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Amsterdam, The Netherlands

Disclaimer:

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Symposia/Plenary Symposia

Saturday, 24 June 2017

Symposium 1 MDS-ES/EAN: The natural history of movement disorders

SYMP01_1

Has deep brain stimulation (DBS) changed the natural history of Parkinson's disease?

W. Poewe
Innsbruck, Austria

DBS can justifiably be viewed as the second therapeutic breakthrough after L-Dopa in the history of PD therapies. Multiple controlled and open-label studies have established efficacy in markedly reducing L-Dopa related motor complications and improving quality of life in moderately advanced PD patients. To what extent these major benefits have altered the course of disease and long-term outcome of PD is difficult to answer from published systematic clinical research. Reasons for this uncertainty include the short duration of RCT's of DBS. The largest series of patients studied long-term over 10 or more years included 79 cases with mean disease durations of 22-25 years (Henriksen, EurJNeurol, 2016;23:53-61). Mortality was 30%, dementia rates varied between 29% (deceased subjects) and 53% in those still alive, and overall 40% had been admitted to nursing homes. Given the long duration of disease these milestone data seem to compare favorably with those from series of unselected patients under conventional drug therapies where mortality rates after 20 years have been as high as 70% and dementia rates reached 80% (Hely, Mov Disord 2008; 23:837). Understanding the longer-term impact of DBS on the course of PD becomes critical when proposals are made to change the timing of these procedures into earlier phases of PD, when medical options have not yet have been fully exploited (Schüpbach, NEJM 20013;368(7):610-22). Long-term follow-up of prospective randomised trials like the EARLYSTIM trial will hopefully provide an answer to the question if and how much DBS has changed the long-term prognosis of PD.
Disclosure: Nothing to disclose

SYMP01_4

Multiple system atrophy (MSA): Does it progress differently in the Western and Asian populations?

W. Meissner
Bordeaux, France

Multiple system atrophy (MSA) is relentlessly progressing fatal neurodegenerative disorder that is characterized by a variable combination of parkinsonism, cerebellar impairment and autonomic dysfunction. The pathological hallmark is the accumulation of aggregated alpha-synuclein in oligodendrocytes forming glial cytoplasmic inclusions, which qualifies MSA as synucleinopathy similar to Parkinson's disease. According to the predominance of parkinsonism or cerebellar impairment, patients are divided into MSA-P and MSA-C subtypes. For still unknown genetic and/or environmental reasons, the MSA-P phenotype accounts for two thirds of cases in the Western hemisphere while MSA-C is more prevalent in Asia. The results of several large cohorts describing the progression and survival of patients with MSA in Europe, North America and Asia were published in recent years. Previous studies including these large natural history cohorts have associated several factors with shorter survival, in particular early autonomic failure, a more rapid progression of Unified MSA Rating Scale scores and a short interval from disease onset to reaching relevant clinical milestone. Survival was also shorter in MSA-P compared to MSA-C in the European study, a finding not confirmed by the North American and Asian cohorts. Median survival ranged between 6 and 10 years, with no difference between the three recent cohorts that reported a median survival of around 10 years. Taken together, currently available results do not suggest distinct progression patterns in Western and Asian populations with MSA.
Disclosure: Nothing to disclose

Symposium 2
Overarching theme: Outcome measures in dementia studies

SYMP02_1

Measuring instrumental activities of daily living (IADL) in dementia: Review of scales

S. Sikkes, A. Hooghiemstra, Y.A. Pijnenburg, P. Scheltens
Amsterdam, The Netherlands

Detecting and monitoring Alzheimer's disease (AD) is becoming increasingly important, stressing the need for clinically relevant outcome measures. Functional decline, as measured with instrumental activities of daily living (IADL) questionnaires, is such an outcome measure. Despite the diversity of available IADL instruments, a clear overview of their usefulness and quality characteristics is lacking. We aim to provide an overview of and evaluate the currently available IADL instruments developed for or validated in the early stages of AD.

Methods: A systematic literature search was conducted in MEDLINE, PsycINFO and Web of Science for psychometric articles on (I)ADL measurement instruments concluding in January 2016. In addition, reviews and reference lists of all retrieved articles were screened for potentially relevant articles and instruments. We selected structured disease-specific questionnaires (developed or validated for use in (preclinical) AD), primarily aimed at measuring IADL.

Findings: The literature search led to a total of 401 articles, and the IADL instruments described in these papers ranged from self-report to informant-report and performance-based instruments. A total of 20 informant-based questionnaires were identified. We will present the selected instruments, their characteristics and quality aspects. These quality aspects will be critically evaluated for potential use in early AD.

Discussion: There is no consensus on specific instruments sensitive to early AD and future cognitive decline. We will discuss the potential use of and differences between various IADL measurement modalities. The results from this study can be used to select instruments for observational studies and clinical trials in subjects with early AD.

Disclosure: Nothing to disclose

SYMP02_2

Using MRI as measure of disease progression: checks and balances

N.C. Fox
London, United Kingdom

Measuring disease progression in the dementias is challenging. Clinical scales have limited ability to differentiate symptomatic from disease-modification effects and brain pathology cannot easily be assessed directly. As a result there is interest in using imaging to track progression. MRI can provide objective measures of the effects of disease on the brain that can safely be repeated many times and are not influenced by "practice effects".

MR-based measures largely attempt to track neurodegeneration – the downstream effects of molecular pathology. In this way it is complementary to molecular-PET or CSF measures. The most established MRI measures for tracking progression in Alzheimer's disease (AD) are measures of atrophy – in particular rates of loss of brain or hippocampal volume or cortical thinning. Natural history studies have shown that losses correlate strongly with cognitive decline and predict clinical outcomes. Moreover estimates of the number of subjects needed to show a given (e.g. 25% slowing) effect on rates of atrophy are lower than similar estimates for clinical scales. Similar power (with different regional atrophy measures) to track progression has been shown in natural history studies in Huntington's disease (e.g. caudate) and frontotemporal dementia (e.g. lobar volumes). However immunotherapy trials in AD challenged assumptions about the effects on therapies on brain volume with several trials showing that therapies could increase volume losses without cognitive worsening. I will discuss these issues and the potential roles, checks and balances for MRI in the context of the move to prevention studies in dementia.

Disclosure: UCL has received payment from Biogen, Eli Lilly, GSK, Janssen, Novartis, and Roche for image analysis services or consultancy from NF: NF receives no personal compensation for this. NF gratefully acknowledges support from the NIHR, the Queen Square BRU in dementia, the Leonard Wolfson Experimental Neurology Centre, the MRC, the Alzheimer's Society, Alzheimer's Research UK and the UK Dementia Research Institute.

SYMP02_4

Is CSF suitable to measure changes in neurodegeneration in dementia?

J.L. Molinuevo Guix
Barcelona, Spain

Introduction: Current research guidelines incorporate several cerebrospinal fluid (CSF) biomarkers for Alzheimer's disease (AD) diagnosis. Contrarily, their use is not well established for other clinical or research purposes. Drug development has proven very challenging and many compounds have failed in showing sufficient improved outcomes for patients. This lecture's objective is to discuss potential intended uses of novel CSF biomarkers, including their use as surrogate markers for measuring neurodegeneration.

Methods: Literature search of the last 15 years was performed to obtain data of the following biomarkers: $A\beta42$, $A\beta40$, neurogranin, Visinin-like protein-1 (VILIP-1), YKL-40, sTREM and neurofilament light (NFL). Based on current definitions of intended biomarker use, the potential utility of each biomarker will be discussed.

Results: $A\beta42/A\beta40$ ratio shows the best correlation with amyloid PET imaging, being a good marker for early detection of amyloid aggregation; Neurogranin levels may reflect synaptic degeneration, predicting future cognitive decline and structural changes; VILIP-1 can predict future cognitive impairment also in cognitively normal individuals; YKL-40 reflects astrogial activity, while sTREM reflects microgial one, having both a non-linear relationship with structural changes observed along the AD continuum; NFL, a component of large-caliber axons, correlates with cognitive decline and disease progression in people with AD and preclinical AD.

Conclusion: Upcoming CSF biomarkers will be very useful not only for AD diagnosis, but also for determining prognosis and as surrogate markers of disease progression and neurodegeneration. Biomarker validation and standardization of prenalytical and analytical conditions are key for advancing in their development and for creating unified testing conditions.

Disclosure: Nothing to disclose.

Symposium 3
DNA repeat syndromes in neuromuscular disorders

SYMP03_1

Amyotrophic lateral sclerosis (ALS)

V. Silani
Milan, Italy

The discovery that a hexanucleotide repeat expansion in C9orf72 is the most numerous genetic variant of both amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD) has opened a rapidly growing field, which may provide promise for advances in the understanding and treatment of these devastating diseases. The clinical and pathological phenotypes associated with expansion of C9orf72 go beyond ALS and FTD to include neurodegeneration more broadly. Pathogenic repeat length is variable but the minimum length that increases risk of disease, and how the repeat size is affecting the phenotype, is still unclear. Related to the current understanding of the C9orf72 expansion and its protein products at a molecular level, three mechanisms are prominent: toxicity mediated directly by RNA transcribed from the repeat; toxicity mediated by dipeptide repeat proteins (DRP) translated from the repeat sequence; and haploinsufficiency resulting from reduced transcription of the C9orf72 exonic sequence. Like in many patients with ALS and FTD, neuronal inclusions that contain TARDBP are seen, but are not universal: the characteristic pathological finding is the dipeptide repeat (DPR) proteins, formed by unconventional repeat-associated non-ATG translation. DRP proteins were recently reported in cerebrospinal fluid and peripheral blood mononuclear cells from C9ALS patients and, notably, from asymptomatic C9orf72 mutation carriers. Moreover, CSF DRP proteins remained relatively constant over time, boding well for their use in gauging biochemical responses to potential treatments. With a view to impact on patient care, we discuss current practice with respect to genetic screening in patients with and without a family history of disease, and the most promising developments towards therapy that have been reported to date: therapeutics that target G4C2 RNA, such as antisense oligonucleotides (ASOs) and small molecules, are thus being actively investigated.

Disclosure: Nothing to disclose.

SYMP03_2

Myotonic dystrophies

B.G. Schoser
Munich, Germany

Myotonic dystrophy types 1 and 2 (DM1 / DM2) are the most frequent adult multisystemic neuromuscular disorders characterized by a plethora of symptoms such as progeric muscle weakness, myotonia, cognitive decline, cardiac, and gastrointestinal symptoms. The estimated patient population for both types in Europe is about 150,000 patients. Both types belong to the group of repeat expansion disorders. DM1 is caused by repeat expansion of a trinucleotide sequence (CTG) in the 3'-untranslated region of the myotonic dystrophy protein kinase (DMPK) gene which, when transcribed into CUG-containing RNA, forms aggregates of mutant transcripts that sequester RNA-binding proteins and cause abnormal splicing of downstream effector genes. DM2 is caused by expansion of a complex repeat motif (TG)n(TCTG) n(CCTG)n in the first intron of the CNBP (cellular nucleic acid-binding protein; previously ZNF 9, zinc finger protein 9) gene. A comparable molecular mechanism of common cellular alterations of mRNA splicing has been proposed. Beyond predominant RNA toxicity, other mechanism may effect protein translation and turnover, and activation of cellular stress pathways. A summary of the current state-of-the-art supervision and treatment of both diseases will be given. In addition, latest results of new studies in the field of DMs will be display. The first large European study termed „Observational Prolonged Trial In Myotonic Dystrophy type I to Improve Stamina, a Target Identification Collaboration", OPTIMISTIC: (ClinicalTrials.gov Identifier: NCT02118779) collected prospectively longitudinal data on phenotype, natural history, fatigue, cognition and biomarkers of 256 DM1 patients from four European countries. DM1 patients receive randomised cognitive behavioural therapy or graded physical training for improving their fatigue, and general activity levels including quality of life. In the UK, in a single centre clinical trial, a GSK3beta inhibitor termed tideglusib is under investigation (ClinicalTrials.gov Identifier: NCT02858908). Furthermore, in 2017 we will gain insight from the outcome of the pilot multicentre Northern-American trial testing the antisense oligonucleotide ISIS-DMPKRx (ClinicalTrials.gov Identifier: NCT02312011).

Conclusion: Myotonic dystrophies are the most variable adult multisystem muscular dystrophies. They are still associated with a premature mortality. We are continuously improving our knowledge on patient´s supervision aiming to reduced morbidity and mortality. Nevertheless, we still need novel avenues integrating the molecular RNA pathogenesis for a specific disease therapy.

Disclosure: Nothing to disclose.

SYMP03_3

Facioscapulohumeral muscular dystrophy (FSHD)

S.M. van der Maarel
Leiden, Netherlands

Facioscapulohumeral dystrophy (FSHD) progressively affects the facial and upper extremity muscles. With disease progression also other muscles can become affected. FSHD can be molecularly recognised by changes in the D4Z4 repeat chromatin structure on chromosome 4 in somatic cells. The polymorphic D4Z4 repeat varies in the population between 8-100 units and adopts a repressive chromatin structure in somatic cells. Because of repeat contractions to a size of 1-10 units (FSHD1), or mutations in chromatin modifiers that are necessary to establish or maintain a repressive D4Z4 chromatin structure (FSHD2), in FSHD this epigenetic silencing is incomplete leading to aberrant expression of DUX4 in skeletal muscle of patients. DUX4 is a germ line transcription factor and ectopic expression of DUX4 in skeletal muscle leads to a cascade of events eventually leading to muscle cell death. SMCHD1 is a chromatin repressor that binds to D4Z4 in somatic cells and often mutated in FSHD2. Partial loss of SMCHD1 repressor activity leads to DUX4 expression in skeletal muscle. Mutations in SMCHD1 can also modify DUX4 expression and disease presentation in FSHD1 families. Rarely, mutations in the DNA methyltransferase 3B (DNMT3B) gene can also cause DUX4 expression and disease presentation in FSHD1 and FSHD2. The presence of damaging variants in these chromatin modifiers may explain the marked inter- and intra-familial variability in disease onset and progression, and the frequent occurrence of borderline FSHD1 repeats in the population. FSHD1 and FSHD2 should therefore not be considered separate disease entities, but opposite extremes of a disease continuum.

Disclosure: Nothing to disclose

Symposium 4
Neuroscience of sleep

SYMP04_1

Effects of sleep/circadian disruption on cognition

P. Maquet

Liege, Belgium

The impact of sleep in neurology practice goes far beyond the sole sleep disorders. Cognitive performance and sleep quality are regulated by circadian rhythms and sleep pressure accrued during wakefulness. Misalignment between sleep debt and circadian rhythmicity jeopardizes cognition, impairs sleep quality, deteriorates memory but also alters peripheral transcriptome, and degrade general health. Starting from human brain physiology, examples will illustrate how sleep and sleep disorders are inherently related to neurological diseases as varied as headaches, vascular diseases, epilepsy, autoimmune encephalitides, and neurodegenerative disorders

SYMP04_2

Sleep deprivation and diabetes/obesity

J.A.H. Romijn

Amsterdam, The Netherlands

The diurnal variation of the geophysical position of the earth in relation to the sun has imposed considerable evolutionary pressure. The suprachiasmatic nucleus, which serves as the central biological clock, receives the input regarding light-dark through the optic nerves. This nucleus in turn conveys output in a diurnal fashion to other hypothalamic nuclei. Sleep is the most extreme phenotypical adaptation to this diurnal light-dark cycle. In recent decades, sleep duration has been reduced and sleep deprivation has become endemic in our modern 24/7 society, either by voluntary sleep restriction, shift work and/or through sleep disorders. These behaviours predispose to metabolic disorders by different mechanisms including circadian misalignment, insulin resistance and disrupted glucose metabolism, and food intake at internal biological times when physiology is unprepared for eating. In epidemiological studies decreased sleep duration is associated with obesity and type 2 diabetes. Experimental studies in humans have documented that sleep deprivation, even of a single night, induces insulin resistance in multiple metabolic pathways in both healthy subjects and patients with type 1 diabetes. Sleep deprivation increases the risk for metabolic disease, including diabetes and obesity.

Disclosure: Nothing to disclose.

SYMP04_3

Memory consolidation during REM sleep

A. Adamantidis

Berne, Switzerland

Rapid eye movement sleep (REMS) has been linked with spatial and emotional memory consolidation. However, establishing direct causality between neural activity during REMS and memory consolidation has proven difficult because of the transient nature of REMS and significant caveats associated with REMS deprivation techniques. This lecture will focus on recent investigation of neural substrate of REMS-dependent memory consolidation in mice using optogenetics. Optogenetically silencing of medial septum inhibitory neurons allows for temporally precise attenuation of the memory-associated theta rhythm during REMS without disturbing sleeping behavior. REMS-specific optogenetic silencing of inhibitory septal neurons selectively during a REMS critical window after learning erased subsequent novel object place recognition and impaired fear-conditioned contextual memory. New results presented in this lecture will demonstrate a role for REMS theta rhythm in memory consolidation.

Disclosure: Nothing to disclose

SYMP04_4

Synaptic function and sleep

V. Vyazovskiy
Oxford, United Kingdom

The importance of sleep for behavioural performance during waking is long-established, but the underlying reasons and mechanisms remain elusive. The neural processes associated with sensory processing, motor functions and learning involve intense synaptic and spiking activity, which are computationally and metabolically demanding. Not surprisingly, staying awake for extended periods of time leads to substantial wake-dependent changes in cortical network activity, which likely contribute to well-known behavioural deficits after sleep deprivation. It has therefore been suggested that prolonged wakefulness needs to be off-set by periods of recovery during which metabolic balance and network function must be restored. Such opposing effects of waking and sleep on brain activity and behaviour may be described conceptually within a framework of homeostatic regulation. The best characterized physiological indicator of sleep-wake history is the level of cortical EEG slow-wave activity during NREM sleep. It is assumed that preceding sleep-wake history, specific waking activities, and circadian time influence subsequent sleep, but neither the relative contribution of these factors, nor the underlying mechanisms are clear. Another prominent type of brain activity - sleep spindles - has been also implicated in synaptic plasticity and memory consolidation. Although originally sleep and wake were considered as global processes, growing evidence suggests differential dynamics of sleep oscillations between cortical regions. Understanding the spatio-temporal pattern of slow waves and spindles during sleep is essential for elucidating their function for recovery processes and synaptic plasticity.

Sunday, 25 June 2017

Plenary Symposium
Presidential Symposium

PLEN02_1

Epilepsy: Where do we stand? Where are we headed?

C.E. Elger

Bonn, Germany

Epilepsy is not a stand-alone disorder, but rather a state of the brain characterized by the fact that epileptic events occur based on chronic alterations. Accepting this, we must then discuss the many types of epilepsies. The treatment of epilepsies is, as a rule, treating seizures by increasing the threshold for generating seizures within the brain. This is a symptomatic, not a curative, therapy. All anticonvulsive drugs developed in recent years have shown no breakthrough effects concerning efficacy. However, when examining single syndromes in epilepsy, a superiority of certain drugs can be seen. A future solution could be phenotyping and genotyping epilepsies with the idea of creating highly specific therapies. However, if we continue on as we have been, then an increase in the quality and efficacy of drug therapies in epilepsy is unlikely. One factor however remains indisputable: solving the problem pertaining to unreliable seizure counting. Seizure counting is the most relevant biomarker and yet the most difficult to document. Without solving this problem, we will probably miss the therapeutic successes necessary to overcome the issues outlined above. The fitness tools currently under development could be a way out if used in an intelligent manner since most of the features run in parallel with an increased heart rate.

PLEN02_2

Autoantibodies and the Nervous System: Depth, Breadth and Challenges

A. Vincent

Oxford, United Kingdom

Over the last 45 years many targets for autoantibodies (Abs) have been discovered in the nervous system. These include receptors and channels at the neuromuscular junction, nodal proteins of peripheral nerves, and intracellular or membrane proteins of glial and neuronal cells in the central nervous system (CNS). Particularly exciting is the evidence that antibodies binding to extracellular domains of neuronal surface proteins can cause severe and often clinically complex diseases that are reversible with immunotherapies. MRI and CSF studies can point to inflammation in the CNS, and antibodies are usually present in both serum and cerebrospinal fluid. Clinical features include limbic encephalitis (seizures, cognitive impairment, psychiatric disturbance, usually with LGI1, CASPR2 or other Abs), autoimmune encephalitis with a characteristic movement disorder, (NMDA receptor Abs) and brainstem/spinal cord dysfunction (glycine receptor Abs). The distinctive features will be illustrated. The difficulties in understanding how the antibodies act in vivo will be addressed by evidence from in-vitro and in-vivo experiments. Although these disorders are relatively rare, their recognition has meant that "autoimmunity" is now often considered in many patients with acute or subacute neurological diseases. Moreover, the possibility that these Abs are related to some cases of epilepsy, dementia or psychiatric disorders is being addressed, although results are far from conclusive. In addition, with an increasing number of requests for testing, and in cases with less characteristic clinical syndromes, the possible significance of positive antibodies has to be carefully evaluated. There are challenges in deciding which antibodies to test, whether they are always relevant, and when, and how aggressively, to treat the patients.

PLEN02_3

WHY NEUROLOGISTS SHOULD BE INTERESTED IN THE HUMAN BRAIN PROJECT: A CHANGE OF CLINICAL PARADIGM

R. Frackowiak

Lausanne, Switzerland; Paris, France

We know that a single human gene mutation may present with any of multiple phenotypes, and vice versa, that a range of genetic abnormalities may cause one disease phenotype. We conclude that a deeper understanding is needed spatial and temporal levels of brain organisation integrate and translate into others, resulting in behaviour and cognition, or their abnormalities. The basic idea is that it is now possible to look for rules underlying the functional and structural organisation of the human brain, exhaustively, at all spatial scales. The methodological approach is to federate and integrate existing knowledge from bottom with new information technologies. The theory is that rules and constraints determining structure and function at one level limit what organisations are possible at the next. The clinical ambition is to link genetic and proteomic levels with rules that govern the cellular segregation of protein expression. From protein expression rules that determine cellular morphology should predict connectivity and so on, until the mechanisms of emergent properties are discovered by a constructive process of predictive simulation, not as isolated but as interacting modules. This novel framework will be used to test new and old theories and generate new hypotheses from clinical and test data. I will describe the practical state-of-the-art with reference to the syndrome of dementia. Frackowiak RSJ, Markram H. (2015) The future of human cerebral cartography: a novel approach. Phil. Trans. R. Soc. B 370: 20-32.

Monday, 26 June 2017

Plenary Symposium
Outcome measures in clinical studies

PLEN03_2

Recent and upcoming new drugs for the treatment of epilepsy

P. Boon
Ghent, Belgium

The diagnosis of epilepsy is typically made in patients with recurrent seizures. Hence, the main outcome measure in intervention studies is seizure counts, assessment of which still relies on documentation of behavioural changes during ictal activity based on patients recall, direct clinical observation and for some seizure types, EEG monitoring. Recent studies have shown that seizure frequency estimation based both on self-reporting by patients and automated seizure detection systems are often unreliable. Development of more sophisticated seizure detection technologies is warranted. Besides assessing seizure frequency, measuring seizure severity may also be indicated. The choice of outcome measures is largely dependent upon trial design. In typical regulatory trials, time to next seizure after randomization or after achievement of target dosage may be used as an index of antiepileptic efficacy. In add-on trials in drug resistant patients, differences in responder rates, defined the number of patients achieving 50%, 75% or 100% reduction of seizure frequency are typically used. For long-term monotherapy trials in newly diagnosed patients, the proportion of patients achieving 6 month or 1 year remission usually represents a meaningful efficacy outcome. Long-term retention of patients on a given treatment is a composite endpoint that is dependent on both efficacy and tolerability. At present, there is no universally accepted method for evaluating AED-related side effects. Typically spontaneous reports of symptoms or use of specific checklists are used. Quality-of-life measures have become increasingly important in assessing overall impact of epilepsy treatment in patients.

Disclosure: Not received

PLEN03_3

Outcome measures in neuromuscular diseases studies

M. de Visser
Amsterdam, The Netherlands

Valid, responsive, reliable and meaningful outcome measures for the measurement of the impairment, activity limitations, and quality of life in patients with neuromuscular disease are crucial to identify the natural history of disease and benefits of therapy in clinical practice and trials. Outcome measures can come in many different forms – from assessing how far a patient can walk in six minutes to looking at changes in their muscle through a biopsy – and using the right outcome measure is a vital step in making sure a trial can really prove whether or not a treatment works. Since there are hundreds of different neuromuscular diseases it is not possible to find "the" single scale that could be used for all studies and all cohorts, irrespective of disease, age and many other variables, but that the choice of measure should be driven by the trial design. Currently, in most trials outcome measures at the ordinal level of assessment are being applied, despite the shortcomings of such scales. New psychometric methods like the Rasch model and the Item Response Theory (IRT) are reportedly able to transform ordinal scales into more accurate interval measures. In this presentation a selection of neuromuscular diseases will be discussed, i.e. spinal muscular atrophy and Pompe's disease, amyotrophic lateral sclerosis, Charcot-Marie-Tooth disease, inflammatory neuropathies and myopathies.

PLEN03_4

Outcome measures in multiple sclerosis studies

B.M.J. Uitdehaag
Amsterdam, The Netherlands

From a measurement perspective multiple sclerosis (MS) is a complex disease. There are several clinical phenotypes and within these phenotypes there is a variety of clinical disease expressions. The dominant clinical feature in relapsing remitting MS is the occurrence of exacerbations. Gradually increasing impairment and disability independent from exacerbations is the key feature of progressive MS.

The present standard for measuring MS-related disability and up to now by far the most widely used outcome measurement in clinical trials in MS is the Expanded Disability Status Scale (EDSS). However, the EDSS has many acknowledged shortcomings. It has been recognized for decades that there is a need for improved clinical outcome measures in MS. Still, so far there is no generally accepted single alternative. Because of the multifaceted nature of the disease combining several measurements is often considered. A good outcome measure captures the extent to which the health status has changed–spontaneously or as a result from treatment – in a valid (to the extent to which the measure truly measures what it intends to

measure) and reliable (free from measurement error) way and is able to detect a true change in a patient's status over time (responsiveness). Available outcome measures and challenges in the search for the optimal outcome measure in MS studies will be discussed.

Symposium 5
ILAE-CEA/EAN: Recent and upcoming new drugs and devices for the treatment of epilepsy

SYMP05_1

Recent and upcoming new drugs for the treatment of epilepsy

E. Trinka
Salzburg, Austria

Epilepsies are one of the most common neurological disorders and they can be gratifying to treat. With the currently available treatments around two thirds of patients will be seizure free and can fully participate in daily life. However, one third of patients will suffer from ongoing seizures, with all consequences on brain function, cognition, neuronal development in case of young patients, injuries, and increased mortality. In addition, the patients suffer from psychosocial consequences and stigmatisation, making epilepsies ranking among the highest in term of burden of disease. The randomness of seizures, and the various aetiologies pose enormous challenges to clinicians and researchers, who strive to develop new drugs for epilepsies. Now, epilepsies are no longer regarded as a homogenous group, but as a large group of disorders, many of them belong to the "rare diseases", which are complex to treat. The approach "one drug for all" will not work for these diseases. A European Reference Network (ERN) for rare and complex epilepsies (epiCARE) has been recently inaugurated reflecting the development of applying more target oriented treatments, directed against the cause of the epileptic disorder and not only to suppress seizures. Nevertheless, newer and better treatments for the common epilepsies are needed. This review will address the achievements in classical drug development over the past decades and the recent development to individualize treatments directed against the causes. Novel drugs developed with classical models are Eslicarbazepineacetate, Brivaracetam, Lacosamide, Retigabine, and Perampanel. More cause specific drugs, such as everolimus, just entered the clinical arena. New and interesting products, such as neurosteroids, or cannabinoids are already at their final stage of clinical development. The presentation will also give an outlook of some treatments for epilepsies, which are still in the early development phase.
Disclosure: Not received

SYMP05_2

New antiepileptic drugs on the horizon: Neurosteroids, cannabinoids, non-teratogenic valproic acid derivatives and YKP3089

M. Bialer
Jerusalem, Israel

Between 1993 and 2016 seventeen new antiepileptic drugs (AEDs) have been approved These AEDs offer appreciable advantages in terms of their favorable pharmacokinetics, improved tolerability and lower potential for drug interactions. In addition, the availability of old and new AEDs with various activity spectra enables clinicians to better tailor drug choice to the characteristics of individual patients. Nevertheless 30% of patients with epilepsy are still not seizure-free and thus, there is a substantial need to develop new AEDs. The new AEDs in development or recently approved can be divided into two categories: a) completely new chemical structures such as allopregenanolone, cannabidio or fenfluramine; b) derivatives of existing AEDs such as: eslicarbazepine acetate, valnoctamide or brivaracetam. Valnoctamide has the potential to be non-teratogenic, more potent valproic acid derivatives with unique activity against benzodiazepine-resistant status epilepticus and organophosphate neuronal damage. Cannabidiol, a non-psychoactive major component of Cannabis Sativa might reduce seizure frequency in children with a highly treatment-resistant epilepsy, although its interaction with clobazam may contribute to its efficacy. Target-based drug design or Targephilia's mantra of: "one gene, one protein, one function" is not useful in the development of antiepileptics or CNS drugs. This is because all successful AEDs have multiple mechanisms of action (MOA) and the two single-mechanism AEDs developed by mechanism-based design are not widely used due to side effects related to their single MOA. In addition, CNS drugs with multiple MOAs have a better probability of being efficacious in refractory epilepsies and other CNS disorders.
Disclosure: Nothing to disclose.

SYMP05_3

Recent advances in neuromodulation

P.A. Boon

Ghent, Belgium

Neurostimulation is making its way into the therapeutic armamentarium of epileptologists treating patients with drug- resistant epilepsy. For vagus nerve stimulation (VNS), deep brain stimulation of the anterior nucleus of the thalamus (ANT- DBS) and the Responsive Neurostimulation System (RNS), efficacy and side effects profile have been demonstrated in large multicenter RCTs. During the blinded phase of the randomized trials seizure frequency was significantly reduced for all modalities. After approximately 5 years of treatment efficacy further increased in the open label studies; up to 55% for VNS, 69% for ANT-DBS and 66% for RNS. Several other neurostimulation modalities are currently under investigation in a pre-clinical or clinical setting: DBS in other brain targets (e.g., hippocampus) and non-invasive neurostimulation techniques such as transcutaneous VNS (tVNS), non-invasive VNS (nVNS), trigeminal nerve stimulation (TNS), repetitive transcranial magnetic stimulation (rTMS) and transcutaneous direct current stimulation (tDCS). Neurostimulation therapies are currently available to patients who are considered unsuitable candidates for epilepsy surgery based on the investigations performed during the presurgical evaluation protocol. To avoid a merely negative selection procedure and in view of an increasing number of neurostimulation options becoming available, the concept of a prestimulation evaluation protocol has recently been introduced.

Disclosure: Not received

SYMP05_4

New potential drugs for super-refractory status epilepticus

S.D. Shorvon

London, United Kingdom

Once a patient has entered the stage of Super Refractory Status Epilepticus (SRSE), the mortality rate is over 30% and many survivors are left with neurological disability which is sometimes severe. Treatment is unsatisfactory and based on open often small case series. There is a debate about the risks of anaesthesia and the treatment starategies which should be imployed. Potential new therapies at this stage include the use of ketamine in place of conventional anaesthetics and the use of adjunctive therapy with neurosteroids. Recent studies have also been carried out on the use of other treatment approaches including hypothermia. In this talk, the recent literature on the therapy of SRSE will be discussed.

Disclosure: Member of Clinical Advisory board of Sage Pharmaceuticals

Symposium 6
Amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD) as a model of interaction between cognition, behaviour and motor impairment

SYMP06_1
The neuropathology of ALS and FTD

M. Neumann
Tübingen, Germany

There is increasing evidence based on clinics, molecular neuropathology and genetics that ALS and FTD are pathomechanistically closely related conditions. This is supported by the presence of similar protein deposits, such as TDP-43 and FUS, as well as similar gene defects, such as the C9orf72 repeat expansion mutation, as common key players in both conditions. However, there are also significant genetic and pathological differences recognized with some gene defects and protein deposits being quite unique to either FTD or ALS, suggesting at least partially divergent pathomechanisms. This presentation will give an overview of the molecular basis of FTD and ALS, their commonalities and differences and will discuss current insights on the topic on whether ALS, ALS with cognitive impairment, ALS with FTD and FTD actually represent a clinical continuum or a spectrum of disorders.

Disclosure: Nothing to disclose

SYMP06_3
Genetics

J. Veldink
Utrecht, Netherlands

Most researchers know the diagram where genetic variants are either common with a small effect (the area of "complex genetics") or rare with a large effect (Mendelian, or "simple genetics"). I will introduce the exciting and highly relevant field of "simplex" genetics, i.e. variants with fairly large effects and not too low or too high frequencies. I will us our recent work combining GWAS and whole genome sequencing on Amyotrophic Lateral Sclerosis (ALS), a lethal neurodegenerative disease with a life-time risk of 1:300 as an example. Apparently, the etiology of all ALS is characterized by a disproportionate contribution of rare genetic variation. ALS is not simply a collection of unique rare diseases with a monogenetic cause nor is it a diagnostic continuum with a complex contribution of thousands of small effect factors. ALS is 'in-between', which I call "simplex", which might also be true for many other human diseases.

Disclosure: Nothing to disclose

SYMP06_4
Clinical interactions

A.C. Ludolph
Ulm, Germany

The phenotypical overlap between ALS and frontotemporal dementias is well recognized since the late 19th century. It has been recently shown that the overlap between cognition, behaviour and motor impairment in these diseases heavily relies on neuroanatomical principles which also have been partially translated into the clinic recently. Heiko Braak has demonstrated that the anatomical connectivity between the motor cortex, the gyrus rectus and the orbitofrontal cortex is the basis of the presumably sequential propagation of phosphorylated TDP-43 into these areas of the cortex. These changes have been recently successfully translated into sequential neuropsychological deficits and also into neuroradiological assessment of the connectom. Also, the involvement of the perforant pathway and the hippocampus has been translated into neuroradiological and neuropsychological findings; this is, however, limited by the small number of patients who reach these later stages of the disease. In contrast, the neuroanatomical interactions between FTD associated behavioural and cognitive changes with motor neuron disease have only been studied to a smaller degree. It seems, however, that in the patients studied a pattern exists that is clearly distinct from primary motor cortex disease. In conclusion, the basis of the understanding of the interaction of cognition, behaviour and motor symptoms is the neuroanatomy of the brain. It seems that FTD and ALS are distinct entities with regard to progression patterns; however within the given entities they seem to include a continuum of deficits.

Disclosure: Nothing to disclose

Tuesday, 27 June 2017

Symposium 7
ESO/EAN: Uncommon cerebrovascular diseases

SYMP07_1

Reversible cerebral vasoconstriction syndrome: How to recognise it?

A. Ducros
Paris, France

During the last 10 years, reversible cerebral vasoconstriction syndrome (RCVS) has emerged as the most frequent cause of thunderclap headache in patients without aneurismal subarachnoid hemorrhage, and as a rare cause of stroke in the young. RCVS can cause any variety of stroke, namely non-aneurismal subarachnoid hemorrhage, intracerebral hemorrhage, or cerebral infarction. The condition is attributed to a transient disturbance in the control of cerebral vascular tone, with a global favorable outcome. More than half the cases occur after exposure to adrenergic or serotoninergic substances or postpartum. RCVS associates severe headache, mostly recurrent thunderclap headaches, and segmental constriction of cerebral arteries that resolves within three months. The typical thunderclap headache of RCVS are multiple, recurring over a few days to weeks, excruciating, short-lived, and brought up by exertion, sexual activities, emotion, Valsalva maneuvers, or bathing, among other triggers. In a minority of cases, they herald stroke (either hemorrhagic or ischemic) and rarely death. RCVS may also occur with milder headaches or without any headache, in patients presenting with stroke, seizures, and/or reversible brain edema. RCVS without thunderclap headache may be more difficult to recognize. Diagnosis should be suspected in any stroke in the young with or without headache. It may be difficult when initial angiography is normal, which occurs in 20% of cases because vasoconstriction scores peak 2 to 3 weeks after clinical onset. Management is based on removal of any vasoactive substances, rest, and blood-pressure monitoring. Nimodipine seems to reduce headaches, but does not completely prevent stroke.

Disclosure: Nothing to disclose

SYMP07_2

Cervical artery dissection: Where are we now?

S. Engelter
Basel, Switzerland

Cervical artery dissection (CAD) is an important cause of stroke in young adults, but 1 out of 14 CAD patients is aged 60 years and older. Diagnosis of CAD requires the detection of characteristic CAD features in vascular imaging, most frequently by visualization of a mural hematoma. Magnetic resonance imaging has a higher sensitivity than neurosonography, but can be falsely negative within the first days after CAD onset. The intramural bleeding is not a reason to withhold IV thrombolysis in patients with acute ischemic stroke attributable to CAD. Acute endovascular treatment has been shown feasible and might be considered an alternative to IV thrombolysis alone, worthwhile to be studied in more detail. Antiplatelets and anticoagulants are both used to prevent stroke in CAD patients. Two randomized controlled trials do compare anticoagulation versus antiplatelets in CAD. One trial has been published, the other is ongoing and participation is encouraged to increase the level of therapeutic evidence. Non-vitamin-K-oral anticoagulants have been used in few CAD-patients. Angioplasty and stenting is usually reserved for CAD patients with recurrent ischemic events despite antithrombotic therapy, when hemodynamic infarction is impending, in ruptured dissecting aneurysms or in iatrogenic CAD.

Disclosure: Nothing to disclose.

SYMP07_4

Causes and clinical course of cerebral venous infarction

P. Canhao
Lisbon, Portugal

Abstract: Cerebral venous thrombosis (CVT) is an unusual type of stroke, representing about 0.5-1% of all strokes. The clinical presentation is highly variable. The most frequent presentations are isolated headache, intracranial hypertension syndrome, seizures, focal signs and encephalopathy. The confirmation of the diagnosis of CVT relies on the demonstration of thrombi in the cerebral veins and/or sinuses by MR/MR venography or veno CT. Many causes or predisposing conditions are associated with CVT. In more than 85% of adult patients, at least one risk factor can be identified. The more frequent risk factors for CVT are inherited and acquired thrombophilias, oral contraceptives or other drugs, puerperium and pregnancy, cancer, local or systemic infections, inflammatory diseases, trauma and mechanical precipitants. Overall, CVT has a good outcome (complete recovery or minor residual symptoms or signs) in approximately 80% of patients. Predictors of poor long-term prognosis include age, Glasgow coma scale score on admission <9, deep CVT location, intracranial hemorrhage, mental status abnormality, male sex, CNS infection, and malignancy. About 5% of patients die in the acute phase of CVT. The main cause of acute death is brain herniation secondary to a large hemorrhagic lesion, multiple lesions or to diffuse brain edema. Treatment in the acute phase includes management of the associated condition, anticoagulation with either low molecular weight or unfractionated heparin, and symptomatic treatment. Decompressive surgery should be considered in patients with large venous infarcts or hemorrhage with impending herniation.
Disclosure: Nothing to disclose

Symposium 8
ECTRIMS/EAN: New developments in MS

SYMP08_1

New aspects in MS pathology

W. Brück
Göttingen, Germany

Multiple sclerosis is an inflammtory demyelinating disease of the central nervous system with focal lesions in the white and grey matter as well as diffuse changes in the normal appearing brain tissue. Recent developments in MS pathology include the nature of white matter lesions in different disease stages, focussing mainly on differences between relasing and progressive MS. In addition, grey matter lesion pathogenesis in relation to meningeal inflammation as well as to immunological mechanisms has been studied in detail. The presentation will focus on the pathology of white matter lesions in different disease stages, as well as the pathogenesis of cortical demyelination. The spectrum of inflammatory demyelinating diseases has increased in the last years with new identities defined such as neuromyelitis optica. Recently, anti-MOG antibody associated demyelination has been described. The heterogeneity of the MS lesion as well as the pathology of these new entities in comparison to MS will additionally be highlighted in the presentation.

Disclosure: The work presented here was supported by the German Research Foundation, The German Ministry for Research and Education as well as the German Multiple Sclerosis Society.

SYMP08_3

New developments in the diagnosis of MS

D. Miller
London, United Kingdom

The diagnosis of multiple sclerosis (MS) is based on specific positive criteria with evidence of dissemination in space (DIS) and time (DIT) and where there is also no better explanation for the clinical presentation and alternative diagnoses are considered and excluded. Historically, a diagnosis of clinically definite MS required clinical evidence of DIS and DIT with symptoms and signs suggesting a CNS demyelinating disease (e.g., 1983 Poser criteria). In 2001, MRI criteria for DIS and DIT were developed that, when fulfilled in patients with a clinically isolated syndrome (CIS, a first clinical event characteristic of CNS demyelination), might enable a diagnosis of MS (2001 McDonald criteria). The McDonald criteria were revised in 2005 and again in 2010. The McDonald criteria often enable an earlier diagnosis of MS, prior to a second clinical event, in young adults presenting with a CIS typical for demyelination. A diagnosis of primary progressive MS using 2010 McDonald criteria may also consider CSF as well as clinical and MRI findings. However, there remain limitations in the accuracy of MS diagnostic criteria and they can be expected to evolve with new knowledge and experience. The talk will consider recent developments including studies of misdiagnosis (when another diagnosis/syndrome is mistakenly thought to be MS), the distinction of MS from NMO spectrum disorders, Radiologically Isolated Syndromes, new and emerging imaging and CSF studies, and new 2016 MAGNIMS guidelines for DIS. An International Panel has also been convened to consider new (2017) revisions to the McDonald criteria.

Disclosure: Nothing to disclose

SYMP08_4

New developments in the treatment of MS

P.S. Sørensen
Copenhagen, Denmark

Treatment of relapsing multiple sclerosis (MS) has improved considerably during the last decade, and several new potent therapies have become available. These drugs are targeting different processes in the complex autoimmune pathology leading to chronic CNS demyelination, neural loss and finally neurological disability. The majority of these new therapies are monoclonal antibodies that have proven to be among the most efficacious disease-modifying therapies in the field of MS. Alemtuzumab, daclizumab and ocrelizumab are new compounds holding promises for fulfilling high efficacy combined with an acceptable safety profile. Whereas effective therapies have been available for treatment of relapsing forms of MS for the last decade, efficacious approved treatments of progressive MS is still an unmet need. However, recently the monoclonal antibody ocrelizumab has been approved for treatment of primary progressive MS by the FDA, and the selective sphingosine-1-phosphate receptor antagonist siponimod has shown beneficial effect in patients with secondary progressive MS. The presently available disease-modifying therapies are all treatments of the inflammatory phase of MS, and although there are highly efficacious anti-inflammatory therapies with an acceptable safety profile, there still is a need of therapies with neuroprotective and remyelinating properties in order to gain control of all phases of the disease course.
Disclosure: Nothing to disclose

Oral Sessions

Saturday, 24 June 2017

Critical Care

O1101

Diagnostic accuracy of quantitative neuromuscular ultrasound for the diagnosis of intensive care unit-acquired weakness

E. Witteveen[1], J. Sommers[2], L. Wieske[1], J. Doorduin[3], N. van Alfen[3], M. Schultz[4], I.N. van Schaik[1], J. Horn[4], C. Verhamme[1]
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Background and aims: Neuromuscular ultrasound is a noninvasive investigation. A reduction in muscle thickness and increase in echo intensity over time have been described in ICU patients, but the relation to ICU-acquired weakness (ICU-AW) is unknown. The aim of this study was to investigate the diagnostic accuracy of neuromuscular ultrasound for diagnosing ICU-AW.
Methods: Newly admitted ICU patients, mechanically ventilated for ≥48 hours were included. As soon as patients were awake and attentive, an ultrasound was made of four muscles and two nerves (index test). ICU-AW was evaluated using muscle strength testing (reference standard; ICU-AW defined as mean Medical Research Council score <4). Diagnostic accuracy of muscle thickness, echo intensity and homogeneity (echo intensity standard deviation) as well as nerve cross sectional area, thickness, and vascularization were evaluated with the area under the curve of the receiver operating characteristic curve (ROC-AUC). Diagnostic accuracy of z-scores of muscle thickness, echo intensity and echo intensity standard deviation were also evaluated.
Results: 71 patients were evaluated of whom 41 had ICU-AW. Ultrasound was done at a median of 7 days after admission in patients without ICU-AW and 9 days in patients with ICU-AW. Diagnostic accuracy of all muscle and nerve parameters was low. ROC-AUC ranged from 51.3% to 68.0% for muscle parameters and from 51.0 to 66.7% for nerve parameters.
Conclusion: Neuromuscular ultrasound does not discriminate between patients with and without ICU-AW at the time the patient awakens, and is therefore not able to reliably diagnose ICU-AW in ICU patients relatively early in the disease course.
Disclosure: Nothing to disclose

O1102

Risk factors for intensive care unit admission in patients with autoimmune encephalitis

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Background and aims: A significant number of patients with autoimmune encephalitis (AE) develop conditions that require admission to an intensive care unit (ICU). Here, we aimed to expand the knowledge about clinical and paraclinical risk factors for ICU care and the impact of ICU admission on short- and long-term outcome.
Methods: We reviewed clinical data of patients evaluated for AE at our university hospital between 2011 and 2016. All patients were re-diagnosed as either "definite" (n=15) or "probable" AE (n=17). We studied demographics, etiology and various clinical and lab examinations on admission, and evaluated their prognostic relevance for ICU admission.
Results: Median age was 62 years (range 25–87), 22 (69%) were men. Thirteen patients (40.6%) required ICU care and the most common underlying causes were seizure (38.5%) and altered mental status (30.7%). Patients with a "definite" diagnosis had a higher risk for ICU admission than "probable" diagnosis (n=10 vs. n=7; p=0.046). Patients with low haematocrit and haemoglobin on hospital admission had higher risk for ICU admission (n=11 vs. n=7, p=0.012, n=10 vs. n=5, p=0.010, respectively). At last follow-up after a median of 31 months (range 2.5–52.4), seven patients had died (23.3%) and the median modified Rankin scale was 3 (range 0–6). ICU care did not impact mortality and outcome.

Table 1. Comparison of characteristics between patients in ICU and ward groups

	Total (n=32)	ICU (n=13)	Ward (n=19)	p value
Age at admission, y	62 (20.5)	64 (14.5)	60.5 (30.25)	0.398
Gender				
Male, n %	22 (69)	11 (50)	11(50)	0.141
Female, n %	10 (31)	2 (20)	6 (80)	
Detection of neuronal antibody, n %	17(53)	10(59)	7(41)	**0.046**
The length of stay, d	14 (14.5)	22 (29.5)	11 (14.75)	**0.025**
Reasons for hospital admission, n %				
AMS	13 (40.6)	8 (61.5)	5 (38.5)	0.071
Seizure	11	4	7	NS
SE	4 (12.5)	1 (25)	3 (75)	0.629
Alcohol, n %	3 (9.4)	1 (33.3)	2 (66.6)	NS
Smoking, n %	9 (28.1)	4 (44.4)	5 (55.5)	NS
Immunotherapy, n %	26 (81.3)	11 (42.3)	15 (57.7)	NS
CCI score	2 (2.75)	2 (3)	2 (2)	0.234
Tumour, n %	10 (31.3)	4 (40)	6 (60)	NS
Autoimmune disease, n %	8 (25)	3 (37.5)	5 (62.5)	NS
Abnormal MRI findings, n %	21 (70)	8 (38.1)	13 (61.9)	0.443
Abnormal EEG findings, n %	26 (86.7)	11 (42.3)	15 (57.7)	NS
Inflammatory CSF*, n %	18 (58.1)	8 (44.4)	10 (55.6)	NS
Outcome, n %				
Good outcome §	19 (63.3)	6 (31.6)	13 (68.4)	0.266
Poor outcome ¶	11 (36.7)	6 (54.5)	5 (45.5)	
Mortality, n %	7 (23.3)	5 (71.54)	2 (28.6)	0.084
Laboratory findings				
Low haematocrit, n %	18 (56.3)	11 (61.1)	7 (38.9)	**0.012**
Low haemoglobin, n %	15 (46.9)	10 (66.7)	5 (33.3)	**0.010**
Laboratory findings				
Median Haematocrit	37.95 (8)	36.3 (5.1)	41.4 (5.4)	**0.007**
Median Haemoglobin	13.7 (2.95)	12.4 (2.7)	14.2 (1.9)	**0.002**

Data shown as median (interquartile range) unless otherwise specified
Fisher exact test and Mann-Whitney test were used to perform this comparison. P values ≤0.05 were considered statistically significant
Abbreviations: ICU, intensive care unit, CCI, Charlson's Comorbidity Index, AMS, altered mental status, SE, status epilepticus, CSF, cerebrospinal fluid, EEG, electroencephalography, MRI, magnetic resonance imaging,
* CSF was considered inflammatory if at least 2 of the following criteria were met
- pleocytosis (≥5 white cells/ml)
- elevated IgG synthesis rate
- increased protein concentration (≥50mg/dl)
- oligoclonal bands
§ A good outcome was defined by an mRs ≤3
¶ A poor outcome was defined by an mRs >3

Table 2. Characteristics of autoimmune encephalitis patients categorized by outcome

	Total** (n=30)	Good (n=19)	Poor (n=11)	p value
Age at admission, y	61 (24.5)	55 (27.5)	64 (26)	0.181
Gender				
Male, n %	22 (73.3)	15 (68.2)	7 (31.8)	0.417
Female, n %	8 (26.7)	4 (50)	4 (50)	
Detection of neuronal antibody, n %	15 (50)	8 (53.3)	7 (46.7)	0.450
The length of stay, d	15 (17.5)	11 (12.25)	37 (53)	0.181
Need for intensive care, n %	12 (40)	6 (50)	6 (50)	0.266
Reasons for hospital admission, n %				
AMS	12 (40)	5 (41.7)	7 (58.3)	0.063
Seizure	10 (33.3)	9 (90)	1 (10)	**0.049**
SE	4 (13.3)	3 (50)	3 (50)	0.611
Alcohol, n %	3 (11.1)	2 (66.7)	1 (33.3)	NS
Smoking, n %	8 (29.6)	4 (50)	4 (50)	0.415
Immunotherapy, n %	24 (80)	17 (70.8)	7 (29.2)	0.156
CCI score	2 (2)	2 (1.25)	3 (4)	0.054
Tumour, n %	10 (33.3)	5 (50)	5 (50)	0.425
Autoimmune disease, n %	8 (26.7)	4 (50)	4 (50)	0.417
Abnormal MRI findings, n %	21 (75)	13 (61.9)	8 (38.1)	NS
Abnormal EEG findings, n %	24 (85.7)	14 (58.3)	10 (41.7)	NS
Inflammatory CSF*, n %	17 (58.6)	10 (58.8)	7 (41.2)	0.717
Laboratory findings, n %				
Low haematocrit	18 (60)	9 (50)	9 (50)	0.121
Low haemoglobin	15 (50)	6 (40)	9 (60)	**0.021**
Laboratory findings				
Median Haematocrit	37.9 (8.15)	42 (6.45)	34.5 (5)	**0.008**
Median Haemoglobin	13.8 (3.4)	14.35 (2.25)	11.3 (2.1)	**0.003**

Data shown as median (interquartile range) unless otherwise specified
Fisher exact test and Mann-Whitney test were used to perform this comparison. P values ≤0.05 were considered statistically significant
Abbreviations: ICU, intensive care unit, CCI, Charlson's Comorbidity Index, AMS, altered mental status, SE, status epilepticus, CSF, cerebrospinal fluid, EEG, electroencephalography, MRI, magnetic resonance imaging,
* CSF was considered inflammatory if at least 2 of the following criteria were met
- pleocytosis (≥5 white cells/ml)
- elevated IgG synthesis rate
- increased protein concentration (≥50mg/dl)
- oligoclonal bands
** Two patients were unavailable for telephone interview
§ A good outcome was defined by an mRs ≤3
¶ A poor outcome was defined by an mRs >3

Conclusion: Our study disclosed that patients with definite AE are at higher risk for ICU admission and identified anemia on admission as a risk factor for ICU care. Interestingly, ICU admission did not determine outcome. This finding contrasts previous reports and deserves further attention in forthcoming studies.
Disclosure: Nothing to disclose

O1103

Clinical predictors of electrographic seizures among neurocritical care patients undergoing continuous EEG monitoring

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Background and aims: Continuous EEG (cEEG) is very useful for the diagnosis of seizures in intensive-care-unit (ICU) since in the majority of studies seizures and status are almost always non convulsive (NCS, NCSE). Many clinicians may have limited access to cEEG, thus the identification of predictors is important in this setting. These results are the preliminary findings of a larger retrospective study of 245 patients who underwent cEEG at Mount Sinai Neurological ICU (NSICU).
Methods: After charts review, we identified 46 patients who developed electrographic seizures (E-Group). We seek to identify possible predictors of electrographic seizures, comparing E-Group to a Control-Group composed of 139 patients who did not experience any seizure. We also identified 29 patients who experienced NCS or NCSE (NCSE-group) in order to identify clinical predictors for this subgroup.
Results: The only past-medical-history (PMH) diagnosis associated with electrographic seizures was Cerebrovascular (CV) (p=0.04). Considering diagnosis at admission (Admission NSICU) Epilepsy was a significant predictor (p = 0.00). Epilepsy was also a significant predictor for the underlying diagnosis (Diagnosis) (p=0.00), as well as CV (p=0.04) and TBI (p= 0.05). Considering clinical predictors, twitches of facial/oral muscles (Subtle movements) were significant predictor of electrographic seizures (p = 0.00, OR 12.5). Considering NCSE-group significant clinical predictors were Subtle movements (p=0.00), and subtle movements and deviation of eyes and gaze (Gaze) (p=0.00).
Conclusion: Our findings show, as recently underlined, that specific clinical features along with patients' history may be used to identify subjects at high risk for seizure or NCSE/NCS in the NSICU.
Disclosure: Nothing to disclose

O1104

Head computed tomography and Neuron specific enolase for early neurological prognostication after cardiac arrest

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Fig. 1 Peak NSE levels in patients with generalised oedema on head CT after cardiac arrest

Fig 1 Peak NSE levels in patients with generalised oedema on head CT after cardiac arrest

Background and aims: A multimodal approach to neurological prognostication of comatose patients after cardiac arrest is recommended. Studies suggest that both head computed tomography (CT) and Neuron specific enolase (NSE) are reliable for prognostication even under sedation and ongoing Targeted Temperature Management (TTM). Little is known of how the combination of CT and NSE contributes to prognosticating the extent of neuronal injury and poor outcome.

Methods: Pre-specified post-hoc analysis of the Target Temperature Management (TTM) trial. 939 patients randomised to treatment at 33°C or 36°C after return of spontaneous circulation. Generalised oedema on head CT post arrest was correlated with poor outcome at 6 months using the Cerebral Performance Category (CPC 3-5). Where possible, NSE was collected at 24; 48; and 72h after cardiac arrest and analysed 6 months after the trial. Peak NSE at either 48; or 72h was correlated with generalised oedema on CT.

Results: 356/939 patients underwent ≥1 head CT. Generalised oedema ≤7 days predicted poor outcome with a sensitivity of 33.7% and a specificity of 97.7%. Peak NSE was available for 70.9% of CT subgroup. Peak NSE was significantly higher with generalised oedema on CT: median 131.2 ng/ml (IQR: 68.9-213.0) vs. median 21.7 ng/ml (IQR: 14.5-70.0) (Fig.1), p<0.001. CT and NSE together improved sensitivity and specificity compared to only CT, and improved specificity compared to only NSE alone (Table 1).

Conclusion: The combination of generalised oedema on head CT with peak NSE seems promising for prognosticating poor outcome after CA with no false positives in this limited population.

Disclosure: Nothing to disclose

Table 1. Prediction of poor outcome with generalised oedema on head computed tomography and/or elevated serum peak Neuron specific enolase at 48 or 72 hours post arrest

Variable	All	TP	FP	TN	FN	Sensitivity	Specificity	PPV	NPV
CT ≤ 7days	361	84	2	110	165	33.7	98.2	97.7	40.0
NSE>37ng/ml	669	209	27	312	121	63.3	92.0	88.6	72.1
NSE >44ng/ml	669	197	13	326	133	59.7	96.2	93.8	71.0
CT+ NSE>37 ng/ml	195	53	0	87	55	49.1	100	100	61.3
CT + NSE>44ng/ml	202	52	0	88	62	45.6	100	100	58.7

Data are given in numbers and percentages. CT: computed tomography with findings of generalised oedema, NSE: Neuron specific enolase, n: number of patients; false positive; TN: true negative; FN: false negative; PPV: positive predictive value; NPV: negative predictive value. More than one CT investigation reported for som

Table 1 Prognostication

O1105

Feasibility of near infra-red spectroscopy in blood pressure management following thrombectomy for acute large vessel occlusion ischemic stroke

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Background and aims: There is no consensus regarding optimal BP targets immediately post-thrombectomy, with uncertainty balancing optimal cerebral perfusion pressure and minimizing reperfusion injury. We sought to investigate the relationship between post-thrombectomy BP targets and cerebral perfusion through non-invasive cerebral oxygen monitoring with Near-Infrared Spectroscopy (NIRS).

Methods: This prospective observational feasibility study was performed through patient enrollment in an IRB approved Neurocritical care registry of patients at the University of Miami. Patients undergoing thrombectomy for acute LVO were monitored for 48 hours post-procedure with NIRS through the INVOS system (Medtronic). Blood pressure parameters were determined at the discretion of the admitting Neurointerventional team. All post-thrombectomy standards of care were followed.

Results: A total of 5 patients have been observed in this ongoing investigation.   sBP goals post-thrombectomy varied from <120 to <140 mmHg. One patient developed L MCA syndrome during monitoring, undergoing repeat angiography showing robust collaterals and L M1 cut-off , followed by thrombectomy. NIRS monitoring showed symmetrical data during the event and immediately post thrombectomy, but then few hours later was observed to have lower values on the affected side, with a poor outcome. The second patient suffered hemorrhagic conversion and NIRS showed higher signals on the affected side. Other patient with successful thrombectomies showed symmetrical data and good outcomes.

Conclusion: NIRS monitoring is a feasible method of evaluating patients undergoing thrombectomy for LVO ischemic strokes. This study is continuing to enroll patients to help determine whether NIRS monitoring may help determine better blood pressure targets following thrombectomy.

Disclosure: Nothing to disclose

Headache and pain 1

O1106

Effects and adverse events possibly related to DBS in cluster headache

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Background and aims: Aim was to stress effects of hypothalamic Deep Brain Stimulation (DBS) in Cluster Headache (CH).

Methods: During 16 years, we observed DBS implanted CH patients versus both Parkinson Disease (PD) sufferers with DBS and chronic Migraine (M) without DBS. CH sufferers= n.14, mean age when implanted 25.9+9.52SEM. In 10 CH sufferes, DBS was truned off   58.9 months+27.9SEM after DBS implant Control Group A= n. 14 PD sufferers who underwent DBS when 52.6 years old+5.8SEM. Control Group B= n. 25 M sufferers matched with CH sufferers.   CH and M similarly overused sumatriptan and opiods. During observation-period, CH and M did not significantly differ in mean pain VAS (0-5) and hrs./month of pain.

Results: Possible effects and adverse effects of DBS were: CH Group

-3 CH sufferers reported -70% pain scores and dropped the observation 16.9 months+1.4SEM following DBS

-1 had a -40% pain if treated with cortisone

-10 0% relief

-2 Auerbach system paralysis

-3 Cardiac arrhythmias

-1 Dystrophic cutaneous lesions

-3 Death for septicemia

-1 Permanently enticed PD (Control Group A)

-14 Relief motor complications = -59,5%+2.9SEM

-2 Weight gain

-1 Mood Changes

A relationship p>0.0025 between DBS exposure and arrhythmias or septicemia resulted by comparing (Odds ratio, MANOVA) CH to Group A (PD) and Group B (M) profiles. Adverse effects had non-significant correlation with familial history positive for headache or for drugs over-use.

Conclusion: DBS in posterior hypothalamus of CH might induce severe adverse events.

Disclosure: Nothing to disclose

O1107

Transcranial sonography (TCS) reveals nigrostriatal dopaminergic system damage in the primary burning mouth syndrome

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Background and aims: Primary burning mouth syndrome (BMS) is chronic intraoral burning sensation without medical or dental cause. Potential causes are neuropathic dysfunction and central mechanisms with involvement of the nigrostriatal dopaminergic system (NDS). BMS could also be premotor symptom of Parkinson's disease (PD). The aim of this study was to determine the frequency of NDS dysfunction in BMS using TCS.

Methods: 120 patients with BMS, 120 with PD and 74 healthy individuals are included. Using standardized transcranial sonography (TCS) protocol, basal ganglia echogenicity as well as ventricular system diameter and brainstem raphe echogenicity were measured. Degree of intraoral burning sensation and affective status were also determined.

Results: Frequency of substantia nigra (SN) echogenicity was the highest in PD, also significantly higher in BMS in comparison to controls (90% vs. 62% vs. 10%; $p<0.01$ respectively), while there were no differences in other basal ganglia echogenitities. The third ventricle diameter was significantly higher in PD and BMS compared to controls (8.4 ± 2.2 vs. 8.2 ± 2.1 vs. 5.3 ± 1.9; $p<0.01$). Frequency of brainstem raphe hypoechogeniicity was significantly higher in both patients groups compared to controls (75% vs. 74% vs. 10%; $p<0.01$ for PD and BMS vs. controls). Significant correlation was found between raphe and substantia nigra echogencity and the degree of depression ($r=0.351$; $p=0.012$).

Conclusion: TCS is noninvasive method to identify BMS patients with NDS damage that in some could be early premotor PD symptom. This finding could have important therapeutic implications.

Disclosure: Nothing to disclose

O1108

Personality traits influence the co-occurrence of migraine and depression

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Background and aims: Migraine frequently co-occur with other neuropsychiatric disorders, from which the most frequent is depression. The exact mechanism of the co-occurrence, which can be partially explained by shared genetic risk factors, is not well understood yet. In our study we investigated the possible personality trait differences between subjects who suffered from migraine type headache in the last 3 months with and without lifetime depression in a large average population cohort. Our hypothesis was, based on previous studies, that we can identify personality factors that prevent comorbidity in subjects with probable migraine.

Methods: Our study, in which reported lifetime depression, ID-Migraine Questionnaire and Big Five Inventory were used to investigate 3026 individuals from Budapest and Manchester, was part of an EU funded research programme, called NewMood (New Molecules in mood Disorders). Multivariate and logistic regression analyses were used to reveal the relationship between lifetime depression, personality traits and headache.

Results: Subjects with lifetime depression reported significantly more migraine, similarly to the scientific literature. Subjects with migraine without lifetime depression had a higher openness score, compared to subjects, who had lifetime depression. Neuroticism was a risk factor for both migraine and lifetime depression.

Conclusion: In our investigation we found, that neuroticism is an independent risk factor for both depression and migraine, conversely openness has a protective role against the co-occurrence of these conditions. These findings may help to comprehend the biopsychosocial background of migraine, and help to find novel strategies in the prevention and intervention of these conditions.

O1109

The relationship between sleep disorders and migraine: Results from the Chronic Migraine Epidemiology and Outcomes (CaMEO) Study

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Background and aims: This cross-sectional analysis from the Chronic Migraine Epidemiology and Outcomes (CaMEO) Study assessed the relationship of sleep disturbances and sleep apnea (SA) as comorbidities of episodic (EM) and chronic migraine (CM).

Methods: CaMEO participants were recruited from an online panel using quota sampling and completed baseline and 3-month follow-up surveys over 1 year. The Comorbidities/Endophenotypes (C/E) survey assessed the risk of SA using the Berlin Scale for Sleep Apnea ("Yes"=high risk; "No"=low risk) and a self-report of a physician diagnosis (SR-PD) of SA. Sleep disturbances were measured using the Medical Outcomes Study (MOS) Sleep Scale.

Results: 16,763 (99.8%) CaMEO Study respondents received C/E survey invitations, of whom 12,810 (76.4%: 11,669 EM; 1,111 CM) provided valid data. Based on the Berlin Scale, 37.0% were "at high risk" for SA (EM, 35.6%; CM, 51.8%; chi-square, 113.7; $P<0.001$). SA risk significantly increased with higher body mass index (Table 1). 10.1% of respondents self-reported SA (n=1,293; EM, 9.7%; CM, 14.1%) (Table 2). Among those reporting SA, 75.7% also reported a physician diagnosis (EM, 74.7%; CM, 82.8%). Commonly reported MOS sleep subscales were Snoring (EM, 32.1%; CM, 33.9%), Shortness of breath (EM, 20.6%; CM, 29.8%), (daytime) Somnolence (EM, 21.2%; CM, 23.4%), and Sleep inadequacy (EM, 22.1%; CM, 24.2%) (Table 3).

Table 1. Risk of Sleep Apnea Relative to Body Mass Index.

	Underweight, <18.5 kg/m² (n=489)	Normal 18.5 to <25.0 kg/m² (n=4,813)	Overweight 25.0 to <30 kg/m² (n=3,534)	Obese >30.0 kg/m² (n=3,974)
Not at Risk for Sleep Apnea, n (%)	439 (89.8)	4,121 (85.6)	2,480 (70.2)	1,031 (25.9)
At Risk for Sleep Apnea, n (%)	50 (10.2)	692 (14.4)	1,054 (29.8)	2,943 (74.1)

Chi-square, 3626.4; $P<0.001$.

Table 2. Self-Reported History of Sleep Apnea.

	EM (n=11,699)	CM (n=1,111)	Total (N=12,810)	Chi-square	P-value
"Have you ever had sleep apnea?"					
No	10,563 (90.3)	954 (85.9)	11,517 (89.9)	21.9	<0.001
Yes	1,136 (9.7)	157 (14.1)	1,293 (10.1)		
Total	11,699 (100.0)	1,111 (100.0)	12,810 (100.0)		
Among those reporting ever having sleep apnea, "Has this condition been diagnosed or confirmed by a healthcare professional?"					
No	287 (25.3)	27 (17.2)	314 (24.3)	4.9	<0.05
Yes	849 (74.7)	130 (82.8)	979 (75.7)		
Total	1,136 (100.0)	157 (100.0)	1,293 (100.0)		

A response of "Yes" denotes high risk; a response of "No" denotes low risk.

Table 3. Medical Outcomes Study Scale (Sleep Quality).

	EM (n=11,699)	CM (n=1,111)	Total (N=12,810)	T-value	P-value
Sleep Index II, mean (SD)	40.2 (17.1)	53.5 (18.7)	41.3 (17.6)	24.6	<0.001
Sleep Disturbance Scale, mean (SD)	37.9 (24.3)	53.2 (26.9)	39.2 (24.9)	19.8	<0.001
Snoring Scale, mean (SD)	31.0 (32.1)	38.0 (33.9)	31.6 (32.3)	6.9	<0.001
Short of Breath Scale, mean (SD)	15.3 (20.6)	34.9 (29.8)	17.0 (22.2)	28.9	<0.001
Somnolence Scale, mean (SD)	32.2 (21.2)	44.1 (23.4)	33.2 (21.7)	17.7	<0.001
Sleep Adequacy Scale, mean (SD)	39.2 (22.1)	34.0 (24.2)	38.7 (22.3)	7.4	<0.001
Raw Number of Hours Slept, mean (SD)	6.8 (1.4)	6.4 (1.7)	6.7 (1.4)	8.9	<0.001
Optimal Hours Slept, n (% yes)	6,403 (54.7)	452 (40.7)	6,855 (53.5)	80.5	<0.001

MOS consists of 12 items to measure 6 sleep dimensions: initiation (time to fall asleep), quantity (hours of sleep each night), maintenance, respiratory problems, perceived adequacy, somnolence (the last 4 items are reported using a 6-item Likert scale ranging from "All of the time" to "None of the time"). The time frame for the responses is "the past 4 weeks."
Two indexes can be derived: Sleep Problems Index I (short form), which is not presented, and Sleep Problems Index II (long form). Additional subscales are derived: sleep disturbance, snoring, sleep shortness of breath or headache, sleep adequacy, sleep somnolence, sleep quantity, and optimal sleep.

Conclusion: Compared with reported general prevalence estimates ranging from 1.0% to 6.0% for SA, we found an increased risk and potential underdiagnosis of sleep apnea and sleep disturbances among those with migraine, especially CM.

Disclosure: The funding source for this study is Allergan plc (Dublin, Ireland)

O1110

Pharmacogenetics in chronic migraine: Role of CALCA and TRPV1 genes in therapeutic response to Onabotulinumtoxin A

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Background and aims: Time from onset of Chronic Migraine (CM), age at therapy onset, and plasma interictal levels of CGRP and VIP have been proposed as predictors of efficacy of OnabotulinumtoxinA (OnabotA). We aimed to analyse influence of single nucleotide polymorphisms (SNPs) of genes associated with migraine in response to OnabotA in CM.

Methods: 176 patients (20 males, 156 females) treated accordingly to PREEMPT paradigm. Age at first procedure was 43.2 ± 11.9 years. Patients were considered responders when reduction of migraine days by at least 50% after two procedures. We analysed 25 SNPs: MEF2D rs1050316; TGFBR2 rs7640543; LRP1 rs11172113; TRPM8 rs10166942; MTDH rs1835740; EAAT2 rs4354668; GRIK3 rs6691840; CALCA rs3781719; GABRE rs1139916; GABRQ rs3810651; GABRA3 rs6627221 and rs2201169; HTR2C rs3813929; DRD2 rs1800497; SCN9A rs6746030; KCNS1 rs734784; P2RX7 rs1718119 and rs2230912; TRPV1 rs222749, rs222747 and rs222741; TRPV3 rs7217270; WFS1 rs734312. Genotyping was performed using KASP probes and data obtained in a LyghtCycler-480 (Roche-Diagnostics). Allelic, genotypic frequencies and dominance hypothesis of each allele between responders and non-responders were compared by X2-test.

Results: 134 responders (76%). Two SNPs showed differences, mainly among female patients: CALCA rs3781719, where allele C represents 40.9% in non-responders and 26.9% in responders (p:0.007, OR: 3.11 (1.33-7.26)); and TRPV1 rs222749, where allele G represents 95.8% in responders and 87.5% in non-responders (p:0.013, OR: 3.29 (1.28-8.43)). No significant differences in rest of SNPs.

Conclusion: Polymorphic variations of CALCA and TRPV1 genes might play a role as a prognostic marker of efficacy of OnabotA in CM female patients in our population.

Disclosure: Nothing to disclose

Motor neurone diseases

O1111

Patterns of cortical atrophy at diagnosis in amyotrophic lateral sclerosis and implications on prognosis

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Background and aims: Up to 30% of patients with amyotrophic lateral sclerosis (ALS) have evidence of cognitive impairment. The presence of clinical evidence of fronto-temporal dementia in ALS is considered as a poor prognostic factor. This project aims to study the prognostic value of cortical atrophy noted radiologically in ALS.

Methods: This is a retrospective, observational study consisting of a conveniently sampled cohort of 249 patients with ALS. The global cortical atrophy (GCA) scale was used to quantify cerebral atrophy on the MRI brain scans. The relationship between cortical atrophy and overall survival is assessed using Kaplan-Meier survival analysis and Cox regression analyses.

Results: 249 patients were studied; males (52.2%) and 119 females (47.8%). The mean age of onset was 61.5 years and the mean diagnostic delay was 15.2 months. The commonest site of onset was lower limb (93 cases) with 79 individuals had bulbar onset disease. The mean survival was 36 months from disease onset. Motor strip atrophy was present in 50% of the cases, 31.3% of them showed bilateral motor strip atrophy. Moderate-to-severe fronto-temporal atrophy was present in 41% of the cases. Brain stem degeneration was seen in 34.2% of the cases.

Kaplan-Meier analysis demonstrated higher degree of cortical atrophy being associated with poorer prognosis. Cox regression analysis (adjusted for gender, El-Escorial category, and diagnostic delay) also demonstrated increasing hazard with increasing atrophy. This was true for fronto-temporal and motor strip atrophy, while brainstem atrophy did not have a significant effect on prognosis.

Conclusion: Cortical atrophy detected radiologically offers an additional prognostic biomarker in ALS.

Disclosure: Nothing to disclose

O1112

Multicenter evaluation of neurofilaments in early symptomatic amyotrophic lateral sclerosis

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Background and aims: Neurofilament (Nf) levels in cerebrospinal fluid (CSF) and serum are increased in patients with amyotrophic lateral sclerosis (ALS), but their diagnostic potential in the early symptomatic phase has not been specifically studied. This multicenter study examined Nf concentrations according to symptom onset and clinical diagnostic certainty categories of ALS.

Methods: Nf light chain (NfL) and phosphorylated Nf heavy chain (pNfH) CSF and NfL serum levels were measured in ALS patients with first symptom onset ≤6 months (n=48), >6 months (n=128) from sampling and neurological disease controls by ELISA and Simoa platform. Nf levels were related to symptom onset and clinical diagnostic category of ALS at baseline and follow-up.

Results: NfL and pNfH in CSF and NfL in serum were increased in both the early and later symptomatic phase ALS patient groups (p<0.0001). CSF and serum NfL and CSF pNfH discriminated ALS patients with early symptom onset from controls with high sensitivity (94%, 88%, 98% respectively) and specificity (86%, 92%, 91%, respectively). NfL and pNfH CSF and NfL serum concentrations did not vary between clinical diagnostic categories of ALS in the early symptomatic phase group. CSF pNfH concentrations were lower in ALS patients with a clinical phenotype of isolated lower motor neuron within the later symptomatic phase (p<0.05). Baseline NfL and pNfH levels were not

significantly different in ALS patients with clinical progression to definite or probable ALS at follow-up.

Conclusion: The study further supports the routine introduction of Nf measurement in those patients where ALS is a diagnostic consideration.

Disclosure: Nothing to disclose

O1113

Unraveling disease burden in familial ALS due to SOD1 mutation through the combination of brain and cervical cord MRI

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Background and aims: Although amyotrophic lateral sclerosis (ALS) patients carrying SOD1 mutations show a clinical phenotype similar to sporadic ALS (sALS), their survival is generally longer for undetermined reasons. This study investigates both brain and cervical cord magnetic resonance imaging (MRI) alterations in SOD1+ ALS patients.

Methods: 20 SOD1+ ALS patients, 11 sALS patients and 33 healthy controls underwent clinical evaluation and a comprehensive MRI protocol assessing brain structural and functional alterations using T1-weighted, diffusion tensor and resting-state (RS) functional MRI. Cortical thickness, tractography of the corticospinal tracts (CST), and RS functional connectivity analyses were performed. Patients also underwent cervical cord MRI to evaluate cord atrophy and magnetization transfer ratio (MTR).

Results: SOD1+ ALS patients showed longer disease duration and slower rate of functional decline relative to sALS cases. Precentral cortical thickness was not different among groups. CST was altered in both patient groups (p ranging 0.001 to 0.02 vs controls), with a trend toward a greater damage in sALS relative to SOD1+ (p=0.06 bilaterally). Functional hyperconnectivity of the motor cortex in the sensorimotor network was observed in sALS patients only. Conversely, SOD1+ patients showed greater cervical cord atrophy at all included myelomeres relative to sALS (p<0.001). No MTR differences were found between SOD1+ and sALS.

Conclusion: SOD1+ ALS subjects showed cervical cord atrophy relative to sALS, despite a similar cord MTR and the relative preservation of brain motor networks. Our results suggest that pathological burden accumulated through presymptomatic stages and longer disease duration in SOD1+ cases might selectively affect the cervical cord.

Disclosure: Nothing to disclose

O1114

A population based study on the prognostic value of the spreading of symptoms at diagnosis in ALS

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Background and aims: The spreading of neurodegeneration in ALS is still unclear. We aimed at assessing in a population-based ALS series the pattern of involvement of body regions (bulbar, upper limbs, lower limbs, and respiratory) at diagnosis and its correlation with survival.

Methods: Of 879 incident cases between 2007 and 2012 in Piemonte and Valle d'Aosta, 810 (92.2%) were included (382 women, 428 men; mean age at onset 66.3 years [SD 10.9]). A site was considered as affected upon the loss of one point from the ALSFRS-R sub-score awarded to that region (bulbar: domains 1, 2, 3; upper limbs: 4, 5; lower limbs: 8, 9; respiratory 10, 11, 12). The different patterns were analyzed according to sex, age at onset, site of onset, PEG, NIV, tracheostomy and survival.

Results: At diagnosis, one region was affected in 367 patients (45.3%), two regions in 217 (26.8%), three in 152 (18.8%), four in 74 (9.1%). With the increase of age at onset, affected sites at diagnosis progressively increased (p=0.0001). This finding was not due to different diagnostic delay according to the number of affected regions at diagnosis (p=0.48) and the age at onset (p=0.30). The number of affected regions at diagnosis correlated with survival (1 region, median survival 3.1 years; 2 regions 2.6 years; 3 regions 1,8 years; 4 regions 1.5 years; p=0.0001) and was independent from the diagnostic delay (p=0.0001) and the age at onset (p=0.0001).

Conclusion: Different spreading patterns at diagnosis are related to ALS survival and can have a prognostic value.

Disclosure: Nothing to disclose

O1115

The impact of spasticity on diaphragm contraction: Electrophysiological assessment

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Background and aims: Respiratory failure is the most common cause of death in Amyotrophic lateral sclerosis (ALS). Diaphragm motor response (PhrenCMAP) is predictive of hypoventilation/survival in ALS. We hypothesize that spasticity could reduce diaphragm contraction in spite of normal motor amplitude; stimulation during muscle contraction causes larger CMAP amplitude, as compared with baseline recording. To test this, we studied PhrenCMAP during both expiration and full-inspiration in ALS, primary lateral sclerosis (PLS) patients and aged-matched controls.

Methods: PhrenCMAP was studied in 111 ALS patients, 11 patients with PLS and 33 aged-matched controls. Electrophysiological assessment was performed on both sides and separately at end-expiration phase and during full-inspiration. We recorded latency, peak-to-peak amplitude (DiaphrAmpl), and negative-peak area and duration. The percentage of change from baseline to full-inspiration (%insp-exp) was calculated for each measure. Patients were also evaluated for the presence of spasticity (Ashworth scale), functionality (ALSFRS-R), respiratory subscore (R) and the forced vital capacity (FVC).

Results: At baseline, PhrenCMAP had longer latency, smaller DiaphrAmpl and area than controls and PLS ($p<0.05$). Furthermore, %insp-exp was significantly reduced in patients with PLS and in patients with ALS and spasticity ($p<0.05$); %insp-exp was independent from baseline DiaphrAmpl.

Conclusion: Investigating the change of the motor response amplitude of the diaphragm by phrenic nerve stimulation we confirmed that spasticity reduces muscle contraction and mobility. This can have a relevant impact on respiratory function, in particular on exercise.

Disclosure: Nothing to disclose

O1116

Amyotrophic Lateral Sclerosis in Nordland County, Norway 2000 – 2015.

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Background and aims: There are indications of increasing incidence of amyotrophic lateral sclerosis (ALS). Awareness of cognitive impairment in ALS has increased in recent years. We describe a cohort of patients collected in northern Norway over a 15-year period.

Methods: All patients with ALS living in Nordland County in the period 2000-2015 were identified and the medical records were scrutinized. The average annual incidence was calculated for the whole period, and for 5-year periods. Point prevalence was January 1, 2015.

Results: We identified 74 cases with motor neuron disease/ALS. The crude point prevalence was 4.1 per 100 000. The average annual incidence was 2.1 per 100 000 for the whole period, 1.4 for women and 2.8 for men. The incidence was 2.0 in the period 2000-2004, 2.3 in 2005-2009, and 2.0 in 2010-2014. Maximum age specific annual incidence was 13.9 per 100 000 in the age group 70-74 year, whereas the mean age at diagnosis was 66.5 years. Mean time from first symptom to diagnosis was 13.7 months. 60 % received the diagnosis within one year, which increased to 90 % within the second year. The survival time from symptom onset ranged from 2 months to nearly 11 years, mean survival time was 3 years and 2 months and median survival time was 2 years and 7 months. In 15 patients, there were evidence of cognitive impairment.

Conclusion: The average annual incidence was stable during the period. Cognitive impairment was noted in 20 % of the patients.

Disclosure: Nothing to disclose

Peripheral nerve disorders

O1117

Statins and polyneuropathy revisited: A Case-control study in Denmark, 1999-2013

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Background and aims: In a previous study we found a positive association between statin use and polyneuropathy risk. Other studies reported equivocal results. We performed the present study with a design similar to our previous study, but on a larger data set.

Methods: We used medical register data to identify patients with incident idiopathic polyneuropathy in 1999–2013 and verified the diagnosis through medical records. Each case was matched to 20 general population controls matched on age, sex, and calendar year. Prior statin use, ascertained through a prescription registry, was classified as ever use and current use; the latter was further classified into long-term (5+ years) use, and as high versus low intensity use. We used conditional logistic regression to calculate odds ratios (ORs), with 95% confidence intervals (CIs) for polyneuropathy associated with statin use.

Results: The study included a total of 370 validated cases and 7,400 controls. Ever use of statins was not associated with an increased risk of polyneuropathy (OR 1.14; 95%CI 0.84-1.54). Similar results were found in analyses of current use (OR 1.11, 95% CI 0.79-1.53), long-term use (OR 1.13, 95%CI 0.66-1.92), and high intensity statin use (1.05, 95%CI 0.59-1.84).

Conclusion: Use of statins was not associated with an increased risk of polyneuropathy.

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O1118

Magnetic resonance neurography including diffusion tensor imaging of the peripheral nerves in patients with CMT Type 1A

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Background and aims: Nerve conduction studies are the gold standard for evaluation of peripheral neuropathies. However, the nerves may be unexcitable in Charcot-Marie-Tooth (CMT) and the degree of severity difficult to assess. These factors indicate the need for more sensitive methods to determine the presence and severity of neuropathy in CMT. The aim of this study was to evaluate Magnetic-Resonance-Neurography (MRN) applying Diffusion-Tensor-Imaging (DTI) for the detection of abnormalities associated with Charcot-Marie-Tooth type 1A (CMT1A).

Methods: MRN was performed in proximal and distal nerve segments of the lower extremity (sciatic and tibial nerve) in 15 patients with CMT1A and 30 healthy controls (HC). MRN consisted of conventional multi-echo MR imaging to calculate T2-relaxation-time (T2) and proton-spin-density (PD), and DTI to determine fractional-anisotropy (FA) and the apparent-diffusion-coefficient (ADC). The findings at MRN were related to severity of neuropathy based on clinical examinations and nerve conduction studies. Sensitivity and specificity of MRN was estimated from receiver-operating-characteristics (ROC).

Results: DTI of the peripheral nerves showed lower FA values (p<0.01) and higher ADC values (p<0.01) in CMT1A patients as compared to HC. T2 showed no difference, but the PD of the sciatic nerve was higher in patients than in controls (p<0.01). There were close associations between neuropathy severity and MRN with the closest correlation between FA and nerve conduction velocity in the sciatic nerve (R2=0.58; p<0.01). ROC analyses showed good separation of CMT1A and HC.

Conclusion: MRN enables detection of neuropathic abnormalities in patients with CMT1A and may be considered for monitoring of the progression of disease in CMT patients.

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O1119

Subcutaneous immunoglobulin for maintenance treatment in chronic inflammatory demyelinating polyneuropathy (CIDP), a multicenter randomized double-blind placebo-controlled trial: The PATH Study

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Background and aims: Approximately two-thirds of CIDP subjects need long-term corticosteroids or intravenous immunoglobulins (IVIg), with IVIg being slightly preferred based on safety profiles. Subcutaneous Ig (SCIg) is an alternative option for Ig delivery but has not previously been investigated in a large-scale clinical trial in CIDP.

Methods: We performed a randomized, double-blind trial in CIDP investigating 0.2 and 0.4 g/kg weekly doses of SCIg IgPro20 (Hizentra®, CSL Behring) versus placebo in 172 subjects for maintenance treatment. IVIg-dependent adults with definite or probable CIDP according to EFNS/PNS criteria were eligible. The primary outcome was the percentage of subjects with a CIDP relapse (1-point deterioration on adjusted INCAT disability score) or who were withdrawn for any other reason during the 24-week SCIg-treatment period. Multiple secondary endpoints were assessed.

Results: The primary outcome occurred in 33% of high-dose SCIg, 39% of low-dose SCIg, and 63% of placebo subjects. Both SCIg doses were superior to placebo (p =< 0.001, p = 0.007) (Table 1). Median INCAT score, MRC sum score, and grip strength remained stable in SCIg subjects. High-dose SCIg prevented the R ODS decline

seen with low-dose SCIg and placebo. All placebo subjects deteriorated on measures of strength and disability (Table 2). Causally related adverse events occurred in 47 (27%) subjects (18% placebo, 30% low dose, and 35% high dose).

Table 1. Primary outcome

	% (number of subjects)			Exact Cochran-Armitage test (p)	Fisher's exact test (p)		
	Placebo N=57	Low-dose SCIg N=57	High-dose SCIg N=58	Overall test	Low-dose vs placebo	High-dose vs placebo	High-dose vs low-dose
Primary outcome	63% (36)	39% (22)	33% (19)	<0.001	0.007	<0.001	0.323
CIDP relapse	56% (32)	33% (19)	19% (11)	<0.001	0.012	<0.001	0.061

CIDP = chronic inflammatory demyelinating polyneuropathy; SCIg = subcutaneous immunoglobulins.
Exact Cochran-Armitage tested statistical significance at a p-value of < 0.025 for superiority of at least one IgPro20 dose over placebo.
All tests are one-sided p-values.

Table 2. Secondary outcomes

		Placebo N=57	Low-dose SCIg N=57	High-dose SCIg N=58	Asymptotic Jonckheere-Terpstra test (p) Overall test	Wilcoxon rank sum test (p) Low-dose vs placebo	High-dose vs placebo	High-dose vs low-dose
INCAT score [total, median (Q1, Q3)]								
	Baseline	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	<0.001	0.005	<0.001	0.102
	Change at last SC post-dose observation	1.0 (0.0, 2.0)	0.0 (0.0, 1.0)	0.0 (0.0, 0.0)				
R-ODS [centile score, median (Q1, Q3)]								
	Baseline	68.0 (51.0, 83.0)	63.0 (51.0, 73.0)	69.0 (54.0, 80.0)	<0.001	0.030	<0.001	0.041
	Change at last SC post-dose observation	-3.0 (-16.0, 0.0)	-2.0 (-7.0, 2.0)	0.0 (-2.0, 3.5)				
Grip strength [kPa, dominant hand, median (Q1, Q3)]								
	Baseline	68.0 (49.3, 83.7)	67.0 (56.7, 86.2)	68.4 (46.0, 93.3)	0.022	0.004	0.014	0.198
	Change at last SC post-dose observation	-6.6 (-21.6, 0.3)	-0.6 (-8.9, 7.0)	-2.7 (-6.6, 2.0)				
MRC [sum score, median (Q1, Q3)]								
	Baseline	76.0 (72.0, 78.0)	75.0 (70.0, 78.0)	76.0 (70.0, 79.0)	0.003	0.003	0.002	0.465
	Change at last SC post-dose observation	-2.0 (-6.0, 0.0)	0.0 (-2.0, 2.0)	0.0 (-2.0, 1.0)				

INCAT = Inflammatory Neuropathy Cause and Treatment; MRC = Medical Research Council; R-ODS = Rasch-built Overall Disability Scale; SC = subcutaneous; SCIg = subcutaneous immunoglobulins.
Baseline scores were the last scores before randomization.
All tests are one-sided p-values. Statistical significance was defined at a p-value of < 0.025.

Conclusion: SCIg IgPro20 was efficacious and safe as maintenance treatment. High-dose and low-dose SCIg were both superior to placebo, with the high dose potentially showing better efficacy.

Disclosure: CSL Behring sponsored the study Clinicaltrials.gov, number NCT01545076

O1120

Transthyretin familial amyloid polyneuropathy: The neuropathy progression on treated patients compared with natural disease progression

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Background and aims: Transthyretin familial amyloid polyneuropathy (TTR-FAP) is an inherited, progressive disease characterized by a sensory, motor, and autonomic neuropathy, resulting in significant disability and death, if not treated. The only approved disease modifying treatments are liver transplant and tafamidis. The main goal of this study was to compare neuropathy progression based on neurophysiological assessments, over 3 years, of treated patients with Tafamidis or Liver Transplant versus untreated patients.

Methods: We analysed nerve conduction data from a total of 76 TTR-FAP patients (27 untreated, 26 liver transplanted and 23 tafamidis treated). At baseline, all subjects were at stage I of the disease. Neurophysiological motor and sensory scores (higher values meaning better nerve function) were used, by summing the amplitudes of motor (CMAP) and sensory (SNAP) evaluations respectively. We used a linear mixed-effects model to investigate how these scores changed over time as a function of each treatment.

Results: At baseline, untreated patients were significantly older than both transplant and tafamidis groups (both p<0.05) and they had shorter disease duration than transplanted cases (p=0.029). At baseline, a significantly higher sensory score in the tafamidis group compared to those without treatment (p=0.012) was found. The regression analysis of changes from baseline at last available follow-up, showed that both transplant and tafamidis groups progressed significantly better than those without treatment on motor and sensory scores (all p<0.05).

Conclusion: Both available disease-modifying therapies have a similar positive impact on neuropathy progression. Our results also highlight the importance of starting treatment in early-stages of the disease.

Disclosure: BM have no disclosures. JC has received support as sub- investigator from Alnylam Pharmaceuticals, ISIS Pharmaceuticals, and Pfizer. IC has received support as primary investigator from Alnylam Pharmaceuticals, ISIS Pharmaceuticals, and Pfizer. Also serves on the advisory board of the Transthyretin Amyloidosis Outcomes Survey (THAOS) that is sponsored by Pfizer.

O1121

Phase 2 open-label extension (OLE) study of patisiran with or without a TTR stabilizer for the treatment of hereditary ATTR (hATTR) amyloidosis with polyneuropathy

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Background and aims: Hereditary ATTR (hATTR) amyloidosis is a rapidly progressive disease induced by a mutation in the transthyretin (TTR) gene, causing misfolded TTR proteins to accumulate in multiple organs leading to significant morbidity and mortality. We present 24-month data addressing the safety and efficacy of patisiran, an investigational RNAi therapeutic, as monotherapy or in combination with a TTR stabilizer (diflunisal or tafamidis).

Methods: Phase 2 open-label extension (OLE) study (NCT01961921) in patients with hATTR amyloidosis; patients received patisiran (0.3mg/kg IV) every 3 weeks for 24 months. Use of a TTR stabilizer was permitted at the discretion of the investigator and based on availability.

Results: Twenty-seven patients (patisiran + stabilizer [combination], n=20; patisiran alone [monotherapy], n=7) were enrolled. Patisiran, both as combination and as monotherapy, was generally well tolerated. Seven patients (combination, n=5; monotherapy, n=2) experienced SAEs unrelated to study drug. Table 1 highlights AEs reported in ≥20% patients by group; the majority of AEs were mild in severity. Sustained mean serum TTR lowering of ~80% was observed over 24 months in both groups. Preliminary 24-month data demonstrate a mean 7.0-point decrease (n=19) and 6.7-point decrease (n=7) in mNIS+7 for the combination and monotherapy groups, respectively. Additional data, including patients who discontinued a stabilizer while continuing patisiran monotherapy, will be presented.

	Patisiran + TTR Stabilizer (Combination Therapy; n=20)	Patisiran Alone (Monotherapy; n=7)
Flushing	7 (35%)	0
Nasopharyngitis	6 (30%)	0
Wound	6 (30%)	0
Diarrhea	5 (25%)	1 (14.3%)
Infusion-related reaction	5 (25%)	1 (14.3%)
Urinary-tract infection	5 (25%)	1 (14.3%)
Pyrexia	4 (20%)	0
Vomiting	4 (20%)	2 (28.6%)
Nausea	3 (15%)	2 (28.6%)
Pain	0	2 (28.6%)

*Occurring in ≥20% of patients in either group

Table 1: Incidence of Treatment-Emergent Adverse Events (TEAE*) by Stabilizer Use

Conclusion: Preliminary 24-month data demonstrated long-term administration of patisiran, with or without a TTR stabilizer, was generally well-tolerated, resulted in robust and sustained serum TTR lowering, and supports the therapeutic hypothesis that TTR knockdown can potentially halt or improve neuropathy progression.

Disclosure: Patisiran is an investigational RNAi therapeutic targeting TTR; study sponsored by Alnylam Pharmaceuticals

O1122

International CIDP Outcome Study (ICOS): A prospective study on clinical and biological predictors of disease course and outcome

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Background and aims: Chronic inflammatory demyelinating polyneuropathy (CIDP) is a heterogeneous immune-mediated disorder with an extensive variation in clinical presentation, electrophysiological phenotype, response to treatment and long-term outcome. This heterogeneity may indicate the presence of distinct subtypes of CIDP with a different pathogenesis that require personalized treatment.

Methods: ICOS is a prospective, observational, international multi-centre study that aims to describe the variation in clinical and electrophysiological subtypes and to define the clinical and biological determinants and predictors of these subtypes, disease activity, treatment response and outcome. Furthermore ICOS will provide an infrastructure for conducting new (therapeutic) studies in CIDP. All patients fulfilling the EFNS/PNS diagnostic criteria for CIDP can participate, independent of age, duration and severity of the disease or treatment. The study collects data on the clinical presentation, diagnostics, validated clinical outcome measures, previous and current treatments, treatment response and the collection of biomaterials (DNA, cerebrospinal fluid and serial serum samples).

Results: Considering the complexity of ICOS, we finalized a pilot study in 3 academic centers in the Netherlands. In January 2017 72 patients are included in ICOS, 29 newly diagnosed and 43 known CIDP patients. 68% males and 32% females with a median age of 65 (IQR 52 - 72). 52 sensory-motor CIDP patients and 20 subtypes are currently included. Further results of ICOS will be presented at the EAN meeting.

Conclusion: Our final aim is to include at least 1000 CIDP patients worldwide with a minimum follow-up period of 2 years.

Disclosure: Nothing to disclose

Cerebrovascular diseases 1

O1201

Safety and complication of contrast-enhanced sonothrombolysis in unselected acute ischaemic stroke population. Results from NOR-SASS.

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Background and aims: Contrast-enhanced sonothrombolysis (CEST) is a promising treatment approach for acute ischaemic stroke within 4.5 hours after stroke symptom onset. Serious adverse events and complications data after CEST in unselected acute ischaemic stroke population are lacking.

Methods: Prospective, randomised, open-label, blinded endpoint study. Patients with neurological deficit measurable on the National Institutes of Health Stroke Scale, admitted within 4.5 hours of symptom onset and eligible for intravenous thrombolysis were enrolled into the Norwegian Sonothrombolysis in Acute Stroke. Randomisation 1:1 to either alteplase (0.9mg/kg) or tenecteplase (0.4mg/kg) and thereafter 1:1 to either CEST with 2MHz pulsed-wave ultrasound, or sham CEST. Microbubble contrast (SonoVue®) or saline 0.9% was administered as continuous infusion for the initial ~30 minutes of in total 60 minutes. Magnetic resonance imaging and angiography were performed within 22-36 hours of stroke symptoms onset. Serious adverse events and complications were assessed blindly in-hospital and following 90 days.

Results: Of 183 patients enrolled in NOR-SASS, 93 received CEST. Any haemorrhagic transformation was observed in 15%, but symptomatic intracerebral hemorrhage and noncerebral bleedings complication occurred in a few patients in the first 36 hours after admission. Early death caused by sICH occurred in 1% patients. There were no statistically significant differences in the occurrence of serious adverse events or complications, neither between the CEST and sham CEST stroke groups. (Final results will be presented at EAN conference 2017).

Conclusion: Contrast-enhanced sonothrombolysis treatment can be safely administered within the first 4.5 hours after symptoms onset in unselected acute ischaemic stroke population.

Disclosure: Nothing to disclose

O1202

Spontaneous intracerebral haemorrhage: Are there any sex-related specifities?

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Background and aims: While sex-related specificities are now regarded as important in the management of patients with ischaemic strokes, few data are available regarding intracerebral haemorrhages (ICH).
We aimed to identify sex-related differences and their impact on outcome in patients with spontaneous ICH.

Methods: From 11/2004 to 03/2009, we prospectively recruited consecutive adults with a spontaneous ICH admitted to Lille University Hospital, France. We compared clinical, radiological and outcome data between men and women in univariate analyses. Independent variables associated with female gender were identified in multivariable analysis (logistic regression).

Results: Among 560 ICH patients (median age 72 years), 269 (48%) were women. Women tended to be older than men (73 vs 70, p=0.089). Women had more often a history of myocardial infarction (11% vs 6%, p=0.023), and diabetes (18% vs 12%, p=0.048), while men were more likely to have excessive alcohol consumption (32% vs 18%, p<0.0001). In multivariable analysis, the only difference between men and women was an excessive alcohol consumption (OR 0.49; 95%CI 0.32-0.75) that was less likely among women. Regarding imaging characteristics, in multivariable analysis there was no gender specificity. At 6-month, 55% of women and 50% of men had died (p=0.250). There was no difference regarding access to rehabilitation (p=0.674). Poor functional outcome (modified Rankin Scale [mRS] score 3-5) was similar in both groups (p=0.920).

Conclusion: Sex-related differences in our study were mainly mediated by age and we could not identify an influence of gender on both vital and functional outcomes at 6 months.

Disclosure: Nothing to disclose

O1203

Rupture risk for familial compared to sporadic intracranial aneurysms

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Background and aims: A 17-times higher rupture rate for patients with familial intracranial aneurysms (IA) compared to patients with sporadic IA has been reported. We aimed to validate these findings in a large independent series of Dutch patients with familial and sporadic IA.

Methods: We included patients with untreated unruptured IA (UIA) from our prospectively collected database of the University Medical Center Utrecht between 1994 and 2016. In patients with familial IA, the IA were identified by screening because of a positive family history for subarachnoid hemorrhage (SAH); patients with a prior history of SAH or UIA were excluded. For sporadic IA, we selected patients with an incidental UIA and no family history of SAH or UIA. We assessed the incidence of SAH in the two patient groups with survival analysis and calculated an incidence ratio by dividing the observed incidence in the familial IA patients by the incidence in sporadic IA patients.

Results: We identified 65 familial IA patients with 93 UIA and 434 sporadic IA patients with 580 UIA. Four familial IA patients had SAH during 3239 patient-years of follow-up compared to ten sporadic IA patients during 1483 patient-years of follow-up. The observed incidence of rupture was 0.12 ruptures per patient-year (95% CI 0.03-0.32) for familial IA and 0.67 ruptures per patient-year (95% CI 0.34-1.20) for sporadic IA (incidence ratio 0.18 (95% CI 0.06-0.59)).

Conclusion: In contrast to previous reports, our results suggest that the risk of aneurysmal rupture is comparable for familial IA and sporadic IA.

Disclosure: Nothing to disclose

O1204

Actovegin in the treatment of post-stroke cognitive impairment: An international multicenter, randomized, double blind, placebo-controlled trial (ARTEMIDA study)

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Background and aims: Post-stroke cognitive impairment (PSCI) is associated with significant morbidity; the treatment strategies to prevent/ameliorate are being investigated. Actovegin (calf blood haemoderivative) showed neuroprotective potential, it ameliorated Aß25–35-induced neuronal apoptosis and decrease reactive oxygen species content in hippocampal neurons. Promising efficacy was demonstrated in small-scale human studies.

Methods: This was a 12-month, parallel-group, randomised, multicentre, double blind, placebo-controlled trial to examine the effect of Actovegin treatment on PSCI in subjects with acute ischaemic stroke recruited from 33 hospitals in 3 countries. The dosage of Actovegin was 2000 mg/day for up to 20 intravenous infusions followed by 1200 mg/day orally for a six-month treatment period and a follow up for six months. The primary endpoint was the change from baseline in the Alzheimer's Disease Assessment Scale (ADAS-Cog+) at month 6.

Results: A total of 503 subjects were randomised. The primary outcome and the key secondary outcome parameters were concordant and demonstrated a significant difference in favor of Actovegin vs. placebo (table 1). At months 3, 6, 12 significantly more patients in the Actovegin group met the definition of responder (>=4 point improvement in ADAS-cog+ score from baseline) vs placebo. Adherence to treatment was high (a mean of 99.6% for the infusions and 93.3% for the tablets). The safety experience was consistent with the known safety and tolerability drug profile. Ischaemic stroke was the most reported serious adverse event, with a non-significantly higher number on Actovegin vs. placebo (table 2).

	Actovegin N=248	Placebo N=255	Actovegin versus placebo (95% CI)
ADAS-cog+			
Baseline (mean, SD)	29.4 (12.5) n=241	29.9 (12.5) n=246	-
Change from baseline at Month 3*	-5.4 (0.5) n=224	-4.3 (0.5) n=234	-1.1 (-2.6, 0.3); p=0.12
Change from baseline at Month 6**	-6.8 (0.6) n=224	-4.6 (0.6) n=234	-2.3 (-3.9, -0.7); p=0.005
Change from baseline at Month 12*	-8.2 (0.7) n=211	-4.5 (0.7) n=219	-3.7 (-5.5, -1.9); p<0.001

Table 1: Summary of primary and key secondary outcomes in the ITT population

Data are LS mean (SE)

*Change from baseline (Imputed data) results based on data which include imputation of missing values. Partially missing ADAS-cog+ scores, with some missing individual question scores, were imputed with the worst scenario score.

** Completely missing ADAS-cog+ scores were imputed by LOCF from Month 3.

	Actovegin N=250	Placebo N=253
Number of patients with at least 1 TEAE	89 (35.6)	96 (37.9)
Number of TEAEs	206	215
Ischemic stroke	13 (5.2)	5 (2.0)
Headache	7 (2.8)	7 (2.8)
Respiratory tract infection viral	5 (2.0)	8 (3.2)

Table 2: Summary of Treatment Emergent Adverse Events (TEAE) occurring in >=2% of patients; safety analysis set

Abstract #1875 (author A. Guekht) Tables 1, 2

Conclusion: Actovegin improved cognitive outcomes in patients with PSCI, compared with placebo.
Disclosure: This study was organized and funded by Takeda Pharmaceuticals.

O1205

Circulating endothelial markers in the monogenic small vessel disease retinal vasculopathy with cerebral leukoencephalopathy and systemic manifestations

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Background and aims: Retinal Vasculopathy with Cerebral Leukoencephalopathy and Systemic manifestations (RVCL-S) is an underdiagnosed monogenic small vessel disease caused by TREX1 mutations. The pathophysiology of RVCL-S is largely unknown, but a systemic endothelial involvement is suggested that leads to pathology in the brain, but also systemically, including retina, liver and kidneys. We investigated circulating levels of endothelial markers to seek confirmation of endothelial involvement in RVCL-S and to identify biomarkers to assess disease activity.
Methods: We measured in a cross-sectional study circulating levels of VWF antigen (VWF:Ag), VWF propeptide (VWFpp) and Ang-2 in members of three Dutch RVCL-S families (31 with and 33 without a TREX1 mutation) and 31 age and sex-matched unrelated healthy controls.
Results: We found elevated levels of VWF:Ag, VWFpp and Ang-2 in TREX1 mutation carriers compared to family members without a TREX1 mutation and unrelated healthy controls (p<0.001 for all three markers and both control groups). Effects were most pronounced in mutation carriers aged ≥40 years (p<0.001 for all three markers and both control groups). All three markers showed strong correlations with RVCL-S symptoms (Spearman's rho>0.6). However, levels of VWF:Ag and Ang-2 were already elevated in mutation carriers aged <40 years compared to healthy controls (p=0.02 and p=0.04, respectively).
Conclusion: VWF:Ag and Ang-2 may serve as (early) biomarkers of disease activity in RVCL-S. Our findings improve mechanistic insight in the pathophysiology of the monogenic cerebral small vessel disease RVCL-S but also may help to understand common neurovascular disorders, including stroke.

O1206

Prevalence of carotid artery stenosis in patients with transient ischaemic attack or ischaemic stroke: A large prospective case series, systematic review and metaregression analysis

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Background and aims: It is suggested that the prevalence of carotid stenosis in patients with transient ischaemic attack (TIA) or ischaemic stroke has declined. We therefore determined the prevalence of carotid stenosis in a comprehensive regional stroke service and reviewed the literature to determine if there has been a change in prevalence over time or geographic location.

Methods: A one year prospective observational study was performed on consecutive patients presenting with ischaemic stroke or TIA. Significant carotid stenosis was defined as atherosclerotic stenosis of the internal carotid artery at the bifurcation measuring $\geq 50\%$ on duplex ultrasonography, computed tomography angiography, or contrast-enhanced magnetic resonance angiography. A systematic review of the literature on the prevalence of carotid stenosis in patients with ischaemic events was conducted.

Results: Carotid imaging studies was performed in 1252 out of 1444 patients diagnosed with acute ischaemic stroke or TIA in our stroke service. The prevalence of carotid stenosis in our study was 19.0% (n=238; 95% CI 16.6% to 21.4%). Carotid stenosis was deemed symptomatic in 99 patients (7.9%; 95% CI 6.3% to 9.5%). A total of 47 studies with data on carotid stenosis from 37,276 patients were included in our systematic review. The pooled prevalence estimate of any significant carotid stenosis described in 37 studies was 16.0% (95% CI 14.3% to 17.7%) and the pooled prevalence estimate of symptomatic carotid stenosis described in 11 studies was 10.4% (95% CI 7.0% to 13.9%).

Conclusion: Atherosclerotic carotid stenosis remains a common disease worldwide, accounting for 10% of all stroke and TIA.

Disclosure: Nothing to disclose

Infection and AIDS

O1207

Clinical and radiological evidence for brainstem invasion of Listeria monocytogenes via the trigeminal nerve

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Background and aims: Listeria monocytogenes is associated with rhombencephalitis but the exact mechanisms by which the pathogen invades the brainstem remain poorly understood. Here we demonstrate clinical and radiological evidence in three patients with listeria rhombencephalitis for invasion of bacteria via the trigeminal nerve.

Methods: Retrospective case series from the departments of neurology and infectious diseases at a university hospital

Results: Three females (age 42-73 years) with serologically proven listeria monocytogenes septicemia and rhombencephalitis were admitted to our institution in the period of 2014-15. T2-weighted and contrast enhanced T1-weighted MRI revealed a cerebellopontine abscess in all three patients, including involvement of the trigeminal nerve root (Figure 1). In two patients, MRI also revealed selective contrast enhancement of the sensory trigeminal tract in the pons and medulla oblongata (Figure 2). Prior to any other neurological symptoms, two patients complained of hypoesthesia and a tingling sensation in the ipsilateral half of the face, consistent with sensory trigeminal nerve dysfunction on that side. (Clinical details were unavailable for the third patient.)
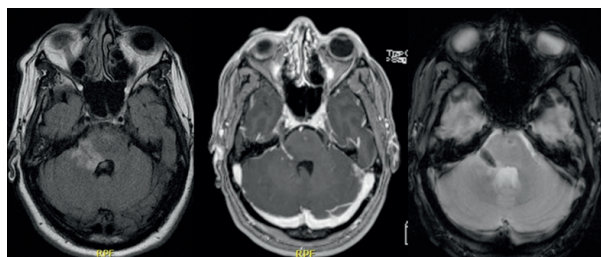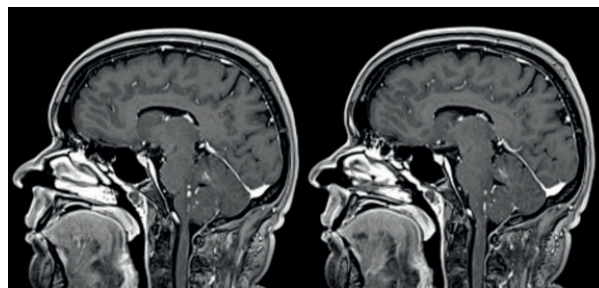

Figure 1

Figure 2

Conclusion: The present clinical and radiological findings corroborate earlier data from animal experiments, showing that Listeria monocytogenes is capable of retrograde intra-axonal migration along cranial nerves and may induce rhombencephalitis in rodents after inoculation of bacteria into the facial musculature. We conclude that in a subset of patients with rhombencephalitis listeria monocytogenes enters the cerebellopontine angle via the trigeminal nerve, invading the brainstem along the sensory trigeminal nuclei.

Disclosure: Nothing to disclose

O1208

Cerebral herniation after lumbar puncture in adults with bacterial meningitis

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Background and aims: We studied the incidence and radiologic findings of fatal cerebral herniation caused by lumbar puncture (LP) in bacterial meningitis.

Methods: In a Dutch prospective cohort study of adults with community-acquired bacterial meningitis (2006- 2015) we identified patients who died shortly after LP. The causal relationship between LP and deterioration was assessed based on clinical course and autopsy findings. All eligible cases were matched to controls with a good clinical outcome, based on age and presenting Glasgow Coma Scale Score. Results of brain imaging prior to LP were blindly reviewed for contraindications for LP by two neurologists specialised in infectious diseases.

Results: Possible cerebral herniation due to LP occurred in 43 of 1533 episodes (3%) with imaging prior to LP. Results of neuroimaging of those episodes, 43 matches and 14 extra episodes with good clinical outcome were assessed. Nine of 25 patients (36%) in whom both examiners reported a contraindication for LP on imaging died after LP, and 11 of 23 patients (48%) in whom one examiner reported a contraindication. No contraindication for LP was reported in 52 patients, of whom 23 (44%) died after LP. Most reported contraindications were basal obliteration and generalized brain oedema.

Conclusion: Cerebral herniation after LP is rare, and determining if it has been caused by LP or by a fulminant course of bacterial meningitis is difficult. We found that LP is sometimes performed while contraindicated, and careful assessment of imaging is essential, as some forms of brain shift, such as generalized oedema, was shown to be overlooked.

Disclosure: Nothing to disclose

O1209

Natalizumab-related progressive multifocal leukoencephalopathy in Austria: An observational nationwide study

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Background and aims: Progressive multifocal leukoencephalopathy (PML) may complicate natalizumab treatment in multiple sclerosis patients. We sought to characterize prevalence as well as clinical course and outcome of all natalizumab-related PML cases in Austria.

Methods: We performed a retrospective observational study of all natalizumab-related PML cases in Austria diagnosed until December 2016. For this purpose, we contacted all hospital-based MS centers in order to collect data.

Results: Twelve natalizumab-related PML cases occurred, seven (58%) were women. The first two cases were diagnosed in 2010 (2011 (1), 2013 (3), 2014 (3), 2015 (3)). The mean age at PML diagnosis was 41 years (range 26 – 56). The number of natalizumab infusions before PML diagnosis ranged from 20 to 94 - nine patients (75%) had received more than 30 infusions. The main presenting symptoms included cognitive symptoms (n=7), hemiparesis (n=6), and gait impairment (n=5). Ten patients (83%) developed IRIS, six had epileptic seizures (50%). The spectrum of outcome was broad but mostly unfavourable, with one fatal case (8%) and five patients (42%) having a more than one point EDSS increase compared to pre-PML. The mean pre-PML EDSS was 3,5, the mean EDSS after PML was 6,5. The impact of the JCV-index could not be assessed as only studied in 3 patients prior to the development of PML.

Conclusion: According to the national MS treatment registry a total of 1477 MS patients were treated with natalizumab until 12/2016, yielding a prevalence for natalizumab-related PML of 0.8%. Cases of natalizumab-related PML seemed to decline over time.

Disclosure: Nothing to disclose

O1210

Bacterial hypervirulence genes in Haemophilus influenzae meningitis identified by whole genome sequencing.

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Background and aims: Haemophilus influenzae is a commensal of the human nasopharynx but can cause invasive disease including bacterial meningitis. Here we studied bacterial virulence genes associated with neuroinvasiveness using whole bacterial genome sequencing.

Methods: We included prospectively collected adult patients with community acquired H. influenzae meningitis in the Netherlands between 1998 and 2002, and between 2006 and 2016, and performed whole genome sequencing on 55 isolates. We collected publically available H. influenzae sequences (GenBank) and compared the presence of 2096 genes in meningitis and non-meningitis isolates using Mantel Haenszel analysis in Plink.

Results: Clinical characteristics for 81 patients were available and showed median age was 58 years, 37 patients (46%) were male; 4 patients (5%) died and 68 (88%) made a full recovery (Table 1). In the phylogenetic tree constructed from 55 sequenced meningitis isolates and 74 public isolates (64 non-meningitis isolates) multiple subclusters were shared (Fig. 1). We identified three gene variants significantly associated with the meningitis phenotype corrected for multiple testing (p<2.4x10-5): rpoB, rplK, and pflA (Fig. 2). These genes are involved in encoding the beta-subunit of RNA polymerase, encoding for the 50S ribosomal protein L11, and activating pyruvate formate-lyase 1.
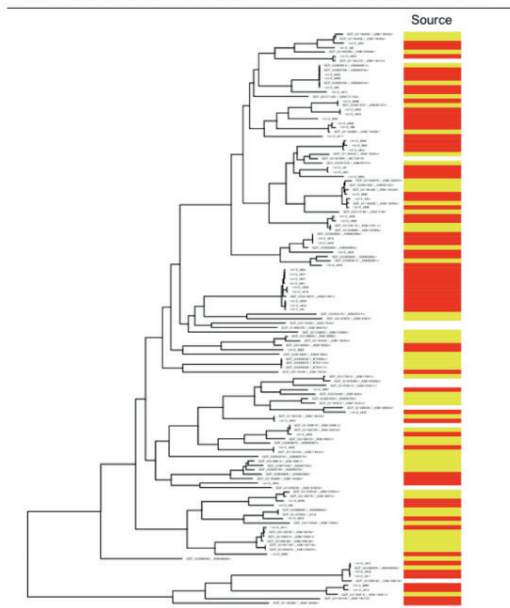
Figure 1. Phylogenetic tree of H. influenzae meningitis and non-meningitis isolates

Maximum likelihood phylogenetic tree of 55 H. influenzae meningitis isolates from the Netherlands and 74 public H. influenzae isolates with their corresponding isolation source. red = cerebrospinal fluid, yellow = other
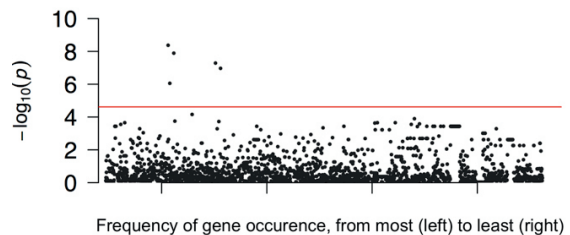
Figure 2

H. influenzae gene versus isolation source

Figure 2

Conclusion: We identified the hypervirulent H. influenzae genes rpoB, rplK, and pflA to be associated with neuroinvasiveness. These proteins may play an important role in the pathophysiology of bacterial meningitis and may be new vaccine targets.

Disclosure: Nothing to disclose

Table 1. Characteristics of patients with *H. Influenzae* meningitis

Features	81 patients
Age, y, median, n=79	58 (41-66)
Male	37/81 (46)
Predisposing factors	
Otitis/Sinusitis	30/74 (41)
Pneumonia	7/70 (10)
Immunocompromised	13/74 (18)
Clinical presentation	
Headache	64/69 (93)
Nausea	47/68 (69)
Neck stiffness	59/71 (83)
Hearing loss	10/63 (16)
Glasgow Coma Scale score at presentation	
≤14	38/74 (51)
≤8	11/74 (25)
≤3	2/74 (3)
Cerebrospinal fluid findings	
Cell count, cells/μL, n=69	3573 (1667-8609)
Total protein, g/L, n=68	4.1 (1.7-4.6)
Glasgow Outcome Scale score at discharge	
1 (death)	4/77 (5)
2 (vegetative state)	0
3 (severe disability)	0
4 (moderate disability)	5/77 (6)
5 (mild or no disability)	68/77 (88)

Data are presented as n/N (%), or median (25th-75th percentile).

Table 1

O1211

An experience from Sudan with tuberculosis of central nervous system: An extensive study of clinical and radiological features, treatment outcomes and predictors of mortality in 60 patients

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Background and aims: Tuberculosis is endemic in Sudan. Tuberculosis of central nervous system (CNS) is associated with high levels of morbidity and mortality.
To study the clinical and radiological features of CNS tuberculosis, treatment outcomes and mortality predicting factors.

Methods: Prospective descriptive study of 60 patients with CNS tuberculosis. Diagnostic methods utilized included histological and/or microbiological evidence of tuberculosis in cerebrospinal fluid analysis or biopsies, magnetic resonance brain imaging, clinical picture and response to anti-tuberculosis treatment.

Results: Mean age was 37.17±1.83 years. Females represented 51.7% of patients. Duration of symptoms was 7.78±0.8 weeks. Symptoms reported were headache (86.7%), fever (66.7%), weight-loss (61.7%), night-sweats (56.7%), and seizures (53.3%). Clinical findings reported were long tract features (46.7%), cranial nerve involvement (45%), papilloedema (43.3%), meningeal irritation (31.7%), and decreased level of consciousness (33.3%). Final diagnosis was cerebral tuberculoma in 65%, tuberculous meningitis (TBM) in 10%; the remaining 25% were having combination of both. Brain tuberculomata were multiple in 51.7% of patients while being single in 38.3%. Brain oedema was observed in 78.3%; mass effect with midline shift was noted in 43.3%. Mean duration of treatment was 17.21 months. Complete recovery was reported in 68.4% of patients, while 13.3% died. Considering single tuberculoma, recovery was complete in 82.1%, whereas in TBM recovery was partial in 83.3%. Death was significantly related to type of diagnosis (P=0.000), number of tuberculomata (P=0.000) and their site (P=0.000), serum sodium (P=0.000), cerebral oedema (P=0.002), and level of consciousness (P=0.05).

Table 1 Details of the clinical features (symptoms & signs) reported in all 60 patients

The clinical feature	No. of patients (%)
Headache	52/60 (86.7%)
Fever	40/60 (66.7%)
Weight loss	37/60 (61.7%)
Night sweats	34/60 (56.7%)
Cranial nerve involvement	27/60 (45%)
Single cranial nerve involvement (7th, 6th, or 3rd)	22/60 (36.7%)
Multiple cranial nerve involvement	5/60 (8.5%)
Papilloedema	26/60 (43.3%)
Choroid tubercle	1/60 (1.7%)
Signs of meningeal irritation	19/60 (31.7%)
Cerebellar signs	3/60 (5%)
Long tract signs	28/60 (46.7%)
Hemiplegia/hemiparesis	20/60 (33.3%)
Paraplegia/paraparesis	3/60 (5%)
Quadreplegia/quadriparesis	3/60 (5%)
Monoplegia	2/60 (3.3%)
Dysphagia	3/60 (5%)
Motor dysphasia	2/60 (3.3%)
Homonomous hemianopia	1/60 (1.7%)
Polyopia	1/60 (1.7%)

Table 2 Radiological features of MRI brain imaging

The feature	No. of patients (%)
Multiple tuberculomata	31/60 (51.7%)
Single tuberculomata	23/60 (38.3%)
Tuberculomata with Size > 1 cm	27/54 (50%)
Tuberculomata with Size < 1 cm	27/54 (50%)
Supratentorial tuberculomata	35/54 (64.8%)
Infratentorial tuberculomata	7/54 (13%)
Tuberculomata sited on both areas	12/54 (22.2%)
Tuberculomata with T1 Weighted hypointensity	27/54 (50%)
Tuberculomata with T1 Weighted isointensity	27/54 (50%)
Tuberculomata with Post-gadolinium enhancement	48/54 (88.9%)
Leptomeneigeal enhancement	21/60 (35%)
Brain oedema (any degree)	47/60 (78.3%)
Marked brain oedema	13/60 (21.7%)
Moderate brain oedema	8/60 (13.3%)
Mild brain oedema	26/60 (43.3%)
Mass effect with midline shift	26/60 (43.3%)
Hydrocephalus	4/60 (6.7%)
Cerebral infarction	1/60 (1.7%)

Conclusion: Cerebral tuberculomata were more prevalent, had more favourable outcomes when compared to TBM.
Disclosure: Nothing to disclose

O1212

Characteristics of headache and its relationship to disease severity in patients with Crimean-Congo hemorrhagic fever

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Background and aims: Crimean-Congo Hemorrhagic Fever (CCHF) is a fatal, tick-borne disease. The classic clinical presentation of CCHF is characterized by a sudden onset of high fever, chills, and severe headache. No previous research has been performed to study the characteristics of headaches caused by CCHF. In this study, the relationship between CCHF-induced headache and the clinical course of the disease was investigated.

Methods: A total of sixty patients diagnosed with CCHF were subdivided into two groups: 'group 1' and 'group 2' consisting of patients with a hospital stay less than seven days and greater than seven days, while 43 hospitalized viral pneumonia patients with fever were included as control group. Patients self-rated headache severity with a numeric pain scale that classified headache as either mild or severe. Patients also described the characteristics of headaches.

Results: In CCHF group 66.7% of all the reported headaches met criteria for a diagnosis of migraine. This ratio was significantly higher than the controls (37.5%). Headache severity scores in group 1 were lower than the scores in group 2. Length of hospitalization was shorter while platelet levels were higher for CCHF patients with mild headaches as compared with patients with severe headache. CCHF patients had more often and severe headaches than the controls.

Conclusion: Severity of headache may be associated with the severity of vascular endothelial damage, vasodilatation and abnormal release of inflammatory cytokines in CCHF. Most CCHF patients experienced migraine like headaches, which suggests that cerebral vessel involvement might be important in both CCHF and migraine.

Disclosure: Nothing to disclose

MS and related disorders 1

O1213

Restriction spectrum imaging in multiple sclerosis

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Background and aims: Restriction spectrum imaging (RSI) is a newly validated diffusion-based magnetic resonance imaging (MRI) sequence that estimates brain tissue in a novel and more specific way. The utility of RSI in multiple sclerosis (MS) is unknown. The aim of this study was to explore the association between diffusion parameters derived from RSI and neurological disability in MS patients.
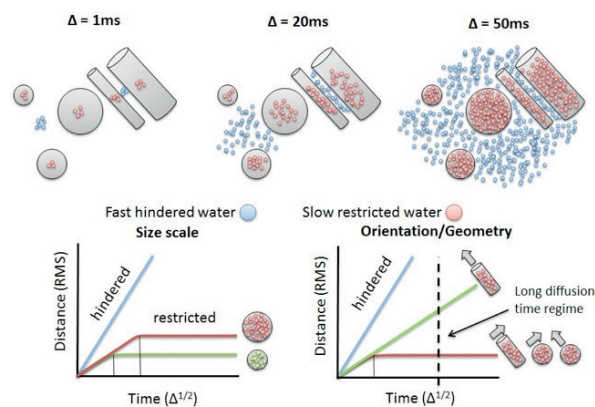

Figure 1. Principles of RSI.

Methods: MRI scans including RSI sequence were acquired on a 3 Tesla scanner in 80 MS patients. Fast (fADC) and slow apparent diffusion coefficient (sADC), fractional anisotropy (FA), restricted FA (rFA), neurite density (ND), cellularity, extracellular water fraction (EWF) and free water fraction (FWF) were extracted from white matter lesions (WML) and from normal appearing white matter (NAWM). Patients were divided into three subgroups according to their expanded disability status scale (EDSS): with minimal, low and substantial disability (<2.5, 2.5–3 and >3, respectively).
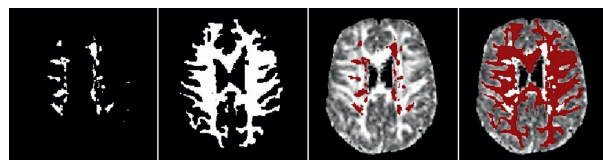
Masks of WML and white matter, and rFA map in a sample patient.

Results: In WML, patients with substantial disability had higher fADC (p=0.009), sADC (p=0.005) and FWF (p=0.031), and lower ND (p=0.018) and cellularity (p=0.015) than patients with minimal disability. In NAWM, patients with substantial disability had higher fADC (p=0.021), sADC (p=0.024) and FWF (p=0.033), and lower FA (p=0.027), rFA (p=0.030) and ND (p=0.015) than patients with minimal disability. Parameter that differentiated best between disability subgroups was sADC in WML (p=0.006). Parameter that correlated best with disability was ND in NAWM (ϱ=-0.38, p=0.011).
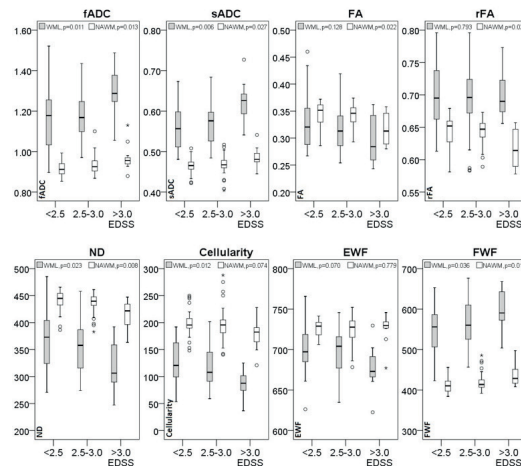
Diffusion parameters derived from RSI sequence in disability subgroups.

Conclusion: The sADC in WML differentiated best between disability subgroups, while ND in NAWM showed best correlation with disability. Diffusion parameters derived from RSI are promising imaging biomarkers in MS.

Disclosure: Piotr Sowa, Hanne F. Harbo, Nathan S. White, Elisabeth G. Celius, Pål Berg-Hansen, Stine M. Moen and Mona K. Beyer received research grants, travel support or speaker's fees from Almirall, Biogen Idec, GE Healthcare, Genzyme, Novartis, Sanofi-Aventis, Teva or UCB.

O1214

Earlier prognostication in primary progressive multiple sclerosis using MRI: A 15-year longitudinal study

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Background and aims: Reliable prognostic markers of primary progressive (PP) multiple sclerosis (MS) evolution are needed. We investigated the added value of conventional and diffusion tensor (DT) MRI measures of brain and cervical cord damage in predicting the long-term clinical evolution of PPMS in comparison to simple clinical assessment.

Methods: In 54 PPMS patients, conventional and DT MRI scans of the brain and T1-weighted scans of the cervical cord were acquired at baseline and after a median follow-up of 15 months. Clinical evaluation was performed after 5 and 15 years of follow-up in 49 patients. Measures of lesion load, brain and cord atrophy were obtained. Histograms of the mean diffusivity (MD) and fractional anisotropy values from the normal-appearing white matter and gray matter (GM) were analyzed. Linear regression models were used to screen the clinical and MRI variables as independent predictors of 15-year expanded disability status scale (EDSS) change.

Results: At 15-year follow-up, 90% of the patients had disability progression. When models including clinical variables only were built, the best model identified baseline EDSS and 5-year EDSS worsening as independent predictors of 15-year EDSS deterioration (R2=0.57; discriminating ability: 74%). When MRI variables were included into the models, the best model identified baseline EDSS and 1-year change of EDSS, T1-hypointense lesions, brain volume and GM MD as independent predictors of 15-year EDSS deterioration (R2=0.61; discriminating ability: 78%).

Conclusion: In PPMS, MRI measures allow an earlier identification of patients at risk of disease progression after 15 years than clinical assessment.

Disclosure: Partially supported by a grant from Fondazione Italiana Sclerosi multipla (FISM 2014/PMS/6).

O1215

Regional patterns of structural damage in neuromyelitis optica spectrum disorders

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Background and aims: The definition of the regional distribution of structural abnormalities in patients with neuromyelitis optica spectrum disorder (NMOSD) could provide useful insights to better understand the pathology in vivo. While atrophy of the white matter (WM) is well established in these patients, the extent of gray matter (GM) involvement remains controversial. Using voxel-based morphometry (VBM), we compared the regional distribution of structural brain abnormalities between NMOSD (2015 criteria), isolated recurrent optic neuritis (ON) and recurrent myelitis patients.

Methods: Brain MR images were acquired from 30 NMOSD, 11 ON, 12 myelitis patients and 30 healthy controls (HC). Between-group comparisons of regional GM and WM volumes and correlations with motor performance were assessed using VBM (SPM12).

Results: Compared with HC, NMOSD patients had atrophy of the thalami, right cuneus and floor of the fourth ventricle; ON patients had atrophy of the cerebellum and calcarine cortex; and myelitis patients had atrophy of the left thalamus and supplementary motor area (SMA). Additionally, NMOSD patients had atrophy of the middle occipital gyrus compared to both ON and myelitis patients.

Conclusion: In recurrent ON and myelitis, structural abnormalities were observed in regions related to the clinical manifestations of such pathologies: visual areas in ON, thalamus and SMA in myelitis patients. Similarly, NMOSD, compared to HC, showed atrophy in brain regions related to clinical manifestations (visual cortex, even more pronounced than in ON), but also consistent with the higher expression of Aquaporin-4 antibodies at this level (thalami and fourth ventricle).

Disclosure: Nothing to disclose

O1216

Impact of ocrelizumab on reducing more severe disability progression in primary progressive multiple sclerosis

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Background and aims: In ORATORIO, ocrelizumab reduced the risk of 12- and 24-week confirmed disability progression (CDP) versus placebo in patients with primary progressive multiple sclerosis (PPMS). Substantial worsening in Expanded Disability Status Scale (EDSS) score may be seen in aggressive PPMS disease, and was investigated by assessing 12- and 24-week CDP using exploratory definitions reflective of more severe events of disability increase.

Methods: In the pre-specified analysis of ORATORIO, CDP events were based on thresholds of increase of ≥1.0/≥0.5 points on the EDSS if the baseline score was ≤5.5/>5.5 points. In this exploratory analysis of the intention-to-treat population of ORATORIO (ocrelizumab n=488; placebo n=244), Kaplan–Meier analyses and Cox proportional hazard modeling were used to estimate the risk of (a) 12- and (b) 24-week CDP using the following definitions (EDSS point increase, baseline): Definition 1: ≥1.5 increase (baseline ≤5.5) or ≥0.5 increase (baseline >5.5); Definition 2: ≥2.0 increase (baseline ≤5.5) or ≥0.5 increase (baseline >5.5); Definition 3: ≥2.0 increase (baseline ≤5.5) or ≥1.0 increase (baseline >5.5).

Results: Compared with placebo, ocrelizumab reduced the risk of (a) 12- and (b) 24-week CDP across the definitions (hazard ratio [95% confidence interval]): Definition 1 ([a] 0.72 [0.54–0.97], p=0.0296; [b] 0.73 [0.54–1.00], p=0.0497); Definition 2 ([a] 0.73 [0.52–1.01], p=0.0584; [b] 0.74 [0.52–1.05], p=0.0861); Definition 3 ([a] 0.52 [0.34–0.81]; p=0.0031; [b] 0.53 [0.34–0.84], p=0.0063).

Conclusion: Despite decreasing overall event rates with stricter definitions, ocrelizumab consistently reduced the likelihood of more severe events of progression in disability in patients with PPMS.

Disclosure: Sponsored by F. Hoffmann-La Roche Ltd.

O1217

The EXPAND study results: Efficacy of siponimod in secondary progressive multiple sclerosis

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Background and aims: The efficacy results of the double-blind, placebo-controlled, phase 3 EXPAND study, evaluating siponimod versus placebo in patients with secondary progressive multiple sclerosis (SPMS), are presented here.

Methods: Patients (N=1651) were randomised 2:1 to once-daily siponimod 2 mg or placebo (with an initial 6-day dose titration). The primary endpoint of this event- and exposure-driven study was the time to 3-month confirmed disability progression (CDP), assessed by the Expanded Disability Status Scale (EDSS). Key secondary endpoints were time-to-confirmed worsening of >=20% from baseline in the Timed 25-Foot Walk test (T25FW) and T2 lesion volume (T2LV) change from baseline. Other secondary endpoints included 6-month CDP, annualized relapse rate (ARR), 12-item MS Walking Scale (MSWS-12), number of T1- gadolinium-enhancing (Gd+) and T2 lesions, and percent brain volume change (PBVC).

Results: Siponimod reduced the risk of 3-month CDP by 21% versus placebo (HR [95%CI]: 0.79 [0.65, 0.95]; p=0.013). Point estimates across predefined subgroups, including patients without relapses in the 2 years prior to study and those without Gd+ lesions at baseline, favoured siponimod. The risk reduction observed for T25FW was 6.2% (p=0.440). Siponimod reduced the risk of 6-month CDP by 26% (p=0.006), ARR by 55.5% (p<0.0001), T1 Gd+ lesion number by 86.6% (p<0.0001), new T2 lesion number by 81% (p<0.0001). Relative difference in change from baseline in T2LV, MSWS-12 and PBVC were 79.1% (p<0.0001), 39.7% (p=0.057) and 23.4% (p=0.0002), respectively, versus placebo.

Conclusion: Siponimod had a robust positive effect on disability progression and other relevant outcomes in SPMS.

Disclosure: This study was funded by Novartis Pharma AG, Basel, Switzerland. Detailed disclosures of each author will be included in the poster/oral presentation.

Neuroimaging

O1218

Altered PDE10A expression detectable early in untreated Parkinson's disease patients

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Background and aims: To investigate in vivo whether loss of PDE10A expression in Parkinson's disease (PD) is an early phenomenon in early untreated PD patients using positron emission tomography (PET) molecular imaging with [11C]IMA107, a highly selective PDE10A radioligand.
Methods: We studied a cohort of 16 early untreated PD patients compared to a group of 16 healthy controls. Subjects undertook one [11C]IMA107 PET and one 3-T MRI scan. Image processing and kinetic modelling was carried out using MIAKATTM. Parametric images of [11C]-IMA107 binding potential relative to nondisplaceable binding (BPND) were generated from the dynamic [11C] IMA107 scans using the simplified reference tissue model with the cerebellum as the reference tissue.
Results: Region of interest analysis showed lower mean [11C]IMA107 BPND in the caudate (38%, P<0.001) and putamen (14%, P<0.001) in PD patients compared to healthy controls, which was confirmed with voxel-based analysis. At structural MRI, PD patients showed no volumetric changes in caudate or putamen but loss of structural connectivity (loss of mean diffusivity in caudate=9%, P=0.005 and putamen=7%, P=0.037). Loss of PDE10A showed no lateralization. Higher Unified Parkinson's Disease Rating Scale part-III motor scores correlated with lower [11C]-IMA107 BPND in the caudate (r=-0.676; P=0.006) and putamen (r=-532; P=0.041).
Conclusion: Our findings demonstrate that loss of PDE10A expression is an early phenomenon in the course of PD over and above structural connectivity changes and is associated with the severity of motor symptoms, independently of levodopa treatment. These data demonstrate that the previous reductions reported in PD are not due to the effects of medication.
Disclosure: Nothing to disclose

O1219

The cerebral metabolic topography of spinocerebellar ataxia type 3

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Background and aims: Spinocerebellar ataxia type 3 (SCA3) is characterized by dysfunction in multiple neuronal networks. Analysis of [18F]-Fluoro-deoxyglucose Positron Emission Tomography (FDG-PET) with the scaled subprofile model and principal component analysis (SSM PCA) may uncover underlying network-level alterations in SCA3.
Methods: 17 ambulatory, genetically-confirmed SCA3 patients and 16 controls underwent static resting-state FDG-PET imaging. The SCA3-related pattern (SCA3-RP) was identified in these images using SSM PCA.
Patients and controls were evaluated with the Scale for Assessment and Rating of Ataxia (SARA) and with a neuropsychological examination which included tests for language, memory, executive functioning and attention (including the Symbol Digits Modalities Test) and emotion recognition. Correlations between expression of the SCA3-RP and SARA or neuropsychology testing scores were evaluated.
Results: The SCA3-RP was characterized by hypometabolism of the cerebellum, caudate nucleus and posterior parietal cortex, and by hypermetabolism in the limbic system and somatosensory areas. This topography correlated significantly with SARA scores (ρ=0.72; P=0.001), but not with neuropsychology testing scores. Patients only showed significantly lower scores compared to controls on the Symbol Digit Modalities Test (P<0.001), which was interpreted as a consequence of impaired motor speed, and not of impaired cognition.
Conclusion: The SCA3-RP reflects local pathological changes (cerebellum and brainstem) and network-level abnormalities (caudate, parietal cortex and limbic areas). Hypometabolism of cerebellum and posterior parietal cortex and hypermetabolism in the somatosensory areas (anterior parietal cortex) may suggest changes in a coherent cerebellar-parietal function. Hypermetabolism of the limbic cortex may reflect relative sparing from the pathological process.
Disclosure: Nothing to disclose

O1220

Nerve ultrasound: A useful screening tool for peripheral nerve sheath tumors?

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Background and aims: Malignant transformation of a peripheral nerve sheath tumor (PNST) is a leading cause of morbidity and mortality in neurofibromatosis type 1 (NF1). However, current consensus is not to screen patients. We performed a cross-sectional pilot-study to explore the role of high-resolution ultrasonography (HRUS) of the nerves as a screening tool.

Methods: Thirteen asymptomatic and four minimally symptomatic patients with NF1 were included in this study to detect asymptomatic abnormalities of the brachial plexus, and upper and lower extremity nerves. Patients underwent clinical examination, nerve conduction studies (NCS) and HRUS.

Results: HRUS showed abnormalities in 16 patients (94%). Neurofibromas were identified in 10 patients (59%): Localized neurofibromas in 3 patients (18%), plexiform neurofibromas in 3 (18%) and both in 4 (24%). In 6 patients (35%) only nerve enlargement without an abnormal fascicular pattern was observed. Severe involvement of the peripheral nervous system with multiple plexiform neurofibromas was observed in 7 patients (41%), while 4 (24%) had no or only minor involvement. Both NCS and HRUS were performed on 73 individual nerve segments. In 6% abnormalities were found with both tests, in 51% only with HRUS and in 1% only with NCS.

Conclusion: HRUS frequently showed subclinical involvement of the peripheral nerves in NF1, also in case of normal NCS. HRUS findings ranged from normal to widespread peripheral nerve involvement. Since the presence of plexiform neurofibromas and the benign tumor load are risk factors for developing a malignant PNST, HRUS may be useful to identify a subgroup of patients that could benefit from regular follow-up.

Disclosure: Nothing to disclose

O1221

Impaired structural brain connectome in patients with systemic lupus erythematosus: A graph theory study

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Background and aims: To explore the topographical organization of structural brain connectome in patients with systemic lupus erythematosus (SLE) and to compare it with that of healthy controls (HC) and relapsing-remitting multiple sclerosis (RRMS) patients.

Methods: Diffusion tensor (DT) and dual-echo MRI scans were obtained from 32 SLE patients (12 with neuropsychiatric-SLE), 32 RRMS patients and 32 HC, matched for age, gender and disease duration (patients only). Structural connectivity matrices between 116 cortical and subcortical brain regions were estimated and global and nodal network metrics were calculated.

Results: Compared to HC, both SLE and MS patients showed decreased (p<0.0001) strength, transitivity, global efficiency and increased average path length of the whole network. The previous abnormalities were less severe in SLE vs MS patients (p from 0.005 to 0.01). Similar hubs were identified in all three groups. In SLE and MS patients, all hubs showed a reduced strength compared to HC (p from <0.0001 to 0.001). Compared to SLE, MS patients showed lower strength in hubs located in fronto-temporo-parieto-occipital cortices, subcortical nuclei (including the thalamus, caudate nucleus and putamen) and cerebellum (p from 0.001 to 0.05). No significant difference of global and regional measures was found in the comparison between SLE patients with and without neuropsychiatric involvement.

Conclusion: Significant abnormalities of global and regional structural connectivity measures occur both in SLE and MS patients, suggesting a diffuse disruption of structural integrity. The extent of such abnormalities is more severe in MS compared to SLE patients.

Disclosure: Nothing to disclose

O1222

Artificial neural networks in the automatic classification of Alzheimer's disease patients

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Background and aims: Neuroimaging can be a potential tool for the diagnosis of Alzheimer's disease (AD). Artificial neural networks (ANNs) are nonlinear regression computational devices that are used in classification in several biomedical systems. This study tested the accuracy of ANNs in the individual AD diagnosis.

Methods: 3D T1-weighted images of a reference group of 676 subjects from the ADNI database (368 healthy subjects, 308 AD patients) were used to train and validate the ANN procedure. The dataset was randomly divided into a training (574 subjects) and a validation set (102 cases). ANN accuracy was increased by adding to the original ADNI dataset 676 synthetic images created using data augmentation algorithms. In a second step, 20 non-ADNI, 3D T1-weighted images (10 AD patients, 10 healthy controls) were added to the ADNI dataset. The number of the new images, whose signal intensity was significantly different from that of the ADNI dataset, was increased using data augmentation.

Results: In the referenced ADNI dataset, we obtained an accuracy of 98% in the binary classification AD patients vs healthy controls. In the second dataset including also non-ADNI images, the ANN procedure was able to discriminate AD patients and healthy controls with an accuracy up to 98%, with no difference between ADNI and non-ADNI images.

Conclusion: AANs provide a powerful tool in the automatic classification of AD patients. Future studies are warranted to test the accuracy of the procedure in identifying subjects in the preclinical or prodromal phase of the disease.

Disclosure: The study was supported by the Italian Ministry of Health (GR-2011-02351217). Data collection and sharing was funded by the Alzheimer's Disease Neuroimaging Initiative (ADNI) (National Institutes of Health Grant U01 AG024904) and DOD ADNI (Department of Defense award number W81XWH-12-2-0012).

O1223

Noradrenergic mechanisms in Parkinson's disease, studied with [18F]FDOPA and [11C]MeNER PET

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Background and aims: Patients with Parkinson´s disease (PD) suffer from a wide range of non-motor symptoms that may be related to loss of noradrenaline. We quantified noradrenaline transporter density and activity of aromatic amino acid decarboxylase (AADC) with [11C]MeNER and [18F]FDOPA PET in the same subjects to elucidate possible compensatory mechanisms in noradrenergic neurons.

Methods: The binding potential (BPND) of [11C]MeNER was estimated in patients (n=11) and controls (n=8) as previously described (Nahimi et al, 2016, submitted). The net rate of fluorodopamine formation (Ki) from [18F] FDOPA was estimated with the Gjedde-Patlak plot using cerebellum as reference region. [11C]MeNER/[18F]FDOPA estimate ratios were calculated using [11C]MeNER and [18F]FDOPA normalized values.

Results: We recently reported [11C]MeNER binding decrease in PD patients (Nahimi et al., presented at BRAIN2017 conference). Estimates of [18F]FDOPA Ki in patients was reduced numerically in Thalamus, Posterior Cingulate Cortex (PCC), significantly reduced in Putamen and numerically increased in other regions. The [11C]MeNER/[18F]FDOPA ratios in patients were decreased numerically in all tested regions except PCC (significantly in Hypothalmus; Table 1 and Figure 1).

Table 1

	Group	FDOPA K_i	p	MeNER/FDOPA ratio	p
FC	PD	0.00099 ± 0.0004	NS	0.81126 ± 0.7185	NS
	HC	0.00098 ± 0.0004		1.16193 ± 0.4526	
PC	PD	0.00063 ± 0.0003	NS	0.70079 ± 0.7227	NS
	HC	0.00059 ± 0.0003		1.13564 ± 0.4041	
ACC	PD	0.00210 ± 0.0008	NS	0.83137 ± 0.6840	NS
	HC	0.00180 ± 0.0005		1.15984 ± 0.5011	
PCC	PD	0.00074 ± 0.0005	NS	1.36091 ± 1.1147	NS
	HC	0.00076 ± 0.0003		1.17587 ± 0.4443	
Thal	PD	0.00139 ± 0.0004	NS	0.82132 ± 0.3369	NS
	HC	0.00161 ± 0.0003		1.06641 ± 0.3241	
Put	PD	0.00389 ± 0.0007	***	-	-
	HC	0.01133 ± 0.0011			
Hypo	PD	0.00589 ± 0.0018	NS	0.41173 ± 0.3583	**
	HC	0.00532 ± 0.0011		1.05927 ± 0.3637	

Table 1 shows 18F-FDOPA Ki values in PD patients compared to healthy controls. The ratio of normalized 11C-MeNER/18F-FDOPA values is shown in the right column. ** = P < 0.01, *** = P-value < 0.001.
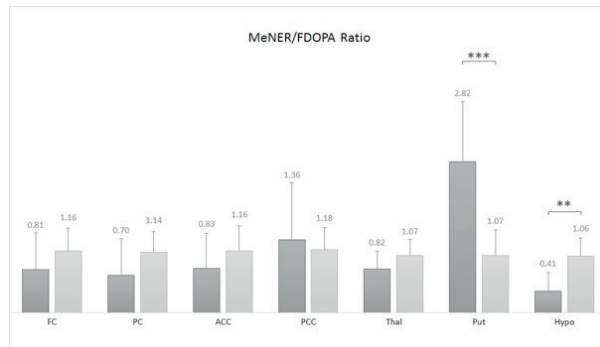
Figure 1 shows the mean±SD of the [11C]MeNER/[18F]FDOPA ratio for patients (dark bars) and controls (light bars). ** = P < 0.01, *** = P-value < 0.001.

Conclusion: AADC activity remained unaffected or slightly increased in areas of the brain with dense noradrenergic projections, in line with previous evidence of increased AADC activity in Frontal Cortex of early stage PD patients (Brück et al., 2005). Compared to AADC activity, the noradrenergic reuptake sites were lost or downregulated to a higher degree, up to 61% in Hypo, as evidenced by the reduction in [11C]MeNER/[18F]FDOPA ratios in patients, in line with previous reports of compensatory mechanisms in PD patients (Lee et al., 1999).

Neuro-oncology

O1224

Detecting insular clinical signs to improve the medical care of neuro-oncologic patients: Interest of a new questionnaire

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Background and aims: Insular localizations of brain tumors are not rare (25% of all glioblastomas in our clinic) but their clinical signs are often undiagnosed because poorly known.

The objective is to build a questionnaire which aimed to identify symptoms associated with an insular lesion in order to improve the medical care of neuro-oncologic patients.

Methods: The questionnaire covered 7 semiotic fields (27 items) related to insular symptomatology. During 2 years, all patients with a histological diagnosis of glioblastoma were included. Questionnaires were administered during the first monthly cure of chemotherapy. Localization of the tumor was assessed afterwards with contrast enhancement MRI images, by an examiner blind to the results of questionnaires. Patients with bifocal lesion, aphasic disorders or altered general state, were excluded.

Results: 44 patients were included (mean age: 57 years). There were 17 (38,63 %) insular localizations. Administration time was about 10 minutes. No patients refused the questionnaire. 26 items distributed among 7 patients (2 insular tumor) have not been answered. Sensory disturbances were the most reported items (62,5%) with 60% of contralateral or bilateral manifestations, which were all judged as "unpleasant". Olfactory, gustatory and auditory signs were less reported.

Conclusion: The questionnaire was well accepted and given its short realization time, it could easily be integrated in medical practice. Furthermore, we observed correlations between insular localization and certain semiotic fields, that is coherent with literature.

The insular questionnaire is a useful tool to detect insular signs and to improve the quality of life of patient by adapting their medical care.

Disclosure: Nothing to disclose

O1225

Neuropsychiatric adverse events of antiepileptic drugs in patients with brain tumour related epilepsy: An Italian multicentre prospective study
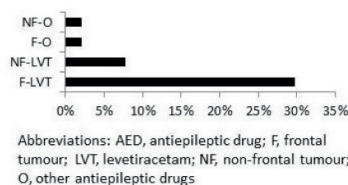
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Background and aims: This study assessed the prevalence and magnitude of neuropsychiatric adverse events (NPAEs) associated with antiepileptic drugs (AEDs) among patients with brain tumour-related wpilepsy (BTRE).

Methods: This observational, prospective, multicentre study enrolled 259 patients with BTRE after neurosurgery. All patients received AED monotherapy: efficacy was assessed through clinical diaries, while NPAEs were collected using the NPI-12 questionnaire.

Results: Tumour localisation in the frontal lobe was associated with a higher prevalence of NPAEs (OR 7.73, p<.001) (Figure 1). Independently from tumour localisation, LVT treatment was associated with higher prevalence and magnitude of NPAEs (OR 7.94, p<.01) compared to other AEDs (Table 1). Patients with oligodendroglioma reported more NPAEs than patients with other tumour type (Figure 2). NPAEs were not influenced by chemotherapy, radiotherapy or steroid treatment. Evaluating non-neurobehavioral adverse events (AEs) of AEDs, no significant differences were found among AEDs, even though patients treated with old AEDs had higher prevalence of AEs than those treated with new AEDs.

Fig.1 – NPAEs occurrence rates depending on tumour localisation and AED used.

Abbreviations: AED, antiepileptic drug; F, frontal tumour; LVT, levetiracetam; NF, non-frontal tumour; O, other antiepileptic drugs

– NPAEs occurrence rates depending on tumour localisation and AED used.

Fig.2 – NPAEs prevalence (bars) and standard error (line) depending on tumour histologic type.
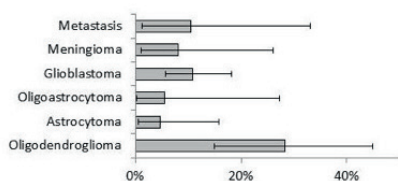
NPAEs prevalence (bars) and standard error (line) depending on tumour histologic type.

Table 2 – NPAEs prevalence and magnitude (NPI-12 score) depending on tumour localisation, considering AED group (A) and multivariate analysis for tumour localisation and AED prescription (B)

A.

Group	NPAEs prevalence Frontal n (%)	Non-frontal n (%)	OR	p-value	NPI-12 score Frontal mean ± SD	Non-frontal mean ± SD	p-value
Overall (n=259)	23/128 (18.0%)	7/131 (5.3%)	3.37	<0.01	0.26 ± 0.08	0.08 ± 0.03	<0.01
LVT (n=151)	22/74 (29.7%)	6/77 (7.8%)	5.00	<0.001	0.44 ± 0.13	0.14 ± 0.06	<0.01
Other AEDs (n=108)	1/54 (1.9%)	1/54 (1.9%)	1.00	1.000	0.01 ± 0.01	0.01 ± 0.01	0.78

B.

Group	NPAEs prevalence OR	95% CI	p-value
LVT (n=151)	7.94	1.68 - 37.56	<0.01
Frontal lobe (n=128)	7.73	2.36 - 25.27	<0.001

Abbreviations: AEDs, antiepileptic drugs; CI, confidence interval; LVT, levetiracetam; NPAEs, neuropsychiatric adverse events; NPI-12, neuropsychiatric inventory test-12 items; OR, odds ratio; RR, relative risk; SD, standard deviation

NPAEs prevalence and magnitude (NPI-12 score) depending on tumour localisation, considering AED group (A) and multivariate analysis for tumour localisation and AED prescription (B)

Conclusion: Both tumour localisation in frontal lobe and LVT treatment are associated with a higher risk of NPAEs in BTRE patients. LVT is regarded as a first-line option in patients with BTRE because of easy titration and few significant drug to drug interactions. Thus, since NPAEs lead to poor compliance and a high dropout rate, clinicians need to accurately monitor NPAEs after AED prescription, especially in patients with frontal lobe tumours receiving LVT.

Disclosure: Nothing to disclose

O1226

Improved survival in primary central nervous system lymphoma up to age 70 only: A population-based study on incidence, primary treatment and survival in the Netherlands, 1989-2015

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Background and aims: PCNSL is a rare, aggressive form of an extranodal non-Hodgkin lymphoma that exclusively affects the CNS. Population-based studies can complement clinical studies by addressing a non-selected group of patients within a well-defined geographic area. The aim of this population-based study was to assess trends in incidence, primary treatment and survival among adult patients diagnosed with PCNSL during a 27-year period in the Netherlands.

Methods: 1,673 adult patients were diagnosed with PCNSL, according to the nationwide Cancer Registry. All diagnoses were pathologically confirmed. Incidence rates were age-standardized to the European standard population and calculated per 100,000 person-years. Data on primary treatment were available for individuals. Patients were categorized into four calendar periods and three age groups (18-60, 61-70 and >70 years). We calculated relative survival as a measure of disease-specific survival.
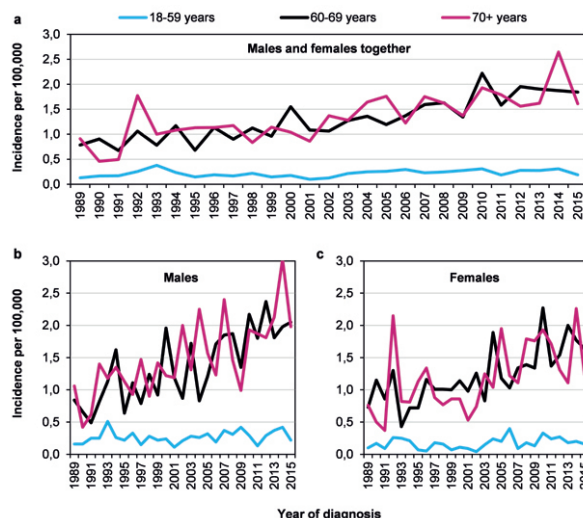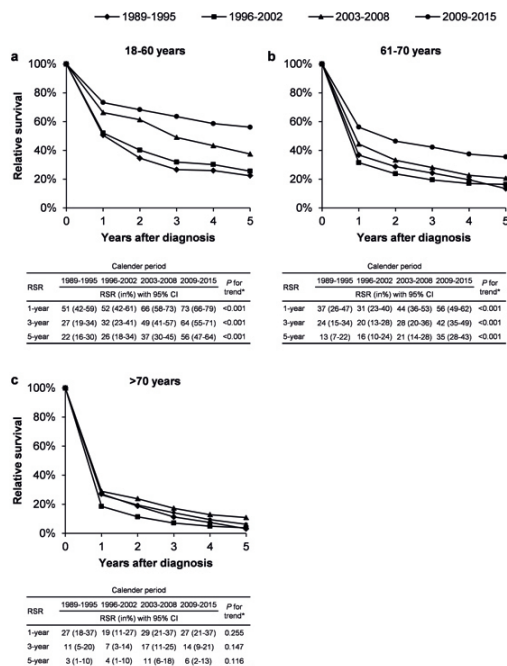

incidence

Results: Overall ASRs increased from 0.28 in the 1989-1995 period to 0.43 in the period 2009-2015. Incresing incidence was only in patients >60 years old.
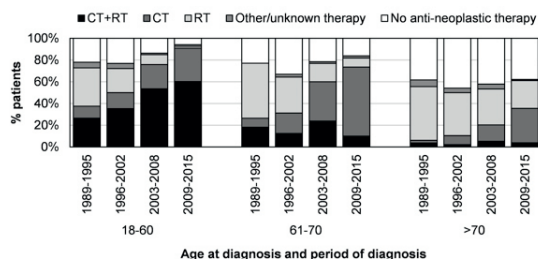
Application of combined chemoradiotherapy increased exclusively among patients age 60 or below. The use of radiotherapy alone among patients above age 60 decreased

with each calendar period, following the wider use of chemotherapy alone over time, especially for patients age 61-70 years. Five-year relative survival only improved over time for patients age 70 or below.

relative survival per era

Conclusion: We foudn in this comprehensive population-based study, a steadily increasing incidence of PCNSL for patients age >60. Survival has improved over time in younger but not in older patients despite increased use of chemotherapy in all age groups.

treatment differences

Disclosure: Nothing to disclose

O1227

Tumor Neuro-Langerhans cell histiocytosis located in the brainstem: A specific entity?

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Background and aims: Langerhans cell histiocytosis (LCH) is a rare multisystemic disease. Central nervous system is involved in ~5% of cases with various types of lesions. Space-occupying mass lesion within the brainstem is a recurrent presentation, poorly documented in the literature.

Methods: From the database of the French Histiocytoses Study Group, we have selected 6 patients with LCH and brainstem tumor lesions with MRI available for analysis. The following characteristics were collected for each patient: first clinical manifestations, systemic involvement, pathological findings, radiological pattern, treatments, response to treatment and outcome.

Results: Median age at LCH diagnosis of patients (4 men and 2 women) was 34 years (range: 10-65), whereas neurological involvement was diagnosed at a median age of 38 years (range: 22-70). The most frequent clinical signs were cerebellar ataxia, cranial nerve palsy and pyramidal tract impairment. All brainstem tumors were hyperintense on T2- images, hypointense on T1-images, sharing a similar pattern with multifocal, patchy, homogenous contrast enhancement. Mass effect in the brainstem was detected in 5/6 patients. Two patients had concurrent cerebellar lesions. Five patients were treated with cladribin; clinical improvement and durable complete radiologic response was achieved in 2/5 evaluable patients.

Conclusion: Tumor Neuro-LCH located in the brainstem is a rare, severe but treatable condition. MRI aspect although not specific may be suggestive especially in the setting of a prior or concomitant LCH systemic disease. Cladribin is active and represents a therapeutic option, in addition to vemurafenib in case of BRAF-mutated LCH and intensive chemotherapy with autologous bone marrow transplantation in aggressive, refractory cases.

Disclosure: Nothing to disclose

O1228

Longitudinal assessment of cognitive functions and quality of life in long surviving patients with glioblastoma

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Background and aims: Neurocognitive defects in patients with glioblastoma (GBM) heavily impact quality of life (QoL) and independence in daily-living. The aim of the study was to perform a longitudinal assessment of neurocognitive function and QoL in a selected population of patients with GBM who survived more than 5 years.

Methods: Patients were monitored with neurological examination, MRI and neurocognitive tests at time of inclusion (T0), 6 months (T1) and every 3 months until disease progression or patient's drop out. Neurocognitive functions were evaluated with Hopkins Verbal Learning Test–Revised (HVLT-R), Trail Making Test (TMT) A/B and Controlled Oral Word Association test (COWA test); QoL with EORTC QLQ-C30, QLQ-BN20 and HADS (Hospital Anxiety and Depression) scale.

Results: Sixteen patients with an histological diagnosis (reevaluated and confirmed) of GBM, were included. Median age was 56 years. Tumor location was supratentorial (13), infratentorial (1) and multicentric (2). Eighty-five percent of patients had a gross total resection, 92% were MGMT methylated and 36% IDH1 mutated. All patients received radio-chemotherapy, 10 a II line chemotherapy and 3 a III line at recurrence.

Neuropsychological tests revealed lower than normal memory and learning performances (HTLV-R) and executive functions (COWA-test). A self-perception of QoL correlated more with levels of depression (HADS) then with the degree of cognitive disability. Fifteen patients are alive, 3 undergoing therapy and 12 in follow-up with stable disease. Median overall survival is 7.8 years.

Baseline characteristics		
Gender	10 M	6 F
Median age	56 aa	
Tumor location		
	supratentorial	13 (81%)
	infratentorial	1 (6%)
	multicentric	2 (12%)
Surgery extension		
	Gross total	14 (85%)
	Partial	2 (14%)
Molecular Pattern		
MGMT (13 patients)	Methylated 12 (92%)	
IDH1 (11 patients)	Mutated 4 (36%)	
KPS > 90	87%	
I line therapy (Stupp regimen)	100%	
Adjuvant Temozolomide (median)	17 months	
II and III line therapies (intensified temozolomide, PCV, fotemustine, antiangiogenic, reirradiation, second surgery)	60 %	

Conclusion: Cognitive impairment in long-term surviving patients with GBM has a minor impact on QoL, compared with newly diagnosed patients reported in the literature.

Disclosure: Nothing to disclose

O1229

Isolated intra-ocular relapses of primary central nervous system lymphoma

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Background and aims: Relapses in primary central nervous system lymphoma (PCNSL) are usually cerebral and severe. Isolated intraocular relapses (IIOR) are much rarer and have not been specifically studied so far.

Methods: We retrospectively selected patients treated within the French national expert network on PCNSL (LOC network). The inclusion criteria were: histologically proven PCNSL with at least a cerebral localization, immunocompetent status, 1st line treatment based on high-dose methotrexate and isolated IIOR subsequently.

Results: 47 patients met the inclusion criteria (median age: 64.5 years (32.8-79.7), median Karnofsky Performance Status (KPS): 70 (40-100)). Initially, 13 patients had an ocular involvement, 16 had no ocular involvement and 18 had unknown status. The IIOR was the first relapse in 80% of cases. Median time from PCNSL diagnosis to IIOR was 14 months (3-51). Median KPS at IIOR was 80 (70-90), the affection was symptomatic in 95%. Decreased visual acuity was the prominent symptom. 76% of the patients received systemic chemotherapy (CT): ifosfamide-based CT (25%), methotrexate-based CT (25%), temozolomide (19%), in association with rituximab in 47%. 32% received a local treatment (intraocular CT or ocular radiotherapy) alone or in association with systemic CT. 31% subsequently received high-dose CT with autologous stem cells rescue). 60% of patients relapsed subsequently (35% in the brain, 62% in the eye) with a median PFS of 10,8 months. 5-year survival rate from relapse was 53.6% (0.28-1).

Conclusion: IIOR of PCNSL seem to have a better prognosis than brain relapses. That might be explained by a better KPS allowing intensification chemotherapy for up to the third of patients.

Disclosure: Nothing to disclose

Sunday, 25 June 2017

Autonomic nervous system

O2101

Early development of orthostatic hypotension distinguishes the parkinsonian variant of multiple system atrophy from idiopathic Parkinson's disease

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Background: Early distinction of the parkinsonian variant of multiple system atrophy (MSA-P) from idiopathic Parkinson's disease (PD) is essential to optimize therapeutic management and enrollment in disease-modifying clinical trials. Orthostatic hypotension (OH) is a key feature of MSA , but develops in 20 to 50% of PD patients as well.
Aims: To evaluate the diagnostic accuracy of early-onset orthostatic hypotension (OH) in distinguishing patients with MSA-P from patients with PD.
Methods: 164 non-demented PD and 62 MSA-P patients were retrospectively included in the present study. Early disease stage was defined as: Hoehn & Yahr (H&Y) stage <3. Short disease duration was defined as: disease duration < 2 years.
Results: 120 PD patients and 15 MSA-P patients were in a H&Y stage <3. Disease duration was significantly shorter in MSA-P patients (p=0.015). OH occurred in 23% of early-stage PD patients versus 60% of early-stage MSA-P patients (p=0.002), with a sensitivity of 60%, specificity of 70%, positive predictive value of 25%, negative predictive value of 94% and diagnostic accuracy of 73%.
23 PD patients and 16 MSA-P had a disease duration < 2 years. MSA-P patients were in a significantly more advanced H&Y stage (p<0.001) and on higher L-Dopa equivalent daily dose (p=0.006). OH occurred in 26% of PD patients after 2 years disease duration versus 56% of MSA-P patients (p=0.058).
Conclusion: The present data suggest that development of OH at early H&Y stages is predictive of a MSA-P diagnosis.
Disclosure: Nothing to disclose

O2102

Fingolimod induced reductions in cardiac autonomic regulation at rest may recover after Fingolimod discontinuation

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Background and aims: Fingolimod-therapy of several months may dampen cardiac autonomic modulation in patients with relapsing-remitting multiple sclerosis (RRMS) (Simula et al., 2016). It is still unclear whether these effects are reversible upon Fingolimod-discontinuation. We therefore intended to assess cardiovascular autonomic modulation under resting conditions during Fingolimod-therapy and after Fingolimod-discontinuation in RRMS-patients.
Methods: In 10 RRMS-patients (mean age 35.8±10.1 years) who were on Fingolimod-therapy for at least six months but then discontinued treatment, we monitored RR-intervals (RRI), systolic and diastolic blood pressure (BPsys, BPdia), and respiration at rest. Measurements were performed before and after six months of continuous daily Fingolimod-therapy (0.5mg/day), and 11.6 (7.6; 16.6) months (median; lower, upper quartile) after Fingolimod-discontinuation. We calculated parameters of total cardiac autonomic modulation [RRI-standard-deviation (RRI-SD), RRI-coefficient-of-variation (RRI-CV), RRI-total-powers], sympathetic [RRI-low-frequency powers (RRI-LF), BPsys-LF-powers] and parasympathetic cardiac modulation [Root-Mean-Square-of-Successive-RRI-Differences (RMSSD), RRI-high-frequency powers (RRI-HF-powers, and baroreflex sensitivity (BRS). We compared the values assessed before, during and after Fingolimod-treatment using the Friedman test and post-hoc Wilcoxon-tests. (significance: p<0.05).
Results: RRI-SD, RRI-CV, RRI-LF-powers, RRI-total-powers, and BRS were significantly lower with six months of Fingolimod-therapy than before Fingolimod-initiation as well as values after Fingolimod-discontinuation. After Fingolimod-discontinuation, these parameters no longer differed from respective parameters before Fingolimod-initiation. The other parameters did not change significantly with Fingolimod-therapy nor after Fingolimod-discontinuation.
Conclusion: Fingolimod reduces cardiac autonomic modulation and BRS. Yet, these changes are reversible after Fingolimod-discontinuation. Fingolimod does not seem to have lasting effects on the cardiac S1P1 receptor-sensitivity which might be down-regulated during continuous Fingolimod-therapy.
Disclosure: This study was in part financially supported by Novartis Pharma, Germany.

O2103

Assessment of the role of autonomic nervous system function on walking performance in patients with clinically isolated syndrome

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Background and aims: The aim of this study was to investigate the role of autonomic nervous system (ANS) function on walking in patients with clinically isolated syndrome (CIS).

Methods: Altogether 124 CIS patients (87 females, age 32.3 ± 8.7 years) were enrolled. Walking was evaluated using the 25-foot walk test (T25FW). Heart rate and blood pressure responses to Valsalva manuever, deep breathing test and head-up tilt were analysed for every patient, and the results were presented in the form of Composite Autonomic Severity Score (CASS). To evaluate the subjective symptoms of autonomic dysfunction 116 patients filled-out the Abbreviated Composite Autonomic Symptom Score (COMPASS31). Additionally, in a subset of patients sweating outputs in the forearm (N=96), proximal and distal leg (N=96) and foot dorsum (N=94) were measured by Quantitative Sudomotor Axon Reflex Test (QSART).

Results: There was no correlations between T25FW and adrenergic (N=119), cardiovagal (N=119), sudomotor (N=95) or total CASS scores (N=93). On the other hand, T25FW positively correlated ($p<0.05$) with several COMPASS31 domains (orthostatic intolerance, vasomotor, secretomotor and pupillomotor function) and total COMPASS31 score. Furthermore, patients with lower sweating output in proximal and distal leg on QSART had worse performance in T25FW (r=-0.201 and -0.320 respectively, $p<0.05$).

Conclusion: The results suggest that ANS has a role in walking performance in patients with CIS, and thermoregulation seems to have the greatest effect. The results further indicate that vasomotor dysfunction, as reported by the patient, may also have an influence on walking in these patients.

Disclosure: This study was funded by Croatian Science Foundation grant HRZZ UIP-11-2013-2622.

O2104

Cancelled

O2105

Interrelation of depression, sexual dysfunction and disease severity in patients with multiple sclerosis

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Background and aims: More than 50% of women with multiple sclerosis (MS) have depression and many have sexual dysfunction (SD). SD in MS could be due to cerebral lesions (primary), MS-related physical disability (secondary) or MS-induced psychological disorders (tertiary). Depression itself also affects SD, and MS-severity affects both depression and SD. So far, the interrelation between MS-severity, depression, and SD is unclear. We, therefore, evaluated the interaction between MS-severity, depression and primary, secondary or tertiary SD in women with MS

Methods: In 83 female MS patients (median age 36.2 years, upper and lower quartile 29.3 and 42.5 years), we assessed depression using Beck Depression Inventory-V (BDI-V), SD using the 19-item Female Sexual Function Index (FSFI), and the Multiple Sclerosis Intimacy and Sexuality Questionaire-19 (MSISQ-19) to classify SD in MS as primary, secondary or tertiary; we graded MS-severity using the Expanded Disability Status Scale (EDSS).We calculated correlations between BDI-V and FSFI-scores, BDI-V, EDSS and MSISQ-19-scores for primary, secondary and tertiary SD using the Spearman-Test.

Results: BDI-V-scores indicated depression in 28/83 (33.7%), FSFI-scores indicated SD in 37/83 (44.6%) patients. FSFI inversely correlated with BDI-V-scores. MSISQ-19 scores showed 28/38 (73.7%) primary, 32/38 (84.2%) secondary, and 22/38 (57.9%) tertiary SD. BDI-V-scores correlated with MSISQ-19 scores of tertiary-SD; EDSS scores correlated with MSISQ-19 scores of secondary-SD.

Conclusion: The association between depression and SD was prominent only in tertiary-SD suggesting that depression furthers SD in MS patients, e.g. due to impaired self-esteem. The association between MS-severity and SD was prominent only in secondary-SD suggesting that increasing MS severity with increasing physical impairment compromise sexual function.

Disclosure: Nothing to disclose

O2106

The cardiac autonomic nervous system response to different daily physiotherapy tasks in patients at the sub-acute phase post-ischemic stroke and healthy controls

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Background and aims: Autonomic disturbances a common phenomenon in patients post- stroke, characterized by hypo function of the para-sympathetic and/or overactive sympathetic system. The impact of autonomic disturbances on physical therapy tasks during the rehabilitation period has not yet been assessed.

Aim: To describe the response of the cardiac autonomic nervous system to different motor and cognitive tasks among patients` post-first ischemic stroke during the sub-acute phase and compared with age and gender-matched healthy controls.

Methods: 19 patients' post first ischemic stroke at the sub-acute phase during rehabilitation and 16 healthy age-matched controls were included in the study. The Polar advanced heart rate monitor (RS800CX) was used to record RR intervals at rest, during paced breathing exercise, while performing different types of muscle contractions and during single and dual task conditions.

Results: At rest, RR intervals and HRV parameters were significantly lower among patients' post- stroke and remained lower during most of the activities tested. In addition, while among the control group a significant autonomic adaptation was seen by a reduction in RR intervals and HRV parameters during muscle contraction and a significant increase in these parameters during slow breathing exercise, no significant changes were observed among patients post- stroke (Figur1).
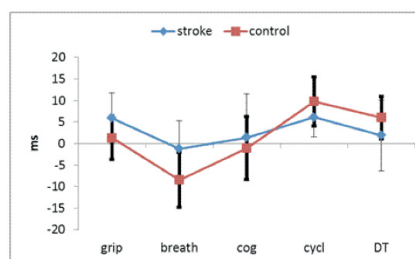

Figure 1: Delta of HRV measure (the Root Mean Square of the Successive Differences - RMSSD values by study and control groups at each study stage from rest: grip test, breathing test, serial three, cycling and serial three while cycling.

Conclusion: Patients post-stroke experience hyper sympathetic function at rest and less adaptive cardiac autonomic control during different activities, which all have an impact on rehabilitation outcomes.

Disclosure: Nothing to disclose

Learning - past and future

O2107

Research trends in neurology literature from 2011 to 2015: A bibliometric analysis

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Background and aims: Literature in neurology has undergone significant developments recently. Analyzing the literature using bibliometrics can facilitate research allocation and enhance research productivity. The aim of this study was to evaluate the research trends in neurology literature from 2011 to 2015 using bibliometric analysis.

Methods: In a descriptive review, Thomson Reuters Web of Science (formerly ISI Web of Knowledge) was evaluated for the most cited articles and journals in neurology from 2011 to 2015. Trend of publications was evaluated for five main categories of neurological disorders: (i) cerebrovascular disorders or stroke, (ii) neuromuscular or peripheral nerve disorders, (iii) epilepsy or seizure, (iv) demyelinative disorders or multiple sclerosis, and (v) degenerative disorders or dementia.

Results: Out of 1,387,980 medical articles in 2015, 440,564 articles (31.7%) were in the field of neurology. Most articles were published about cerebrovascular disorders (92502) with the increase rate of 149% from 2011 to 2015 (fig-1). The majority of articles were original research (68.8%). Characteristics of the 10 highest cited articles in neurology are shown in fig-2. The highest H-index (292) belonged to the "Neurology" journal. Top 10 journals with the highest citations in each category of neurological disorders were extracted; fig-3 provides data about cerebrovascular disorders. The United States, Japan, Germany, United Kingdom, and Italy published the highest number of articles.

Name of Journal	Field of Publication	Number of Citations
Annals of Neurology	Multiple Sclerosis	1747
Neurology	Dementia	773
Lancet Neurology	Anti-NMDA Encephalitis	596
Neurology	Dementia	273
Neurology	Epilepsy	255
Movement Disorders	Parkinson's Disease	228
Neurological Care	Subarachnoid Hemorrhage	204
Neurology	Evidence-based Guideline by AAN	192
Neurology	Dementia	187
Neurology	Epilepsy	166

Fig-2. Characteristics of top 10 most cited articles in neurology from 2011 to 2015

Name of Journal	Number of Citations
Clinical Neurology	24242
Peripheral Vascular Disease	9916
Neurosciences	4629
Surgery	1729
Psychiatry	950
Radiology Nuclear Medicine Medical Imaging	876
Neuroimaging	800
Rehabilitation	697
Pediatrics	395
Critical Care Medicine	291

Fig-3. Top 10 journals with the highest number of citations in the category of cerebrovascular disorders
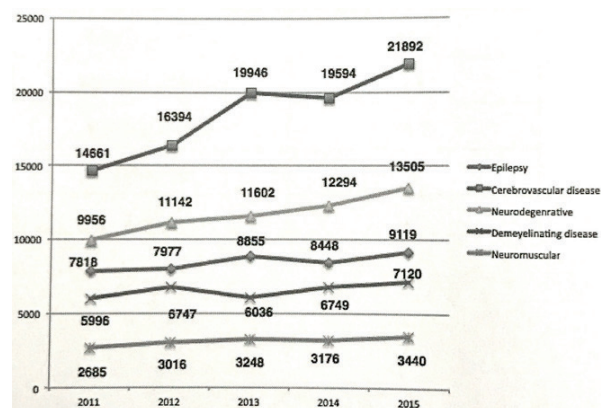

Fig-1. Publication trend in the five categories of neurological disorders

Conclusion: Neurology is one the most studied fields of medicine; the number of neurological publications has grown by a rate of 133.9% from 2011 to 2015. Within this time period, cerebrovascular disorders have gained the most attention.

Disclosure: Nothing to disclose

O2108

Inter-professional neurology simulation training

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Introduction: Inter-professional simulation immerses participants in realistic scenarios in a safe and reproducible environment. To date its use in neurology education is limited.

Learning Objectives: (i)Technical skills and knowledge in neurological emergencies (ii)Non-technical skills including communication and leadership.

Methods: Three acute neurology scenarios (refractory status epilepticus, coma and neuromuscular respiratory failure) with high fidelity mannequin over 4 hours. 30 participants (7 nursing; 8 physician's associates; 15 medical). Mixed-methods evaluation before and after training and statistical analysis with Mann–Whitney U test.

Results: Analysis of pre and post course questionnaires. 56% (14/25) had previous experience of simulation. On scale of 1=poor to 7 good: scored 5.66 (SD±1.14) for enjoyment and 6.28 (SD± 1.21) for relevance to clinical practice. Improvement in technical skills with increased confidence in managing emergency neurology situations (pre-course: 3.5[SD±1.45] post-course:4.63 [SD±0.956] p=0.00736).No improvement in non-technical skills:communication skills (pre-course:4.31[SD±1.12] post-course:4.75[SD±0.737]p=0.187 NS) and leadership skills (pre-course:3.92[SD±1.13] post-course: 4.33[SD±0.868]p=0.271 NS).

Discussion: Surprisingly, simulation improved technical but not non-technical skills. Participants started with a higher opinion of their non-technical skill than their knowledge. Knowledge is learnt during a scenario but improvement in non-technical skills are only realised later so may be underestimated. In future sessions we plan to add an introduction about non-technical skills and use the diamond debrief approach.

Disclosure: Nothing to disclose

O2109

"The Move Europe"- an innovative teaching programme for European medical students

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Background and aims: Graduating medical students often consider the neurological examination as the clinical skill they are least comfortable with. This can in turn lead to neurophobia. One way to enhance how one learns neurological semiology is to design innovative learner-friendly educational methods, including simulation training.

Methods: The program "The move" was proposed to third-year medical students of Pierre and Marie Curie University (UPMC) in Paris during their neurology rotation. The students were trained to role-play patients by miming various neurological syndromes. We thereafter investigated the students' experience. From this initial experience we decided to develop the programme in other European countries.

Results: More than 700 students chose to participate in the programme during the last two years at UPMC. The majority of students considered that "The Move" increased their motivation, and improved both their understanding of the subject and their long-term memorization of the teaching content. During a pilot session at University College Dublin (UCD) students reported a similar experience. The program is currently implemented at UCD. The first "The move Europe" tournament will be held in Paris in July 2017 between medical students from Ireland and France. We plan to have a similar meeting on an annual basis and to increase the number of European countries involved.

Conclusion: "The Move Europe" may be a valuable instrument for training medical students. It may also be a beneficial tool to foster collaborations in the fields of patient care or neuroscience, and to promote friendship and fraternity between European students.

Disclosure: Nothing to disclose

O2110

All the Rembrandt's ptoses – differential diagnosis of ptosis in Rembrandt's paintings

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Background and aims: Rembrandt van Rijn unintentionally captured medical conditions in his vivid and naturalistic masterpieces. His works frequently feature uni- or bilateral ptosis.

Methods: In Rembrandt's portraits, eye details, facial features, other clinical signs, historical, demographic data and model's social status were studied, aiming to reveal the etiology of ptosis.

Results: The following diagnoses are considered possible:

1. Aponeurotic (senile) ptosis (Picture 1a) is suspected in elderly people with symmetric ptosis and overactive frontalis muscle without additional facial symptoms. Found in the majority of Rembrandt's depictions of the elderly, senile ptosis was perhaps used ichnographically to emphasise advanced age or may be explained by frequent eye inflammation caused by poor hygiene and polluted air.

2. Brainstem stroke in portrait of the old Jew who shows signs of 3rd nerve palsy with contralateral hemiparesis (Picture 2a)

3. Wernicke encephalopathy (Picture 2b) is suspected in the soldier with known history of alcohol abuse and promiscuity, who also shows non-conjugated gaze. Alternative diagnosis is neurosyphillis.

4. Myasthenia gravis may be suspected in portraits of younger people or in an older man with asymmetrical ptosis and non-conjugated gaze, which is inconsistently found in repeated portraits of the same person (Picture 3).

5. Pseudo-ptosis and Veraguth's eyelid folds: depression may cause tone alterations of facial muscles, giving a typical facial appearance (Picture 1b). Suspected in portraits of people with history of troublesome life experience or in portraits with religious context of profound sorrow.

Picture 1a (senile ptosis) and 1b (pseudoptosis in depression): Portrait of Rembrandt's mother (1630), Self-portrait (1668), Simeon in The Temple (1669), Apostole Simon (1661), The Virgin of Sorrows (1661), Self portrait after his son's death.

Picture 2a (ptosis due to brainstem stroke) and 2b (ptosis due to B1 deficiency or neurosyphillis): Portrait of an Old Man in Red (1652), The laughing soldier (1629)

Picture 3 (ptosis due to myasthenia gravis): Bearded Man with a Beret (1655), Titus (1657), Jewish young man (1648), The Syndics of the Drapers' Guild (1662),

Conclusion: Ptosis in Rembrandt's portraits can be explained with relatively common and, in Rembrandt's time, incurable diseases.

Disclosure: Nothing to disclose

O2111

Hepatolenticular Degeneration: Wilson, Westphal, Strümpell, Konovalov: Who Was First?

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Background and aims: Wilson's disease in the Western World remains he only eponim of this hereditary disorder, although in German speaking countries Westphal and Strümpell disease after Karl Friedrich Otto Westphal (1833-1890) and Ernst Adolf Gustav Gottfried von Strümpell (1853-1925) who credited with providing an early diagnosis of "pseudosclerosis", a disease known today as hepatolenticular degeneration (HD). In Russia and number of Eastern European countries Wilson-Konovalov disease calling still takes place.

Methods: We archives of Wilson, Westphal, von Strümpel and Konovalov and two monographies devoted to HD by the last author.

Results: Samuel Alexander Kinnier Wilson (1878–1937) was an American born-British neurologist whom we consider the first to describe Wilson's disease. He practiced clinical neurology and made important contributions in his studies of epilepsy, narcolepsy, apraxia and speech disorders. He described hepatolenticular degeneration in his Gold Medal winning doctor's dissertation of 1912 titled "Progressive lenticular degeneration" from the University of Edinburgh Medical School. Nikolai V. Konovalov (1900-1966) has left a significant imprint in the history of Russian neuroscience. He became well known by international neurologists only in 1950s. Along with the large number of fundamental scientific papers that have determined several aspects of neuroscience, his two monographies devoted to HD remain a useful manuals for contemporary Russian neurologists.

Conclusion: First papers on hepatolenticular degeneration were presented by Nikolai Konovalov a long before 1937 when this diseas was "firstly" described by Wilson. Absence of close contacts between Western and Soviet neurologists and strict publication of last ones only in Russian precluded his recognition in the West.

Disclosure: Nothing to disclose

O2112

Short-term performance improvement after neurological exam training sessions for undergraduate medical students: Motor lasts longer

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Background and aims: Neurological examination is an essential part of the assessment of any patient. Learning of these procedures demands practice, which most often is left to occur in an unstructured way during clinical attachments. We aimed at assessing the impact of extracurricular training sessions on the neurological exam for 3rd year medical students and the decline in performance on the short term.

Methods: Performance of neurological examination is listed in the learning objectives of students in the 3rd of a 6-year medical undergraduate program. We offered 90min sessions on "Motor examination" and "Sensory examination". Attendance was voluntary. Students' perceptions were assessed and their self-reported confidence compared at entrance and exit of the session. Performance was also assessed using a checklist at the end of the session and after three months. A matched control group that did not attend the sessions was also tested at the 3 months timepoint.

Results: Initially, students reported a moderately-low confidence level (median=3.5; 1-7 scale) that increased after the session (end: median=6 vs 4.5). Compared with the end of the session, performance sharply declined afer three months only for the sensory examination, but not for the motor examination, although in both cases it was significantly higher in training participants than in controls.

Conclusion: Learning of the neurological examination can be potentiated by complementary extracurricular training sessions. Motor examination skills last longer than sensory examination skills.

Disclosure: Nothing to disclose

MS and related disorders 2

O2113

Treatment outcomes of daclizumab in patients at high risk of transitioning to secondary progressive multiple sclerosis in DECIDE

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Background and aims: Daclizumab HYP (daclizumab), a structurally distinct form of daclizumab, demonstrated superior efficacy to intramuscular interferon beta-1a on several clinical and radiologic outcomes in DECIDE (ITT: daclizumab, n=919; interferon beta-1a, n=922). This post hoc analysis evaluated treatment outcomes in DECIDE patients with baseline characteristics predictive of transition to secondary progressive multiple sclerosis (SPMS) and higher risk of further progression: moderate/severe disability at baseline (EDSS ≥3.5) and confirmed disability progression (CDP) during study independent, or in the absence, of clinical relapses.

Methods: CDP was defined as 24-week confirmed worsening on ≥1 of: Timed 25-Foot Walk (≥20% worsening), 9-Hole Peg Test (≥20% worsening), or EDSS (≥1.0-point increase from baseline). Progression was confirmed ≥24 weeks after initial worsening and at last study visit. Treatment effects on new/newly enlarging T2 lesions were also evaluated.

Results: In patients with baseline EDSS ≥3.5 who remained relapse free during DECIDE (daclizumab, n=154; interferon beta-1a, n=163), 14.3% of daclizumab versus 23.4% of interferon beta-1a patients had CDP (relative risk reduction [RRR], 33%; hazard ratio [HR]:0.67; 95%CI:0.36–1.22) and daclizumab reduced the number of new/newly enlarging T2 lesions at Week 96 by 45.7% (P=0.004) versus interferon beta-1a (n=138 both groups). Similar results favouring daclizumab were observed on CDP outcomes in relapse-free patients with baseline EDSS ≥4.0 (RRR:50%; HR:0.50; 95%CI:0.22–1.15) and ≥4.5 (RRR:51%; HR:0.49; 95%CI:0.17–1.39). Outcomes in patients with CDP independent of relapses were similar.

Conclusion: In moderately/severely disabled patients at high risk of transitioning to SPMS, daclizumab was associated with greater benefits than interferon beta-1a in reducing further relapse-unrelated disability progression.

O2114

Secondary progressive patients show higher demyelination and neurodegeneration along the visual pathway than primary progressive patients in multiple sclerosis

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Background and aims: The pathophysiologic distinction between primary progressive (PP) and secondary progressive (SP) multiple sclerosis is debatable. We explored demyelination and neurodegeneration among the visual system using visual evoked potentials-VEPs and optical coherence tomography-OCT.

Methods: 55 SP (disease duration-DD 19.6±7.6 years, median EDSS 6.0), 28 PP patients (DD 8.9±4.5 years, EDSS 6.0) and 42 healthy subjects (HC) underwent OCT with RNFL measurement and VEPs. Eyes with previous optic neuritis-ON were excluded.

Results: Mean High and Low-Contrast Visual Acuity were similar in SP and PP (HCVA 0.90 vs 0.97 decimal, p=0.589; LCVA 0.19 vs 0.29, p=0.198), but significantly lower in SP than HC (HCVA 1.03, p=0.018; LCVA 0.31, p=0.03). Mean binocular RNFL was significantly thinner in SP vs PP (81.2±12.01 vs 89.1±9.8 µm, p=0.003), and in both subgropus vs HC (mean 96.9±5.7 µm, p=0.003). VEPs latency was significantly delayed in SP vs PP (149.3±23.8 vs 135.6±16.2 ms, p<0.001), and in both subgroups vs HC (115.9±5.1 ms, p<0.001). RNFL and latency differences were however no longer significant after correction for DD. The proportion between demyelination and axonal loss was expressed as Z-scores sum of latency (positive=delayed) and RNFL (negative=reduced). The Z-score sum was higher in SP (3.7±3.7) vs PP (2.4±2.9) with a trend towards significance (p=0.053), not identifiable after correction for DD (p=0.195).

Conclusion: Despite similar disability, visual pathway showed greater demyelination and neurodegeneration in SP than PP, possibly owing to a longer DD and a higher likelihood of subclinical episodes during the relapsing phase even in eyes without ON.

O2115

Fingolimod significantly lowers neurofilament light chain blood levels in relapsing-remitting multiple sclerosis patients as compared with interferon beta-1a or placebo

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Background and aims: To assess the effect of fingolimod (0.5mg) in lowering blood neurofilament light chain (NfL) levels in patients with relapsing-remitting multiple sclerosis compared with interferon beta-1a q.w. (IFN) or placebo.

Methods: NfL was measured in two phase 3 studies (FREEDOMS, TRANSFORMS): in patients with five (FREEDOMS; month (M)0, M6, M12, M18, M24, N=165) or three (TRANSFORMS; M0, M6, M12, N=222) available sampling time points using the Single Molecule Array (SIMOA) technology, and compared with healthy subjects of similar age group (N=35). Geometric means were used for comparing NfL levels.

Results: NfL baseline levels were well-balanced between treatment groups in both studies (p=not significant). In TRANSFORMS, NfL levels significantly decreased with fingolimod versus IFN at month (M)6 (p=0.0001) and M12 (p=0.0010). At M12, NfL levels decreased by 18.9% with IFN (26.0 to 21.1pg/ml) and 40.0% with fingolimod (29.8 to 17.9pg/ml), approaching levels of healthy controls (16.4pg/ml). Fingolimod lowered NfL levels from baseline to M12 by at least 20% in 60.9% (67/110) of patients, while IFN did so in 44.6% (50/112) of patients (p=0.0404). In FREEDOMS, fingolimod reduced NfL levels versus placebo at M6, M12, M18 and M24 (p<0.0001, all). From baseline to M24, NfL levels decreased by 39.0% with fingolimod (30.4 to 18.6pg/ml) and 3.8% with placebo (28.6 to 27.5pg/ml;p<0.0001).

Conclusion: Fingolimod treatment was associated with early and sustained reduction in blood NfL levels compared with IFN or placebo with values approaching those of healthy controls.

Disclosure: This study was funded by Novartis Pharma AG, Basel, Switzerland. Detailed disclosure of each author will be included in the poster.

O2116

Individual remyelination profiles in cortical grey matter and in white matter lesions in multiple sclerosis: a combined PET and MTR study

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Background and aims: Reduced magnetization transfer ratio (MTR) has been associated with decreased myelin content in cortical grey matter in patients with multiple sclerosis (MS). The aim of this study is to explore for the first time in-vivo cortical remyelination using MTR, and to investigate its relationship with WM lesional myelin repair, measured with [11C]PIB-PET, and its clinical relevance.

Methods: Patients with MS were clinically assessed, and underwent [11C]PIB-PET and MT imaging at baseline and after 2-4 months. Voxel-wise maps of WM lesional [11C] PIB binding and cortical MTR were generated, and indices of WM and cortical remyelination were derived (Fig.1). Spearman's rank coefficient was used to investigate the correlation between the two indices of remyelination, and between the index of cortical remyelination and clinical scores.
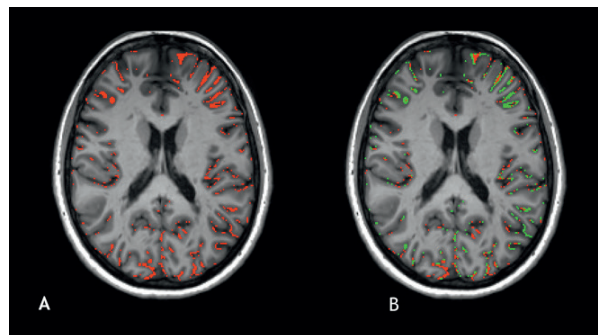
Example of an individual patient map of demyelinated voxels in the cortical grey matter at baseline (voxels in red in A), generated with MTR maps, and overlayed onto the corresponding MPRAGE. Remyelinating cortical voxels over the follow-up period are displayed in green in B, overlayed onto demyelinated regions at baseline (voxels in red).

Results: The index of cortical remyelination was highly variable across the cohort, ranging from 12% to 28% of the baseline demyelinated cortical volume. The index of cortical remyelination correlated with the index of WM remyelination (p=0.01, rho=0.61). There was a strong, inverse correlation between the index of cortical remyelination and both the Expanded Disability Status Scale (p=0.001, rho=-0.74) and the MS Severity Scale (p=0.001, rho=-0.73).

Conclusion: Longitudinal analysis of cortical MTR may allow to measure individual profiles of cortical remyelination, which significantly correlate with the WM remyelination index measured with [11C]PIB PET, and with clinical scores. A combined approach of WM PET and cortical MTR should be considered to stratify patients according to their global remyelination potential and to measure the effects of novel promyelinating drugs.

Disclosure: B. Bodini is funded by the ARSEP foundation. This study has been supported by ELA, INSERM-DHOS and the ECTRIMS post-doctoral fellowship.

O2117

Prognostic factors for multiple sclerosis in patients with spinal isolated syndromes.

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Background and aims: The early identification of patients with spinal isolated syndromes at high risk of multiple sclerosis (MS) represents the main purpose of the evolving MS diagnostic criteria and of clinicians in everyday clinical practice. The aim of this study was to investigate the prognostic role of different biomarkers in patients with a spinal isolated syndrome.

Methods: We evaluated baseline clinical, MRI, CSF and neurophysiological data of 218 patients (mean age 32.9 years) with a first spinal demyelinating episode. We used discrimination and calibration characteristics and reclassification of risk categories to assess incremental utility of different biomarkers for MS prediction.

Results: During follow-up (median 7.3 years), 112 patients (51.4%) developed clinically definte MS (CDMS). In Cox proportional-hazards models adjusted for age at onset and gender, the number of brain T2 lesions (>9 vs < 2 lesions, HR 6.5 95% CIs 1.4 -15.7), the presence of CSF OCBs (HR 2.3 95% CIs 1.0-4.0) and the multimodal evoked potential score (4th quartile vs 1 quartile, HR 2.5 CIs 1.2-4.2) significantly predicted the subsequent development of CDMS. The use of multiple biomarkers led to a 27% net-reclassification improvement (p < 0.001) over the use of current MRI criteria for MS in the prediction of patients with spinal isolated syndromes who develop multiple sclerosis at 2 years.

Conclusion: The use of several biomarkers improves the risk stratification for MS in patients with spinal isolated syndromes beyond that of a model that is based only on MRI criteria.

Disclosure: Nothing to disclose

O2118

CHS-131, an oral, once-daily selective modulator of PPARγ inhibited contrast enhancing lesions and reduced cortical atrophy over a 6-month phase 2B study in RRMS

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Background and aims: CHS-131 is a first-in-class, selective PPARγ modulator. CHS-131 crosses the BBB and appears to be anti-inflammatory in the CNS without demonstrable immunosuppression. This study evaluated safety and efficacy of CHS-131 in treatment-naïve subjects with RRMS.

Methods: This double-blind, parallel-group, study randomized patients into oral CHS-131 at 3 mg/day; 1 mg/day: or oral placebo in a 1:1:1 ratio at 21 sites in Russian. Patients (18-50 years old) had RRMS for ≤3 years, ≥1 gadolinium-positive lesion within 12-months of enrollment, and an EDSS of 0-6 at screening. Monthly MRIs were read blind at a U.S. imaging center (Buffalo Neuroimaging Analysis Centre, Buffalo, NY). Cumulative number of new gadolinium contrast-enhancing (CE) lesions on monthly MRI over 6-months was the primary endpoint. A recently concluded open label extension is not reported here.

Results: 227 subjects with RRMS enrolled (mean age 31-years; 65% female; 97% completed Part 1). Treatment with 3 mg CHS-131 was associated with a 52% reduction in CE lesions compared to placebo (p=0.003), and 1 mg CHS-131 associated with a 21% reduction (p=ns). Treatment with 3 mg of CHS-131 reduced cortical atrophy 42.6% at 3 months and 34.2% at 6 month, as compared to placebo. Cortical atrophy was similar between placebo and 1mg/d CHS-131. Safety with CHS-131 was similar to placebo. Neither immunosuppression nor toxicities (e.g., edema, weight gain) common to full PPARγ agonists were seen.

Conclusion: Daily treatment with 3 mg CHS-131 was well-tolerated, decreased CE lesions and attenuated neural atrophy. Additional study is warranted.

Disclosure: The work was supported by Coherus Biosciences, Inc.

Clinical neurophysiology

O2201

3Hz postural tremor in patients with spinocerebellar ataxia

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Background and aims: Cerebellar ataxias are a heterogeneous group of degenerative diseases characterized by progressive instability, impairment of speech, dyscoordination of the limbs due to progressive degeneration of the cerebellum. Despite a great progress in molecular genetics, diagnostic evaluation is often problematic. Clinical findings in initial stages are often nonspecific. Some studies imply that 3Hz postural tremor is specific for cerebellar impairment.

The aim of the study was to analyze posturography findings, to assess the prevalence of 3Hz postural tremor in patients with spinocerebellar ataxia and to compare these findings with a group of patients with balance problems of non-cerebellar etiology and with healthy controls.

Methods: 30 patients with spinocerebellar ataxias were examined (1 SCA-1, 5 SCA-2, 1 SCA-3, 1 SCA-8, 1 SCA-17, 1 SCA-28, 19 ILOCA, 1 FRDA), results were compared with results of 30 patients with peripheral vestibulopathy and 30 healthy persons. Subjects were examined with static posturography, spectral analysis of Centre of pressure displacement was performed. Vestibular reactivity was examined by means of ENG with rotational and caloric testing. Range of impairment in patients with cerebellar ataxia was assessed by SARA.

Results: Posturography is able to distinguish patients with cerebellar and vestibular impairment from healthy controls. Finding of 3Hz postural tremor can differentiate patient groups among themselves. Prevalence of 3Hz tremor in SCA patients was 90%, including those with mild impairment. 3 Hz tremor did not appear neither in patients with vestibulopathy nor in healthy controls.

Conclusion: This finding can serve as an objective correlative of cerebellar impairment.

Disclosure: Nothing to disclose

O2202

Multimodal brainstem evoked potential in evaluation of brainstem involvement in multiple sclerosis

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Background and aims: Several studies have shown the importance of brainstem lesions in the prediction of disability in multiple sclerosis (MS). The aim of this study was to evaluate the brainstem evoked potential score (BEP score) in detection of brainstem lesions in patients with early MS.

Methods: Fifty-eight MS patients were enrolled, (38 females), mean age 32.2±7.4. Brainstem functional system score (part of the EDSS), 9-Hole Peg Test (9HPT) and Timed 25-Foot Walk test (T25FW) were performed in all patients. Latencies of the major components for both sides of vestibular evoked myogenic potentials (P13, N23, N10 and P13, VEMP), brainstem auditory evoked potentials (III and V wave, BAEP), tongue somatosensory evoked potentials (P1, tSSEP) and somatosensory evoked potentials of the medial nerve (P14, mSSEP) were analyzed and z score for each EP was calculated and combined into BEP score.

Results: Patients with brainstem lesions on the MRI had significantly higher BEP score compared to patients without brainstem MRI lesions (0.15 vs -0.17, respectively; p=0.027). When looking into each evoked potential zscore separately, the significant difference was evident for VEMP zscore (0.19 vs -0.20, respectively; p=0.05) and mSSEP zscore (-0.03vs -0.37, respectively; p=0.013). We found significant correlations between BEP score and 9HPT for the dominant and non-dominant hand (r s =0.437, p=0.001 and r s =0.276, p=0.036,

respectively).

Conclusion: These data indicate that the BEP score is a valuable tool in evaluation of brainstem involvement in patients with early MS. Further studies evaluating the role of combination of different brainstem evoked potentials in MS are warranted.

Disclosure: Funding: Croatian Science Foundation grant HRZZ UIP-11- 2013-2622

O2203

Evaluation of Neostigmine responsiveness with concentric-needle single fiber electromyography in myasthenia gravis: A comparative study.

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Background and aims: Response to acetylcholinesterase-inhibitors (AchEI) is a specific clue in Myasthenia Gravis (MG) diagnosis. Neostigmine Test (NT) is a pharmacological test, demonstrating an improvement of clinical deficits lasting 2-4 hours in MG patients. We aim to compare clinical and neurophysiological response to AchEI in ocular and generalized MG patients, evaluating MG-Composite (MGC) scale and Concentric-Needle-Single-Fiber-Electromyography (CN-SFEMG) before and after NT.

Methods: MG patients underwent CN-SFEMG and MGC scale before and after 90 minutes neostigmine 0.5 mg administration. Mean value of consecutive differences (MCD), single-pair-jitter and blocks were compared before and after NT. Clinical responsiveness to NT was assessed by MGC scale.

Results: 23 patients, whose 10 with ocular MG and 13 with generalized form, were enrolled. MCD and single-pair-jitter significantly improved after NT in ocular patients (MCD: 50.8 ± 22.7 vs $40.1\pm22.9\mu s$; $p=0.01$. Single-pair-jitter: 35.9 ± 23.7 vs $20.0\pm25.1\%$; $p=0.001$). All neurophysiological parameters significantly improved after NT in generalized patients (MCD: 58.9 ± 18.8 vs $45.9\pm23.2\mu s$; $p=0.003$. Single-pair-jitter: 49.8 ± 26.9 vs $24.1\pm26.7\%$; $p=0.0001$. Blocks: 6.2 ± 9.5 vs $2.6\pm7.4\%$; $p=0.03$). MGC score significantly improved after NT in generalized patients (11.1 ± 7.6 vs 9.1 ± 6.7; $p=0.02$), whereas the decrement was not statistically significant in ocular group.
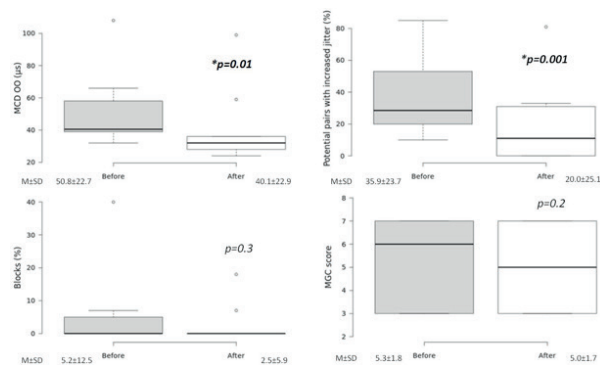
Figure 1: Box plot graphs show electrophysiological and clinical results in patients with ocular Myasthenia Gravis before and after neostigmine test. Abbreviations: MCD= mean value of consecutive differences; OO= Orbicularis Oculi; MGC= Myasthenia Gravis Composite scale.
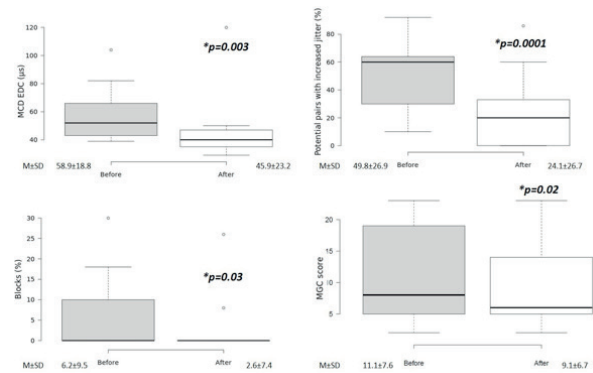
Figure 2: Box plot graphs show electrophysiological and clinical results in patients with generalized Myasthenia Gravis before and after neostigmine test. Abbreviations: MCD= mean value of consecutive differences; EDC= Extensor DigitorumCommunis; MGC= Myasthenia Gravis Composite scale.

Conclusion: MCD and single-pair-jitter are reliable indexes to evaluate the subclinical response to AchEI in both forms of MG. Clinical response to NT has been demonstrated by MGC scale in generalized patients, but not in ocular form. The use of CN-SFEMG before and after NT in ocular MG patients could be an objective instrument to assess and predict their responsiveness to AchEI treatment.

Disclosure: Nothing to disclose

O2204

3D printed scalp model for electroencephalography training

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Background and aims: Three-dimensional (3D) printing has made a fast entrance to the field of medicine and is currently used in a great variety of medical and educational applications. Here in, we report our initial experience of using 3D printing for medical educational purpose. A 3D scalp model was printed for the aim of training the students of Electroneurophysiology.

Methods: Reconstruction and 3D printing was performed in university 3D Printing Facilities (NEU3D Laboratories). The 3D scalp model (figure 1) was rendered from patient CT database using Synapse 3D software and prepared for 3D printing in Meshmixer software. Three-dimensional printing was performed using 2.85mm polylactic acid filament in Ultimaker 2+ Extended 3D printer.
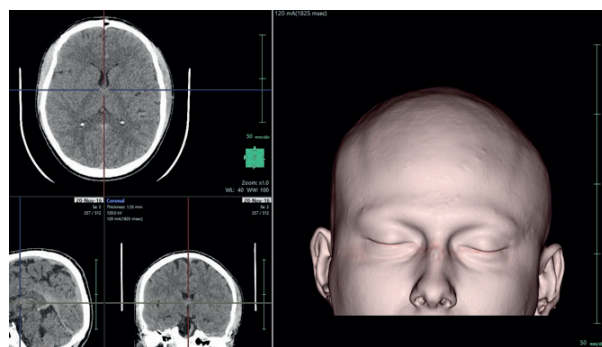
3D construction and rendering from CT images.

Results: Learning to place EEG electrodes in the 10-20 system requires three-dimensional thinking and teaching to the students. 3D printing model of the scalp gives us the opportunity to provide education by showing and pointing anatomical structures, which are free from hair on a head which is an exact copy of the real (figure 2). The other great advantage of 3D printing is the ability to scale the models to any size needed, so that students can work on models for babies and toddlers, who are unlikely to be practiced on.

Instruction of placement of electrodes according to 10-20 system on scalp

Conclusion: In conclusion, 3D printed models of the parts of nervous system provides an important contribution in education, research and preparation for invasive procedures and it seems that 3D printing technology will hold a great importance in our clinical practice in the near future.
Disclosure: Nothing to disclose

O2205

Neurophysiological findings in asymptomatic stage of familial amyloid neuropathy: A case control study

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Background and aims: Familial amyloid neuropathy (FAP) is a life-threatening disease of autosomal dominant inheritance. Current treatments slow down its natural course and are indicated from the very first objective symptoms. We aimed to evaluate two neurophysiological markers: sympathetic skin response (SSR) and heart rate variability (HRV) in the early detection of neurovegetative damages due to FAP.

Methods: SSR and HRV were assessed in 21 cases: TTR gene mutated patients with neither clinic nor electroneuromyographic abnormalities and 21 controls matched on gender and age. Cases were recruited consecutively from current care in the French Reference Center for Rare Diseases of Kremlin-Bicêtre Hospital. SSR was recorded on the two palms and on the sole of the left foot. HRV was registered during three conditions of 60 seconds each: normal breathing, deep breathing and Valsalva manoeuver.

Results: Valsalva ratio, defined by the ratio between the longest and shortest RR intervals, was significantly higher in the control groups after Bonferroni correction (means of 1.556 and 1.929, respectively, $p < 0.0001$). There was no significant difference between the two groups for any SSR parameter, although means of amplitudes were systematically higher in controls than among cases.

Conclusion: Our results confirm that autonomic nervous fibers are damaged early in both clinical and electroneuromyographic asymptomatic patients mutated on the TTR gene. Valsalva ratio seemed to be the most discriminative marker. Long-term follow-up and confrontation with cardiologic assessment will help to precise, how these tests could be used to stratify high risk patients and propose them an appropriate early treatment.
Disclosure: Nothing to disclose

O2206

EEG reactivity for prognosis after cardiac arrest; preliminary study results

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Background and aims: Electroencephalographic (EEG) reactivity testing is often presented as a very valuable and clear-cut element of electrophysiological testing. In a recent systematic review we showed that method of testing varies greatly and also definitions are poorly defined.(Admiraal et al., Eur J Neurol. 2016) To investigate the prognostic value of standardized EEG reactivity testing in patients after cardiac arrest we started a multicenter prospective observational study.

Methods: We aim to include 160 patients admitted after cardiac arrest to an ICU who are monitored with continuous EEG (cEEG). cEEG is started <24 hours after arrest and continued for up to 3 days. EEG reactivity is tested twice a day according to a strict stimulation protocol comprising of multiple types of stimuli. All EEGs and stimuli are assessed by three blinded experts. Prognostic value of EEG reactivity is calculated as sensitivity, specificity and false positive rate. Added prognostic value of EEG reactivity besides other known prognostic markers is given as the increased accuracy of a random forest classifier if EEG reactivity is included compared to excluded. Outcome is assessed after 6 months, poor outcome is defined as maximal score on the Cerebral Performance Category scale of 3-5.

Results: Currently, 100 patients have been included and inclusion is expected to be completed in august 2017. Analyses are in progress and we will present the first results at the conference in June.

Conclusion: EEG reactivity might be a valuable prognostic marker for neurological outcome in patients after cardiac arrest. Results of a dedicated prospective study will be presented.

Disclosure: Nothing to disclose

O2207

The effect of repetitive transcranial magnetic stimulation on spasticity: A meta-analysis of randomized controlled trials

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Background and aims: Spasticity is a common feature and major cause of long-term disability in various neurological disorders. Small-scale clinical trials reported that repetitive transcranial magnetic stimulation (rTMS) may improve spasticity. However, its' efficacy has not been conclusively proved. Accordingly, the objective of this study is to perform a meta-analysis of trials exploring the effects of rTMS on spasticity in patients with stroke, multiple sclerosis and spinal cord lesions.

Methods: We searched PubMed, CENTRAL, ScienceDirect, Scopus and PEDro for randomized controlled trials using the keywords "spasticity OR repetitive transcranial magnetic stimulation OR rTMS". We used random-effects models to estimate the mean difference (MD) and a 95% CI for the spasticity outcomes.

Results: Nine studies,involving 218 patients with spasticity, were eligible and included in the meta-analysis. A significant effect size of -0.71 was found for the primary outcome "decrease in the Modified Ashworth Scale (MAS) score" (95% CI=-1.00 to -0.43, P=<0.00001) with significant heterogeneity (I2=83%, P=<0.00001). Further analyses revealed statistically significant decrease of the MAS score at 1 week follow-up, but failed to demonstrate significant effects for the reduction of the Hmax/Mmax ratio. Subgroup analysis was undertaken based on the rTMS protocol, the underlying neurological disease and the anatomical area that was targeted.

Conclusion: rTMS has a positive effect on spasticity in patients with stroke, multiple sclerosis and spinal cord lesions. Further well-designed studies, including larger patient populations, are warranted in order to explore the long-term effects of rTMS in the treatment of spasticity.

Disclosure: Nothing to disclose

Cognitive neurology/neuropsychology

O2208

Role of cognitive reserve on cognitive function and regional brain atrophy in multiple sclerosis: A two-year longitudinal study

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Background and aims: The cognitive reserve (CR) hypothesis states that enriching experiences protect against dementia and cognitive decline in multiple sclerosis (MS). We investigated the role of CR on cognitive decline and gray matter (GM) and white matter (WM) atrophy progression in MS patients.

Methods: 3D T1-weighted scans and Rao's Brief Repeatable Battery were obtained from 54 MS patients and 20 healthy controls (HC) at baseline and after two years of follow-up (FU). A cognitive reserve index (CRI) was calculated. Regional GM/WM atrophy was estimated using voxel-based-morphometry, whereas longitudinal changes were investigated using tensor-based-morphometry (SPM12). Linear regression models were applied to evaluate the effect of CRI on cognitive performance and GM/WM atrophy at baseline and over time, controlling for demographic, clinical and structural MRI measures.

Results: At baseline, compared to HC, MS patients showed atrophy of the deep GM nuclei, GM/WM fronto-temporal-parietal-occipital regions, and left cerebellum. Controlling for atrophy within the previous regions, higher CRI predicted better performances at verbal memory (β=0.43, p<0.001; β=0.39, p=0.002; β=0.27, p=0.03) and verbal fluency (β=0.37, p=0.002). No effect of CRI on GM/WM atrophy was detected. At FU, memory and attention performance changes were associated with local and global variations of GM/WM volumes and T2 lesions. No effect of CRI on cognitive and longitudinal structural changes was found.

Conclusion: In MS patients, CR might have a protective role on recovery of semantic knowledges over and above the effect of GM/WM atrophy on cognitive functions. This protective role might lose efficacy with disease progression.

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O2209

Cognitive performance is highly stable over A 2-year follow-up in chronic kidney disease patients in a dedicated medical environment

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Background and aims: Kidney and brain functions decline with aging, chronic kidney disease (CKD) and dementia becoming increasing health burdens worldwide. Among the risk factors for cognitive impairment, CKD is increasingly recognized. The precise impact of CKD on the development of cognitive impairment is poorly understood.

Methods: In the New Tools for the Prevention of Cardiovascular Disease in Chronic Kidney Disease (NTCVD) cohort, which was recruited in a dedicated nephrology department, we examined the 2-year course of cognitive performance in 120 patients (73 patients with CKD stages 3–5D, 47 control patients without CKD with similar vascular risk profile) using a comprehensive battery of 10 neuropsychological tests.

Results: Kidney function, vascular risk factors and cognitive performance were highly stable both in CKD and control patients. The summary score of cognitive performance in CKD patients was very similar at baseline (z=-0.63±0.76) and follow-up (z=-0.54±0.79, p=0.113), as was cognitive performance in control patients (z=-0.01±0.59 and 0.01±0.70, p=0.862, at baseline and follow-up, respectively). Total serum cholesterol (199.6±36.0 and 186.0±32.9, p=0.005 in controls; 194.4±46.1 and 181.2±41.2, p=0.008 in CKD) and common carotid intima-media thickness (0.87±0.18 and 0.84±0.17, p=0.351 in controls; 0.88±0.21 and 0.82±0.16, p=0.002 in CKD) moderately but significantly decreased during the follow-up. In multivariable regression analyses, high age (β=-0.28, 95%CI=-0.48 to 0.08, p=0.007) predicted decrease in cognitive performance.

Conclusion: In this well-defined cohort receiving state-of-the-art therapy, cognitive performance did not decrease over 2 years. Our data emphasize the aspect of risk factor control, suggesting that dedicated medical care might prevent cognitive decline in CKD patients.

Disclosure: Nothing to disclose

O2210

Cognitive decline of MCI patients by amyloid-PET positivity at 12 months follow-up

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Background and aims: Patients with mild cognitive impairment (MCI) and brain amyloidosis show greater cognitive decline than MCI patients without amyloidosis (Doraiswamy et al., 2012; 2014). This work investigates, using a wide neuropsychological battery, which cognitive functions are more vulnerable to decline in amyloid-positive patients on a 12 months follow-up.

Methods: Ninety-two MCI patients underwent a standardized neuropsychological multi-domain battery and amyloid-PET at baseline, and repeated neuropsychological battery after 12 months. We performed linear models for each test (dependent variables: scores; factors: amyloid-PET result -positive/negative- and time -pre/post-scan-), and computed effect size indices (Cohen's d; 0.20: small, 0.50: medium, 0.80: large) in order to assess the magnitude of pre-scan differences and longitudinal changes.

Results: Fifty-five MCI patients were amyloid-positive and 37 were amyloid-negative. Pre-scan, amyloid-positive patients had worse performances than amyloid-negative ($p<0.05$) primarily in memory (Rey AVLT–Delayed recall, d=0.70; Story recall test, d=0.66; Rey-Osterrieth complex figure–Recall, d=0.54), but also in language (BADA–Object naming, d=0.50; Token, d=0.23), global cognition (MMSE, d=0.40; ADAS-COG, d=0.37), and non-verbal reasoning (Raven's CPM, d=0.28). Over 12 months, amyloid-positive patients showed decline ($p<0.05$) in visuospatial abilities (Rey-Osterrieth complex figure–Copy, d=0.66), global cognition (ADAS-COG, d=0.50; MMSE, d=0.29), Letter and Category fluencies (d=0.35), attention (TMT-A, d=0.29) and non-verbal reasoning (Raven's CPM, d=0.29). Amyloid-negative patients remained stable in all tests (d between 0.00 and 0.35).

Conclusion: Only amyloid-positive patients declined on global cognition and non-memory functions. ADAS-COG and Rey-Osterrieth figure–Copy showed the greatest change, while amyloid-negativity may be a prognostic index of cognitive stability over 12 months.

O2211

Long-term cognitive sequelae and quality of life after pneumococcal meningitis

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Background and aims: Pneumococcal meningitis is a severe disease with high mortality (18%) and morbidity (41%). Even patients with good recovery often suffer from cognitive impairments such as cognitive slowness and memory deficits. We performed neuropsychological evaluation to determine the rate and nature of cognitive impairments after pneumococcal meningitis.

Methods: We included adult survivors of community acquired pneumococcal meningitis which participated in a Dutch prospective observational cohort study, the MeninGene study. Cognitive domains were tested with the Vienna Test System Cognitive Basic Assessment Test set. Differences between group scores were tested with a multivariate analysis of variance (MANOVA). Questionnaires were taken to assess subjective cognitive functioning and quality of life.

Results: In total 80 patients and 69 controls were included and cognitive impairment was found in 11 (14%) of the patients. Patients performed significantly worse on overall cognitive test scores (p=0.008) compared to controls. Alertness (p=0.01) and cognitive flexibility (p=0.03) were the most affected domains. On a subjective scale, patients experienced substantial cognitive impairment on all domains and their proxies noticed these impairments as well. The quality of life of patients was significantly lower in physical ($p<0.001$) and social (p=0.003) functioning and perceived health (p=0.005). There was a positive association between alertness score and perception of physical functioning (p=0.046).

Conclusion: Survivors of pneumococcal meningitis have cognitive impairments and experience a decreased quality of life. Standardized cognitive testing should be performed to determine the rate of cognitive sequelae and can be used as an outcome measure of pneumococcal meningitis when assessing novel treatments.

Disclosure: Nothing to disclose

O2212

Persistent spatial navigation deficits in patients with transient global amnesia

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Background and aims: Transient global amnesia (TGA) typically presents with sudden anterograde amnesia due to hippocampal dysfunction. Although mnestic function subjectively improves within 24 hours, previous studies showed longer-lasting deficits on neuropsychological tests. We here tested spatial orientation performance longitudinally in TGA patients to delineate enduring hippocampal impairment in this disorder.

Methods: 21 TGA patients and 19 healthy controls completed a spatial navigation task in a real-space environment. The TGA patients performed the task within ~3.15 days of their attack (post-acute TGA), and ~4.1 months later (follow-up). The spatial navigation task consisted of 5 distributed target items, which had to be found in a pseudo-randomised order after a investigator-guided exploration phase. Throughout, the subjects wore a gaze-controlled head camera, allowing recording of individual "navigograms" for visual exploration and path trajectory.

Results: Post-acute TGA patients showed a significantly impaired spatial navigation performance when compared to healthy controls (p<0.008). In subgroup analyses TGA patients with hippocampal DWI lesions did not have a higher error rate than those without lesions; younger patients outperformed older patients. Navigograms showed all TGAs did not make use of short-cuts between stimuli. During follow-up testing error rate was still significantly increased in TGA patients as compared to controls (p<0.03). Navigograms during follow-up were identical to post-acute stage.

Conclusion: The higher error rates and non-use of short-cuts during the navigation task suggest that TGA patients are unable to generate cognitive maps of their environment. This deficit persisted several months. This study supports the view of a longer-lasting hippocampal dysfunction in TGA.

Disclosure: The study was supported by the German Federal Ministry of Education and Health (BMBF) in the context of the foundation of the German Center for Vertigo and Balance Disorders (DSGZ).

O2213

Brain activity related to tool-associated actions: An fMRI study in acute stroke patients

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Background and aims: Acute left-hemispheric stroke frequently leads to apraxia with impaired tool-use capacities. However, despite similar lesion size and location, patients present with different behavioral deficits. Our study aims at understanding the praxis network after acute stroke on a functional level.

Methods: We correlated performance in tool use tasks (pantomime and imitation of tool-use gestures as well as actual tool use) with activation patterns of functional stimulus-based MRI, acquired during the presentation of video sequences of tool-associated actions from a first-person perspective. A total of 48 acute left-hemispheric stroke patients (63.3 years ± SD 13.6; 13 female) with first stroke in the territory of the middle cerebral artery were tested 4.8 days ± SD 2.9 post-stroke.

Results: Intact performance of tool-associated tasks (principal component analysis over test scores) correlated with activation in the left supramarginal gyrus and superior temporal lobe (corrected for left-hemispheric lesion volume). Activation of the left posterior middle temporal gyrus was found in patients with low behavioral performance in tool-associated tasks.

Conclusion: Deficient performance of tool-associated actions was associated with lower activity within the left supramarginal gyrus, a key region for tool-associated tasks. This decreased activity was not only found in patients with lesions in this area, but also in patients with more remote lesions, i.e., potentially due to diaschisis effects. Conversely, patients with deficits in tool use-associated tasks showed higher activity in the posterior middle temporal gyrus. This may reflect that apraxic patients rely to a greater extent on higher-order visual areas during action recognition, possibly as compensatory effort.

Disclosure: Nothing to disclose

Epilepsy 1

O2214

Do serum levels contribute to define the optimal lacosamide loading dose in status epilepticus?

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Background and aims: Intravenous lacosamide (LCM) is increasingly used in status epilepticus (SE) treatment, but optimal loading dose and target serum levels are unclear. We analysed the correlation between LCM serum levels after intravenous loading, and clinical response.
Methods: Retrospective study in two centres from December 2014 to May 2016, including consecutive adult SE patients treated with LCM, in which trough serum levels after intravenous loading were available. Trough levels were correlated with loading doses and clinical responses, defined as LCM introduction terminating SE without the need of further treatment. Correlations were adjusted for other SE characteristics.
Results: Among 41 SE episodes, 17 (41%) responded to LCM. A loading dose of more than 8mg/kg was associated with LCM serum concentrations within the reference interval of 10-20mg/l (p=0.04; χ2). However, we observed no difference between LCM serum levels in responders versus non-responders (median 10.9 mg/l versus 9.5 mg/l; p=0.24; U-test), even after adjusting for other outcome prognosticators (SE severity, potentially fatal aetiology and number of previous treatments).
Conclusion: High intravenous LCM loading (more than 8 mg/kg) was associated with serum levels within the reference interval, there was however no correlation with the clinical response. Increasing the LCM loading dose in SE appears to bear little clinical benefit.
Disclosure: Nothing to disclose

O2215

How to withdraw highly-sedating treatment after control of refractory status epilepticus

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Background and aims: Refractory status epilepticus (RSE) often prompts 'aggressive treatment' (AT) with continuous i.v. midazolam, pentobarbital, propofol, or thiopental. Recently, concerns have been raised about AT worsening outcomes, in part due to prolonging intensive care hospitalizations. We sought to discern how to withdraw patients from AT more expeditiously and successfully.
Methods: Literature review on the treatment of RSE, focusing on practices (and particularly, other medication use) facilitating the successful withdrawal of AT after control of RSE.
Results: Sufficiently detailed information about AT withdrawal was found almost exclusively in the 14 case reports on prolonged RSE. Five reports of 'super RSE' (134 patients) and 4 on new-onset RSE ('NORSE') (24 patients) yielded consistent case fatality rates of >30% and good functional outcome in <35% of cases but, with large patient cohorts, gave essentially no details on HOW to withdraw AT. Papers on ketamine, ketogenic diet, and stimulation procedures deemed them helpful, often after AT failed. Case reports (likely biased toward successful management) often described reliance on tapering doses of (other) benzodiazepines and phenobarbital, sometimes starting with extremely high doses. Immunosuppression helped in cases with auto-immune etiologies.
Conclusion: AT is often necessary in RSE, but withdrawing patients from AT sooner may improve outcome, sometimes as facilitated by tapering doses of benzodiazepines and (originally high-dose) phenobarbital. Alternatively, non-coma-inducing treatments should be studied further. Other recommendations from these papers on how to get patients out of 'therapeutic coma' will be discussed, including tolerating epileptiform discharges (and even some seizures) on the EEG, and attention to serious medical co-morbidities.
Disclosure: Nothing to disclose

O2216

MiR-22 down-modulation is associated to P2X7 receptors brain overexpression in mesial temporal lobe epilepsy patients

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Background and aims: Several evidences implicate the participation of ATP-gated ionotropic P2X7 receptors in epilepsy. Upregulation in P2X7R has been demonstrated in patients with Mesial Temporal Lobe Epilepsy with Hippocampal Sclerosis (MTLE-HS) (Jimenez-Pacheco et al., 2013; Barros-Barbosa et al., 2016). The P2X7R modulates glial activation, cytokines production and neurotransmitter levels after brain injury. Recent experimental studies indicate that the P2X7R expression may be downmodulated by miR-22 in status epilepticus (Jimenez-Mateos et al., 2015; Engel et al., 2017). Taking into consideration that miR levels are very stable in biological fluids and normally reflect tissue production, here we compared the expression of P2X7R and miR-22 respectively in the brain and serum of MTLE-HS patients.

Methods: P2X7R expression was quantified in brain samples of 23 patients with MTLE-HS and 10 cadaveric controls. MiR-22 expression levels were evaluated in serum of 43 MTLE-HS patients and 36 healthy individuals.

Results: The P2X7R expression was higher in the hippocampus and adjacent neocortex (p=0.023) of MTLE-HS patients compared to control individuals. The opposite was observed in miR-22 serum levels.

Conclusion: Our results show for the first time that downmodulation of miR-22 production is associated with P2X7R overexpression in human MTLE-HS. The putative implication of miR-22 de-repression of P2X7R in epileptogenesis and seizure propagation linked to exacerbation of inflammatory responses and excitatory over inhibitory neurotransmission (Barros-Barbosa et al, 2016) requires further elucidation. Nevertheless, our hypothesis is that targeting the miR-22 – P2X7R axis may be a novel strategy to develop novel antiepileptic drugs.

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O2217

Genetics of sleep-related hypermotor epilepsy (SHE): Whole exome sequencing (WES) in a large Italian cohort

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Background and aims: To identify genetic determinants of SHE in patients without mutations in CHRNA4, CHRNB2, CHRNA2 tested by Denaturing High Performance Liquid Cromatography (DHPLC).

Methods: We performed WES analysis in patients with video/video-EEG documented SHE, both familial (the proband and one affected relative) and sporadic cases (TRIO approach).

Results: We studied 62 probands and 78 affected/not affected relatives. Eleven were familial cases: 5 Autosomal Dominant SHE (ADSHE), 6 Familial Focal Epilepsy with Variable Foci (FFEVF). Of the 51 sporadic cases, 31 were studied as TRIOs.

We identified 5 mutations in genes coding for GATOR1 components: (i)a mutation of NPRL2 (p.L105P) in 6 members of a FFEVF pedigree with prevalent SHE phenotype; (ii)4 mutations in DEPDC5: a frameshift mutation (p.T329Lfs*7) in 9 patients of a pedigree with lesional/nonlesional epilepsy; a novel mutation (p.M1126I) in a pedigree with variable epilepsy phenotype and intellectual disability (ID); 2 frameshift mutations (p.R165Yfs*13;c.193+1G>A) in sporadic cases, inherited from a healthy parent. Moreover, we found (iii) a de novo mutation of KCNT1 (p.A889T) in a patient with ID; (iv) 3 variants in CHRNA4: a novel change (p.G307V) in an ADSHE pedigree; 2 mutations (de novo p.S284L; p.S284W) in 2 sporadic cases.

Conclusion: Mutations in GATOR1 genes account for 8% of our cases; DEPDC5 showed the highest mutation rate, strengthening its role in focal epilepsies possiblyassociated with malformations of cortical development. KCNT1 is confirmed to be involved in SHE and ID. The unexpected detection of CHRNA4 mutations confirms the low sensitivity of DHPLC.

Disclosure: Nothing to disclose

O2218

An economic evaluation of a multi-component self-management intervention for adults with epilepsy (ZMILE study)

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Background and aims: Objective of this (trial-based) economic evaluation was to compare the cost-effectiveness of a multi component self-management intervention (MCI) compared to care as usual (CAU) in adult patients with epilepsy from a societal perspective with a follow-up of 6 and 12 months.

Methods: Participants were randomized into intervention or CAU group. Adherence, self-efficacy (ESES), quality adjusted life years (QALYs), health care costs, production losses, and patient & family costs were assessed at baseline and during the 12-month study period. Incremental cost-effectiveness ratios (ICERs) (i.e. cost per increased adherence, self-efficacy or QALY), and cost-effectiveness acceptability curves were calculated and presented.

Results: In total 103 patients were included in the study, of which 52 in the intervention group. Adherence rates over 6 months were 70.3% for the CAU group and 74.3% for the intervention group. Adherence, ESES and quality of life were not significantly different between groups. An ICER of €52 per point increase in ESES-score at 6 months and €979 per point increase at 12 months follow-up was found. The intervention resulted in an ICER of €488 per percentage of adherence increase at 12 months. An ICER of €7,677 per QALY gain was found at 6 months follow-up and an ICER of €13,404 per QALY gained at 12 months follow-up.

Conclusion: Although there was no statistically significant difference found after baseline adjustments, cost-effectiveness estimates appear to be promising. In addition, it has been argued that rules of inference are arbitrary and entirely irrelevant to the decisions which clinical and economic evaluations aim to inform.

Disclosure: Nothing to disclose

O2219

Identifying items responsive to treatment and impairing QoL in people with epilepsy

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Background and aims: Depression and anxiety, frequent co-morbidities in epilepsy, and adverse events (AE) of antiepileptic drugs (AED) are reducing QoL in people with epilepsy (PwE). Often occurrence of those is missed. Screening tools can identify individuals likely to suffer from those conditions. The aim of the present study is to identify the rate of depression, anxiety and AE as well as QoL in consecutive PwE attending an epilepsy clinic.

Methods: PwE attending the local epilepsy clinic were asked routinely to fill a questionnaire whilst waiting for their appointment. The questionnaire consisted of the Liverpool adverse event profile (LEAP), the neurological disorders depression inventory for epilepsy (NDDI-E), the emotional thermometers (ET4/5), and a scale for QoL (EQ-VAS). In case of multiple attendances, only the first questionnaire from each patient was included in the study.

Results: In total 546 questionnaires were returned during the study period. 12% of PwE were screened positive for depression with NDDI-E, 18% with ET4 (scale 5 was not included in the analysis), 9% for pure anxiety and 23% for significant adverse events. Statistical analysis showed that these 3 complains explained 28% of the variance of EQ-VAS, with lower QoL if screened positive.

Conclusion: QoL is significantly impaired by depression, anxiety and adverse events in PwE. Screening tools can help to identify those comorbidities easily. Given that all three comorbidities are responding well to treatment, such screening should be routinely performed to improve QoL in PwE.

Disclosure: Nothing to disclose

Neurogenetics

O2220

Genetic and clinical analysis of cerebral calcification

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Background and aims: Cerebral calcification is associated with a variety of disorders of different aetiologies. To date, the primary form of cerebral calcification is thought to be a genetically and clinically heterogeneous disease with variable penetrance within and between families.

Methods: In-depth, phenotype-genotype and radiological analysis of patients with cerebral calcifications. Genetic testing was performed using Whole Exome Sequencing. Visual calcification rating of total calcification scores(TCC) was performed by two separate investigators.

Results: We analysed 58 cases of brain calcifications suggestive of Fahr's syndrome of which 72% of patients presented with primary brain calcification and 28% had secondary forms. Whole exome sequencing performed in 32 patients identified a causal mutation in 17.4% of cases. The most frequent gene in this cohort was SLC20A2. In the familial form, movement disorders (65%), psychiatric (60%) and cognitive symptoms (56%) were most common clinical presentation with high familial and interfamilial variability. In the secondary forms, 12.5% of cases had a mitochondrial disorder presenting with cerebral calcification and 15.5% were due to other pathology. TCC scores were highly variable even within family members.

Conclusion: This UK series of genetic and clinical analysis of cerebral calcification shows high phenotype variability and calcification patterns, absence of calcification score correlations and contributes with novel mutations. Less than one third of the patients with primary familial brain calcification were found to have a genetic cause suggesting further thorough genetic studies are necessary with potential for the discovery of new causal genes.

Disclosure: Nothing to disclose

O2221

Contribution of the NGS analysis to the HyperCKemia

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Background and aims: Genetic study using new generation techniques (NGS) is a tool that is increasingly being used in the diagnosis of myopathies. However, its usefulness in hyperCKemia (HCK) is not known. The aim is to evaluate the diagnostic performance of a panel of genes potentially involved in HCK.

Methods: We studied 138 patients that remained undiagnosed after performing all the steps of the EFNS guidelines over a series of 371 cases with pauci-or-asymptomatic HCK. Ion Torrent technology was applied to a home design panel of 40 genes (LGMD / myofibrillar / glycosylation), which allows to study the gene coding and intronic flanking regions.

Results: Significant changes were found in 45% of patients; 16% of them were of pathological significance (reported mutations or new/uncertain variants expressing biopsy marker); the other 29% represented possible pathogenic changes (heterozygous dominant and recessive mutations as well as new or uncertain variants without biopsy marker). As a whole this NGS procedure increment on a 6-16% the rate of 30% of detection yielded by the classical EFNS algorithm applied to the total series of HCK patients. This increment corresponds mainly to genes not screened by conventional methods.

Conclusion: This study proves that the NGS is a very useful tool in HCK investigation. It can permit to change the algorithm of HCK investigation increasing the rate of diagnoses and reducing the proportion of muscle biopsies when used as first tier. However this procedure provides a deal of raw data that requires expertise and sometimes biological analysis on tissue or cells to confirm pathogenicity.

Disclosure: Nothing to disclose

O2222

The multiple faces of TUBB4A mutations: from hypomyelination to adult dystonia

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Background and aims: For an increasing number of monogenetic disorders the classic one-gene, one-phenotype paradigm is no longer valid. In this study we describe the broad spectrum of disease phenotypes associated with dominant mutations in the TUBB4A gene, which encodes β-tubulin. This gene was initially associated with the severe childhood leukodystrophy Hypomyelination with Atrophy of the Basal Ganglia and Cerebellum (H-ABC) as well as with adult Dystonia type 4 (DYT4). Mutations were subsequently found in patients with isolated hypomyelination of variable degree.
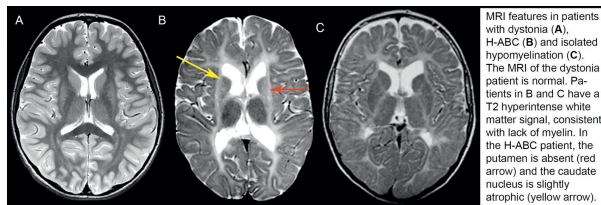
MRI characteristics in TUBB4A-related disorders

Methods: We performed a cross-sectional observational study of the radiological, clinical and genetic characteristics of the H-ABC patients in our database. Sequential MRIs of patients were evaluated via a standard protocol, DNA was analysed via Sanger sequencing and clinical information was collected via questionnaires for physicians. Next, we studied the characteristics of additional patients with isolated hypomyelination and analysed the available literature on TUBB4A-related disease variants.

Results: In our cohort of 42 H-ABC patients, we described a phenotypic range extending from neonatal up to childhood disease onset and slowly to more rapidly progressive neurological deterioration. Furthermore, we identified 12 patients with isolated hypomyelination. An additional 20 cases have been described in literature. The presence of extrapyramidal movements is a common hallmark in TUBB4A-related disorders. All results support a strong genotype-phenotype correlation with evidence for cell type-specific effects of mutations.

Conclusion: The phenotypic spectrum associated with TUBB4A mutations is a continuum, with DYT4 and H-ABC representing the ends. The cell type specificity is focus for further investigation aiming at unravelling the underlying pathophysiology.

Disclosure: Nothing to disclose

O2223

Adult-onset hypomyelinating leukodystrophies: a clinical and genetic study of 15 individuals

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Background and aims: Hypomyelinating leukodystrophies (HLDs), the prototype of which is PLP1-associated Pelizaeus-Merzbacher disease (PMD), are a genetically heterogeneous group of white matter diseases characterized by impaired myelin formation and typical onset in the first years of life. Adult-onset (AO) HLDs may be considered as milder variants of their early-onset counterparts, but little is known about these diseases and their genetic basis. Aim of this work is to genetically characterize a cohort of 15 individuals with AO-HLD.

Methods: A probe-based customized panel covering 142 known genes associated with genetic leukoencephalopathies was used for the screening of 15 individuals (8 males; 13 sporadic) with HLD and adult-onset (>16 years). Hypomyelination was defined as an unchanged pattern of diffuse mild T2-hyperintensity with (near-)normal T1 signal on two brain MRIs at least 6 months apart.

Results: In six out of 15 patients (40%; mean age at onset 37 years) we identified pathogenic mutations in the following genes: CYP7B1, GJA1, POLR3A, RARS, SPG11, TUBB4A. Key clinical feature of these patients was progressive spastic gait in all but one (i.e., the patient with POLR3A-associated HLD who presented with mild cerebellar ataxia and cognitive impairment). Poor performance at school was reported in 3 cases. The course of the diseases was slowly progressive over years.

Conclusion: A brain MRI pattern suggestive of hypomyelination can be the prominent feature of adult-onset genetic conditions. An inclusive screening approach allowed the diagnosis in 40% of AO-HLD cases. Interestingly, AO-HLD can be caused by mutations in the genes associated with the more severe early-onset hypomyelinating forms.

Disclosure: Nothing to disclose

O2224

mineRARE: Semantic text-mining of electronic medical records as diagnostic decision support tool to search for rare neurologic diseases such as Pompe disease, Fabry disease and Niemann-Pick type C disease

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Background and aims: Diagnosis of rare neurogenetic disorders is often challenging, particularly adult-onset presentations, with long diagnostic delays and misdiagnosis. As therapies become available, it is increasingly important to identify patients with rare neurologic diseases.

Methods: This multicenter project on ten rare neurogenetic diseases was approved by local Ethics committees and data protection authorities of six German University medical centers. Semantic text mining software structures medical data by ranking documents according to probability of disease, based on disease-specific lists of weighted signs and symptoms. Software and search algorithms were optimised in a pilot phase. Existing electronic medical records from the Department of Neurology of each center, corresponding to 10 years of activity, were screened, and patients ranked by probability of having the respective disease. An experienced team of physicians reviewed the data for the top ranked patients and those without a confirmed diagnosis were contacted for testing for the respective disease.

Results: In the pilot phase, 4 patients with Pompe disease and 4 heterozygous NPC1 mutation carriers were identified in Munich. More than 400.000 datasets from four centers were analysed for three diseases: Niemann-Pick type C disease, Pompe disease and Fabry disease. Four novel Pompe patients and 3 heterozygous NPC1 or NPC2 mutation carriers were identified, who had not previously been diagnosed. Data from more centers will be provided.

Conclusion: Electronic medical records-based diagnostic data mining seems to be a promising tool to help diagnosing rare neurologic diseases. It may allow effective screening, re-evaluation of patients with uncertain diagnosis, and identification of patients for clinical trials.

Disclosure: This research was supported by research grants from Sanofi Genzyme and Actelion.

O2225

CSF neurotransmitter depletion and brain atrophy in adult phenylketonuria patients

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Background and aims: Neurotransmitter synthesis in PKU patients with high phenylalanine (phe) concentration is impaired by inhibition of tyrosine- hydroxylase activity and by competition through the blood brain barrier. The neurotransmitter CSF levels have never been tested in adult PKU and might explain the neuropsychiatric alterations in the aging PKU population.

Methods: The study included eleven early treated classical PKU patients older than 30 years who underwent CSF analyses and 14 age-matched controls. CSF Phenylalanine (Phe), 5-hydroxyindoleacetic acid (5-HIAA), 5-OH-Tryptophan (5-HTP),), L-3-(3,4-Dihydroxyphenyl) alanine (L-DOPA) and homovanillic acid (HVA) were evaluated in patients and controls. Voxel-based morphometry (VBM) was used to test the correlation between Gray matter (GM) atrophy and CSF amine levels corrected for age, gender, educational levels (uncorrected $p < 0.005$) .

Results: Phe was increased in CSF and strongly related to plasma Phe levels and current treatment. 5-HIAA and 5-HTP were significantly reduced in PKU patients compared to controls, while L-Dopa and HVA were reduced only in a subset of patients. A significant inverse correlation was found between 5-HIAA / HVA/ 5-HTP and plasma Phe levels. The reduction in 5-HIAA and 5-HTP correlated with frontal and parietal gray matter atrophy, respectively.

Conclusion: High plasma phe levels probably lead to neurotransmitter depletion in adult PKU patients, is associated with specific gray matter brain atrophy and might explain neurological and psychiatric symptoms of adult PKU patients. Replication of these findings in larger samples with CSF analyses are necessary in order to confirm the clinical relevance of neurotransmitter deficits in adult PKU patients.

Disclosure: The study was supported by VItaflo, a Nestlè company, the University of Tuebingen and of Heidelberg.

Sleep disorders

O2226

H1N1 HA-specific T-cells can be readily detected in patients with narcolepsy

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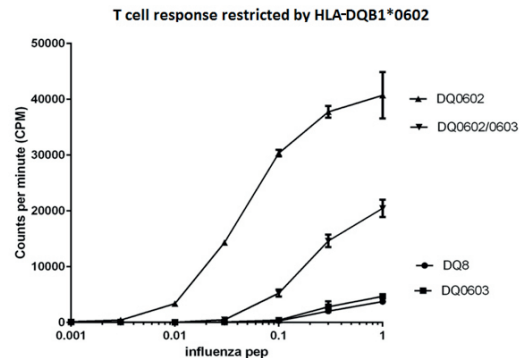
Background and aims: Following the 2009 influenza A(H1N1)pdm09 pandemic, and subsequent vaccination campaign, in China and several European countries an increased risk of narcolepsy type 1 was observed. Narcolepsy type 1, a rare sleeping disorder resulting from a selective loss of hypocretin-producing neurons in the hypothalamus, is strongly associated with HLA-DQB1*06:02 (carrier status: 95% in narcolepsy patients vs. 20% in healthy controls). Moreover, polymorphisms in T-cell receptor-α loci and P2RY11 have been associated with narcolepsy. Together this implies that narcolepsy is an autoimmune disease, in which activation of HLA-DQB1*0602-restricted CD4+ T-cells leads to destruction of hypocretin-producing cells. The hypothesized role for H1N1-specific T-cells in the pathogenesis of narcolepsy remains to be elucidated.

Methods: In the current study we determined whether H1N1-specific T-cell responses could be detected in type 1 narcolepsy (N = 80) and if these responses were restricted by HLA-DQB1*06:02. T-cell clones were generated from a subset of 13 patients. In these clones, T-cell receptors were sequenced.

Results: H1N1 hemagglutenin(HA)-specific CD4+ T-cell responses were detected in 26% of patients after stimulation with one particular HA-derived peptide. Generated T-cell clones proliferate only in the presence of HLA-DQB1*06:02 positive antigen-presenting cells. T-cell receptor sequences provided preliminary evidence for overrepresentation of particular T-cell receptor beta chain variable (TRBV) gene segments.

T cell responses restricted by HLA-DQB1*0602

Conclusion: H1N1 HA-specific T-cells can be readily detected in patients with narcolepsy. As these T-cells are restricted by HLA-DQB1*06:02, such T-cells may be implicated in the pathogenesis of narcolepsy.
Disclosure: Nothing to disclose

	Narcolepsy Type 1	Controls
N	80	10
Age ± SD	33 ± 20	53 ± 7.3
Male	41 (52%)	5 (50%)
HLA DQB1:0602	80 (100%)	10 (100%)
Reaction to HCRT seq.	0 (0%)	0 (0%)
Reaction to H1N1 seq.	21 (26%)	0 (0%)
No growth	5 (6%)	0 (0%)

H1N1 responses in narcolepsy patients

O2227

Polysomnographic findings in Restless Legs Syndrome (RLS) patients with severe augmentation

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Background and aims: An increasing number of RLS patients with severe augmentation due to dopaminergic therapy is currently reported in Germany. Polysomnographic (PSG) data of augmented RLS patients are scarce. In this context, we aimed to present the PSG characteristics of patients with severe augmentation.

Methods: We enrolled in the study consecutive RLS patients who presented augmentation and underwent a PSG examination in the acute phase. All patients underwent one night PSG. Patients with a sleep efficiency of < 25% were excluded from the study due to invalid data.

Results: 30 consecutive inpatients were included in the study: 18 women (60%) and 12 men (40%) with a mean age of 63.37 ± 13.58 years. The severity of RLS on the IRLS was 33.21 ± 3.79. The PSG investigation revealed a reduced sleep efficiency of 61.75 ± 22.4 %, prolonged sleep latency of 40.9 ± 42.06 min and a reduced amount of slow wave sleep of 8.49 % ± 13.71 %. The periodic limb movements index (total PLMI) was high with 52.43 ± 41.23, for wakefulness (PLMW): 84.43 ± 53.41, vs sleep (PLMS): 33.7 ± 42.7. During PSG 29 (96.67%) patients were still under dopaminergic medication.

Conclusion: This study objectively showed the markedly reduced quality of sleep in RLS patients with severe augmentation and the increased number of leg movements, although medication was not withdrawn at the night of PSG. Dopaminergic medication seems to increase PLM and restlessness during augmentation.

Disclosure: Nothing to disclose

O2228

Vitamin D in a large sample of patients with restless legs syndrome: A case-control study

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Background and aims: Restless Legs Syndrome (RLS) is a common sensorimotor disorder characterised by discomfort during rest and urge to move the limbs, accompanied by abnormal sensations. Genetic factors, brain iron dysregulation and dopaminergic dysfunction play a role in the pathogenesis of RLS. Vitamin D affects the nigrostriatal dopaminergic pathway and has been suggested to be involved in RLS pathogenesis. We investigated vitamin D levels in RLS patients and matched controls.

Methods: 107 RLS patients and 107 age- and sex-matched healthy controls were included. All RLS patients were clinically evaluated using different scales (IRLS, RLS-6, CGI) and underwent a structured interview. All patients and controls underwent laboratory examination including vitamin D.

Results: 8.4% (9/107) of RLS patients had vitamin D deficiency as compared to 0.9% (1/107) of matched controls (p=0.021). Among RLS patients, vitamin D deficiency correlated weakly with all used severity scales (RLS-6:r=0.199, p=0.040; IRLS:r=0.214, p=0.027; CGI:r=0.276, p=0.004). After stratification for sex, the correlation between vitamin D deficiency and CGI was moderate in males (r=0.320, p=0.022). After stratification for early/late onset RLS, in late onset RLS a moderate correlation between both IRLS and CGI and vitamin D deficiency was found (r=0.391, p=0.027, and r=0.405, p=0.021, respectively).

Conclusion: These results corroborate an association between vitamin D deficiency and RLS. The correlation between vitamin D deficiency and RLS symptom severity, which was stronger in males and in patients with late onset RLS, suggests that vitamin D levels interact with RLS symptoms. The role of vitamin D in RLS pathogenesis needs to be further investigated.

Disclosure: Nothing to disclose

O2229

Sleepwalking in adults: Any differences between onset in childhood or adulthood?

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Background and aims: Sleepwalking (SW) affects mostly children but can persist or appear de novo in adulthood. The main aim of the study was to assess the clinical, epidemiological and polysomnographic profile of adults sleepwalkers with onset in childhood (CO-SW) vs adulthood (AO-SW).
Methods: Over a period of 12 years we consecutively assessed adults with SW with a protocol which included subjective (scales, questionnaires and detailed sleep interview) and objective (polysomnography) sleep-wake measures.
Results: Among 63 adults with SW (65% males, mean±SD age 39±15 years), 45% had ≥1 episode/month, 54% had partial recall of the episodes and 36% reported at least one trigger factor for SW. Episodes of sleepwalking and confusional arousals were observed during polysomnography in 4% and 17% of patients respectively. In AO-SW, a positive family history for parasomnias was found in 33% (vs 49% in CO-SW), neurological comorbidities in 33% (vs 14%), psychiatric comorbidities in 25% (vs 32%), and EEG abnormalities in 50% (vs 29%). In addition, violence during SW episodes were more frequent in AO-SW compared to CO-SW (45% vs 33% for self-injury and 44% vs 29% for violent behavior).
Conclusion: The characteristics of the AO-SW often differ from those of CO-SW. The highlighted differences indicate that AO-SW represents a more complex and potentially dangerous condition compared to CO-SW. Whether or not a different neuropathology underlies these two conditions requires further investigation.
Disclosure: Nothing to disclose

O2230

Cardiovascular autonomic modulation during sleep is absent in patients with mild acute ischemic stroke: an analysis of the SAS-CARE Study cohort.

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Background and aims: Cardiac autonomic changes are described in acute ischemic stroke (AIS). Insula seems to play a prominent role in autonomic cortical control. Cardiovascular autonomic control (CAC) varies across sleep stages, with a sympathetic predominance during REM and a vagal predominance during NREM sleep. However, no data are available on CAC in AIS patients during sleep. Aim of the study was to assess CAC during wake and different sleep stages in patients with AIS.
Methods: From the population of the SAS-CARE prospective study, 45 patients with a diagnosis of AIS, without relevant sleep apneas (Apnea Hypopnea Index <15) and cardiac arrhythmias were selected. Mean NIHSS on admission was 5.1. Polysomnography (PSG) was conducted within seven days from AIS. ECG and respiration were extracted from PSG and divided in 4 stages: wake (S0), non-REM 2 (S2), non-REM 3 (S3) and REM. Linear spectral (Sp) and non linear symbolic analysis (SA) were used for the analysis of CAC. Site and size of lesions were analyzed.
Results: Sp and SA showed no differences among wake, non-REM and REM sleep. A reduction of total power of HRV was found in NREM sleep. Patients with insular involvement showed a lower sympathetic modulation compared to patients without insular involvement during both wakefulness and sleep, without differences across these states.
Conclusion: This study shows that patients with AIS do not display the physiological autonomic modulation during sleep. Moreover, a negative correlation between CAC impairment and clinical outcome is confirmed. Insular involvement seems to be associated with a predominance of vagal modulation.
Disclosure: Funded by: Swiss National Fond (SNF) Grant 320030-125069 and Swissheart Foundation

O2231

Screening for antibodies in narcolepsy type 1 and type 2

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Background and aims: Narcolepsy (NC) is caused by loss of hypothalamic hypocretin-secreting cells, and has been proposed to be autoimmune. However, to date, clear evidence of an ongoing autoimmune process is still missing. The hypocretin receptor 2 (HCRTR2) was recently shown to be a possible antigen in post-vaccination patients. Our aim was to identify potential pathogenic autoantibodies in the serum of narcoleptic patients by screening for these antibodies and the presence of possible novel antigens.

Methods: We studied 61 narcoleptic (NC) patients, including 50 patients with narcolepsy type 1 (NT1; only one post-vaccination with Focetria) and 11 with narcolepsy type 2 (NT2), and 15 healthy controls (HC). Antibodies against HCRTR2 were tested using a cell based assay (CBA). For potential novel antigens we used immunohistochemistry on rat brain sections and immunofluorescence on primary rat hippocampal neurons.

Results: In the NT1 cohort, 5/50 patient had antibodies directed against neuronal antigens. These included two patients with serum IgG antibodies binding to the HCRTR2, one that stained rat neuropil of the hippocampus, cortex, thalamus and cerebellum, and two that bound to the surface of live hippocampal neurons. Among the NT2 patients, 2/11 were positive. One patient serum had low levels of HCRTR2-Abs and one bound to neuropil of the hippocampus and also to the surface of hippocampal neurons.

Conclusion: Very few narcolepsy patients, either NT1 or NT2, had detectable antibodies to neuronal antigens and their presence was not associated with a distinctive phenotype.

Disclosure: This research has been supported by the EAN Scientific fellowship 2015

Neuro-ophthalmology/neuro-otology

O2233

Strabismus measurements with novel video goggles

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Background and aims: Measurement of ocular motility and alignment is essential for the diagnosis of eye muscle palsies and strabismus, preparation for strabismus surgery, and post-surgical follow-up. The traditional Hess screen test is time-proven for documenting squint angles at different gaze directions, but the test is subjective and requires good patient cooperation. The goal of the study is to develop automated strabismus video goggles and compare their accuracy and precision to the Hess screen test in a prospective medical device study with a case-control design.

Methods: We designed novel strabismus video goggles with built-in laser target projection and LCD shutters for automated alternate occlusion of the eyes. We measured 41 adult and child patients ≥6 years with acquired paralytic strabismus (third, fourth and sixth nerve palsy) or comitant strabismus (esotropia and exotropia) and 17 healthy controls, and compared the results to the Hess screen test.

Results: Measurements with strabismus video goggles and Hess screen test were closely comparable across patients and healthy controls, reproducing the individual strabismus patterns up to deviations of about 40 degrees. Unlike with Hess screen testing, measurements with the strabismus video goggles were even possible in patients with comitant strabismus and visual suppression.

Conclusion: The novel strabismus video goggles are simple, fast and accurate in measuring ocular deviations and the results are closely comparable to the conventional Hess screen test. The device can be used in patients with visual suppression, who are not suitable for the Hess screen test, as well as children as young as 6 years of age.

Disclosure: The study was supported by the Albert Bruppacher Foundation for Eye Research, University Hospital Zurich, Switzerland; the OPOS Foundation, St. Gallen, Switzerland; the Dr. Dabbous Foundation, University of Zurich, Switzerland; and the Betty and David Koetser Foundation for Brain Research, Zurich, Switzerland. K. P. Weber and H. G. MacDougall act as unpaid consultants and have received funding for travel from GN Otometrics.

O2234

Diagnostic accuracy of optical coherence tomography inter-eye difference in optic neuritis

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Background and aims: Multiple sclerosis associated optic neuritis (MSON) causes loss of retinal axons and corresponding retinal ganglion cells. The degree of inner retinal layer atrophy can be quantified by optical coherence tomography (OCT). Therefore, it has been suggested that the inter-eye difference of inner retinal layers may be of diagnostic value in unilateral MSON.

Methods: A prospective, cross-sectional study in patients with multiple sclerosis and healthy control subjects (HCs). Spectral-domain OCT of both eyes was performed at the optic disc and macula, followed by automated retinal layer segmentation and OSCAR-IB quality control. Data were used for the peripapillary retinal nerve fibre layer (pRNFL) and macular ganglion cell and inner plexiform (GCIPL) layers. Receiver Operating Characteristic curves were plotted and the area under the curve (AUC) was calculated for percentage inter-eye differences of inner retinal layers comparing unilateral MSON patients to HCs and to patients without MSON.

Results: There were 62 patients with unilateral MSON (mean age 53.4 years), 106 without MSON (mean age 55.6 years) and 63 HCs (mean age 50.5 years). In the model with unilateral MSON patients and HCs the AUCs were 0.85 for pRNFL and 0.89 for GCIPL. In the model with unilateral MSON patients and no-MSON patients the respective AUCs were 0.80 and 0.74. A cutoff of 10% inter-eye difference gave a diagnostic sensitivity of 100% for the GCIPL.

Conclusion: The percentage inter-eye difference of inner retinal layer thickness is a sensitive diagnostic measure for unilateral MSON and may be useful in screening for suspected subclinical episodes of MSON.

Disclosure: Nothing to disclose

O2235

Glial activation accelerates compensation of acute unilateral vestibulopathy

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Background and aims: Reactive gliosis may improve recovery after acute unilateral vestibulopathy (AUV). In the present study glial activation was visualized in vivo by [18F]GE180-PET in a rat model of unilateral labyrinthectomy (UL) and compared to behavioural vestibular compensation (VC) over time.

Methods: 14 Sprague-Dawley rats underwent a UL by transtympanic injection of bupivacaine/arsenilate, 14 rats a SHAM-UL (injection of normal saline). Glial activation was visualized with [18F]GE180-PET and ex vivo autoradiography at baseline and 7,15,30 days after UL/SHAM-UL. Postural asymmetry and nystagmus were registered at 1,2,3,7,15,30 days after UL/SHAM-UL.

Results: Signs of vestibular imbalance were found only after UL, which significantly decreased until days 15 and 30. In parallel, [18F]GE180-PET and ex vivo autoradiography depicted glial activation in the ipsilesional vestibular nerve and nucleus on days 7 and 15 after UL. Correlation analysis revealed a strong negative association of [18F]GE180 uptake in the ipsilesional vestibular nucleus on day 7 with the rate of postural recovery (R=-0.90, p<0.001), suggesting that glial activation accelerates VC. In analogy to the rat model a pilot patient with AUV showed increased [18F]GE180 binding in the ipsilesional vestibular nerve and nucleus 7 days after symptom onset.

Conclusion: In the rat glial activation takes place in the ipsilesional vestibular nerve and nucleus within the first 30 days after UL and can be visualized in vivo by [18F]GE180-PET. Comparative analysis of behavioural and [18F]GE180-PET data proves that glial activation is beneficial for VC. In human AUV neuroinflammation seems to similarly take place in the ipsilesional vestibular nerve and nucleus.

Disclosure: The study was supported by the German Federal Ministry of Education and Health (BMBF) in the context of the foundation of the German Center for Vertigo and Balance Disorders (DSGZ) and General Electric (GE Healthcare Ltd.).

O2232

Autosomal dominant optic atrophy related to OPA1 gene mutation: a clinical and molecular study of 14 families

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Background and aims: Autosomal Dominant Optic Atrophy (ADOA) is a congenital optic neuropathy, usually presenting in childhood with bilateral, progressive visual loss due to Retinal Ganglion Cells neurodegeneration. Mutations in OPA1, a nuclear gene encoding a mitochondrial dynamin-related protein, have been reported in 32-89% of ADOA.

Methods: Complete neuro-ophthalmological examination was performed in 61 patients belonging to 14 families (27 males, mean-age:37.19), with genetically-confirmed OPA1-related ADOA. 12 symptomatic subjects (11 females, mean-age:34.7) underwent Optical Coherence Tomography (OCT) study. We compared the different genotypes in terms of visual acuity/OCT with Kruskal-Wallis test.

Results: 54 patients were symptomatic. Onset was variable, typically first/second decade. We identified 4 known mutations, the most common being c.1034 G>A (p. Arg345Gln; exon 10) and a new missense mutation, c1193A>C (p.Asp398Ala; exon 12), with a late-onset clinical manifestation. Visual acuity ranged from 0 to 1.70 LogMAR. A significant lower visual acuity was found in association with c.1034 G>A, with respect to c1193A>C. Moreover, a negative effect of age on visual performances was observed in c.1034 G>A mutated patients. 50 % of affected had cup-to-disk ratio higher than 0.5. All had diffuse/temporal paleness of optic discs. OCT showed a global reduction of RNFL thickness, with no differences between genotypes. OPA-plus phenotype was observed in four subjects.

Conclusion: Our data confirm the clinical variability in a cohort of OPA1-related ADOA. We found a new mutation, associated with a late onset and mild phenotype. Visual acuity, color sensitivity and optic disc atrophy were sensitive indicator of disease. OCT confirmed the neurodegeneration of RNFL.

Disclosure: Nothing to disclose

O2236

Stroke and transient ischemic attack incidence after acute microvascular ocular motor palsies

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Background and aims: Microvascular ocular motor palsies (mOMP) have been regarded as a benign vascular condition with excellent prognosis. Despite being acknowledged that mOMP and lacunar stroke (LS) share common risk factors, little is known about stroke incidence after mOMP. We sought to determine the incidence of subsequent stroke or transient ischemic attack (TIA) in acute isolated mOMP.

Methods: Retrospective observational case-control study enrolling patients presenting either with mOMP or LS(controls) in the Emergency Department between January 2007 and October 2012. Outcome was defined as stroke or TIA during 36-months follow-up. Propensity score matching of patients and controls was used to ensure balance between the two groups.

Results: Fifty-seven mOMP patients and 53 controls were included with a mean age of 66.6±13.4 and 65.3±12.4, respectively (p>0.05); 35,0% (OMP) and 35.8% (LS) were male (p>0.05). There were no differences between groups (p>0.05) regarding previous history of diabetes, high blood pressure, dyslipidemia, ischemic heart disease, previous stroke or antiplatelet drug medication. Six mOMP patients (10.5%) and three LS patients (5.6%) had subsequent stroke. No significant differences were found between groups concerning global/annual stroke rate or its cumulative incidence (p=0.352 and 0.081, respectively) Neither risk factors, nor antiplatelet drug medication status, nor group status showed a significant impact on stroke recurrence in logistic-regression analysis.

Conclusion: Microvascular ocular motor palsies patients and lacunar stroke patients seem to share similar stroke/TIA recurrence. This finding emphasizes the importance of secondary prevention strategies in patients with microvascular ocular motor palsies.

Disclosure: Nothing to disclose

O2237

Frequency of acute vestibular symptoms in the emergency department of a tertiary referral centre: A retrospective cross-sectional study

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Background and aims: Vestibular symptoms are common complaints in the general population with prevalences of up to 60%. In emergency departments (ED) dizziness has been reported in 3.3% of all patients. We assessed frequency and aetiology of vestibular symptoms in a large interdisciplinary tertiary ED.

Methods: We manually screened medical reports of all 23.608 patients admitted to the ED 01/2013-12/2013. We included patients older than 16 years with vestibular symptoms as a chief or accompanying complaint. We extracted clinical, radiological and laboratory findings as well as presumed aetiologies from medical records. Symptoms were classified according to the Classification of Vestibular Disorders of the Bárány Society.

Results: 2690 patients (11.3%; mean age 52/SD 19.6 years; 50.2% females) complained about any vestibular symptom with 62% as a chief complaint. Vestibular symptoms were classified as vertigo (48%), dizziness (44%), postural symptoms (25%) and unknown vestibular symptoms (1%). Most frequent aetiologies were cerebrovascular events (10.7%; 167 ischemic strokes, 87 TIAs, 35 intracranial bleedings, 15 dissections, 3 sinus venous thrombosis, 2 ischemic events of the eye), internistic causes (9.5%), and other CNS-disorders (8.5%). In 20%, no diagnosis was assigned. 12% of underlying causes were potentially life threatening.

Conclusion: Reported one-year prevalence of vestibular symptoms was 11% in emergency setting, which is higher than previously described. Every 9th patient with vestibular symptoms suffers from a stroke and/or any other potentially life threatening condition. Improvement of diagnostic accuracy should be pursued to reduce the risk of missing severe pathologies.

Disclosure: Nothing to disclose

Monday, 26 June 2017

Child neurology

O3101

Refractory status epilepticus as de novo epileptic event: tertiary center experience in 80 children

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Background and aims: Evaluation of specific clinical features and outcome of refractory status epilepticus (RSE) as de novo epileptic event in children.

Methods: The retrospective study included children aged 0.2-18 years with RSE as de novo epileptic event hospitalized in Institute from 1995-2011. RSE is defined as SE with duration >60 minutes. The etiology was summarized in five categories. All patients were treated by the same hospital protocol. The outcome of RSE was assessed at the end of hospitalization in relation to SE recurrence, neurological consequences and death. Logistic regression analyses were used to determine predictors for poor outcome.

Results: The study included 80 children mean aged 4.2 years. Etiology was: acute symptomatic in 32 (40%), febrile SE in 19 (23.8%), idiopathic/cryptogenic in 15 (18.7%), remote symptomatic in 9 (11.3%) and progressive encephalopathy in 5 (6.3%). Inflammation of CNS makes 78.1% of the all acute RSE etiology. Prehospital treatment started in 65%. SE recurrence rate was 28.7%, neurological consequences in 35% and lethal outcome in three children. SE duration > 60 minutes has impact to recurrence rate (QR 0.30; 0.15-0.61; p=0.001) and neurological consequences (QR 0.44; 0.24-0.81; p=0.009).

Conclusion: RSE as de novo epileptic event is commonly caused by acute disorders, and it is important to explore underlying etiology, especially CNS inflammation and to start early appropriate etiological treatment. The outcome is unfavorable. The acute symptomatic SE etiology and prolonged SE duration have the main impact to the outcome.

Disclosure: Nothing to disclose

O3102

The natural history of vanishing white matter

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Background and aims: Vanishing White Matter (VWM) is a leukodystrophy caused by mutations in 1 of the 5 genes encoding eukaryotic initiation factor 2B (eIF2B), characterized by chronic and stress-provoked deterioration. The disease was initially described as a childhood onset, fatal disorder, but the spectrum is now known to be much broader. This study investigates the natural history of VWM in relation to age of onset and genotype, to improve counselling of families and provide natural history data for future therapeutic trials.

Methods: We performed a longitudinal multicentre observational study among 296 genetically confirmed VWM patients. DNA analysis was performed by Sanger sequencing and clinical information was obtained via questionnaires for physicians and chart review.

Results: Median age of onset was 3 years (mode 2 years, range antenatal - 54 years). 103 patients were deceased; median age at death was 6 years (range 3 months - 60 years). Kaplan-Meier survival analysis estimated an overall median survival of 20 years from onset. Multivariable Cox regression analysis revealed a positive relation between age of onset and both preservation of ambulation and survival. Absence of stress-provoked episodes favoured outcome. Disease onset <2 years was associated with early death, onset ≥4 years was associated with neurological deterioration of variable degree and low mortality independent of the exact age of onset. There was a high genetic heterogeneity with evidence for a genotype-phenotype correlation.

Conclusion: This study describes the natural history in a large cohort of VWM patients. Age of onset is a relatively strong predictor for disease course.

Disclosure: Nothing to disclose

O3103

Structural connectivity abnormalities underlying cognitive impairment in pediatric multiple sclerosis

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Background and aims: The factors associated with cognitive impairment in pediatric multiple sclerosis (MS) remain largely unexplored. Aims of this study are to describe brain structural network architecture in pediatric MS patients applying graph-analysis and to identify structural connectivity abnormalities associated with cognitive dysfunction.

Methods: Diffusion tensor and dual-echo MRI scans were obtained from 53 pediatric MS patients and 26 age- and gender-matched healthy controls (HC). Between-group differences of global and local network metrics were investigated. Partial correlations between network metrics and Z-scores for each cognitive domain and a global Z-score of cognitive function were assessed.

Results: All global network metrics differed significantly between pediatric MS patients and HC. Compared to HC, pediatric MS patients showed only an additional hub in the left post-central gyrus. A significant reduction of strength in all network nodes identified as hubs was detected. Global cognitive functioning was positively correlated with strength of connections of hubs located in right superior parietal lobe and bilateral precuneus. Impairment in language and verbal memory functions was related to reduced strength of hubs located in frontal and temporal lobes, while visual-spatial memory, attention and information processing speed impairment were associated to a reduced strength in several hubs located in frontal, parietal and occipital lobes.

Conclusion: A partial preservation of brain network architecture has been observed. Cognitive impairment is likely to be mainly associated to globally reduced strength of connections of the hub nodes, due to diffuse normal-appearing white matter damage, resulting in efficiency loss in information transmission.

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O3104

Diagnostic algorithm for relapsing inflammatory demyelinating syndromes of the central nervous system in children

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Background and aims: Paediatric relapsing demyelinating syndromes (RDS) of the CNS include different diseases, such as multiple sclerosis (MS) and neuromyelitis optica spectrum disorder (NMOSD), whilst in other cases there remain diagnostic uncertainties. We studied a cohort of children with relapsing ADS to unify phenotypes and propose a diagnostic algorithm.

Methods: A panel reviewed the clinical characteristics, MOG and AQP4 antibodies, intrathecal oligoclonal bands and Epstein-Barr virus serology results of 110 children with RDS. A neuroradiologist, blinded to the diagnosis, scored the MRI scans. Clinical, radiological, and immunological tests results were compared.

Results: 56% of children were diagnosed with MS, 25% with NMOSD (31% of these cases were AQP4-Ab-positive), 13% with multiphasic disseminated encephalomyelitis (MDEM), and 5.5% with relapsing idiopathic optic neuritis (RION). Blinded analysis defined baseline MRI as typical (or suggestive) of MS in 97% of MS children. MOG-Ab were found in 83% of AQP4-Ab negative NMOSD, 100% MDEM, and 33% with RION. Children with MOG-Ab were younger, less likely to present with area postrema syndrome, had lower disability, longer time to relapse, and more poorly-marginated cerebellar peduncle lesions.

A diagnostic algorithm, applicable to any episode of CNS demyelination, leads to four main phenotypes MS, APQ4-Ab NMOSD, MOG-Ab-associated disease, and antibody-negative RDS; MRI, testing for AQP4-Ab and MOG-Ab are the sequential diagnostic tests. Consideration of alternative diagnoses and monitoring are recommended in antibody-negative RDS.

Conclusion: Since MOG-Ab positive children showed notable and distinctive clinical and MRI features, they were grouped into a unified phenotype (MOG-Ab-associated disease), which is included in a new diagnostic algorithm.

Disclosure: Nothing to disclose

O3105

Changing pattern of anti-epileptic drug prescription in children in the Netherlands

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Background and aims: In the last decade several new, so-called second-generation antiepileptic drugs (AED) have become available. The aim of our study was to analyse whether prescription patterns of AEDs in children in the Netherlands have changed during the last 10 years.

Methods: We identified children aged 0-19 years who received at least one prescription for an AED (ATC-group N03A, ATC-code N05BA09) between 2006 and 2014 from the IADB.nl database. This database contains pharmacy-dispensing data from community pharmacies in the Netherlands. Children who also received prescriptions for migraine (ATC-group N02C, N07CA03, C07AA05), mood disorders (ATC-group N06A), and/or anti-psychotics (ATC-group N05A) were excluded. We calculated year-prevalences and -incidences of AED use for all AEDs together; for first- and second generation AEDs; and for individual AEDs. We also evaluated patterns of AED prescriptions including duration of treatment.

Results: Until 2011, first-generation AEDs (mainly valproic acid) were significantly more often prescribed. Prescription of second-generation AEDs (mainly levetiracetam) increased over the years at the expense of first-generation AEDs, becoming equal since 2012 (Figure 1). From 2012 onwards, levetiracetam was the most often initiated AED (Figure 2). Only 5.5% of the children used combination therapy. Of those on monotherapy, 88.2% used one single AED, duration of treatment being less than 200 days in approximately 60% of them.

Figure 2: Initial use of individual AEDs per 1000 children (aged 0 – 19 years)

Conclusion: Levetiracetam has replaced valproic acid as the most frequently prescribed first line antiepileptic drug in children since 2012, which is in line with national guidelines. On the other hand, an expected increase of prescription of lamotrigine was not found.

Disclosure: Nothing to disclose

First-generation AEDs: carbamazepine, clobazam, clonazepam, ethosuximide, phenobarbital, phenytoin, primidone, sulthiame, valproic acid

Second-generation AEDs: felbamate, gabapentin, lacosamide, lamotrigine, levetiracetam, oxcarbazepine, perampanel, pregabalin, retigabine, rufinamide, stiripentol, topiramate, vigabatrin, zonisamide

Figure 1: Prevalences of all, first- and second-generation AED use per 1000 children (aged 0 – 19 years)

O3106

Regional patterns of brain atrophy development in pediatric and adult multiple sclerosis patients: A 3.5-year study

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Background and aims: It has been widely demonstrated that pediatric multiple sclerosis (MS) patients have, at short-medium term, a more favorable clinical course than adult ones. A few studies investigated pathobiological basis of such a different clinical course identifying brain plasticity and heightened myelin reparative capacity as possible causes. We compared brain atrophy development between pediatric and adult MS patients.

Methods: Using 3 T scanner dual-echo and 3DT1-weighted images were acquired from 31 pediatric and 30 adult disease duration-matched MS patients at baseline and after a mean follow-up of 3.5 years. As control groups, 26 pediatric and 30 adult age- and sex matched healthy controls (HC) were enrolled. Voxel-wise techniques were used to assess volumetric differences at baseline and atrophy progression.

Results: Compared to age-matched HC, pediatric MS patients showed atrophy of the bilateral thalamus, right hippocampus, middle frontal gyrus, left inferior temporal gyrus and calcarine cortex. Compared to age-matched HC, adult MS patients showed a broader pattern of atrophy, involving bilateral thalamus, hippocampus, cingulate cortex and corpus callosum and several cortical areas in the frontal, temporal and parietal lobes. At baseline, compared to pediatric, adult MS patients had atrophy of the cingulate cortex and right precentral gyrus. During the follow-up, compared to adult, pediatric MS patients developed less atrophy in bilateral temporal pole, precentral and postcentral gyrus, left insula, hippocampus, middle frontal gyrus and cerebellum.

Conclusion: Pediatric MS patients compared to disease duration-matched adult patients showed less atrophy, indicating increased resilience against structural damage and neurodegeneration.

Cerebrovascular diseases 2

O3201

Decreased GABA levels in the symptomatic hemisphere after transient ischaemic attack

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Background and aims: In patients with stroke the GABA level is decreased in the lesioned hemisphere which may facilitate neurological recovery. In this study we aimed to determine the cortical levels of GABA and glutamate in patients after transient ischemic attack (TIA).

Methods: Ten first-time TIA patients with unilateral motor symptoms from upper limb and 10 healthy subjects underwent Magnetic Resonance Spectroscopy with SPECIAL technique. GABA and glutamate were measured in the hand area of the primary motor cortex (M1) in the symptomatic hemisphere.

Results: Both GABA:Cr ($p=0.003$) and Glutamate:Cr ($p=0.0035$) ratios were significantly lower in the symptomatic hemisphere of TIA patients than in healthy subjects. No difference was found in grey matter content within the scanned voxel ($p=0.26$)

Conclusion: Even though the neuroligial function was reestablished, our study showed reduced GABA- and Glutamate ratios in the symptomatic hemisphere. In the affected hemisphere of TIA patients, the lower GABA level may facilitate re-establishment of normal function. This finding should be explored in future studies. MRS could be a useful biomarker in the acute assessment of patients with suspected TIA.

Disclosure: Nothing to disclose

O3202

CRP in atherosclerosis - A risk marker but not a causal factor. A 13-year population-based longitudinal study. The Tromsø Study.

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Background and aims: CRP predicts cardiovascular disease (CVD) in large epidemiologic studies. The aim of the present study was to investigate the cross-sectional and longitudinal association between serum CRP levels and carotid atherosclerosis in a prospective population-based study.

Methods: 6503 middle-aged subjects from The Tromsø Study, had serum CRP and carotid ultrasound examination at baseline in 1994. The subjects were invited to follow-up surveys with repeated assessments in 2001 and in 2007. Mean attendance was 2.2 surveys. The cross-sectional association between CRP and subclinical carotid atherosclerosis, and the association between baseline CRP and future plaque formation and progression was assessed in linear mixed models stratified by sex.

Results: At baseline, traditional risk factors and plaque prevalence increased by CRP risk categories (<1mg/l, 1-3mg/l, and >3mg/L) in both sexes. In age-adjusted models, baseline CRP was associated with baseline total plaque area (TPA) in men ($\beta=0.28$ (CI 0.21-0.35) and women ($\beta=0.11$ (CI 0.04-0.17). In multivariable-adjusted models, baseline CRP was associated with TPA ($\beta=0.20$ (CI 0.12-0.27) in men only. Baseline CRP did not predict TPA-progression in multivariable adjusted analyses for either sex. In age-adjusted models, baseline CRP was associated with novel plaque formation in men (OR 1.10 (CI 1.01-1.21), but not after multivariable adjustment.

Conclusion: CRP was associated with plaque presence and TPA independent of traditional CVD risk factors in cross-sectional analyses, but did not predict novel plaque formation or TPA progression. Our findings suggest that CRP links to CVD by other mechanisms than promoting plaque formation and progression.

Disclosure: Nothing to disclose

O3203

Intravenous thrombolysis in posterior circulation stroke – risk of intracranial hemorrhage and clinical outcome: results from the SITS-EAST registry

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Background and aims: In patients treated with intravenous thrombolysis (IVT), previous studies demonstrated lower risk of symptomatic intracranial hemorrhage (SICH) in posterior (PCS) versus anterior circulation strokes (ACS). However, data regarding clinical outcomes are controversial. The aim was to assess the SICH risk and clinical outcome in PCS versus ACS patients treated with IVT.
Methods: Prospectively collected data in the Safe Implementation of Treatments in Stroke – Eastern Europe (SITS-EAST) registry between 2010 and 2015 were analyzed. NINDS criteria were used for SICH definition. 90-day outcome was assessed using mRS with good clinical outcome defined as 0-2 points. Method of generalized linear mixed models estimates was used for statistical analysis.
Results: Set consisted of 2738 patients – 363 (13.3%) with PCS, 2375 (86.7%) with ACS. SICH occurred in 0.55% of PCS and 5.51% of ACS patients (P>0.05). The following independent predictors of SICH were: age (OR 1.025;P=0.004), baseline diastolic blood pressure (OR 1.016;P=0.02), intravenous antihypertensive therapy before/during IVT (OR 1.632;P=0.01). Good 90-day clinical outcome was achieved in 68.6% of PCS and 58.9% of ACS patients (P=0.02). The following independent predictors of good 90-day clinical outcome were: age (OR 0.953;P<0.0001), pre-stroke mRS (OR 0.611;P<0.0001), baseline glycemia (OR 0.927;P=0.0005), intravenous antihypertensive therapy before/during IVT (OR 0.526;P<0.0001), SICH occurrence (OR 0.096;P<0.0001), PCS (OR 1.413;P=0.03).
Conclusion: In patients treated with IVT, data from SITS-EAST registry showed that localization of stroke in the posterior circulation was associated with better 90-day clinical outcome than in the anterior circulation. Nevertheless, the SICH risk was only statistically insignificantly lower in PCS versus ACS patients.
Disclosure: Nothing to disclose

O3204

Outcomes of thrombolysis treatment in patients with dementia and acute ischemic stroke: A longitudinal cohort study from SveDem and Riksstroke, Swedish Dementia and Stroke Registries

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Background and aims: In Sweden, 25,000 strokes occur each year, 10% in persons with pre-existing dementia. The aim of this study was to investigate outcomes of thrombolysis in patients with dementia and acute ischemic stroke.
Methods: Longitudinal analysis combining SveDem, the Swedish dementia registry, and Riksstroke, the Swedish stroke registry. Patients with pre-existing dementia who suffered an ischemic stroke 2010-2014 (n=1356) were compared with matched non-dementia subjects (n=6755).
Results: In both groups, the median age at stroke onset was 83 years. Thrombolysis was administered to 94 (7.0%) dementia and 639 (9.5%) non-dementia patients. The corresponding OR for the dementia group was 0.68 (p=0.010) after adjusting for demographics, medication and comorbidities. However, when the analysis was repeated exclusively among patients who were independent in mobility, dressing and toileting before stroke, the difference between dementia and non-dementia group was not significant. In patients who received thrombolysis, change in NIHSS (National Institutes of Health Stroke Scale, p=0.305), the incidence of intracerebral hemorrhage (ICH, p=0.96) and death at 3 months (p=0.169) did not differ significantly between the two groups. On the other hand, physical functional outcome was worse among dementia patients after 3 months, with OR 3.67 (p<0.001) for a higher mRS (modified Rankin Scale).
Conclusion: In Sweden, patients with dementia and acute ischemic stroke are less likely to receive thrombolysis. Among patients who receive thrombolysis, there are no significant differences in NIHSS change, ICH or death at 3 months. However, dementia patients have worse functional outcomes. These findings might be explained by comorbidities or worse baseline functional status.
Disclosure: We received financial support from Swedish Stroke Association, the Swedish Order of Saint John, Swedish Brain Power and Swedish Association of Communities and Regions.

O3205

Long-term predictors of mortality and functional outcome after decompressive hemicraniectomy for malignant middle cerebral artery infarction.

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Background and aims: Decompressive hemicraniectomy (DH) is recommended in patients at high risk of malignant middle cerebral artery territory infarct. However, predictors of outcome after DH remain unknown.
The aim of our study was to identify predictors of mortality, and of functional outcome in 1-year survivors.
Methods: We evaluated prospectively consecutive patients who underwent DH between May 2005 and September 2015. We performed logistic regression analyses to identify predictors of mortality, and predictors of poor functional outcome in 1-year survivors, defined as a modified Rankin scale [mRS] of 4 or 5.
Results: Of 139 patients (88 men, 63%; median age 49 years, interquartile range 43-57), 22 (16%) patients died before discharge 6 (4%) between discharge and 1 year. The only predictor of inhospital death was a higher volume of infarct measured on diffusion-weighted images before DH (odds ratio [OR] 1.6; 95% confidence interval [CI] 1.004-2.6). The only predictor of mortality at 1-year was an increasing age (OR 1.08; 95% CI: 1.02-1.14). Of 111 survivors at 1-year, 43 (39%) had a mRS 4-5. Predictors of mRS 4-5 in survivors were excessive alcohol consumption (OR 6.5; 95% CI 2.1-20.2) and arterial hypertension (OR 8.8; 95% CI 2.7-29.2).
Conclusion: Short term mortality depends only on the volume of diffusion abnormality before surgery, while long-term outcome depends mainly on the pre-existing status of the patient (age, excessive alcohol consumption and arterial hypertension). These findings may help identifying patients who may benefit the most from DH.
Disclosure: Nothing to disclose

O3206

PORTYWHITE - Portuguese registry on incidental white matter lesions of presumed vascular etiology in young adults: Preliminary results

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Background and aims: Frequently assumed to be age-related changes, white matter lesions (WML) are sometimes incidentally found in young adults. Etiology frequently remains unexplained or is attributed to "sporadic" small vessel disease (SVD) but sometimes patients with inherited SVD present with WML. We aimed to characterize the population of young adults with WML referred to neurology consultation.
Methods: During two years, consecutive patients aged 18-55 years, referred to neurology outpatient consultation of twelve Portuguese hospitals, with WML of presumed vascular etiology that scored II/III or III/III in the Fazekas scale, were included in an on-line database. Demographic and clinical data were collected as well as results of investigations (according to the decision of the neurologist). Central imaging analysis was performed by two independent, blinded, neuroradiologists.
Results: Between July 2014 and June 2016, 85 patients were included. After central imaging analysis, 8 patients were excluded. Among the 77 patients studied, mean age was 47.7% years (25-34 n=5; 35-44 n=11; 45-55 n=61) and 72.7% were female. Reasons for referral were: focal symptoms (40.3%), headache (20.8%), vertigo (6.5%) syncope (3.9%), cognitive complaints (3.9%), epilepsy (2.6%) and others (22.1%). Hypertension was the most common risk factor (53.2%). WML scored II/III in 49 and III/III in 28 patients. A genetic disorder was identified in 6 patients: CADASIL n=5; COL4A1 n=1.
Conclusion: In the study population, only one in five patients has less than 45 years and females outweigh males. More than half of the patients are hypertensive. Genetic disorders are responsible for more than 7% of patients.
Disclosure: The PORTYWHITE study was supported by an unrestricted grant from SANOFI-Genzyme.

Movement disorders 1

O3207

Deep sleep and progression of Parkinson's disease

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Background and aims: Deep sleep, quantified by delta-power on electroencephalography during polysomnography (PSG), might influence the course of neurodegenerative disorders. We investigated the relationship between delta-power and clinical progression in patients with Parkinson's disease (PD) and whether disease duration modulated this relationship.
Methods: Clinical data were retrospectively collected from consecutive patients with PD who underwent PSG not later than 12 months after baseline visit (n=79, mean age=63±9.9 years, disease duration at baseline=5.2±5.1 years). We quantified delta-power based on spectral analysis of electroencephalography during PSG. Baseline measures and annual increases of the Unified-Parkinson's-Disease-Rating-Scale part III (UPDRS) and the daily levodopa-equivalent-dose (LED) were calculated and correlated with delta-power using partial-correlation controlling for relevant covariates. The analysis was conducted in all patients and separately in those with de novo and early PD (disease duration≤5years).
Results: Delta-power was associated with lower annual increase of the UPDRS in all patients (r=-0.23; p=0.05). This association was stronger in patients with de novo (r=-0.63; p=0.02) and early PD (r=-0.3; p=0.03). Only in patients with de novo PD, higher delta-power correlated with higher UPDRS at baseline (r=0.54, p=0.05). Delta-power was not associated with LED at baseline or its annual increase in any of the subgroups.
Conclusion: Deep sleep relates to a mild motor progression in PD, particularly during early stages, suggesting beneficial effects. As higher delta-power relates to higher motor symptoms in drug-naïve de novo patients, deep sleep might support nigrostriatal reserve, compensating during pre-motor PD until the breakdown of compensatory mechanisms.
Disclosure: Nothing to disclose

O3208

Poor cognitive functioning is associated with an increased risk of incident parkinsonism: the Rotterdam Study

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Background and aims: Cognitive impairment is a common feature among patients with parkinsonism, but there is a scarcity of data on cognitive functioning before parkinsonism diagnosis.
Methods: Between 2002 and 2008, we assessed baseline cognitive function in 7,386 participants of the Rotterdam Study who were free of parkinsonism and dementia. We used four tests (Stroop, Letter-Digit-Substitution-Test[LDST], Verbal Fluency, Word Learning Test[WLT]) and derived a Global cognition score from principal component analysis. Subsequently, we followed participants until 1 January 2015 for the onset of parkinsonism. We determined the association of cognitive test scores with incident parkinsonism, adjusting for age, sex, study subcohort, and level of education.
Results: During follow-up (median 8.3 years), 79 persons were diagnosed with incident parkinsonism, []49 (61%) with Parkinson Disease. Among incident parkinsonism patients, 24 also developed dementia (10 before and 14 after parkinsonism onset). Poor global cognition at baseline was associated with a higher risk of incident parkinsonism (hazard ratio per standard deviation decrease HR=1.79, 95% confidence interval [1.37;2.33]). The association remained robust even beyond the first five years, after removing persons with dementia onset before parkinsonism or removing those with secondary parkinsonism diagnoses. (Figure 1) The LDST (HR=1.68 [1.30;2.18]), verbal fluency (HR=1.63 [1.27;2.08]), and inverted interference-task Stroop (HR=1.35 [1.10;1.69]) scores were each strongly associated with incident parkinsonism, whereas the association of delayed-task WLT scores was distinctly weaker (HR=1.16 [0.91;1.49]).
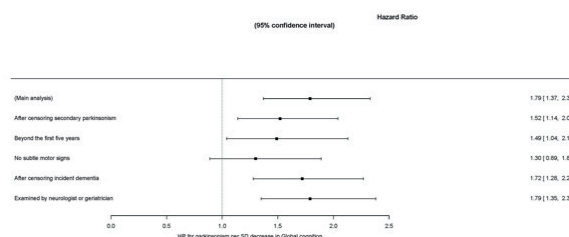
Figure 1. Sensitivity analyses of the association between Global cognition and incident parkinsonism

Table 1. Combining cognitive functioning and motor features

	N no incident parkinsonism	N incident parkinsonism	HR [95%CI]
Normal cognition, no subtle motor features	4809 [65.8]	40 [50.6]	(reference)
Any subtle motor feature with normal cognition	1339 [18.3]	17 [21.5]	1.42 [0.80; 2.52]
Low cognitive functioning with no subtle motor features	673 [9.2]	8 [10.1]	1.57 [0.73; 3.36]
Low cognitive functioning + any subtle motor feature	486 [6.7]	14 [17.7]	3.80 [2.06; 7.01]

HR, hazard ratio for incident parkinsonism.
95% CI, 95% confidence interval. Analyses are adjusted for age, sex, education and subcohort.
Low cognitive functioning, ≤-1 standard deviation in Global cognition score compared to age-&sex-adjusted means.
Subtle motor feature, parkinsonian sign or ≤-1 standard deviation manual dexterity score.

Table 1. Combining cognitive functioning and motor features

Conclusion: Poor cognitive functioning is associated with an increased risk of incident parkinsonism. Importantly, cognition predicts parkinsonism even over long intervals, and extends beyond patients with secondary parkinsonism.
Disclosure: Nothing to disclose

O3209

Skin nerve phosphorylated α-synuclein deposits in idiopathic REM sleep behavior disorder

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Background and aims: REM sleep behavior disorder (RBD) represents a powerful heralding symptom of impending neurodegeneration. We tested if p-α-syn deposits can be detected by means of skin biopsy in patients with idiopathic RBD (iRBD), as a potential early histopathological marker of impending synucleinopathy.
Methods: Proximal (cervical) and distal (legs) samples of skin biopsy have been obtained from 12 patients with polysomnographically-confirmed iRBD and 55 sex and age-matched healthy controls (HC). P-α-syn deposits were assessed by a monoclonal antibody against phosphorylated α-synuclein at Serine 129, disclosed by an immunofluorescence method. Additionally, patients underwent an extensive work-up in order to search for non-motor symptoms and neuroimaging findings usually associated with impending neurodegeneration and to exclude subtle motor or cognitive signs.
Results: P-α-syn deposits were detected in nine (75%) out of 12 patients with iRBD and none of the HC. In iRBD, the sensitivity of the test was higher at the cervical site (67%), when compared to the leg site (58%).
Conclusion: Our preliminary findings suggest that skin biopsy in patients with iRBD might be a safe and sensitive procedure to be further tested in order to detect p-α-syn deposits in the pre-motor stage of synucleinopaties.
Disclosure: Nothing to disclose

O3210

Cortical involvement in early Parkinson's disease: evidence from multimodal MRI

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Background and aims: MRI studies in early Parkinson's disease (PD) have shown promise in the detection of disease-related brain changes in vivo in the white and deep grey matter. While neuropsychology points to early cortical dysfunction even in early PD, MRI data on cortical involvement in early PD is lacking. We set out to establish if cortical pathology in early PD can be detected with MRI.

Methods: We collected a rich, multi-modal dataset including diffusion MRI, T1 relaxometry, and T1-weighted images to perform cortical morphometry in 20 early PD patients (disease duration 2±0.9 years, Hoehn & Yahr 1-2), and a set of matched controls.

The cortex was reconstructed using Freesurfer. Data analysis proceeded with linked independent component analysis (ICA), a novel data-driven technique that allows for data fusion and extraction of relevant multi-modal components before statistical analysis. For comparison, we performed standard unimodal GLM analysis.

Results: Linked ICA detected concomitant multi-modal cortical changes in early PD (p=0.015, Figure). Receiver operating characteristic (ROC) analysis separated PD from controls with 71% accuracy based on imaging results alone. Unimodal GLM detected no significant group difference on any imaging modality.
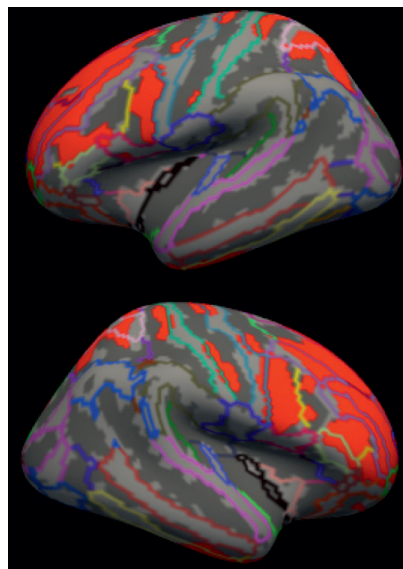
Cortical microstructural dysintegrity in Parkinson's Disease

Conclusion: Linked ICA detects multi-modal, predominantly microstructural cortical pathology in early PD. This cannot be explained by loss of dopaminergic terminals alone, as their volume fraction is too small. Excitingly, MRI opens a window into the study of early cortical involvement in PD. Our data suggest that cortical neurodegeneration occurs earlier than previously thought, leaving a signature in the diffusion signal that can be detected with advanced MRI methods.

O3211

Ventral striatal dopaminergic defect is a risk factor for hallucinations in Parkinson's disease

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Background and aims: Visual hallucinations (VHs) are common in patients with Parkinson's disease (PD). However, the pathogenesis of VHs in PD is unclear as the stimulation by dopaminergic medications is not sufficient to fully explain the emergence of hallucinations. The aim of this study was to investigate dopaminergic mechanisms of VHs and specifically weather the degree of striatal or extrastriatal dopamine transporter (DAT) or serotonin transporter (SERT) function can predict the appearance of VHs in patients with PD.

Methods: We identified twenty-two PD patients scanned with [123I]FP-CIT SPECT at the time of diagnosis who developed visual hallucinations, and compared them with matched 48 non-hallucinating PD patients. The groups were matched for age, medication, disease duration and motor symptom severity. Imaging analyses were performed with regions-of-interest –based and voxel-based (SPM) methods.

Results: Median interval between scan and the emergence of VHs was 4.8 years. Patients who developed VHs had 18.4% lower DAT binding in the right ventral striatum (p=0.009), 16.7% lower binding in the left ventral striatum and 18.8% lower binding in the right putamen (p=0.03) when compared to patients without VHs. No extrastriatal differences (SERT) were detected.

Conclusion: Low striatal DAT function may predispose PD patients to VHs. The regional distribution of the findings suggests a particular role of the ventral striatum. This is in line with non-PD research that has demonstrated alterations in ventral striatal function in psychosis. Susceptibility to medication-induced VHs may be increased in PD patients with relatively low baseline DAT activity in the limbic system.

Disclosure: Tyks (Erva-funds)

O3212

Cognitive decline relates to reversal of information flow in cortico-subcortical networks in the Parkinson's disease brain

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Background and aims: The pathophysiological mechanisms underlying the development of Parkinson's disease (PD)-related cognitive decline and the conversion to PD dementia (PDD) are poorly understood. Previous magnetoencephalograpy (MEG) studies aimed at resting-state functional brain networks have demonstrated decreases in cortico-cortical functional connectivity associated with PD-related cognitive decline. In these studies, directionality of information flow and the contribution of subcortical brain regions have not yet been taken into account. The aim of the present MEG-study was to analyse the relationship between the preferential direction of information flow in the brain (including subcortical brain regions) and cognitive performance in PD.

Methods: Eyes-closed resting-state MEG recordings and clinical measures of disease severity were acquired in moderately advanced PD patients (n=34) and healthy controls (n=12). Using an atlas-based beamforming approach, MEG signals were projected to both cortical and subcortical brain regions, following which we estimated PD-related changes in the direction of cortico-subcortical and cortico-cortical information flow.

Results: We observed that in PD patients, compared to healthy controls, preferential beta band information outflow was significantly higher for the basal ganglia and frontotemporal brain regions, and significantly lower for parieto-occipital brain regions (Figure 1, Figure 2). In addition, in patients, a low preferential information outflow from occipital brain regions correlated with poor global cognitive performance (Table 1).
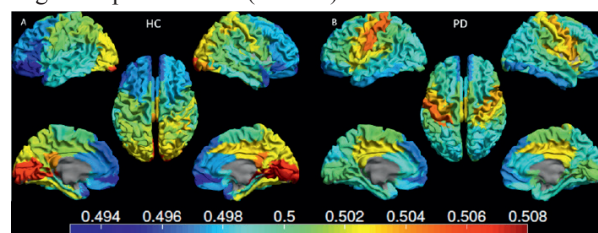
Figure 1: Distribution of beta band mean dPTE values for cortical regions
Directed phase transfer entropy (dPTE) indicating whether information flow is mainly 'incoming' (0 ≤ dPTE < 0.5 ; cold colours) or 'outgoing' (0.5 < dPTE ≤ 1 ; hot colours) for a region of interest (ROI) in relation to another. Note the pattern of preferential information outflow from posterior brain regions in the healthy controls (HC), whereas in Parkinson's disease (PD) the pattern of preferential information flow is dominated by outflow from pre- and postcentral gyri.

Figure 1
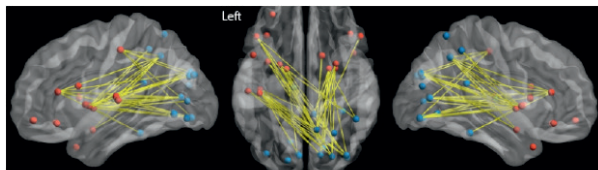
Figure 2: Significant differences in information flow between Parkinson's disease (PD) patients and healthy controls (HC)
Note that compared to the healthy controls, in PD the frontotemporal and subcortical regions consistently display a significantly higher (red) preferential information outflow, while the parieto-occipital regions show a significantly lower (blue) preferential information outflow. The latter is most pronounced for the right hemisphere. Significantly different individual connections between ROIs are displayed in yellow. For visualization purposes, only links with an absolute t-value larger than 4.17 are shown. Note that all but one connection are between ROIs that ROIs that had shown significantly different mean dPTE values between the groups in the first analysis. Furthermore, the parieto-occipital regions displayed a right-sided dominance in differences in individual connections.

Figure 2

Table 1 Correlations between clinical measures of disease severity and beta band dPTE values

Brain regions	Clinical measures of disease severity	
	CAMCOG	UPDRS-III
Occipital*	$\beta = .429, t(29) = 2.31, p = .029$	$\beta = -.230, t(30) = -1.216\ p = .234$
Basal ganglia**	$\beta = .139\ t(29) = .731, p = .471$	$\beta = .019, t(30) = .102, p = .919$

CAMCOG, Cambridge Cognitive Examination; UPDRS-III, Unified Parkinson's Disease Rating Scale motor ratings
* Superior/middle/inferior occipital gyrus, calcarine area, cuneus, lingual gyrus and fusiform gyrus (all bilateral)
** Caudate nucleus, putamen, globus pallidus (bilateral)

Beta coefficients are standardized in order to facilitate interpretability

Table 1

Conclusion: Our results indicate that changes in the physiological posterior-to-anterior flow of information are an important mechanism in PD-related cognitive decline. The relevance of these findings is not restricted to PD, as similar mechanisms may be involved in other neurodegenerative disorders.
Disclosure: Nothing to disclose

Muscle and neuromuscular junction disease

O3213

Outcome and antibody profile in ocular myasthenia gravis

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Background and aims: Myasthenia gravis (MG) ranges from ocular (OMG) to generalized disease (GMG). MG has autoantibodies (Abs) targetting acetylcholine receptor (AChR) and muscle-specific tyrosine kinase (MuSK).We surveyed cohort of 173 OMG, comparing outcome of double seronegative, anti-AChR, anti-MuSK Ab positive patients to find prognostic predictors.

Methods: MuSK positive were 3.5%, anti-AChR Ab positive 38.4%, double seronegative 57.9%. Gender, age, time to generalization,ocular scores were analyzed with parametric, non parametric measures.Survival statistics was used to predictive value of clinical variables .

Results: Males were 102 (59%), females 71 (41%). Males prevailed among anti-AChR Ab positive (76.8%), females among seronegative (50.9%) and MuSK positive (67%). Late onset OMG were 79%, the remaining had early onset (EOMG). Among anti-MuSk positive, 50% had EOMG. Median disease duration was 95 months for anti-AChR Ab positive, 93 for seronegative, 74 for anti-Musk positive. 21% of OMG progressed to GMG: 31% of females, 13% of males, 83% of anti-MuSK positive vs 14 % of seronegative and 26% of anti-AChR Ab positive.Median time to GMG for anti-MuSK was 37 months, 93 months for seronegative, 91 for anti-AChR positive. 95% of anti-AChR positive MGO received steroids, all MuSK-positive had immunesuppresion.A MuSK positive MGO had hyperplastic thymus at thymectomy.Regression analysis showed that sex, anti-MuSK positivity independently predicted conversion to GMG (p:0.005 and p:0.014, respectively). Diplopia onset was associated with good outcome (p0.02). Seronegative subjects showed significant lower risk of progression (p0.008)

Conclusion: MuSK related OMG is associated with worse prognosis in comparaison with anti-AChR positive and seronegative subjects.

Disclosure: Nothing to disclose

O3214

Respiratory involvement in facioscapulohumeral dystrophy

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Background and aims: Respiratory compromise in FSHD has only been addressed in a few studies without full understanding of the mechanisms and the extension of the problem.
We aimed at evaluating respiratory function in the FSHD population followed at the JWMDRC.

Methods: Retrospective study of 100 FSHD patients. According to the Clinical Severity Scale (CSS), patients were classified as mildly affected (score <3.5) or moderate/severely affected (score $\geq$ 3.5). Patients with FCV < 50% predicted were classified as severely impaired (SR group) and compared to the group with FVC $\geq$ 50% predicted (NSR group).

Results: Forty six patients were classified as mildly affected and 54 as moderate/severely affected. Fifty five patients (58.5%) had normal spirometry results and 36 (38.3%) had a restrictive pattern, 38.9% of which showed FVC < 50% predicted (SR group). A significant correlation was found between FVC; CSS score and D4Z4 fragment size for fragments up to 18kb. A higher probability of severe respiratory involvement was found in patients with early onset, moderate/severe disease and fragments up to 18kb. The SR group showed higher proportion of wheelchair bound patients and spine deformities. Seventeen patients with sleep disordered breathing (SDB) showed higher frequency of severe respiratory involvement. Mean FVC decline in the SR group was 3.6 $\pm$ 3.3% per year.

Conclusion: Respiratory involvement in FSHD is more frequent and severe than previously suggested. Smaller D4Z4 repeats and early onset are more useful than severity as early predictors of respiratory involvement. Regular spirometry and clinical screening of respiratory symptoms is warranted in FSHD patients.

Disclosure: Nothing to disclose

O3215

Assessing the impact of gender on the phenotype of myotonic dystrophy type 2: a cohort of 307 patients

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Background and aims: Myotonic dystrophies are autosomal dominant diseases characterized by a combination of muscular and multisystemic involvement. Gender has been recently found to influence the phenotype of myotonic dystrophy type 1. Our aim was to study the impact of gender on myotonic dystrophy type 2 (DM2) phenotype.

Methods: We retrospectively studied 307 patients with DM2 analysing the following data: i) demographics (age, gender), ii) clinical features (first symptom, diagnostic delay, presence of myotonia, weakness and/or pain, comorbidities), and iii) diagnostic assessments (serological tests, electromyography, muscle biopsy). Statistical analyses were performed

Results: Our cohort comprised 186 females (61%) and 121 males. Muscle weakness was more common in women than men (64.9% vs. 43.8%, p=0.0006), while pain was a more frequent presentation in men (49.5% vs. 29.9%, p=0.001). Patients with weakness at onset were older than those with pain and myotonia (median 49, vs. 39 and 30 years, p<0.0001). A multinomial regression model revealed that age at onset and sex were significantly and independently associated with specific types of symptoms. Cataract and thyroid diseases occurred more frequently in women (p=0.002 and p<0.001). CK and GGT were more frequently abnormal in men (p<0.001 and p=0.019) whereas no differences were found for electromyography and biopsy results. Lastly, females were diagnosed later than males (diagnostic delay: median 6 vs. 2 years, p<0.0001).

Conclusion: In conclusion it seems that, as in DM1, gender influences, independently from age, the phenotype of DM2. These gender-specific manifestations should be considered in the diagnosis and management of patients.

Disclosure: Nothing to disclose

O3216

Functional outcome measures and muscle MRI pattern recognition in dysferlinopathy: The JAIN COS Study

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Background and aims: The Jain Clinical Outcome Study (COS) is the largest international natural history study in patients with genetically confirmed dysferlinopathy. 203 adults have been recruited across 15 sites in 8 countries.

Aims: To analyse longitudinal clinical data over the first year of the study and to describe the pattern and selective distribution of muscle pathology by MRI.

Methods: An adapted North Star Ambulatory Assessment (aNSAA), MFM-20 and timed tests (rise from floor, 10 metre walk/run, four stair climb and descend, Timed Up and Go (TUG) and 6MWD) were completed at baseline, six months and year 1. A semi-quantitative MRI analysis was performed on T1-weighted axial sequences at baseline in 182 patients using the Mercuri scale modified by Fisher. Hierarchical analysis was performed to define the selective pattern of involvement. Results of the MRI scans were correlated with appropriate functional tests.

Results: aNSAA, MFM-20, 10m walk test, and TUG demonstrated consistent deterioration in scores or time taken over each 6 month window, although variation in the change of scores was wide. The rise from floor, stair climb and stair descend detected significant change over one year. On muscle MRI scans, the gastrocnemius medialis and soleus were the most frequently affected muscles. A similar pattern of involvement was identified regardless of the clinical phenotype. The increase of fat replacement on MRI correlated positively with disease duration and functional tests.

Conclusion: Functional tests showed changes in 6 month and 1 year time. Semi-quantitative MRI can help to define target muscles to monitor in quantitative muscle MRI studies.

Disclosure: This study is sponsored by the JAIN Foundation. based in Seattle, USA, which is entirely focused on LGMD2B/ dysferlinopathy/Miyoshi Myopathy. Please visit www.jain-foundation.org for more information. The Jain COS consortium would like to thank the study participants and their families for their invaluable contribution.

O3217

Poly-autoimmunity and associated autoantibodies in a nationwide juvenile myasthenia gravis cohort

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Background and aims: Autoimmune disorders (AD) are multifactorial in origin and affect at least 5% of the World's population. Juvenile myasthenia gravis (MG) is a rare autoimmune disorder targeting the neuromuscular junction, most commonly through autoantibodies against the acetylcholine receptors (AChR ab). Poly-autoimmunity, the presence of a second AD in an individual, is a well-known phenomenon, also among adult MG patients where it occurs in 13-22%. Another characteristic of Ads, is the presence of diverse ADs in members of a nuclear family, familial autoimmunity. We aimed to assess the frequency of poly-autoimmunity, AD associated autoantibodies and familial autoimmunity in a juvenile MG cohort in Norway.

Methods: Patients were identified through multiple strategies from January 2012 to April 2016. A total of 75 unique patients with MG onset ≤18 years of age were identified. 63 subjects gave written consent and were included. Retrospective clinical data were collected by means of medical chart and a questionnaire. 51 patients gave new blood samples for autoantibody analysis. Females constituted 84%. Onset was prepubertal in 33%. AChR ab were present in 73%, and 50% underwent thymectomy.

Results: We found that a total of 20 (32%) juvenile MG patients had at least one additional autoimmune disorder, in all but one with onset after MG diagnosis. In addition, 21 cases had autoantibodies associated with an AD without other signs. Familial autoimmunity was reported in 29. Details will be presented.

Conclusion: We show that poly-autoimmunity is common among juvenile MG cases in Norway, and also the presence of autoantibodies associated with an autoimmune disorder.

Disclosure: Nothing to disclose

O3218

The utility of next generation sequencing in a muscle specialist service

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Background and aims: Diagnosis of inherited myopathies can be a challenging process due to broad genetic heterogeneity. Next generation sequencing (NGS) is a promising technique for diagnosing neuromuscular disorders enabling the screening of multiple genes simultaneously. In this study we evaluated the utility of a focused clinical exome in our muscle specialist service.

Methods: We used targeted exome sequencing (Agilent Focused Exome) on undiagnosed patients attending our service with likely genetic myopathy supported by clinical, electromyography and/or muscle biopsy findings. We screened 340 genes known to be related to neuromuscular diseases and cardiomyopathies. We filtered out variants with an allele frequency higher than 1% in public databases. We then excluded all synonymous and deep intronic variants.

Results: We currently recruited 80 cases (mean age 54 ± 15.67 SD). Most were sporadic and had previous extensive genetic investigation. We identified a likely pathogenic candidate variant in 28/80 patients (35% of cases). 48% of these variants were already reported in the literature as causing neuromuscular disorders. In distal myopathy subgroup (n=28) we identified likely pathogenic variants in 46% of cases. Muscle biopsy was non-specific in 35% of the whole distal myopathy group. In two cases genes previously associated with motor neuropathy were found.

Conclusion: NGS targeted sequencing is an effective tool in the diagnostic process of our muscle specialist service. Muscle biopsy was non-specific for diagnosis in a significant proportion of cases, especially in distal myopathies subgroup. The latter may benefit in particular from the use of a broad neuromuscular genetic panel due to their genetic heterogeneity.

Disclosure: Nothing to disclose

Neurorehabilitation & Neurotraumatology

O3219

Long-term outcome after mild traumatic brain injury: The effect of age on health related quality of life

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Background and aims: Although most patients show full recovery within 3-6 months after mild traumatic brain injury (MTBI), 15-25% still experiences persistent post-traumatic complaints interfering with resumption of activities. Epidemiological patterns for TBI show more injuries occurring among elderly patients. The aim is to determine the effect of age on quality of life and functional outcome after MTBI.

Methods: 670 patients with MTBI admitted to the Emergency Department (January 2013 - January 2015) of three Dutch Level-1 hospitals were included. Data on post-traumatic complaints (head injury symptoms checklist), anxiety and depression (hospital anxiety and depression scale) and functional outcome (Glasgow Outcome Scale Extended) were collected at 2 weeks and 12 months post-injury. The following age-groups were formed: young adults (16-40), adults (41-60) and elderly ($\geq$ 61 years).

Results: 12 months post-injury 67% of patients had favorable outcome, and 1 in 10 patients either was depressed or anxious. Adults showed highest rates of post-traumatic complaints at both intervals and lowest resumption of activities (79% young adults; 63% adults; 74% elderly). In addition, adults reported the poorest health related quality of life (QoL) (30% on domain physical health (p=0.04) and 32% on mental health (p=0.21). Global scores show a decreasing trend of QoL up to age-group 51-60, with an increasing trend beyond this age-group.

Conclusion: Elderly patients show a good recovery after MTBI, with even better global QoL scores compared to adults, suggesting a greater impact of psychosocial factors than age on long term outcome and QoL in patients after mild traumatic brain injury.

Disclosure: This study is supported by the Dutch Brain Foundation (Grant Ps2012-06)

O3220

Transcranial direct current stimulation boosts spontaneous motor plasticity in subacute stroke

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Background and aims: Transcranial direct current stimulation (tDCS) and repetitive transcranial magnetic stimulation (rTMS) can improve motor recovery in stroke patients. However, we lack information on their neural effects and their interaction with spontaneous brain plasticity. Here, we conducted a randomized trial comparing the effects of tDCS, rTMS, or sham stimulation on functional and structural markers of brain plasticity and upper limb motor recovery.

Methods: Forty-one patients with subacute hemispheric stroke and impaired upper limb motor function were randomized to neuro-navigated continuous theta-burst stimulation (a form of inhibitory rTMS, N=14), cathodal tDCS (N=14), or sham stimulation (N=13) over the contralesional primary motor area. Each participant completed nine stimulation sessions over three weeks, combined with physical therapy. Patients were assessed with standardized motor tests, high-density electroencephalography (EEG), and diffusion tensor imaging (DTI) before and after all sessions.

Results: Cathodal tDCS induced an increase in EEG resting-state beta-band functional connectivity between ipsilesional primary motor cortex and the rest of the brain which was greater than after sham stimulation and even compared to rTMS (Fig. 1). Patients with poor motor recovery in the rTMS and sham groups showed a degradation of white-matter tracts in the affected hemisphere, which did not occur in patients treated with tDCS (Fig. 2). However, these neural effects translated to improved motor recovery only in patients in whom tDCS could be started within the first 4.5 weeks after stroke.
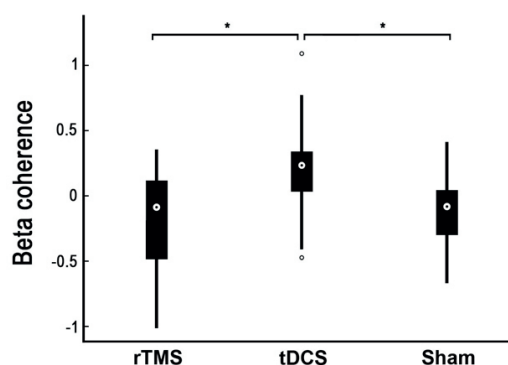
Figure 1. tDCS enhanced beta-band functional connectivity between the ipsilesional primary motor cortex and the rest of the brain. This pattern has previously been found to be associated with future motor improvement.
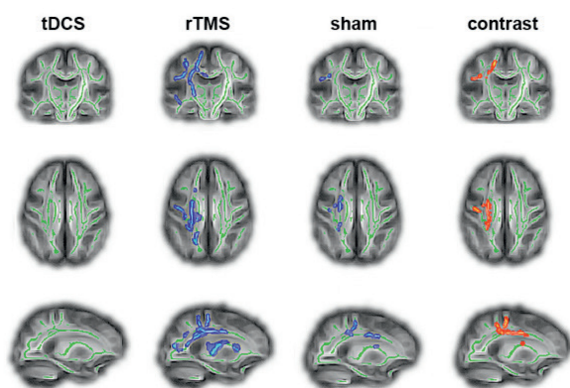
Figure 2. tDCS was associated with a prevention of white-matter tract degradation in the affected hemisphere, which occurred only in the other groups (blue colors). Red indicates significant differences between groups. All lesions are aligned to the left hemisphere (shown left).

Conclusion: tDCS specifically enhanced functional markers for cortical plasticity and prevented the structural signature for poor motor outcome. However, the time of application was critical.
Disclosure: Nothing to disclose

O3221

24-hour close observation may not be necessary in patients with mild traumatic brain injury (mTBI) during anticoagulation therapy

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Background and aims: Patients with mild traumatic brain injury (mTBI) using anticoagulants have an increased risk of intracranial haemorrhage (ICH). However, there is no consensus whether these patients should be admitted for observation when cranial computed tomography (CT) is normal. Therefore, we evaluated the yield of 24 hour close neurological observation in these patients.
Methods: Retrospective multicenter study. We included patients admitted between January 2010 and December 2014. Inclusion criteria were: age $\geq$ 16; mTBI; anticoagulation use (therapeutic dose heparin, direct oral anticoagulant, or vitamin K antagonist (VKA) and an international normalized ratio (INR) $\geq$ 1.7); normal cranial CT obtained within 24 hours after trauma. Primary endpoint was the frequency of ICH within 24 hours of injury. Secondary endpoint was ICH > 24 hours after trauma.
Results: Of 17,822 patients with mTBI, 1445 used anticoagulants. Of these, 905 met our inclusion criteria. Median age was 82 years [IQR 74-87] and 47% were men. 97% used VKA, with a median INR of 2.9 [IQR 2.5-3.6]). A total of 4/905 patients (0.4%, 95% CI 0.14-1.2) developed ICH within 24 hours. Upon reevaluation of the initial imaging, ICH was already present at baseline in all four patients. Five other patients developed ICH after 1, 7, 21, 35 and 51 days, respectively.
Conclusion: Development of ICH within 24 hours is extremely rare in patients with mTBI on anticoagulants when initial cranial CT fails to reveal ICH. Routine hospitalization of these patients seems unwarranted, but scrupulous evaluation of the initial CT is required.
Disclosure: Nothing to disclose

O3222

Factors influencing adherence to tibial nerve stimulation for the management of neurogenic overactive bladder

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Background and aims: Bladder dysfunction is common following neurological disease and Percutaneous Tibial Nerve Stimulation (PTNS) is an established minimally-invasive outpatient treatment for managing neurogenic overactive bladder symptoms (OAB). Following a 10-12 week course of once-weekly treatment, responders return for top-up treatments (top-ups) when OAB recurs. Not all responders return however, and this study aims to evaluate factors influencing patients's decision to return for top-ups.
Methods: Patients with neurogenic OAB attending a standard 12-week PTNS treatment were prospectively evaluated using standardised bladder questionnaires (ICIQ-OAB, ICIQ-LUTSqol), three-day bladder diary and satisfaction questionnaire. Responders to treatment were invited to return for top-ups and were divided into those actually returning for top-ups (group-1) and those not returning (group-2). PTNS service evaluation questionnaire (PTNS-SEQ) retrospectively enquired about treatment effects, side-effects, and procedural/ logistical difficulties with treatment.
Results: 73 patients completed PTNS-SEQ (non-responders (n=25), responders returning group-1 (n=31) and responders not returning for top-ups group-2 (n=17)). Age, gender, and neurological diagnosis were comparable across groups. Responders experienced significant improvement in OAB symptoms(group-1: -1.85±2.28, $p<0.001$; group-2: -1.54±1.85, $p<0.05$) and (group-1: -5.35±6.90, $p<0.001$; group-2: -4.27±10.98, $p>0.05$) following treatment. Group-1 experienced a greater improvement compared to group-2 in 24-hour urinary frequency ($p<0.01$), number of incontinence episodes($p<0.01$) and severity of leakage ($p<0.01$). In the PTNS-SEQ, differences between group 1 and 2 were satisfaction with the PTNS Service and lack of treatment effect ($p<0.05$).
Conclusion: PTNS is a safe and effective treatment for the management of neurogenic OAB. Improvements in 24-hour urinary frequency and severity of urinary incontinence impact patient´s satisfaction with the PTNS service and their decision to return for top-ups.
Disclosure: Nothing to disclose

O3223

Management of mild traumatic brain injury at the emergency department and hospital admission in Europe: A survey of 71 neurotrauma centers participating in the CENTER-TBI study

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Background and aims: Previous studies have indicated that there is no consensus about management of mild traumatic brain injury (mTBI) at the emergency department (ED) and during hospital admission. We aim to study variability between management policies for TBI patients at the ED and hospital ward across Europe.
Methods: Centers participating in the Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI) study received questionnaires about different phases of TBI care. These questionnaires included 77 questions about TBI management at the ED and at the hospital ward.
Results: We found differences in how centers defined mTBI. For example, 40 centers (59%) defined mTBI as a Glasgow Coma Scale (GCS) score between 13-15 and 26 (38%) as a GCS score between 14-15. At the ED various guidelines for the use of head CT in mTBI patients were used; 32 centers (49%) used national guidelines, 10 centers (15%) local guidelines and 14 centers (21%) used no guidelines at all. Also differences in indication for admission between centers were found. After ED discharge, 7 centers (10%) scheduled a routine follow-up appointment, while 38 (54%) did so only after ward admission.
Conclusion: In conclusion, large between-center variation exists in policies for diagnostics, admission and discharge decisions in patients with mTBI at the ED and in hospital. Guidelines are not always operational in centers, and reported policies systematically diverge from what is recommended in those guidelines. The results of this study show the need for further studies on the effectiveness of different policies on outcome.
Disclosure: Data used in this manuscript were obtained in the context of CENTER-TBI study with support of the European Commission 7th Framework program (602150).

O3224

There is still recovery at least until one year after severe traumatic brain injury. Results from the Danish Headtrauma Database before and after sub acute rehabilitation.

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Background and aims: Survival after severe traumatic brain injury (sTBI) has increased in recent years and recovery seems to be regained for a longer period than other brain injuries such as stroke and meningitis. We investigated the recovery of adult patients in the Danish Headtrauma Database (DHD) a national database based upon levels of consciousness, and performance at admission to our rehabilitation department, at discharge and one year after the trauma

Methods: Data was obtained from DHD on the following scores: Rancho Los Amigos (RLA), Functional independence measure (FIMTM) and Early functional abilities (EFA) scores in years 2011-2013 (n= 249).

Results: Recovery in level of consciousness is seen in this patient group at hospital discharge, and a trend towards a recovery in up to a year is seen, measured by RLA at admission; mean value 4 (range 2-8), at discharge mean value 6 (range 2-8) and at 12 months outpatient follow-up mean value 8 (range 3-8). FIMTM shows mean values of 20 (range 18-125) at admission, 91 (range 18-126) at discharge and 113 (range 18-126) at 12-months follow-up. EFA showed mean values of 52 (range 22-100) at admission, and 95 (range 26-100) at discharge and 99 (39-100) at 12 month follow-up.

Conclusion: Our patients are survivors of severe head trauma and show recovery in at least up to one year after trauma in levels of consciousness and by functional level, measured by RLA, FIMTM and EFA score. This must be considered in a rehabilitation unit, when predicting outcome of rehabilitation and level of consciousness

Disclosure: Nothing to disclose

Ageing and dementia

O3225

The independent effect of cerebral microbleeds on cognition

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Background and aims: The presence of small vessel disease (SVD) is associated with cognitive impairment. However, among the many components of SVD, the contribution of cerebral microbleeds (CMBs) to cognitive impairment remains elusive. Our aim was to determine if CMBs contribute to global and specific cognitive domains in addition to that contributed by other measures of SVD burden.
Methods: Subjects in a multimodal imaging study diagnosed with mild cognitive impairment (MCI), Alzheimer's disease (AD) and healthy controls (HC) were recruited. A neurologist blinded to the clinical and cognitive measures quantified CMBs using SWI. FLAIR was utilized for white matter hyperintensity (WMH) and lacunes. Global, frontal and non-frontal cognitive domains were evaluated. The isolated effects of CMBs (location and number) on specific cognitive domains were determined using linear regression analysis.
Results: 143 subjects (37 MCI, 56 AD and 50 HC), with mean 64 years of age and 11 years of education were analyzed. AD subjects had the highest Fazekas WMH burden of 5.9±3.8 compared to MCI 4.4±3.6 and HC 3.7±3.0 (p=0.005). The presence of CMBs acted as an independent predictor for worsening non-frontal cognition among patients with SVD (β=-0.8; p=0.038). At the multivariable level, the total number of lobar CMBs correlated to worsening global cognition (β=-0.2; p=0.021), after adjusting for demographics, education and other SVD parameters. The presence of lacunes correlated negatively with frontal cognition (β=-1.1; p=0.038).
Conclusion: CMBs contribute to cognitive impairment, specifically to non-frontal cognition, independent of WMH and lacunes.
Disclosure: Nothing to disclose

O3226

Diabetes mellitus in a large dementia cohort. A study of clinical characteristics and treatment from the Swedish Dementia Registry.

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Background and aims: We aimed to investigate clinical characteristics of diabetes mellitus (DM) in a large dementia cohort and analyse relationships between DM and different types of dementia disorders.
Methods: A cross-sectional registry-based study was conducted using data from the Swedish Dementia Registry (SveDem), the Swedish National Patient Register and the Swedish Prescribed Drug Register. Data on dementia diagnosis, dementia type and demographic determinants were extracted from SveDem. Data from Swedish National Patient Register and Prescribed Drug Register were combined for the diagnosis of DM. Data on antidiabetic, dementia, cardiovascular and psychotropic medication were extracted from the Swedish Prescribed Drug Register. Logistic regression was used to determine whether the variables were associated with DM after adjustment for confounders. In total 29,630 patients were included in the study and 4881 (16.5%) of them were diagnosed with DM.
Results: In the fully adjusted model, DM was associated with lower age at dementia diagnosis (odds ratio [OR] 0.97 [95% CI 0.97-0.98]), male gender (1.41 [1.30-1.52]), vascular (1.17 [1.04-1.31]) and mixed dementia (1.21 [1.09-1.35]). Dementia with Lewy bodies (0.64 [0.48-0.86]) and Parkinson's disease dementia (0.46 [0.31-0.67]) were less common among DM patients, as well as treatment with antidepressants (0.85 [0.79-0.92]). DM patients with Alzheimer's disease obtained significantly less treatment with acetylcholinesterase inhibitors (0.78 [0.66-0.91]) and memantine (0.68 [0.57-0.81]).
Conclusion: Patients with DM were younger at dementia diagnosis and obtained less dementia medication for Alzheimer's disease, suggesting less optimal dementia treatment. Future studies should focus on factors determining dementia treatment in DM patients.
Disclosure: This study was supported by the Swedish Brain Power, Swedish Association of Local Authorities and Regions, the Swedish Research Council (grant 2012-2291)

O3227

Predicting development of amyotrophic lateral sclerosis in frontotemporal dementia

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Background and aims: We aimed to establish the risk of developing amyotrophic lateral sclerosis (ALS) in patients presenting with frontotemporal dementia (FTD) and to identify the relevant clinical variables associated with progression from FTD to FTD-ALS.

Methods: Of 218 consecutive patients with FTD, 22 (10.1%) had a dual FTD-ALS diagnosis at presentation. The remaining 152 FTD patients with follow-up of at least 12 months were included in the present study. We calculated the rate of progression to FTD-ALS and compared the baseline characteristics of FTD patients that developed ALS to those that did not develop ALS.

Results: 5% of FTD patients developed ALS. The incidence rate of ALS was 6.7/100 patient-years in patients with FTD symptoms since 1 year, which declined with duration of FTD symptoms. No FTD patients developed ALS after 5 years. Five out of 8 FTD patients who developed ALS had presented with a mixed behavioural variant FTD and progressive non-fluent aphasia (bvFTD+PNFA) phenotype, 2 with bvFTD and 1 with PNFA. Progression to FTD-ALS was significantly more frequent in patients with bvFTD+PNFA compared to those without this phenotype (p<0.0001, OR 38.3, 95%CI: 7.3 to 199.2), and in FTD patients who carried the C9orf72 repeat expansion compared to those without the repeat expansion (p=0.02, OR 8.0, 95%CI: 1.7 to 38.6).

Conclusion: FTD patients with a mixed bvFTD+PNFA phenotype and a C9orf72 repeat expansion should be closely monitored for the possible development of ALS. Of particular clinical relevance is that the risk of developing ALS in FTD declines with the duration of FTD symptoms.

Disclosure: Nothing to disclose

O3228

Multimodal structural MRI differentiates in vivo the three clinical variants of primary progressive aphasia

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Background and aims: Primary progressive aphasia (PPA) variants may present with an overlapping picture and diagnosis in the clinical practice can be challenging. The aim of this study was to discriminate the non-fluent (nfvPPA), semantic (svPPA) and logopenic (lvPPA) variants using a multimodal magnetic resonance imaging (MRI) approach including cortical thickness and white matter microstructure metrics.

Methods: 56 patients (28 nfvPPA, 15 svPPA, 13 lvPPA) and 50 healthy controls underwent 3D T1-weighted and diffusion tensor (DT) MRI. Individual patient classification was performed using receiver operator characteristic curve analysis.

Results: The best markers to differentiate svPPA from both nfvPPA and lvPPA patients were the thickness of the temporal pole and DT MRI metrics of the left inferior longitudinal and uncinate fasciculi (area under the curve [AUC] ranging from 0.81 to 0.90). Cortical thickness of the superior temporal gyrus bilaterally and DT MRI metrics of the left frontal aslant tract distinguished nfvPPA and lvPPA with an AUC of 0.70.

Conclusion: Structural and DT MRI are powerful tools to help distinguishing the PPA variants in vivo. svPPA showed a prevalent cortical damage of the anterior temporal lobe and microstructural alterations of the temporal structural connections. The involvement of the superior temporal gyrus and left frontal aslant is crucial for distinguishing nfvPPA from lvPPA cases, which can be challenging in the clinical practice.

Disclosure: Italian Ministry of Health (#GR-2010-2303035).

O3229

COMAJ (Early onset Alzheimer's disease cohort): Vascular risk factors impact on early onset Alzheimer's disease

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Background and aims: Vascular risk factors (VRF) are risk factors of Alzheimer's disease (AD) in the elderly, whereas its impact on disease course is more controversial. Data about impact of VRF on early onset AD (EOAD, disease onset before 60) are poor. We studied the influence of VRF on EOAD course on two-year follow-up.

Methods: All the patients with probable or certain EOAD according to NIA and IGW criteria of the prospective COMAJ cohort in Lille entered between the 01/06/09 and the 01/05/14 were included, except autosomal dominant diseases. Demographical, neuropsychological and medical-social data, VRF, APOE4 status, medical history, autonomy and mortality were collected according to a standardized protocol. For each VRF, carriers and non-carriers were compared on these parameters. Results were adjusted on disease duration, gender, age, number of VRF and APOE4 status.

Results: 94 patients were included with a mean age of 59.3 (3.9) years; 78% showed at least one VRF: overweight (51%), HTA (41%), hypercholesterolemia (41%), smoking (36%), diabetes (4%); 52% were APOE4 carriers. At baseline no difference was observed. On follow-up, hypercholesterolemia was associated with a slower MMSE decline (-5 (3.4) vs -6.6 (4.9), p = 0.048), a lower risk of first hospitalization (p = 0.0223) or institutionalization (p = 0.0249), but not with lower mortality. This association seemed independent from APOE4 status and statin treatment.

Long-term follow-up

Two-year outcome of patients with (red) or without (blue) hypercholesterolemia on the parameters « first hospitalization » (A) and « institutionalization » (B)
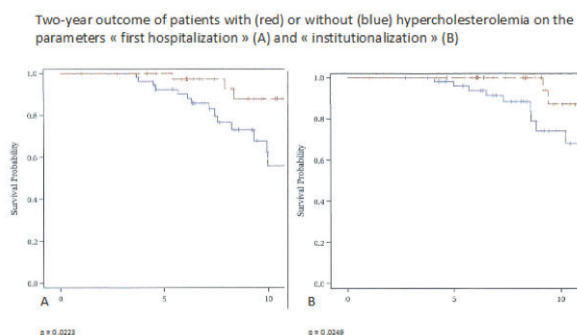
Conclusion: VRF has no impact on EOAD course except hypercholesterolemia which was associated with a slower cognitive decline and loss of autonomy.

Disclosure: Fund:Labex DistALZ

O3230

Negative association between peripheral blood NLRP3 levels and CA1 and subiculum in MCI patients with AD pathology: an innate immune pathway leading to hippocampal neurodegeneration

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Background and aims: Amyloid plaques and tangles, the two major lesions of AD, are strongly associated with central inflammation. Enhanced inflammation occurs also in cerebrospinal fluid and blood of AD patients.

This study aimed at investigating the correlation between immune and inflammatory signaling and structural alterations in MCI patients with or without AD pathology.

Methods: 89 consecutive amnestic MCI patients were enrolled in the WP5 of PharmaCog (E-ADNI) and were classified into positives or negatives based on their baseline CSF Aβ42/P-tau level. AD-related structural MRI (hippocampus and its subfields, entorhinal cortex, lateral

ventricles) and diffusion MRI (in the splenium of the corpus callosum) biomarkers were extracted with Freesurfer and an atlas-based approach, respectively. Expression of pro-inflammatory factors (IL-6, IL-1beta, TNF-alpha, NLRP3) were measured by Real Time PCR Assay. The human biological samples were sourced ethically and subjects provided written informed consent.

Results: Volume reduction in positive compared to negative patients was reported in the right hippocampus (p=.011), presubiculum (p=.013) and CA1 (p=.040), among the first brain regions affected by tangle pathology in AD. Moreover, positive patients showed higher expression of the innate immunity regulator NLRP3 (p=,038), an inflammasome component essential for the maturation of several pro-inflammatory cytokines, and of the pro-inflammatory cytokine IL-8 (p=,010). NLPR3 negatively correlated with all the right hippocampal measures: whole hippocampus (r=-.33, p=.018), presubiculum (r=-.28, p=.046) and CA1 (r=-.28, p=.049), but only in aMCI positive patients.

Conclusion: This data suggest a role of the inflammasome complex in AD-related hippocampal neurodegeneration and thus a key role of innate immune responses in AD pathology.

Disclosure: Nothing to disclose

Epilepsy 2

O3231

Fidelity of a Self-Management course for people with epILEpsy (SMILE (UK))

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Background and aims: People with epilepsy want self-management courses. We undertook a trial of a two-day interactive course for people with epilepsy, and examined the fidelity with which the course was delivered.

Methods: We tape recorded all 18 courses delivered and analysed audio-recordings of five courses selected to maximise the number of facilitators evaluated. Adherence in delivering specific topics according to a manual was assessed by a checklist. Competence of facilitators (i.e. how well they delivered the course) was evaluated by group interaction, overall impression and didacticism. Didacticism was measured in a novel way by using computer software to calculate the total percentage of facilitator speech during each course.

Results: Two independent raters assessed implementation fidelity. The adherence measurement had substantial agreement with weighted Kappa of 0.67 and agreement of 81.2%. The new didacticism measurement was highly reproducible with an intra-class coefficient of 0.97 (p < 0.0001). When testing implementation fidelity of SMILE (UK), we found a high level of adherence and high competence. Didacticism varied from 42% to 93% of total module time and was not correlated with the other competence scores.

Conclusion: This method of measuring implementation fidelity was reproducible and assessed multiple components of fidelity. SMILE(UK) was delivered with high adherence to topics outlined in the protocol, while not compromising the interactivity of the course.

Trial registration: ISRCTN57937389.

Disclosure: Funding: NIHR-HTA 09/165/01. The views and opinions expressed in this evaluation are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health.

O3232

Interictal versus ictal high frequency oscillations in temporal lobe epilepsy: A time-frequency analysis study

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Background and aims: High frequency oscillations (HFOs) have been previously shown to be related to epileptogenicity. The aim of this study is to elucidate the differences in spectral power of ictal and interictal HFOs. We hypothesized that HFOs have a higher increase in power compared to baseline in the Seizure Onset Zone (SOZ) contacts in both ictal and interictal epochs.

Methods: 5 patients with pharmacoresistant epilepsy who were implanted with subdural grids for presurgical evaluation were included in this study. Time-frequency analysis of SOZ and non-SOZ contacts was used to study the increase in power of HFOs compared to baseline in ictal and interictal epochs.

Results: SOZ contacts had a higher increase in power of HFOs compared to baseline in ictal and interictal epochs (Mean Difference [95% Confidence Interval]); (45.98% [18.54% - 73.42%]; 20.05% [3.10% - 37.00%], respectively). Ictal HFOs also had a higher power compared to interictal HFOs in the SOZ and non-SOZ contacts (32.05% [9.25% - 54.87%]; 6.12% [0.36% - 12.59%]). Interictal discharges from the SOZ had higher power of HFOs compared to interictal discharges from outside the SOZ (9.44% [0.002% – 18.88%]).
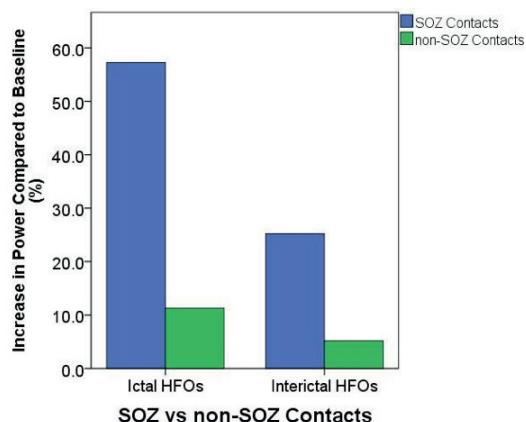
This chart shows that SOZ contacts have a higher power in ictal and interictal HFOs compared to non-SOZ contacts.
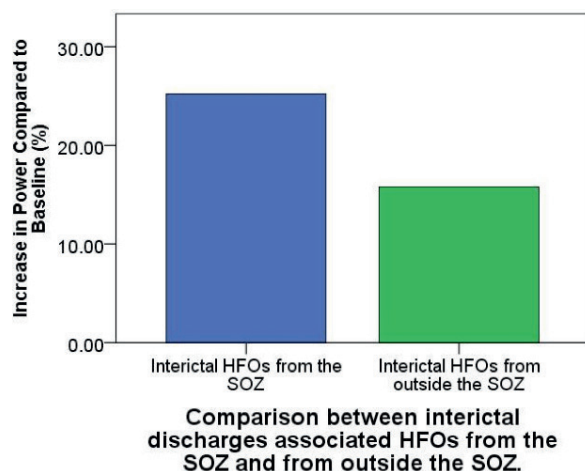
HFOs associated with interictal discharges have higher power when the discharges are from the SOZ.

Conclusion: It seems that SOZ contacts have higher increase in power of ictal and interictal HFOs compared to non-SOZ contacts. Additionally, it looks like ictal HFOs are more likely to spread to non-SOZ contacts compared to interictal HFOs.

Disclosure: Nothing to disclose

O3233

Motor phenomena in transient loss of consciousness: How to differentiate vasovagal syncope from convulsive seizures

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Background and aims: Myoclonic jerks are common in vasovagal syncope (VVS). We assessed motor phenomena in VVS and convulsive seizures (CS) to aid differential diagnosis, and studied the association between motor phenomena and EEG patterns.

Methods: We studied video-EEG records of tilt-table induced VVS and CS of subjects >15 years. Definite VVS was defined using the triad: (1) loss of consciousness, (2) circulatory changes (abrupt blood pressure decrease with or without bradycardia/asystole), and (3) EEG changes (slow or slow-flat-slow). We studied tonic postures and jerks of the arms and noted time of occurrence, laterality, synchronicity and rhythmicity (mean consecutive differences (MCD)) of interclonic intervals (ICI).

Results: Video-EEG records of 65 VVS cases and 50 CS were included. In VVS postures occurred in 42 cases (65%) and jerks in 33 (51%). Mean number of jerks in CS (62 ± 36, range 20-191) was higher than in VVS (4 ± 3, range 1-19; $p<0.001$; Figure 1). Jerks were more rhythmic in CS compared to VVS ($p<0.001$). Jerks predominantly seen during the slow and postures during the flat EEG phase (Figure 2).
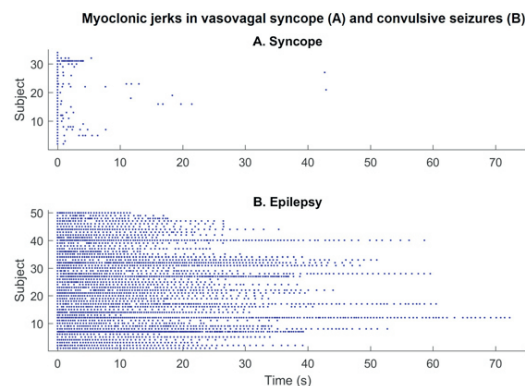
Figure 1: Myoclonic jerks in vasovagal syncope (A) and convulsive seizures (B). Every dot represents one jerk.
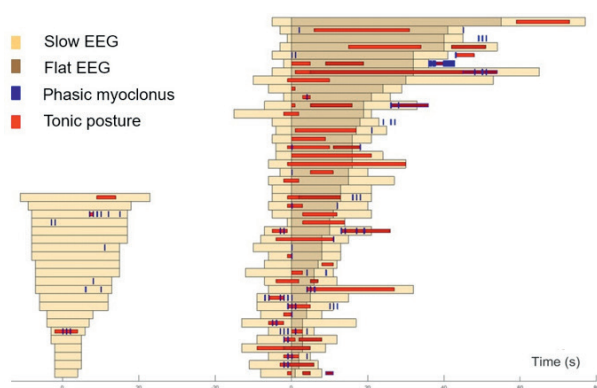
Figure 2: Duration of EEG phases and timing of the myoclonic jerks and tonic postures. The group with EEG slowing is shown on the left and with a slow-flat-slow EEG on the right. Each horizontal bar represents one person.

Conclusion: Jerks were common in VVS, but semiology differed from that of CS: fewer in number, less rhythmic and coincided with loss of tone. The lack of any overlap in the number of jerks suggests that less than 10 signifies syncope and more than 20 a CS ('10/20 rule'). These features may help to distinguish syncope from epilepsy.
Disclosure: Nothing to disclose

O3234

Complement system dysregulation in untreated patients affected by primary generalized epilepsy and the influence of anti-epileptic drugs.

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Background and aims: Complement system activation has been invoked as a possible pathogenetic factor for epileptogenesis in animal model and human bioptic studies. The aim of the present study is to evaluate the complement factors C3 and C4 in patients affected by idiopathic generalized epilepsy (IGE).
Methods: We enrolled patients affected by IGE admitted to our Epilepsy Centre undergoing neurological investigation, epilepsy diary, 24-h EEG recording, and blood sample for the assessment of C3, C4, fibrinogen and C-reactive protein (CRP) serum levels.
Results: We observed decreased C3 and C4 serum levels in EGI patients (n=37) with respect to controls (n=20) (p<0.05). We did no document differences in C3 and C4 serum levels between seizures free patients and patients with al least 1 seizure in the past year, as well as between patients treated by VPA and patients under other antilepeptic treatments. However, we documented lower C3 and C4 serum levels in drug-naive IGE patients compared to treated IGE patients (p<0.05). Finally, we found significant correlations linking C3 to C4 (R=0.34), CRP (R=0.49), and fibrinogen serum levels (R=0.61).
Conclusion: This study documented the significant alteration of complement system in IGE patients. The reduction of C3 and C4 serum levels may be the expression of the hyperactivation of the complement system. Since drug-naive IGE patients showed the lowest C3 and C4 levels, it is conceivable that antiepileptic treatments may modulate the complement system reducing its hyperactivation. Therefore, this study highlights the finding that complement system dysregulation may concur in epilepeptogenesis, also in IGE.
Disclosure: Nothing to disclose

O3235

Efficacy and safety of external trigeminal nerve stimulation in drug-resistant focal epilepsy.

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Background and aims: External trigeminal nerve stimulation (ETNS) through adhesive cutaneous electrodes is a novel, non-invasive and reversible therapy to treat drug resistant epilepsy (DRE). In previous pilot and controlled studies, trigeminal stimulation has been shown to decrease seizure frequency in patients with DRE and has improved scores in depression scales.
The objectives of our study are to find out the efficacy and tolerability of this therapy, whether its profile of efficacy varies depending on the location of the epileptogenic zone and if its long term use is associated to significant changes in mood, cognitive function or trigeminal nerve excitability.
Methods: Forty consecutive patients with frontal or temporal DRE who meet inclusion criteria and give their informed consent will be randomized to receive either stimulation or medical treatment (control group). We will analyze (before-after treatment and also respect to the control group) changes in seizure frequency (at 3, 6 and 12 months), percentage of responders, treatment-related adverse effects, changes in scores in HADS and Beck scales (6 and 12 months), changes in the neuropsychological study (12 months), changes in quality of life (scores in QUOLIE-31, 6 and 12 months), and changes in trigeminal nerve excitability (blink reflex).
Results: The study is ongoing: 32 patients have already been randomized, from whom 17 are treated with ETNS. We will present our preliminary results at one year of follow-up.
Conclusion: ETNS seems to be effective to reduce seizure frequency in DRE. Nevertheless, results at one year of follow-up are needed to obtain solid definite conclusions.
Disclosure: This study is supported by a Sanitary Research Fund of Health Institute Carlos III ("Fondo de Investigaciones Sanitarias del Instituto de Salud Carlos III"). We use the Monarch eTNS system by NeuroSigma because it is the only external trigeminal nerve stimulation device available on the market.

O3236

Retrospective single-center study of drug-resistant epilepsies: a survey on two decades of presurgical evaluations and surgical treatments.

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Background and aims: Drug-resistant epilepsies represent 30-50% of all epilepsies and surgery is an effective option to treat those patients. However, attitudes and tools are changing over time, which could lead to earlier referral or better outcome. This study reviews two decades of presurgical evaluation and surgical treatment at our Epilepsy Program Geneva-Lausanne.
Methods: We reviewed surgical outcomes of 828 patients who underwent to preoperative evaluation from 1995 to 2016. It has been performed a statistical analysis taking in account an early (1995-2002) vs a later time periods (2003-2009; 2010-2016).
Results: Seizure onset was 11.2±11.4 yrs (mean±sd), the duration of epilepsy was 13.7±11.9 yrs. 370 patients underwent surgical treatment of which 72% are seizure-free. Outcome did not change over time (p=0.787). A positive MRI for hippocampal sclerosis, focal cortical dysplasia, and tumors, is associated to better outcome compared to vascular, traumatisms or negative MRI-findings (p<0.001). There were more extratemporal resections during the late time (70%) with respect to the early time period (23%). Among operated patients, there was no change of epilepsy duration over time (p=0.320), but patients reported younger age at onset (p=0.034) and at evaluation (p=0.021).
Conclusion: Despite more complex operations, the outcome was stable over time which is due to a comprehensive battery of non-invasive imaging tools (ESI, PET, ictal SPECT, EEG-fMRI). Patients are younger at referral, reflecting a more positive attitude towards epilepsy surgery in Switzerland
Disclosure: Nothing to disclose

Tuesday, 27 June 2017

Neuroimmunology

O4101

Human aquaporin 4 auto-antibody alters blood brain barrier permeability

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Background and aims: Although blood brain barrier (BBB) breakdown is considered a key step in the development of neuromyelitis optica (NMO) lesion formation, little is known about the molecular mechanisms involved. We evaluate the effect of immunoglobulins of NMO patients (NMO-IgG) on BBB properties.

Methods: Firstly, brain isolated microvessels (BIM) from OFA rats (n=7) were exposed to NMO-IgG, control-IgG or Modified Eagle's Medium (MEM) for 20 hours. In parallel, primary cultures of endothelial cells (PCEC) isolated from lateral ventricle of OFA rats were exposed to NMO-IgG (n=6), control-IgG and MEM for 20 hours. We analyzed by Western Blotting (WB), the expression of claudin-5, occludin and ZO-1 in both experiments. Secondly, based on chronic intraventricular infusion of a NMO-IgG patient (rat-NMO) or control-IgG (control-rat) in brain rat, we investigated by immunohistochemistry (IHC) the expression of these proteins, and by WB the rat-IgG brain parenchyma deposition. Finally, a bicameral model (rat blood-CSF barrier) was established to measure clearance of NMO-IgG (n=3) and control-IgG over 24 hours.

Results: In BIM, claudin-5 levels decreased by 25% after NMO-IgG exposition compared to MEM (p=0.03). Similarly, there was a claudin-5 diminution in 5/6 PCEC exposed to NMO-IgG compared to those exposed to control-IgG or MEM. By IHC, there was a claudin-5 decrease in certain periventricular areas and, by WB, a rat-IgG parenchyma deposition in rat-NMO compared to control-rat. Bicameral model indicated that NMO-IgG clearance was increased compared to control-IgG (p<0.05).

Conclusion: Human NMO-IgG induces both structural and functional alteration in BBB, suggesting a direct role of NMO-IgG on modulation of BBB permeability.

Disclosure: Nothing to disclose

O4102

Immunemediated necrotizing autoimmune myopathy: Dutch and Belgian experience

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Background and aims: Immune-mediated necrotizing myopathy (IMNM) - a rare subtype of myositis - is clinically characterized by subacute onset of proximal muscle weakness. Histologically necrotic muscle fibres are the main finding with no/sparse cell infiltration. Solo treatment with corticosteroids is often insufficient necessitating second-line treatment. IMNM can be associated with myositis-specific autoantibodies. We report clinical features, serological data and outcome of 48 patients of Dutch and Belgian origin.

Methods: All patients in whom a diagnosis of IMNM was established over a period of 2012 to 2017 were included. Data on the clinical features and treatment at onset and during the disease course was extracted from the medical charts. Myositis antibodies were assessed (by a commercial lineblot).

Results: Forty-eight patients (33 females) were included with a median age of onset of 54 years (range 20-87). All had proximal muscle weakness, 16 also had dysphagia, 7 dropped head, 2 camptocormia and one required ventilation. IMNM was associated with interstitial lung disease in 5 patients, 11 had another connective tissue disease (mostly systemic sclerosis), 5 had had cancer. Anti-HMGCR antibodies were found in 9 patients, anti-SRP in 13, anti-MDA5 in 1. In 13 patients solo treatment with corticosteroids sufficed, 30 patients needed other immunosuppressants and 14 patients needed IVIg. Five patients had died, 1 myositis-related. In twenty-two patients recovery was good to excellent, in 13 moderate, in 6 poor, 2 were lost-to-follow up.

Conclusion: Immune-mediated necrotizing myopathy is a severe disease often necessitating multimodality treatment resulting in good or excellent recovery in less than half of the patients.

Disclosure: Nothing to disclose

O4103

Spectrum of autoantibodies against myelin oligodendrocyte glycoprotein

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Background and aims: The identification of antibodies to myelin oligodendrocyte glycoprotein (MOG-IgG) may allow stratification of patients with inflammatory CNS disorders. Here, we investigated the abundance of MOG-IgG in a cohort of Turkish patients and determined antibody characteristics.

Methods: 150 serum samples from pediatric and adult patients with multiple sclerosis (MS), non-MS demyelinating CNS disorders including neuromyelitis optica-spectrum disorders (NMOSD), and other inflammatory neurological disorders were tested for MOG-IgG with a cell based assay and flow cytometry. Patients with anti-MOG reactivity were further analyzed for the Ig-subtype and epitope recognition pattern.

Results: 5 adult (1 recurrent optic neuritis, 2 NMOSD, 2 MS) and 4 pediatric patients (2 acute disseminated encephalomyelitis, 1 recurrent optic neuritis, 1 MS) tested positive for MOG-IgG. One additional adult (NMOSD) with an unusually high background on control cells and a high MOG-IgG signal scored positive only after pre-absorption with the non-transfected control cells. Two NMOSD patients had both Aqp4 and MOG-IgGs. Two adult patients had additional Sjögren's syndrome. Two patients reported unusually severe episodes of headache before relapses. Recognized epitopes were unrelated with specific disorders or age groups. IgG1 was the dominant MOG-IgG isotype in 7 patients, IgM was dominant in one adult patient (with Aqp4+ NMOSD) and IgG3 was detected in addition to IgG1 in one pediatric patient with MS.

Conclusion: (1) Some patients with MOG-Ig have additional autoantibodies (AQP4, anti-SSA/SSB, ANA). (2) The isotype may be in addition to the commonly described IgG1 also IgG3 and IgM. (3) Pre-absorption of serum may increase sensitivity to identify MOG-Ig positive patients.

Disclosure: Atay Vural was supported by postdoctoral research fellowship grants from EAN and The Scientific And Technological Research Council Of Turkey (TUBITAK) to do this project in Ludwig-Maximilians University, Munich.

O4104

Clinical utility of 18FDG PET-CT in the diagnosis of neurosarcoidosis

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Background and aims: Sarcoidosis is a multisystem disorder, which affects the nervous system in 5% of cases. The diagnostic process is strived towards determining these granulomas in affected tissue, and 18FDG PET-CT can be used to assess for the optimal biopsy location. The aim of our study was to evaluate the results of 18FDG PET-CT in patients suspected of neurosarcoidosis at our tertiary referral centre.

Methods: In a retrospective observational study we included patients suspected of neurosarcoidosis who underwent a 18FDG PET-CT between 2009 and 2016 at the AMC in Amsterdam.

Results: We found that FDG avidity suggestive for sarcoidosis was found in 24 of 110 patients suspected of neurosarcoidosis (22%), of which 14 (58%) eventually had a biopsy suggestive for sarcoidosis. Of these 24 patients, 3 (18%) also had a chest X-ray and 7 patients (58%) a chest CT-scan suggestive for sarcoidosis (see figure 1). Overall, 18FDG PET-CT led to an additional 2 patients with a biopsy result suggestive for sarcoidosis in patients who also underwent a chest CT-scan. Furthermore, 18FDG PET-CT showed disease activity irrespective of serological markers for disease activity, most notably ACE. Incidental findings were found in 24 of 110 patients (22%). Neurological disease activity in patients with neurosarcoidosis could be detected with 18FDG PET-CT scan in 59% of the cases compared to gadolinium enhancement on MRI of the brain or spinal cord (see figure 2).
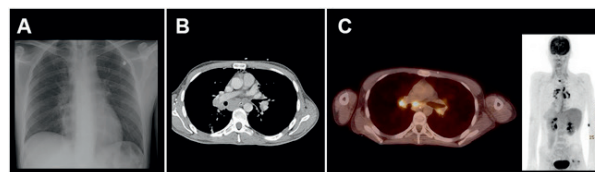
39 year old patient with lymphadenopathy suggestive for sarcoidosis on chest X-ray (A), chest CT-scan (B) and 18FDG PET-CT (C).
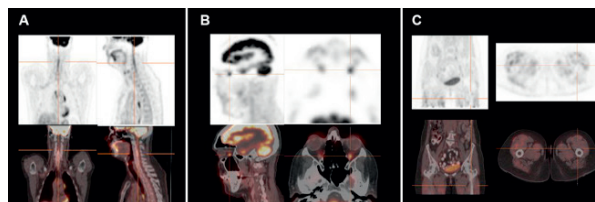
Neurological abnormalities suggestive for neurosarcoidosis on 18FDG PET-CT consisting out of FDG avidity of the spinal cord (A), of the richt optical nerve (B) and muscles (C).

Conclusion: 18FDG PET-CT is a useful investigation when neurosarcoidosis is considered, even in patients with a prior normal CT-thorax and/or normal serological markers.

Disclosure: Nothing to disclose

O4105

Clinical characterization and long-term outcome of patients with autoimmune encephalitis with antibodies against the metabotropic glutamate receptor 5 (mGluR5)

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Background and aims: Few patients have been reported with autoimmune encephalitis and Hodgkin's lymphoma (Ophelia's syndrome) associated with antibodies to the metabotropic glutamate receptor 5 (mGluR5). However, the clinical spectrum and long-term outcome are largely unknown

Methods: Antibodies were determined using known techniques.

Results: We identified 10 patients (2006-2016): median age 29 years, 4/10 females. The main clinical manifestations were psychiatric (9/10), cognitive (8/10), movement disorders (7/10), seizures (6/10), altered consciousness (4/10), and sleep dysfunction (5/8). Median mRS at disease peak was 4.5; 5/10 patients required intensive care. Six patients had a tumor: 5 Hodgkin's lymphoma, 1 small cell lung cancer; the latter had progressive ophthalmoplegia, cognitive changes, gait ataxia and SOX1 antibodies. Of the 6 patients with tumor, 3 received immunotherapy and cancer treatment, and 3 cancer treatment only. The 4 patients without tumor received immunotherapy. At last follow-up (median 30 months) 9/10 patients had complete (6) or partial (3) recovery; 1 patient died. One patient with Hodgkin's lymphoma had a neurological relapse 2.5 years after the first neurologic episode. Ancillary tests showed: CSF pleocytosis in 10/10 patients; oligoclonal bands in 4/7; MRI abnormalities in 5/10 involving temporal (2/5) or extra-temporal regions (3/5), and EEG abnormalities in 5/7. Antibodies were identified in serum and CSF of all paired samples (5/10).

Conclusion: Anti-mGluR5 encephalitis is characterized by limbic and extra-limbic manifestations and can occur in the absence of a tumor. Patients with tumors other than Hodgkin's lymphoma may develop an atypical clinical syndrome. Patients respond to immunotherapy (and cancer treatment), but relapses can occur.

O4106

Discrimination of spinal cord sarcoidosis from neuromyelitis optica spectrum disorder or spondylotic myelopathy

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Background and aims: Spinal cord sarcoidosis (SCS) often manifests as long myelitis or mimics spondylotic myelopathy. We aimed to reveal clinical and radiological features of SCS to discriminate the disease from neuromyelitis optica spectrum disorder (NMOSD) or spondylotic myelopathy.

Methods: We retrospectively reviewed clinical data and MRI findings of patients with SCS; compared the features to those with NMOSD or spondylotic myelopathy.

Results: Numbers of patients and spinal cord lesions (SCLs) were SCS (n = 19, 24 SCLs), NMOSD (n = 43, 46 SCLs), and spondylotic myelopathy (n = 20, 20 SCLs). The predilection for SCL was C5 vertebral segment (11/24, 46%) in SCS, Th6 and Th7 (18/46, 39%) in NMOSD, and C5 (16/20, 80%) in spondylotic myelopathy. The prevalence of long myelitis ($\geq$ 3 vertebral segments) was SCS (11/19, 58%), NMOSD (36/43, 84%), and spondylotic myelopathy (6/20, 30%). The characteristic enhancement pattern on MRI was vascular-territorial in SCS, gray-matter predominant in NMOSD, and circumferential in spondylotic myelopathy. The coincidence rate of SCL with spondylotic compression was higher in SCS (11/24, 46%) than that in NMOSD (2/46, 4.3%) (P < 0.01). Such coincidence was observed exclusively in elder patients (> 50 years old) with SCS. The SCS patients harboring spondylotic compression showed recurrent and intractable clinical course.

Conclusion: SCS manifested as long myelitis at considerably high prevalence. The vascular-territorial enhancement was a discriminative MRI feature of SCS. SCS frequently affected the spinal cord with spondylotic compression especially in elder patients; showed intractable clinical course in patients with spondylotic compression.

O4107

Clinical and immunological characteristics of the spectrum of GFAP autoimmunity: Novel findings in a case series of 20 patients

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Background and aims: Autoantibodies specific for the glial fibrillary acidic protein (GFAP) have been recently detected in patients with autoimmune meningoencephalomyelitis. (Fang et al. JAMA Neurol., 2016). Here we report the clinical and immunological characteristics of 20 new patients.

Methods: From January 2012 to December 2016 we recruited 436 patients with suspected neurological autoimmunity admitted to our Institution. Patients' Serum and CSF samples were tested for neural autoantibodies by immunohistochemistry on mouse and rat brain, by cell-based assays (CBA) using HEK293 cells transfected with neuronal plasma membrane antigens and by immunocytochemistry on rat cortical and hippocampal neurons. GFAP autoantibody positivity was confirmed by CBA using cells transfected with the cDNA encoding the human alpha or delta GFAP and by immunoblot employing recombinant GFAP proteins

Results: Serum and/or CSF IgG of 20/436 (5%) patients bound to human GFAP (20/20 bound to the human GFAP alpha isoform and 13/20 to both the GFAP alpha and the GFAP delta isoforms, none to the GFAP delta isoform only). The neurological presentation was: meningoencephalitis in 9, movement disorder (choreoathetosis or myoclonus) in 3, AED-resistant epilepsy in 3, myelitis in 2, cerebellar ataxia in 2, optic neuritis in 1. Coexisting neural autoantibodies were detected in 5 patients. Neoplasms were found in 3 patients (breast carcinoma, 1; ovarian carcinoma, 1; thymoma, 1). Eighteen patients were treated with immunotherapy and 14 patients improved.

Conclusion: GFAP autoimmunity is not rare. The clinical spectrum encompasses meningoencephalitis, myelitis, movement disorders, epilepsy and cerebellar ataxia. Coexisting neurological autoimmunity is common. Immunotherapy is beneficial.

Disclosure: Nothing to disclose

Headache and pain 2

O4108

Real-world treatment utilisation and safety of onabotulinumtoxinA for chronic migraine: results from an observational study in the European Union

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Background and aims: This post-authorisation study monitored utilisation patterns and safety of prophylactic treatment of onabotulinumtoxinA for chronic migraine (CM) in routine clinical practice.
Methods: This prospective, multinational (Germany, Spain, Sweden, United Kingdom [UK]) study observed onabotulinumtoxinA treatment in adults with CM. Data were collected at the first study treatment and at each subsequent treatment for ≤52 weeks for utilisation or ≤64 weeks for safety data.
Results: A total of 1160 patients (Germany, 287 patients; Spain, 232; Sweden, 219; UK, 422) had ≥1 treatment, with 4017 treatments administered overall. The median number of injection sites (n=31) and total dose (155U) was consistent across all treatment sessions and similar across countries. The mean time between treatment sessions was 14.3 weeks (Germany, 14.6; Spain, 14.6; Sweden, 12.6; UK, 15.0) Most patients (74.4%) were satisfied/extremely satisfied with onabotulinumtoxinA treatment (Germany, 61.3%; Spain 86.0%; Sweden, 78.8%; UK, 74.1%). At least one treatment-related adverse event was reported by 25.1% of patients (Germany, 30.7%; Spain 11.2%; Sweden, 17.8%; UK, 32.7%), most frequently neck pain (4.4%). There were no treatment-related deaths.
Conclusion: Utilisation of onabotulinumtoxinA treatment for CM appears to be consistent across Europe. Inter-country variability in patient satisfaction and treatment-related adverse events was observed. No new safety signals were identified.
Disclosure: The funding source for this study is Allergan plc (Dublin, Ireland)

O4109

Prospective testing of ICHD-3 beta diagnostic criteria for migraine with aura and migraine with typical aura in patients with transient ischemic attacks

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Background and aims: The International Classification of Headache Disorders 3rd edition beta (ICHD-3 beta) gave alternative diagnostic criteria for 1.2 migraine with aura (MA) and 1.2.1 migraine with typical aura (MTA) in the appendix. The latter were presumed to better differentiate transient ischemic attacks (TIA) from MA. The aim of the present study was to field test that.
Methods: A neurologist interviewed soon after admission 120 consecutive patients diagnosed with TIA after MRI or CT. Semi-structured interview forms addressed all details of the TIA episode and all information necessary to apply the ICHD-3beta diagnostic criteria for 1.2,1.2.1, A1.2 and A1.2.1.
Results: Requiring at least one identical previous attack, the main body and the appendix criteria performed almost equally well. But requiring only one attack, more than a quarter of TIA patients also fulfilled the main body criteria for 1.2. Specificity was as follows for one attack: 1.2: 0.73, A1.2: 0.91, 1.2.1: 0.88 and A1.2.1: 1.0. Sensitivity when tested against ICHD-2 criteria were 100% for the main body criteria (because they were unchanged) and 96% for A1.2 and 94% for A1.2.1.
Conclusion: The appendix criteria performed much better than the main body criteria for 1.2 MA and 1.2.1 MTA when diagnosing one attack (probable MA). We recommend that the appendix criteria should replace the main body criteria in the ICHD-3.
Disclosure: Nothing to disclose

O4110

Dynamic mechanical hyperalgesia in women with migraine: the dynamic pressure algometry

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Background and aims: We aim to explore the association between dynamic pressure algometry (DPA) with headache features and widespread pressure pain hypersensitivity in migraine and to assess if DPA differentiate between episodic and chronic migraine.

Methods: 120 women with migraine (42% chronic, 58% episodic) participated. Dynamic hyperalgesia was assessed with a DPA set (Aalborg University, Denmark©) consisting of 11 rollers with fixed pressure levels from 500g to 5300g. Each roller was moved at a speed of 0.5 cm/sec over a 60mm horizontal line covering the temporalis muscle. Dynamic pain threshold (DPT-pressure level of the first painful roller) was calculated. Migraine pain features were collected on a headache-diary. As golden standard, static pressure pain thresholds (PPTs) were assessed over the temporalis muscle, C5/C6 joint, second metacarpal and tibialis anterior.

Results: Side-to-side consistency between DPT (r=.769, P<.001) was found. DPT was moderately associated with widespread PPTs (.364>r>.769, all P<.001). No significant association with migraine pain were shown (all, P>.129). Women with chronic migraine exhibited bilateral lower DPT (P<.032), but similar widespread PPTs (all, P>.141) than those with episodic migraine.

Conclusion: DPA was valid for assessing dynamic mechanical hyperalgesia in migraine. DPT was associated with widespread pressure pain sensitivity independently of migraine frequency supporting that dynamic pressure hyperalgesia in the trigeminal area is consistent with generalized pressure pain hyperalgesia. Dynamic, but not static, pressure pain hyperalgesia was able to differentiate between episodic and chronic migraine. Assessing dynamic deep somatic tissue sensitivity may provide a new tool for assessing treatment effects.

Disclosure: Nothing to disclose

O4111

Efficacy of levothyroxine in migraine patients with subclinical hypothyroidism

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Background and aims: Hypothyroidism can be an aggravating factor on primary headaches especially migraine. However, data on outcomes after treatment with levothyroxine are widely lacking. The purpose of this study was to evaluate the effect of treatment of subclinical hypothyroidism in migraine patients

Methods: In this cross-sectional study we evaluated the severity and monthly headache frequency from 45 patients with migraine according to International Classification of Headache Disorders, third edition beta criteria, who referred to outpatient of Eginition Hospital between January 2015 and February 2016 and treated with levothyroxine for two months by completing the questionnaire quality of life (Short-Form questionnaire-36) before and after treatment.

Results: Twenty two women (52%) and 23 males (48%) with a mean age of 62 years were included in the study. In patients with hypothyroidism, the monthly headache attack frequency were (mean ± SD) 14.68 ± 8.8 $1.2 \pm$ attacks vs. 1.86 ± 1.08 p<0.05) and severity of headache (mean ± SD: 6.54 ± 1.6 vs. 1.23 ± 0.77 p<0.05) score and the scores of the quality of life showed a statistically significant decrease after treatment.

Conclusion: To the best of our knowledge, this is the first study showing that treatment of subclinical hypothyroidism was effective in reducing both the frequency and severity of migraine attacks and improvement of quality of life in those patients. Therefore, control tests of thyroid function should be made in migraine patients.

Disclosure: Nothing to disclose

O4112

Phase 3, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of erenumab (AMG 334) in migraine prevention: primary results of the STRIVE Trial

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Background and aims: Efficacy and safety/tolerability of erenumab, a human anti-CGRP receptor monoclonal antibody, were evaluated in episodic migraine (EM) subjects in a multinational, phase 3 trial (NCT02456740).
Methods: Adults with EM (n=955) were randomized 1:1:1 to subcutaneous monthly placebo or erenumab 70mg or 140mg for 24 weeks. The primary endpoint was change from baseline in mean monthly migraine days (MMDs) over weeks 13-24. Secondary endpoints were ≥50% reduction in MMDs; change in acute migraine-specific medication days; change in Physical Impairment (PI) and Impact on Everyday Activities (EA) (as measured by the Migraine Physical Function Impact Diary [MPFID]). P-values are for pairwise comparisons of each erenumab dose with placebo, statistical significance determined after multiplicity adjustment.
Results: Subjects reported 8.3 MMDs at baseline and experienced -3.2, -3.7, and -1.8-day reductions in the 70mg, 140mg, and placebo groups, respectively (p<0.001). A ≥50% reduction in MMDs was achieved by 43%, 50%, and 27% in the 70mg, 140 mg, and placebo groups (p<0.001), and monthly acute migraine-specific medication was reduced by -1.1, -1.6, and -0.2 days (p<0.001). Subjects had improved PI scores (-4.2, -4.8, -2.4 points in the 70mg, 140mg, and placebo groups; p<0.001) and EA scores (-5.5, -5.9, and -3.3 points; p<0.001). The safety/tolerability profile of erenumab was similar to placebo; subjects most frequently reported nasopharyngitis, upper-respiratory-tract infection, and sinusitis.
Conclusion: Erenumab 70mg and 140mg significantly reduced migraine frequency and use of migraine-specific medications, reducing migraine's impact on physical impairment and everyday activities in this EM trial. Numerically greater efficacy was observed for the 140mg dose consistently across endpoints.

O4113

Representation of minorities in clinical trials for migraine in the United States and Europe

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Background and aims: Recognising that minorities have historically been underrepresented in clinical research trials despite poorer health indicators1-3, the U.S. National Institute of Health[NIH] mandates the inclusion and reporting of minorities in NIH-funded studies.4 Europe has no comparable mandate. In this study, we compared the representation of minorities in migraine clinical trials from the U.S. and Europe.
Methods: We searched PubMed using the terms "migraine randomised controlled trial" to identify controlled-trials for migraine treatment published in English since 2011. We excluded pilot studies with <50 participants. We determined the frequency of reporting of minority representation;factors correlated with reporting; and whether minority inclusion rates were representative of the general population.
Results: 36 of 128 trials met our inclusion criteria. 25 of 36 (69.4%) reported ethnicity or race. Exclusively European studies were less likely to report ethnicity than studies conducted at least partly in the U.S. [3 of 7 (42.9%) verses 22 of 27 (81.5%), Chi-square=4.26;p=0.04]. No studies stratified efficacy or safety by ethnicity. Minority representation in European trials could not be compared with the populations of Europe or of European migraineurs since few trials and countries provide data on ethnicity.5
Conclusion: In contrast to those conducted in the U.S., few European migraine clinical trials report ethnicity. Since minorities have disproportionately poor health outcomes, and since medication effectiveness and toxicity can differ by race and genetic make-up6-9, future studies should strive to increase minority participation and investigate race-based differences in migraine expression, treatment response, and medication toxicity.

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Abstract references

Table 1. Migraine controlled treatment trials 2011-2016, n=36

lead author, year	n	intervention*	gender or sex data reported	ethnicity or race data reported	% of sample female	% of sample white	results by gender	results by race	study region	industry funded
Sun, 2016[3]	483	CGRP* antagonist	yes	yes	81	92	no	no	Worldwide	yes
Bigal, 2015[7]	297	CGRP antagonist	yes	yes	88	78	no	no	US	yes
Bigal, 2015[5]	264	CGRP antagonist	yes	yes	86	83	no	no	US	yes
Buettner, 2015[4]	57	vitamin D / simvastatin[b]	yes	yes	91	79	no	no	US	no
Tepper, 2015[5]	275	intranasal sumatriptan	yes	no	85	n/a	no	no	US	yes
Hagen, 2015[6]	72	acetylcarnitine	yes	no	83	n/a	no	no	Europe	no
Dilli, 2015[7]	69	occipital nerve block	yes	no	80	n/a	no	no	US	no
Cady, 2015[8]	230	intranasal sumatriptan	yes	yes	84	86	no	no	US	yes
Dodick, 2014[9]	163	CGRP antagonist	yes	yes	82	81	no	no	US	yes
Dodick, 2014[10]	218	CGRP antagonist	yes	yes	85	69	no	no	US	yes
Ho, 2014[11]	660	CGRP antagonist	yes	yes	84	90	no	no	US	yes
Chabi, 2015[12]	235	orexin antagonist	yes	yes	84	82	no	no	US	yes
Friedman, 2014[13]	330	valproate v metoclopramide v ketorolac[c]	yes	yes	84	2	no	no	US	no
Tullo, 2014[14]	314	frovatriptan +/- dexketoprofen[d]	yes	no	87	n/a	no	no	Europe	yes
Asadollahi, 2014[15]	216	sumatriptan +/- promethazine	yes	no	74	n/a	no	no	Near East	yes
Silberstein, 2014[16]	443	sumatriptan / naproxen	yes	yes	75	91	no	no	US	yes
Marcus, 2014[17]	885	CGRP antagonist	yes	yes	83	84	no	no	US	yes
Gomez, 2014[18]	75	AMPA* antagonist	yes	yes	85	91	no	no	Worldwide	yes
Schoenen, 2013[19]	67	supraorbital nerve stimulator	yes	no	91	n/a	no	no	Europe	no
Silberstein, 2013[20]	523	gabapentin	yes	yes	82	83	no	no	US/Canada	yes
Silberstein, 2012[21]	157	occipital nerve stimulator	yes	no	78	n/a	no	no	US	yes
Pfaffenrath, 2012[22]	140	intranasal toradol	yes	yes	92	99	no	no	Europe	yes
Farkkila, 2012[23]	512	5-HT[1F] agonist	yes	yes	87	99	no	no	Europe	yes
Silberstein, 2012[24]	171	topiramate +/- propranolol	yes	yes	90	85	no	no	US	yes
Ho, 2012[25]	165	CGRP antagonist	yes	yes	60	83	no	no	Worldwide	yes
Derosier, 2012[26]	442	naproxen/sumatriptan v butalbital	yes	yes	88	83	no	no	US	yes
Seeburger, 2012[27]	100	rizatriptan	yes	yes	92	99	no	no	Worldwide	yes
Yang 2011[28]	66	acupuncture v topiramate	yes	no	89	n/a	no	no	Asia	no
Varkey, 2011[29]	91	exercise v topiramate	yes	no	90	n/a	no	no	Europe	no
Hewitt, 2011[30]	543	CGRP antagonist + ibuprofen v acetaminophen	yes	no	87	n/a	no	no	Worldwide	yes
Aurora, 2011[31]	903	inhaled dihydroergotamine	yes	yes	92	86	no	no	US	yes
Hewitt, 2011[32]	547	CGRP antagonist	yes	yes	87	94	no	no	Worldwide	yes
Latsko, 2011[33]	75	frovatriptan	yes	no	78	n/a	no	no	US	yes
Diener,2011[34]	341	CGRP antagonist	yes	yes	83	87	no	no	Europe	yes
Connor, 2011[35]	1068	CGRP antagonist	yes	yes	77	85	no	no	Worldwide	yes
Lipton, 2011[36]	340	topiramate	yes	yes	89	82	no	no	US	yes

*when a single agent is provided, this drug is compared with placebo; *CGRP = calcitonin-gene related peptide; * / * = combination therapy; ° v * = verses (comparison study); *+ / - x* = comparison with or without the study drug x; *AMPA = α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid; [F]5-HT = serotonin

Table 1. Migraine controlled treatment trials 2011-2016, n=36

Table 1 references

Disclosure: Nothing to disclose

Movement disorders 2

O4114

Differential diagnosis between Parkinson's disease and essential tremor using the smartphone built-in accelerometer

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Background and aims: Differential diagnosis of tremors is still challenging, particularly between Parkinson's disease (PD) and essential tremor (ET) patients. We examined whether recording with the built-in accelerometers of a smartphone, and time-frequency analysis of the signal, could show differences in tremor characteristics between PD and ET. This might help neurologists in environments where more sophisticated diagnostic techniques are unavailable.

Methods: We recorded with the smartphone 30 s of rest and postural tremor in 17 patients with PD, 16 patients with ET and 12 healthy volunteers. Data were fed into a personal computer for signal processing. We generated frequency power spectra and calculated receiver operating characteristics (ROC) curve of total spectral power index, to establish a threshold to separate subjects with and without tremor. Patients who showed relevant tremor based on this threshold were further analysed, and ROC curve measure of relative energy index was computed to establish a threshold to discriminate PD from ET.

Results: Total spectral power showed $96.6 \pm 2.1\%$ accuracy in the discrimination of subjects with and without tremor (sensitivity 97.6%; specificity 83.3%). In subjects with tremor, relative energy index of tremor discriminated PD from ET with $84.6 \pm 7.2\%$ accuracy, with a sensitivity of 82.4% and specificity of 81.2% (interval of confidence: 95%).
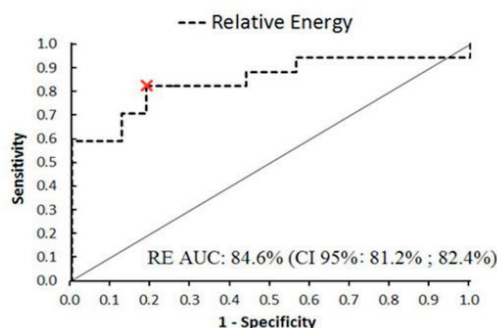
FIGURE. Receiver Operating Characteristics (ROC) curve of Relative Energy A (rest tremor) / B (postural tremor) in Essential Tremor and Parkinson disease shows 82.4% sensibility and 81.2% specificity in discrimination. AUC, area under the curve. CI, Confidence Interval.

Figure

Conclusion: This study demonstrates that smartphones can detect tremor and accurately discriminate PD from ET under unsophisticated clinical conditions. Our method can be implemented into a smartphone application to give immediate results for the clinician to gain valuable information for the diagnosis of tremor.
Disclosure: Nothing to disclose

O4115

Severity of impulsive compulsive behaviours in early and prodromal Parkinson's disease

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Background and aims: Impulse control behaviours (ICB's) are a recognised side-effect of dopaminergic medication in Parkinson's disease (PD). In their severe form, they are known as impulsive control disorders (ICD). The severity varies significantly, some patients report mild ICB, while others exhibit severe symptoms. The severity of ICB's (including mild symptoms) in early Parkinson's is not well known. In this cross-sectional study, we report the severity of ICB's in early PD, prodromal PD (using a group with (REM sleep behaviour disorder (RBD)) and a control group.

Methods: We embedded a detailed cross-sectional study within the Discovery study (Thames Valley, UK). Participants were identified as being at risk of ICD using the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's (QUIP) and those above threshold were invited to an interview using the Parkinson's impulse-control scale to grade severity.

Results: In September 2015 there were 1,544 patients enrolled into the Discovery cohort, of which 317 (20.5%, 95% CI 18.5, 22.6)) were at risk of ICD following screening; 142 participants were subsequently interviewed. Of those initially screening positive on the QUIP: 39/90 PD patients (43.3%, 95% CI 32.9, 54.2) were affected with ICB and 10 met the criteria for ICD (11.1%, 95% CI 5.5, 19.5%); 5/19 RBD patients (26.3%, 95% CI 9.1, 51.2%) and 7/33 controls (21.2, 95% CI 9.0, 38.9) were affected with ICB.

Conclusion: This study demonstrates that ICB are common in early Parkinson's and future studies should consider syndromal and subsyndromal symptoms.
Disclosure: Nothing to disclose

O4116

Prevalence of C9orf72 expansion in a Portuguese cohort of Huntington's disease phenocopies

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Background and aims: Around 1% of patients in whom Huntington disease (HD) is clinically suspected, CAG repeat expansion in HTT gene is not identified. Several genetic diseases are known to cause HD phenocopies. Recently, the expansion in C9orf72 gene was reported as the most common genetic cause. We aimed to determine the prevalence of C9orf72 expansion in a cohort of HD phenocopies.

Methods: We identified HD phenotype patients in whom expansion in HTT gene was tested, assisted in the Movement Disorders Unit in a tertiary centre. The expansion in C9orf72 gene was tested in HD phenotype patients without diagnosis. We analysed the prevalence of this mutation and revised demographic and clinical characteristics.

Results: We identified 192 patients: 165 had HD, 3 neuroacanthocytosis, 2 vascular chorea, 1 PARK7 and 1 PKAN. The expansion in C9orf72 gene was tested in 20 HD phenocopy patients without diagnosis and was identified in 2 (10%). A man (case 1) and a woman (case 2) presented chorea, dementia and behaviour disorder since the age of 62 and 50, respectively. Autosomal dominant inheritance was identified in both. Oromandibular chorea was the most prominent motor symptom in both, along with segmental dystonia. Case 1 had multi-domain cognitive impairment and profound apathy; while in case 2 prevailed psychotic activity. Brain MRI showed subcortical generalized atrophy in both.

Conclusion: In our cohort, the expansion in C9orf72 gene was identified in 10% of HD phenocopies without diagnosis, corroborating the necessity of being considered in the differential diagnosis. We emphasize the clinical variability, particularly in the neuropsychiatric presentation.

Disclosure: Nothing to disclose

O4117

A multimodal magnetic resonance imaging study of brain structural changes in spasmodic dysphonia

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Background and aims: The pathophysiology of spasmodic dysphonia is poorly understood. This study evaluated patterns of cortical morphology, basal ganglia, and white matter microstructural alterations in patients with spasmodic dysphonia relative to healthy controls.

Methods: T1-weighted and diffusion tensor magnetic resonance imaging (MRI) scans were obtained from 13 spasmodic dysphonia patients and 30 controls. Tract-based spatial statistics was applied to compare diffusion tensor MRI indices (i.e., mean, radial and axial diffusivities, and fractional anisotropy) between groups on a voxel-by-voxel basis. Cortical measures were analyzed using surface-based morphometry. Basal ganglia were segmented on T1-weighted images, and volumes and diffusion tensor MRI metrics of nuclei were measured.

Results: Relative to controls, patients with spasmodic dysphonia showed increased cortical surface area of the primary somatosensory cortex bilaterally in a region consistent with the buccal sensory representation, as well as right primary motor cortex, left superior temporal, supramarginal and superior frontal gyri. A decreased cortical area was found in the rolandic operculum bilaterally, left superior/inferior parietal and lingual gyri, as well as in the right angular gyrus. Compared to controls, spasmodic dysphonia patients showed increased diffusivities and decreased fractional anisotropy of the corpus callosum and major white matter tracts, in the right hemisphere. Altered diffusion tensor MRI measures were found in the right caudate and putamen nuclei with no volumetric changes.

Conclusion: Multi-level alterations in voice-controlling networks, that included regions devoted not only to sensorimotor integration, motor preparation and motor execution, but also processing of auditory and visual information during speech, might have a role in the pathophysiology of spasmodic dysphonia.

Disclosure: Nothing to disclose

O4118

TGF beta 1 as Huntington's disease biomarker

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Background and aims: Huntington's disease (HD) in genetically determined neurodegenerative disorder. Typically triad of symptoms occurs – involuntary movements, psychiatric and cognitive deterioration. Here we present evaluation of serum TGF beta1 level usefulness as HD biomarker. The TGF beta was correlated with psychological assessment, motor disorders and cognitive tests in different severity stages – based on Unified Huntington's disease scale (UHDRS).

Methods: 100 HD-subjects (mean age 46 years old, 51 females) and 40 healthy control matched for age and sex were included to the study. Subjects distribution was based on UHDRS scale: 0-13 early, 14-37 mild, 38-67 moderate, >68 severe stage (study groups: 24,23,32,21) mean disease duration was 8 years and average UHDRS - 52. All patients underwent psychological assessment (Stroop tests (ST), Trialmaking test (TT), Symbol Digital Modality test(SDMT), Verbal fluency VF) and neurological examination. Blood was collected from all patients and control group.

Results: Mean level of TGF beta in HD was lower than controls (570 vs controls 648). TGF beta 1 in early stage patients was higher than mild and moderate stage patients, that supports previous theories (662 vs 517 vs 526) [pg/ml], however there were no significant difference in values of TGF between any HD stage or controls. Age of patients in early stage of HD was significantly lower (p=0,0001)and disease duration(including all signs) in early and mild stage significantly varied (p=0.005).

Conclusion: TGF beta 1 can serve as biomarker of transition into the symptomatic phase of Huntington disease

Disclosure: Funds from statutory work for PhD candidates obtained from Medical University of Silesia, Katowice Poland.

O4119

Results from a phase 1b multiple ascending-dose study of PRX002, an anti–alpha-synuclein monoclonal antibody, in patients with Parkinson's Disease

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Background and aims: PRX002 (RG7935) is an investigational monoclonal antibody designed to neutralise extracellular neurotoxic forms of alpha-synuclein. This may inhibit the cell-to-cell transmission of the aggregated form of alpha-synuclein and modify Parkinson's disease (PD) progression. We evaluated PRX002 in patients with PD in a double-blind, placebo-controlled, phase 1b multiple ascending-dose study.

Methods: Patients with mild-moderate PD (Hoehn and Yahr stages 1-3) were enrolled to six escalating-dose cohorts and randomised to receive intravenous PRX002 or placebo (2:1 for 0.3, 1, 3 or 10 mg/kg [n=48] and 3:1 for 30 or 60 mg/kg [n=32]). Safety and tolerability (primary objectives), pharmacokinetics, immunogenicity, pharmacodynamics and clinical effects were assessed.

Results: The intent-to-treat population (n=80) consisted predominantly of Caucasian (97.5%) males (80%; mean age 58.3 years). PRX002 was well tolerated; no serious or severe treatment-emergent adverse events (TEAEs) were reported. TEAEs experienced by ≥5% of patients and >placebo were constipation, infusion-related reactions (IRRs; the only dose-dependent TEAEs), diarrhoea, peripheral oedema and post-lumbar puncture headache. CNS penetration was demonstrated by a dose-dependent increase in PRX002 levels in the CSF. Across all doses, the mean PRX002 concentration in CSF was 0.3% relative to serum. Results showed a rapid dose- and time-dependent mean reduction of serum free alpha-synuclein levels of up to 97% after a single dose (P<0.0001), consistently observed after two additional monthly doses. New trial data will be presented.

Conclusion: PRX002 had an acceptable safety and tolerability profile, penetrated the CNS and reduced serum free alpha-synuclein. A planned phase 2 study will evaluate PRX002 as a disease-modifying treatment for PD.

Disclosure: This study was sponsored by Prothena Biosciences Limited (South San Francisco, CA, USA).

ePoster Session

Saturday, 24 June 2017

Ageing and dementia 1

EP1001

ASL MRI in early diagnosis of Alzheimer's disease: A biomarker suitable for clinical settings?

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Background and aims: Early diagnosis is very important in Alzheimer's Disease as the pathological process, starts years before cognitive impairment gets attention and the patient seeks medical advice. ASL MRI (Arterial Spin Labeling) is a functional MRI,which is a quick and a relatively cheaper method. Also it is safer as it does not require a radioactive material or a contrast agent injection.
Methods: In our study, we used ASL MRI as an early biomarker in patients with cognitive problems. 85 patients were included and 24 of patients had MCI (minimal cognitive impairment), 23 had Alzheimer's Disease, 31 of the patients were diagnosed as having depression and 7 of the patients had subjective memory impairment (SMI).
Results: Bilateral parietal hypoperfusion pattern were found statistically significantly more in the AD and MCI group than depression and SMI group (p<0.001). Additionally a difference, which was significant, was found between MCI and AD. Hypoperfusion rates were 67% among MCI and 83% in AD group. Hypoperfusion rate of ASL maps in depressive patients who did not show cognitive deficits according to neuropsychiatric evaluation was 13% which was significantly lower than MCI and AD groups and similar to the subjective cognitive deficit group (SMI) who also did not show any cognitive deficit in Neuropsychiatric tests.
Conclusion: This study shows that ASL MRI is quick, cheap and easy to access in a clinic where MRI is avaible. It is a valuable method in early evaluation of cognitive deficits and differentiation of the pathology which causes forgetfulness.
Disclosure: Nothing to disclose

EP1002

A trend towards associative binding impairment but not delayed recall impairment of explicit memory by healthy aging decliners vs supernormals: Preliminary data

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Background and aims: We endeavored to investigate if we can find predictors of cognitive decline in healthy aging. Specifically, we wanted to examine Benjamin-Naveh´s associative-deficit hypothesis (ADH) in episodic memory: a major factor in older adults' poorer episodic memory is their deficiency in creating and retrieving links between the representation of two mental codes.
Methods: Healthy participants were followed with cognitive test measures for four years. Afterward, we aimed to compare supernormals (N=20; (73.9±(SD)7.7 years)) with decliners (N=6; (75.8±(SD)8.0 years)) and we wanted to find out if the decliners will show abnormal rates of cognitive decline in episodic memory and brain atrophy. Measures of brain volumes derived from 3 Tesla magnetic resonance imaging scanner (MRI) were acquired, and an automated system (FreeSurfer) was used for further analyses.
Results: Regarding explicit memory measures we found only a trend towards difference based on Mann-Whitney U test between supernormals and decliners in Memory Binding test, an associative binding measure (p=.072, one-tailed), other measures, such as Philadelphia Verbal Learning Test or Logical Memory delayed free recall were not significant (p>.10). Automated segmentation by Freesurfer (version 5.3) did not reveal any groupwise volumetric differences between supernormals and decliners.
Conclusion: There is a trend towards significance in associative binding impairment in healthy aging decliners in comparison to supernormals despite non-significant differences in their brain volume. The data are consistent with Benjamin-Nave's ADH. However, these preliminary results need to be taken with caution and replicated on larger samples.
Disclosure: Supported by the grant "Cognitive Predictors of Neurodegeneration from the Czech Science Foundation," under grant number 16-01781S.

EP1003
Cancelled

EP1004
Computerized attention test web based (CVST) as the key to a screening tool for attention and cognition deficits (http://neurocenter.nl/en_GB)

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Background and aims: The perspective of effective treatment of neurodegenerative cognitive disorders implies an early intervention and therefore a reliable, easy screening tool.

Methods: Clinical neurological experience of over 25 years with regards to early detection and evolution of cognitive impairment by computerized screening tools, was extracted out of a private practice database.Determining cut-off scores for pathology. Explanation of mechanisms leading to false positive results.

Results: Matching of this screening exam with the M.M.S.E., the neuropsychological testing, imaging and the liquor analysis (beta amyloid, tau - fosfotau protein) was done for all diagnosed cases. A normal CVST score lies between 8 and 13 seconds. With a score above 20 seconds., the attention problems interfere with daily life on a significant manner (e.a. driving). Severely abnormal scores (above 25-30 seconds) are a reliable indicator (a warning sign') for underlying organic disorder: MCI and all variants of beginning cognitive impairment (AD, FLD, PDD , LBD e.g.). This clinical finding pushed us to use the test systematically, as vague complaints of headache, vertigo, fear or depression can be the first symptoms of a degenerative process in a population above 65.

Conclusion: 1- The web based CVST is a reliable test for screening attention and memory deficits in first line. Repeating the test over time, gives a consistent and reliable image of the clinical situation and evolution. 2- False positive results are mostly related to anxiety, slowing due to an obsessive behavior, and/or computer-aversion.

Disclosure: Nothing to disclose

EP1005
Complement system dysregulation and quantitative EEG changes in Alzheimer's disease

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Background and aims: Complement dysregulation has been related to Alzheimer's disease (AD) and epileptogenesis. Consistently, it has been demonstrated in animal model studies the role of complement system activation in causing both seizures and neurodegeneration. The aim of the present study is to measure the complement factors in AD patients and correlate their levels with quantitative EEG (qEEG) and CSF AD biomarkers changes.

Methods: Patients affected by AD pathology were compared to patients affected by other neurological disorders (OND). Both AD and OND underwent a protocol including neurological examination, neuropsychological testing, CSF AD biomarkers analysis, EEG, and quantification of serum complement factors concentrations (C3, C4, C1q, CH50, C1inh). In particular, we correlate CSF, serum and clinical data with qEEG analysis selecting the temporal lobe regions (F7, T3, T5, F8, T4, T6). Relative power of EEG bands (delta, theta, alpha and beta) was considered as reference parameter.

Results: We documented the significant reduction of serum C3 levels in AD patients compared to OND (p<0.05). Considering the correlation analysis in the AD group we documented the significant interplay between C1q serum levels and tau/Ab42 ratio (R=-0.61) and between C4 and CSF Ab42 concentrations (R=-0.73). Moreover, we documented significant correlations between lower C1q serum levels and slowing of EEG. Conversely, the reduction of C3 serum concentrations was related to the reduction of faster EEG rhythms

Conclusion: This pilot study reported that complement system dysregulation may occur in AD pathology and may be related to a more severe neurodegeneration and to the pathological slowing of qEEG.

Disclosure: Nothing to disclose

EP1006
Cancelled

EP1007

Effects of physical exercise on Alzheimer´s biomarkers: A systematic review of intervention studies

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Background and aims: Physical exercise may ameliorate symptoms of Alzheimer´s disease (AD). Animal studies have suggested this may be mediated through an effect on AD pathology. Therefore, we undertook a systematic review of randomised trials examining effects of physical exercise on validated AD biomarkers.

Methods: Studies eligible for inclusion were intervention studies of physical exercise with 1 or more of the following AD biomarkers as outcome measures: a) Aβ1-42, Total-tau and/or Phosphorylated-tau in cerebrospinal fluid; b) 18F-FDG-PET imaging, c) amyloid-PET imaging or d) hippocampal volume measured on MRI in healthy subjects, subjects with subjective cognitive complaints, patients with MCI or AD dementia. Databases searched: MEDLINE, EMBASE, Cochrane Register of Controlled Clinical Trials, PsycInfo and Web of Science.

Results: 54205 citations were identified. Of these 7 papers were included, containing 508 participants (252 in intervention group, 256 in control group) (figure 1). Outcome measure was change in hippocampal volume on MRI and AD biomarkers in CSF. Two studies reported an effect of aerobic exercise on hippocampal volume. One study found an absolute increase in the volume of the anterior hippocampus, which was significant compared to the control group. Another study found a detrimental effect of aerobic exercise in CA2/3 and dentate gyrus/CA4 subregions relative to the control group.

Time of Examination	Indicators	Group 1	Group 2	
		Tempo-rhythmic correction	Control	
Initial	Step Variability Factor (SVF)	0.51±0.09	0.52±0.06	
	Average Step Length (ASL)	38.00±6.44	36.2±3.96	
In 6 months	Step Variability Factor (SVF)	0.27±0.07*	0.40±0.06	
	Average Step Length (ASL)	46.85±5.89*	38.21±3.73	

*-p 0.05 (vs. control)

Figure 1: PRISMA flow chart showing flow of citations in the study

Conclusion: The present findings do not support an effect of physical activity on AD biomarkers and subsequently AD pathology. However, evidence is sparse, and therefore a possible effect of physical exercise on AD pathology cannot be ruled out. Further studies applying AD biomarkers in rigorously conducted studies are needed.
Disclosure: Nothing to disclose

EP1008

Association of plasma β-amyloid with cognitive performance and decline in chronic kidney disease

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Background and aims: Decreased β-amyloid (Aβ) clearance from the brain has been suggested to contribute to cerebral Aβ accumulation in Alzheimer's disease. Based on the idea of a dynamic Aβ equilibrium in different body compartments, plasma Aβ levels have been investigated as biomarker candidates for preclinical Alzheimer's pathology, yet with inconsistent results. Since the kidneys are involved in Aβ elimination from the blood, we evaluated how chronic kidney disease (CKD) affects the association between plasma Aβ and cognitive deficits and cognitive decline.

Methods: In 28 CKD patients stages 3-5D and 26 control subjects with comparable vascular risk profile from the New Tools for the Prevention of Cardiovascular Disease in Chronic Kidney Disease (NTCVD) cohort, plasma total Aβ was determined with a highly sensitive electro-chemiluminescence-immunoassay. Cognition was evaluated using a comprehensive battery of ten neuropsychological tests at baseline and 2-year follow-up.

Results: Subjects with high plasma Aβ level (above median) demonstrated a significantly worse baseline cognitive performance than subjects exhibiting low Aβ level (summary score of global cognitive performance at baseline z=-0.46±0.76 vs z=-0.08±0.57, p=0.045). Cognitive performance moderately decreased over the 2-year-follow-up in subjects with high plasma Aβ level (Δz=-0.13±0.51), but increased in subjects with low plasma Aβ level (Δz=0.16±0.41, p=0.023). In linear regression analyses, baseline plasma Aβ was significantly associated with cognitive decline both in unadjusted analyses (β=-0.28, 95% CI= -0.55 to -0.01) and analyses adjusted for age (β=-0.27, 95% CI= -0.54 to -0.01).

Conclusion: Our results suggest the utility of plasma Aβ level in predicting cognitive decline in patients suffering from CKD.
Disclosure: Nothing to disclose

EP1009

Peripheral neuropathy as clinical onset in E200K familial Creutzfeldt-Jakob disease

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Background and aims: To report a case of familial Creutzfeldt-Jakob disease (fCJD) with peripheral neuropathy as unusual clinical presentation and a cluster of 8 members with fCJD in Guadalajara, Spain.

Methods: A non-diabetic 65-year-old male presented a history of 6 middle-aged family members, in an autosomal dominant inheritance pattern, who died of neurological diseases, described as rapidly progressive cognitive and gait impairment. Our patient presented with a history of 4 months characterized by unsteady gait, numbness and paresthesias on both feet. Initial examination evidenced mild gait ataxia, generalized osteotendinous hyporeflexia and distal lower extremities vibratory and tactile hypoesthesia. 2-3 months later, he developed progressive and severe gait ataxia, bilateral appendicular dysmetria, "nocturnal jerks", bilateral hypoacusis, slow and hypometric saccades, decreased visual acuity and lately temporospatial disorientation, visual hallucinations and insomnia that persist daily.

Results: Complementary blood tests for potential causes of acquired ataxia and peripheral neuropathy, including onconeuronal antibodies were negative. 2 craneal MRI showed unspecific brain atrophy, including cerebellum, panmedular MRI was normal and EEG was normal . EMG evidenced a mixed and severe sensory-motor neuropathy. Audiometry exam found a bilateral 50% hearing loss. CSF exam revealed a positive 14-3-3 protein. Genetic testing for PRPN gene evidenced the E200K mutation and a polymorphism in the codon 129 methionine/valine, in heterozygosis.
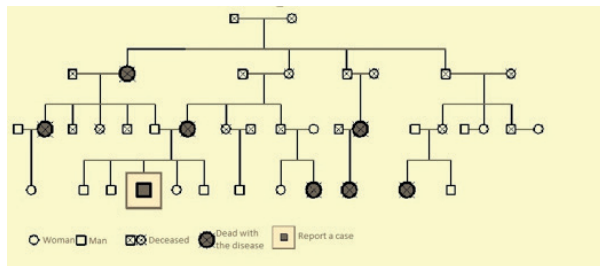
Family tree

Neurophysiological study

Conclusion: An atypical case of familial Creutzfeldt-Jakob disease, presenting with peripheral neuropathy and having delayed central symptoms, is described. A cluster Spanish family with 7 affected members is reported.

Disclosure: Nothing to disclose

EP1010

Cancelled

EP1011

Basal forebrain atrophy is associated with elevated plasmatic homocysteine levels in subjects at risk of Alzheimer's disease

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Background and aims: Increased homocysteine plasmatic level (HPL) is recognized as risk factor for Alzheimer's disease (AD). Basal forebrain (BF) neurons, that are major source of acetylcholine, degenerate early in the course of AD. Recent findings suggest increased HPL lowers the number of BF cholinergic neurons. We aimed to assess the association between HLP, BF and hippocampal volumes in cognitively normal elderly (NC), subjects with subjective cognitive decline (SCD), mild cognitive impairment (MCI) and AD dementia.

Methods: In total 96 subjects; NC (n=11); SCD (n=30); MCI (n=39); AD (n=14) had volumetric brain MRI at 1.5T and blood sampling. Hippocampal and BF volumes were computed using a mask based on cytoarchitectonic map derived from a postmortem brain. MRI scans were time-matched with HLP blood sampling. Analysis of variance and multiple linear regression were used to assess mutual associations.

Results: Elevated HPL was associated with lower BF volumes (R2=0.52; p=0.016). Analysis of separate BF nuclei showed associations of HPL with medial septum, vertical limb of diagonal band (DB) (R2=0.25; p=0.01), nucleus subputaminalis (R2=0.38; p=0.04) and horizontal DB limb (R2=0.48; p=0.03). There was no association between HPL and hippocampal volume.

Conclusion: The HPL is associated with BF but not with

hippocampal atrophy. This agrees with animal studies showing that hyperhomocysteinemia is associated with reduction in number of BF cholinergic neurons. Our data suggest that increased HPL may be one of the factors contributing to early degeneration of BF during the course of AD.

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EP1012

Cancelled

EP1013

Hypothalamic dysfunction is related to sleep impairment and CSF biomarkers in Alzheimer's disease

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Background and aims: Hypothalamus is a key brain region affected by the Alzheimer's disease (AD) pathology and regulating several essential homeostatic functions, including the sleep-wake cycle. We investigated the possible in vivo alteration of the hypothalamus and its correlations with sleep impairment and cerebrospinal-fluid (CSF) AD biomarkers changes in a population of AD patients compared to non-demented elderly controls.

Methods: We measured the polysomnographic sleep, the CSF AD biomarkers and orexin levels, and the hypothalamic [18F] FDG PET uptake in a population of AD patients.

Results: We documented the significant reduction of hypothalamic [18F]FDG PET uptake in the AD group (n=18) compared to the Control 2 group (n=18) (p<0.01). Moreover, we found the increase of CSF orexin levels coupled with the marked alteration of the nocturnal sleep in the AD group as compared to the Control 1 group (n=15) (p<0.05). Finally, we observed the significant association linking the reduction of both sleep efficiency and REM sleep to the reduction of hypothalamic [18F]FDG PET uptake in the AD group. Moreover, [18F]FDG PET hypothalamic uptake correlated with the higher ratio of total-tau/beta-amyloid42 CSF levels (index of more marked neurodegeneration). Finally, we documented a connection between the hypothalamus and the limbic system in the control group, which was not evident in the AD group.

Conclusion: In conclusion, we documented the in vivo dysfunction of the hypothalamus in AD patients, which was correlated with both the impairment of nocturnal sleep and the CSF index of more marked AD neurodegeneration.

Disclosure: Nothing to disclose

EP1014

Frequency and risk factors for appetite and eating disturbances in Alzheimer's disease

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Background and aims: Our goal is to evaluate the frequency of appetite/eating disturbances in Alzheimer's disease (AD) and to determine the features associated with its development.

Methods: A cross-sectional study in 173 consecutive patients with probable AD (NIA-AA criteria) followed-up in a Dementia Unit in Spain (mean age at onset 75.2±6.7 years and mean duration of dementia 3.8±2.0 years, 71.7% women, Mini-Mental State Examination 16.7±6.1). The 12th item in Neuropsychiatric Inventory (NPI) was used to assess appetite/eating disturbances.

Results: Overall, appetite/eating disturbances occurred in 44.5% of participants, and in 35.8% were "clinically relevant" [NPI $\geq$ 4]. These were associated with depression (p=0.042), apathy (p<0.0001), disinhibition (p=0.026), aberrant motor behaviour (p=0.047) and antidepressants use (p=0.013). By domains, 30.6% experienced appetite loss (15% of them coexistent with dysphagia), and it was significantly more prevalent in women, subjects with depression, apathy or antidepressant medication. In contrast, 15.0% presented increase in appetite, change that was more frequent in those individuals with more severe dementia [CDR-3], disinhibition or higher MMSE/year decline. 6.9% had an unusual eating behaviour (e.g. tending to overfill mouth) which was associated with more severe dementia, hallucinations, agitation, multiple drug therapy and rapid progression. Other 6.9% had suffered a change in his/her food preference (e.g. preferring sweet foods more than before) in which a widower status, disinhibition and aberrant motor behaviour were associated factors.

Conclusion: Appetite disturbances are frequent in AD, but risk factors for them differ according to the type of appetite/eating disturbance assessed.

Disclosure: Nothing to disclose

Cerebrovascular diseases 1

EP1015
Cancelled

EP1016
Cancelled

EP1017

Focal cerebral arteriopathy: A well-characterized cause of stroke in pediatric age

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Background and aims: Focal cerebral arteriopathy is an uncommon cause of stroke in pediatric age. This idiopathic clinical syndrome consists of unilateral intracranial arteriopathy involving distal carotid artery and proximal segments of middle and anterior cerebral artery. We present our clinical experience in the management of this entity.
Methods: We present 3 cases of girls with ages between 10 and 16-year-old, admitted to our center with the diagnosis of acute ischemic stroke between 2013 and 2016. Complementary tests including angiography and their evolution, were consistent with the diagnosis of focal cerebral arteriopathy.
Results: At initial evaluation their National Institute of Health Stroke Scale (NIHSS) score was 16 or greater. One patient received intravenous thrombolysis treatment, the other two were beyond the time window. Another patient underwent endovascular treatment 8 hours from stroke onset. In all cases, the angiographic studies showed supraclinoid carotid and ipsilateral proximal middle cerebral artery involvement, which consisted of focal stenosis. Radiological worsening at 6 months was observed in one patient, without clinical relevance. All patients had characteristic lenticulostriate infarction demonstrated on MRI. A complete etiological study was performed, with no additional findings. None presented new ischemic events and all showed a trend for clinical improvement.
Conclusion: Focal cerebral arteriopathy is a typical pediatric disease with a characteristic vascular involvement pattern. It has an overall good prognosis although it is necessary to consider the possibility of radiological worsening.
Disclosure: Nothing to disclose

EP1018

Optimal glucose control may prevent small-artery occlusion subtype of ischemic stroke in patients with type 2 diabetes mellitus

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Background and aims: Although optimal glycemic control is recommended in patients with type 2 diabetes mellitus (DM), whether this can prevent ischemic stroke, remains unclear. Our study investigated whether optimal glycemic control could influence etiologic patho-mechanism of acute stroke in patients with DM.
Methods: We studied acute ischemic stroke patients who were admitted between January 2009 and December 2013 and had been treated with hypoglycemic agents. The controlled group comprised patients with less than glycated hemoglobin level (HbA1c) 7% at admission. The clinical characteristics, laboratory results, antidiabetic drugs, and stroke subtypes (large-artery atherosclerosis, cardioembolism, and small-artery occlusion) were compared between controlled and uncontrolled groups.
Results: Of 259 patients with DM (female 43.7%, mean age 68.5±9.6 years), only 82 patients (31.7%) showed a controlled HbA1c. Small-artery occlusion subtype was most common (43.5%) in uncontrolled group and was the least common (26.8%) in controlled group. The HbA1c showed 7.9% (IQR 7.1–9.2) in small-artery occlusion, 7.4% (IQR 6.8–8.5, p=0.029) in large-artery atherosclerosis, and 7.2% (IQR 6.3–7.8, p=0.001) in cardioembolism. In addition to low density lipoprotein-cholesterol and high density lipoprotein-cholesterol levels, small-artery occlusion subtype was independently associated with HbA1c (odd ratio 1.26; 95% confidence interval 1.05-1.51, p=0.011). However, HbA1c was not associated with large-artery atherosclerosis subtype, and with the class of antidiabetic agents.
Conclusion: In patients with DM, optimal glycemic control may reduce the incidence of the small-artery occlusion subtype of ischemic stroke, not large-artery atherosclerosis subtype.
Disclosure: Nothing to disclose

EP1019

Why are there so many cerebral infarcts in the same hemisphere? Adult presentation of Dyke-Davidoff-Masson Syndrome or acquired hemiatrophy.

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Background and aims: To present a patient with Dyke-Davidoff-Masson syndrome as a rare cause of susceptibility to repetitive ischemic strokes in the same cerebral hemisphere.

Methods: A 62-year-old woman with history of severe mitral valvulopathy associated with atrial fibrillation, partial seizures and recurrent stroke in the left cerebral hemisphere. She had no pre or perinatal complications. However, she had meningoencephalitis with seizures at the age of 28 months. At age 45, she presented a first ischemic event in territory of left posterior cerebral artery that recovered without sequelae, 5 years later she had a isquemic stroke of left middle cerebral artery with mixed aphasia and right hemiplegia that did not improve. 12 years after the first stroke she presented a new infarct of left anterior cerebral artery despite always maintaining therapeutic levels of INR (International Normalized Ratio), dying by respiratory infection during this process.

Results: The vascular study to causes of recurrent stroke was normal after extensive study, however, in all the neuroimaging performed, additionally to the areas of malacia corresponding to the previous infarctions, marked atrophy of the left hemisphere was evident, predominantly in the cerebral peduncle, cerebellar hemisphere, thalamus and frontoparietal cortex. Given this clinical context, we established the diagnosis of Dyke-Davidoff-Masson Syndrome acquired.
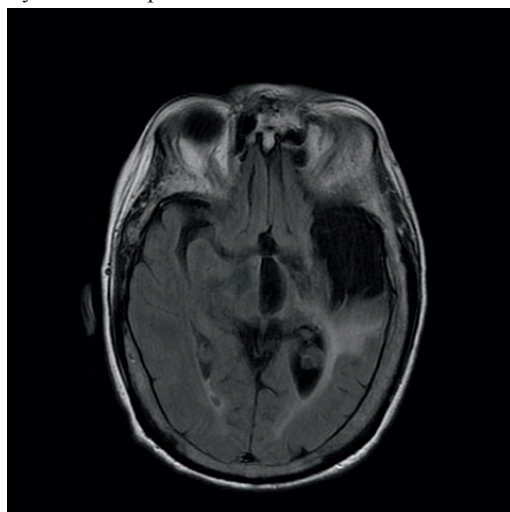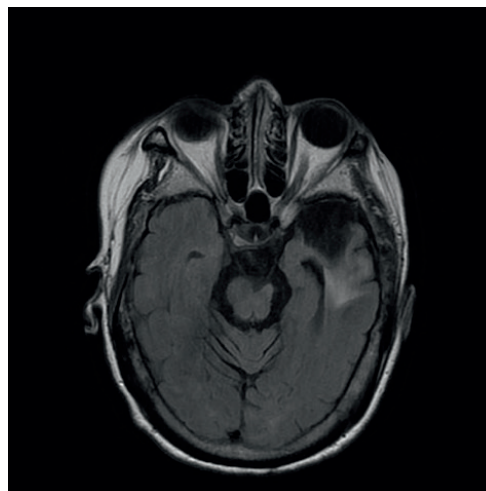
Left cerebral peduncle atrophy.
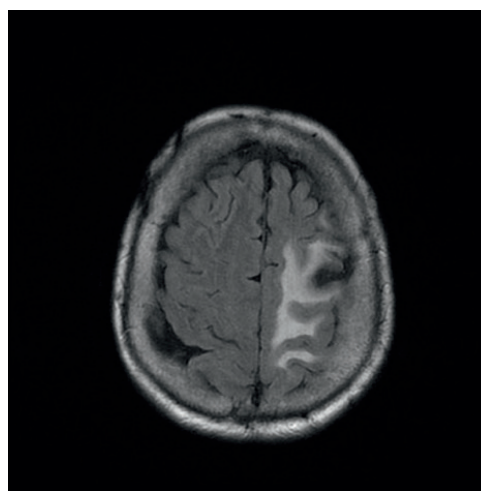
Left cortical atrophy.

Conclusion: This case shows a rare form of recurrent ictus in a hemisphere and its identification would allow to generate longitudinal studies to ascertain the natural course of this syndrome especially in an adult population, which would help in planning approaches to the time, nature of interventions and management accordingly.

Disclosure: Nothing to disclose

Left thalamic atrophy.

EP1020

Voluntary control of plegic limb during yawning after stroke

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Background and aims: Stereotyped movements of paretic limbs during yawning in stroke patients are common, although rarely reported. They are described as involuntary actions.

Methods: We present the first report of voluntary control of a plegic superior limb during yawning.

Results: 59-year-old patient, admitted with an acute left middle cerebral artery stroke (NIHSS 12). Endovenous thrombolysis was administered but plegia of the right superior limb persisted. Since the first hours of stroke, the patient presented with a stereotyped movement with flexion of the elbow of the plegic limb while yawing. Remarkably, at day 6, patient started to have voluntary movement control of the plegic limb while yawning. Ability to touch the chin or the left shoulder with the right hand according to the request of the observer was documented by video. MRI showed an ischemic lesion involving lenticular nucleus, anterior and posterior limbs of internal capsule, body of caudate nucleus and corona radiate. We performed an overlay study using two patients with lenticulo-capsulo-radiate lesions as controls. Softwares FSL and MRIcron were used. Analysis showed that this patient had more involvement of the anterior, posterior and inferior regions of the putamen, although the difference was not significant. Motor deficit improved to paresis after 30 days. The described phenomenon remained.

Conclusion: To our knowledge this is the first report of voluntary control of a plegic limbic during yawning. Lesion overlay studies with more controls can contribute to the identification of a specific lesion pattern underlying this singular phenomenon.

Disclosure: Nothing to disclose

EP1021

Prognostic value of prealbumin in patients with ischemic stroke

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Background and aims: Blood–cerebrospinal fluid barrier (BCSFB) maintains stable and well controlled environment which is essential for the central nervous system functions. The probable link between brain ischemia and capabilities of BCSFB located in choroid plexus has not been extensively explored. Prealbumin (PA) is a protein synthesized in the liver as well as in the choroid plexus. We investigated the possible association between levels of this protein and outcome in ischemic stroke.

Methods: In this prospective observational study 81 patients with acute ischemic stroke consecutively admitted to Stroke Unit were included. The functional status at the day of hospital discharge was evaluated with the modified Rankin Scale (mRS) and the patients were classified into two groups: unfavorable (mRS score $\geq$ 3) and good (mRS score<3) outcome. In multivariate analysis we assesed the relations of PA levels with the unfavorable outcome. One-year mortality was analyzed by Kaplan–Meier survival curves stratified by mean value of PA.

Results: Compared with patients with mRS <3, patients with an unfavorable outcome at hospital discharge had significantly lower PA levels (P<0.0001). In multivariate analysis, PA was an independent predictor for unfavorable outcome at the day of hospital discharge (adjusted odds ratio =0.96; 95% CI: 0.9–0.99, P<0.05). Patients with lower PA concentration had a higher risk for death, in contrast with patients in whom PA levels exceeded mean value=46.9 mg/dl (p=0.02).

Conclusion: The serum PA level status is associated with the functional outcome in patients with acute ischemic stroke. It coud be useful factor in stroke outcome prognosis.

Disclosure: Nothing to disclose

EP1022

Cerebrovascular disease in a Sicilian elderly community: Results from a population based study

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Background and aims: Stroke is one of the most disabling and burdensome health conditions worldwide. Our aim was to assess incidence and mortality rates of cerebrovascular disease, in a Sicilian population using data from a population-based survey of elderly participants.

Methods: A door-to-door survey was carried out in the city of Bagheria, Sicily (prevalence day September 30th, 2006). A cohort of 2,200 persons was randomly stratified, obtaining a 25% sample of the whole population aged 65 years or more. We obtained clinical data for the whole cohort after nine year from local Health Institution. Individuals were evaluated at baseline (2007-2008) and at the end of follow-up period (2016). We calculated crude, and age and sex specific incidence rates, as well as cause specific mortality rates, with 95% confidence intervals.

Results: We identified 176 incident patients with cerebrovascular disease during the follow up giving a total incidence of 888.9/100,000 person years (CI: 888.86-888.94). Incidence rate was higher in men (1010.00, CI: 1009.94-1010.06) than women (790.30; CI: 790.24-790.36). Cause specific mortality rate for CVD was 353.54/100,000 (CI: 353.50-353.58) in the whol cohort, 420.12 in men (CI: 420.06-420.18) and 297.54 in women (CI: 297.48-297.60). Age-specific incidence rates of cerebrovascular disease increased with advancing age.

Conclusion: In the Bagheria Cohort study, incidence of cerebrovascular diseases increased with age. Stroke incidence rates and mortality were significantly higher for men compared to women. Our incidence rates provide new estimates for projection of future burden of disease in Italy and should be considered when planning prevention and stroke care services in this region.

Disclosure: Nothing to disclose

EP1023

ECG changes and its effect on prognosis in acute ischemic stroke patients without cardiac pathology

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Background and aims: Acute ischemic stroke has effect on ECG results and cardiac enzyme levels, but its mechanism has not been clearly established. Our aim in this study is to research ECG and cardiac enzyme changes in acute ischemic stroke and to investigate association between these changes and stroke localization, infarct volume.

Methods: The study included 241 acute ischemic stroke patients. Patients with any cardiac pathology and stroke history were excluded. Only patients with normal echocardiography results were included. The risk factors for stroke, CK-MB and TnI levels were recorded. The infarct sizes, localizations and volumes were analysed in MR images. In addition NIHSS scores were noted at application and discharge. ECG results (QTc interval, PR interval, QRS duration, RR interval, ST depression) were measured by a cardiologist. Bazett's formula was utilized to analyse ECG results and abnormality.

Results: 123 patients were with right hemisphere infarcts (mean age: 68.07+11.37 years) and 118 patients were with left hemisphere infarcts (mean age: 68.20+12.59). HT was more common in right hemisphere infarcts (p=0.013). The most common ECG abnormality was QTc extension (31%). TnI levels were higher in 42 patients. CK-MB and TnI levels were significantly higher in patients with right hemispheric infarts(p<0.05) and TnI levels were also higher in cerebellar infarcts (p=0.008)). NIHSS scores and infarct volumes were higher in left hemisphere and cerebellar infarcts (p<0.05).

Conclusion: The most common ECG abnormality was QTc extension. Right hemisphere and cerebellar infarcts may induce ECG changes and increase cardiac enzymes more often.

Disclosure: Nothing to disclose

EP1024

Rheological properties of blood in different subtypes of acute ischemic stroke

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Background and aims: Despite of the diversity and heterogeneity of clinical manifestations of ischemic cerebrovascular diseases, there are universal pathogenetic mechanisms underlying stroke. Blood rheology has extremely important role in vascularisation of the brain: disturbances in hemorheological parameters provoke the development of zone of ischemia, local stasis, hypoxia.

Methods: The study included 94 patients with acute ischemic stroke (age 62 [53;69] years). Subtypes of stroke were indentified according to criteria TOAST (Figure 1). Rheological properties were assessed: blood viscosity, plasma viscosity, fibrinogen concentration, hematocrit, red blood cell aggregation and deformability. The data is presented in the form of Me [Q1; Q3], Me - median, Q1 and Q3 - the lower and upper quartiles. For statistical analysis was been used χ2 Pearson criterion. The critical level of significance was p<0,05.

Results: Analysis of blood viscosity in all of shear rates had not showed statistically significant differences between groups with different subtypes of stroke (Figure 2). Statistical analysis of plasma viscosity(PV),hematocrit (Ht), deformability in different shear rate (D 90-890), red blood cell aggregation (T1/2) and fibrinogen concentration (Fb) had not showed statistically significant differences between groups with different subtypes of stroke (Figure 3).
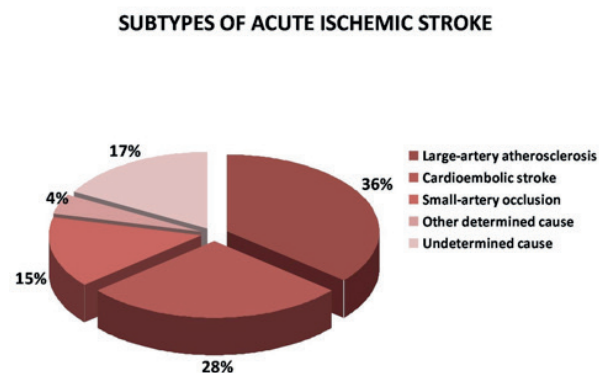
Stroke subtype	Large-artery aterosclerosis	Cardioembolic stroke	Small-artery occlusion	Undetermined cause	p, χ²
vk_3	13,4 [11,9;14,6]	12,2 [10,0;14,1]	13,4 [12,8;16,4]	13,3 [10,4;16,5]	p=0,398, χ2=5,1
vk_5	10,9 [9,9;12,1]	9,9 [8,4;11,8]	10,9 [10,0;12,3]	10,8 [9,0;12,6]	p=0,439, χ2=4,8
vk_7	10,0 [8,9;10,8]	8,3 [7,7;10,5]	9,8 [8,9;10,6]	9,4 [8,8;10,9]	p=0,748, χ2=2,7
vk_10	8,9 [8,2;10,0]	7,5 [7,3;9,9]	9,0 [7,7;9,4]	8,4 [7,0;9,7]	p=0,670, χ2=3,2
vk_50	6,0 [5,8;6,7]	5,5 [5,2;6,6]	6,4 [5,4;6,5]	5,9 [5,0;6,6]	p=0,676, χ2=3,2
vk_100	5,3 [5,2;6,0]	5,1 [4,7;5,7]	5,8 [4,9;6,0]	5,4 [4,6;6,0]	p=0,615, χ2=3,6
vk_300	5,0 [4,7;5,4]	4,7 [4,5;5,1]	5,3 [4,6;5,5]	5,0 [4,4;5,5]	p=0,568, χ2=3,9

Figure 2. Blood viscosity with different subtypes of ischemic stroke (in shear rate 3-300 s-1)

Stroke subtype	Large-artery aterosclerosis	Cardioembolic stroke	Small-artery occlusion	Undetermined cause	p, χ²
PV	1,6 [1,6;1,7]	1,6 [1,6;1,7]	1,7 [1,7;1,8]	1,7 [1,6;1,8]	p=0,797, χ2=2,4
Ht	43,6 [40,3;47,0]	41,4 [39,5;45,0]	44,4 [42,1;47,9]	40,6 [38,9;41,8]	p=0,666, χ2=3,2
D_90	0,190 [0,159;0,210]	0,157 [0,121;0,204]	0,190 [0,186;0,214]	0,195 [0,179;0,212]	p=0,368, χ2=5,4
D_180	0,212 [0,189;0,297]	0,208 [0,173;0,249]	0,211 [0,203;0,240]	0,260 [0,238;0,271]	p=0,471, χ2=4,6
D_360	0,297 [0,263;0,340]	0,262 [0,232;0,279]	0,263 [0,247;0,293]	0,299 [0,247;0,349]	p=0,439, χ2=4,8
D_890	0,365 [0,329;0,394]	0,320 [0,278;0,336]	0,388 [0,311;0,396]	0,375 [0,311;0,389]	p=0,217, χ2=7,0
T$_{1/2}$	4,6 [3,5;6,6]	4,1 [2,0;6,2]	3,3 [3,0;3,9]	2,9 [2,2;6,5]	p=0,906, χ2=1,6
Fb	3,7 [3,2;4,0]	3,3 [3,1;3,5]	3,3 [2,9;3,6]	3,1 [2,9;3,7]	p=0,530, χ2=3,6

Figure 3. Rheological properties with different subtypes of ischemic stroke

Conclusion: The lack of significant differences in rheological parameters at different subtypes of ischemic stroke shows that the change in blood rheology is a universal pathophysiological mechanism of acute cerebral ischemia.

Disclosure: Nothing to disclose

SUBTYPES OF ACUTE ISCHEMIC STROKE

- 36% Large-artery atherosclerosis
- 28% Cardioembolic stroke
- 15% Small-artery occlusion
- 4% Other determined cause
- 17% Undetermined cause

Figure 1. Subtypes of acute ischemic stroke (TOAST criteria)

EP1025

Blood viscosity in acute ischemic stroke

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Background and aims: Important role in the pathogenesis of ischemic stroke belongs hemorheological properties, leading to diffuse and focal changes in the brain tissue.

Blood viscosity (BV) is one of the main rheological parameters, what is measuring the resistance of blood to flow. The aim of study is evaluation of BV at ischemic stroke in dynamic within 20 days after onset.

Methods: The study included 94 patients with acute ischemic stroke (IS) (age 62 [53;69] years) and 20 control patients, age 55 [54;59]. BV was assessed by rotational viscometry at shear rates 3-300 s-1. BV was been measured in the first 12 hours, in 3-5 and 18 - 20 days of stroke. The data is presented in Me [Q1; Q3]. For statistical analysis was been used nonparametric Mann-Whitney U-test. The critical level was p<0.05.

Results: Patients in the first 12 hours after IS had significant changes in BV in all shear rates compared with control group (Table 1, Figure 1). Patients in 3-5 days after IS had significant changes in blood viscosity: 38% in shear rate 3 s-1 (p=0.002, U=203), 35% in 5 s-1 (p=0.003, U=205), 27% in 7 s-1 (p=0.011, U=232), 19% in 10 s-1(p=0.03, U=257). In 18-20 days after IS patients had difference in BV for 24% in 3 s-1(p=0.023, U=175) and 19% 5 s-1(p=0.03, U=181).
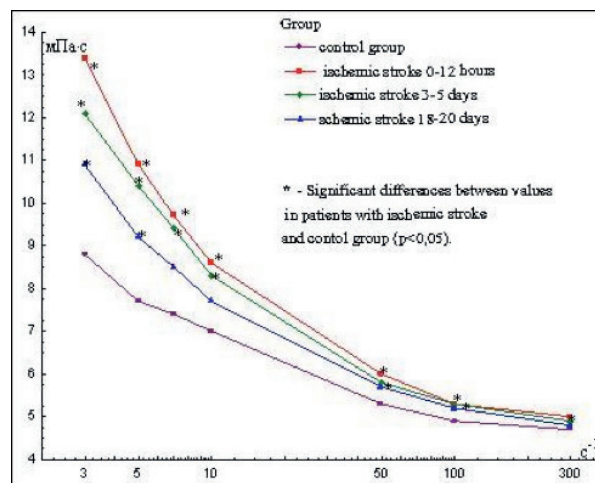
Figure 1. Blood viscosity at different shear rates in patients with ischemic stroke in dynamic within 20 days after onset

Conclusion: We found long-term preservation of increased blood viscosity at low shear rates in ischemic stroke. Hyperviscosity syndrome is the important pathogenetic mechanism at the level of microcirculation in patients with acute cerebral ischemia.

Disclosure: Nothing to disclose

	Ischemic stroke, n=94			Control group, n=20
	0-12 hours	3-5 days	18-20 days	
3 s⁻¹	13,4 [10,4;15,2] *	12,1 [9,5;16,3] *	10,9[10,2;13,6]*	8,8 [8,0;12,5]
5 s⁻¹	10,9 [9,0;12,2]*	10,4 [8,1;12,0] *	9,2 [8,5;10,7] *	7,7[6,4;10,4]
7 s⁻¹	9,7[8,3;10,8]*	9,4[7,5;10,2]*	8,5[7,5;9,7]	7,4[5,9;9,3]
10 s⁻¹	8,6 [7,4;9,9] *	8,3[6,7;9,1] *	7,7[6,8;8,8]	7,0[5,7;8,2]
50 s⁻¹	6,0 [5,4;6,6] *	5,8[5,2;6,3]	5,7[5,2;6,7]	5,3[4,8;5,9]
100 s⁻¹	5,3 [4,9;6,0] *	5,3[4,8;5,6]	5,2[4,7;5,8]	4,9[4,5;5,3]
300 s⁻¹	5,0 [4,5;5,5] *	4,9[4,4;5,2]	4,8[4,4;5,4]	4,7[4,3;4,9]

Table 1. Blood viscosity in patients with ischemic stroke and control group (* – significant differences between values in patients with ischemic stroke and control group)

EP1026
Cancelled

EP1027

Recurrent intracerebral hemorrhage in young age – can traumatic brain injury induce cerebral amyloid angiopathy?

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Background and aims: Cerebral amyloid angiopathy (CAA) by deposition of amyloid-β protein (Aβ) characteristically occurs sporadically in persons aged ≥55 years. Some rare familiar forms can occur at younger ages. We report the case of a young woman with recurrent cerebral hemorrhages with pathological evidence of amyloid-β angiopathy

Results: 33-year-old female, with past history of traumatic brain injury at the age of 1 year with right parietal fracture, requiring cranioplasty at ages of 3,7,8 years, was admitted with sudden onset of left hemiparesis and sensory loss. CT scan showed a right fronto-parietal hematoma. Etiologic investigation, including Digital Subtraction Angiography (DSA), was negative. Six years later, she was readmitted with headache. CT scan showed a lobar hemorrhage in the left frontal lobe. Repeated DSA was normal, lumbar puncture showed low levels of β-amyloid protein. Cerebral biopsy showed severe CAA, with extensive capillary involvement, with scarce amyloid plaques and without tau-pathology or associated-inflammation. Genotyping of APP gene was negative and apolipoprotein-E showed heterozigosiy for ApoE4. In the next months she suffered multiple spontaneous cortical hematomas and she died two months after the last admission.

Conclusion: At younger ages CAA is a rare disease and is normally associated with genetic disease. In our case, the previous history of traumatic brain history cannot be ignore and although its role is not clear, evidence has accumulated about the possible association between traumatic brain injury and CAA particularly at younger ages.

Disclosure: Nothing to disclose

Cerebrovascular diseases 2

EP1028
Cancelled

EP1029

On the role of Na+ in controlling cerebrospinal fluid (CSF) osmolality

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Background and aims: Osmolality plays a relevant role in controlling neuronal cell volume as well as swelling or shrinking under ipo- and iper-osmolality status. Na+ is the major, although the non exclusive, determinant of both CSF and serum osmolality. Serum and CSF osmolalities are in equilibrium due to the equilibrium of major osmolites across the blood-brain barrier. The present study was planned in order to investigate the possibility that CSF Na+ could play an independent role in controlling CSF osmolality

Methods: CSF and sera from 60 patients were employed in this study. Na+, glucose, nitrogen urea were measured using Siemens ADVIA 1800 Chemistry. Osmolality was measured directly or calculated using three different algorithms employing the concentrations of Na+, glucose and urea nitrogen. The osmolality gap was calculated by subtracting the calculated to the measured values.

Table I: computational algorithms employed to calculate serum or CSF osmolality

Algorithms	Furmulae
Alg 1	Osmolality = (2*Na$^+$) + (glucose/18) + (urea nitrogen/2.8)
Alg 2	Osmolality = (1.86*Na$^+$) + (glucose/18) + (urea nitrogen/2.8) + 9
Alg 3	Osmolality = ((1.86*Na$^+$) + (glucose/18) + (urea nitrogen/2.8)) * 1.09

Table I

Results: CSF and serum Na+ concentrations were correlated although, in approximately 25% of cases (all characterized by a moderate hyponatremia,) CSF Na+ was definitely higher that serum Na+. Despite these differences, CSF and serum osmolalities were superimposable and correlated. The CSF-serum Na+ difference was (a) inversely related to serum (but not CSF) Na+ concentration, (b) directly correlated with serum (but not CSF) osmolality gaps, (c) inversely correlated with the CSF-serum osmolality gap difference, (d) directly correlated with serum (but not CSF) Na±independent osmolality and (e) directly correlated with CSF-serum Na±independent osmolality.

Table II: Differentiation of Na$^+$ S, Osmolality gap, Difference (CSF-S) in osmolality gap, Na$^+$-independent osmolality serum and difference (CSF-serum) of Na$^+$-independent osmolality according to quartiles of difference in CSF-serum Na$^+$ concentration

Quartiles of CSF-S difference in Na$^+$	Difference (CSF-S) in Na$^+$, mEq/L	Na$^+$ S, mEq/L	Osmolality gap (alg 1) S, mOsm/Kg	Difference (CSF-S) in osmolality gap (alg 1), mOsm/Kg	Na$^+$-independent osmolality serum, mOsm/Kg	Difference (CSF-serum) of Na$^+$-independent osmolality mOsm/Kg
Quartile 1	-0,87 ± 0,91	142,8±2,1	-8,55 ± 4,67	5,95 ± 4,31	2,60±5,17	3,87±4,58
Quartile 2	1,67 ± 0,62	137,8±3,5	-2,92 ± 5,49	2,68 ± 5,46	9,33±6,51	-0,47±5,75
Quartile 3	4,12 ± 1,15	138,3±3,1	-0,81 ± 5,14	0,01 ± 4,75	11,00±4,90	-2,31±4,91
Quartile 4	8,07 ± 1,62	134,9±4,5	4,55 ± 4,65	-4,83 ± 5,98	17,47±6,15	-7,27±6,51

Table II

Conclusion: these data suggest that CSF Na+ plays a specific role in controlling CSF osmolality in cases of moderate normoosmolal hyponatremia.

Disclosure: Nothing to disclose

EP1030

Nutritional status measurement using body mass index, waist-to-hip ratio and waist circumference to predict stroke outcome in both genders

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Background and aims: We investigated whether increased waist-to hip ratio (WHC), waist circumference (WC) or improper body mass index (BMI) may differently predict short-term outcome in females and males with first-ever ischemic stroke.

Methods: We retrospectively analyzed data collected in a detailed registry regarding consecutive patients (1109 females and 939 males) admitted due to first-ever ischaemic stroke between 2003 and 2015. BMI 18.5-24.9 kg/m^2 and gender specific normal values of WHC and WC were used as references for comparisons. Logistic regression was used to calculate odds of in-hospital death or death or dependency at discharge, adjusted for patients' age and prestroke disability.

Results: In both sexes high WHR increased the odds of death or dependency at discharge (OR:1.8, 95%CI:1.05-3.08 for females and 1.43, 95%CI:1.00-2.04 for males), but not in-hospital death alone. Increased WC was significantly associated with lower odds of death or death and dependency at discharge in females only (OR:0.36, 95%CI:0.22-0.58 and 0.69, 95%CI:0.48-0.97, respectively). BMI had no clear predictive value in neither sex.

Conclusion: Among evaluated measure methods only increased WHR was a predictor of poor outcome in both genders, but more significant in females. Abdominal obesity, measured with abnormal WC, was a strong predictor of good outcome in women, but not in men. BMI seemed to have the least clinical value in predicting stroke outcome in both gender.

Disclosure: Nothing to disclose

EP1031

Acid sphingomyelinase inhibitor amitriptyline induces angiogenesis of cerebral microvascular cells by mechanisms involving the Notch pathway

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Background and aims: Post-stroke, new microvessels are formed in the peri-infarct brain, which via release of trophic factors contribute to the remodeling of the brain parenchyma. Strong efforts are currently made in the stroke field to promote neurological recovery by enhancing brain remodeling.

Methods: Following in-vivo observations that the acid sphingomyelinase (ASM) inhibitor and anti-depressant amitriptyline promotes post-stroke angiogenesis, we herein evaluated effects of amitriptyline on the proliferation, migration and tube formation of cerebral microvascular HCMEC/ D3 cells in cell culture. HCMEC/ D3 cells were seeded in proliferation, migration and tube formation assays and treated with various concentrations of amitriptyline.

Results: Amitriptyline dose-dependently increased the migration and tube formation of cerebral microvascular HCMEC/ D3 cells when administered at doses of 5-50 mg/ml, at the same time reducing the proliferation of HCMEC/ D3 cells. These effects were attenuated by N-[N-(3,5-difluorophenacetyl)-L-alanyl]-S-phenylglycine t-butyl ester (DAPT), an inhibitor of Notch signaling pathway.
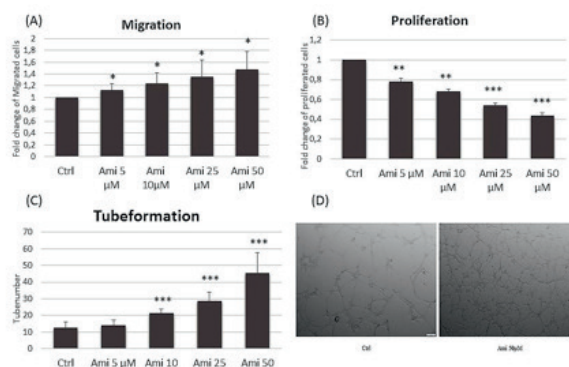
Figure : quantification of tube formation (A), migration (B) or proliferation (C) in human cerebral microvascular endothelial cell line (hCMEC/D3) treated with increasing concentrations of amitriptyline; (D) representative pictures showing increased tube formation with 50 μM amitriptyline treatment, scale bar represents 200 μm.

Conclusion: Our data suggest that DLL-4/ Notch signaling is involved in the angiogenic actions of amitriptyline.

Disclosure: Nothing to disclose

EP1032

Floating thrombi complicating aortic arch atherosclerosis – probably an under diagnosed cause for embolic stroke

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Background and aims: It is viewed that the most frequent causes of ischemic stroke are cardioembolism with atrial fibrillation or atherosclerosis of the cervico-cerebral vessels. However, in up to a third of cases none are present and this is when, among others, an aortic embolic source should be taken into consideration.

Methods: An 82-year-old woman with no prior medical history, was admitted for sudden loss of consciousness. Upon arrival at the hospital she was disoriented, aphasic, tetraparetic, with choreoathetosis of the right arm, head and eyes deviated toward the left. The initial head Computer Tomography (CT) showed no lesions but upon repeating it the next day, there were left occipito-parahippocampal, bilateral thalamic and left cerebellar hypointensities consistent with multiple acute ischemic strokes. Cervical vessel ultrasound and angio CT showed no severe atheromatosis and 24 hour electrocardiographic monitoring was normal. Blood cultures were negative and transthoracic echocardiography was not suggestive of endocarditis.
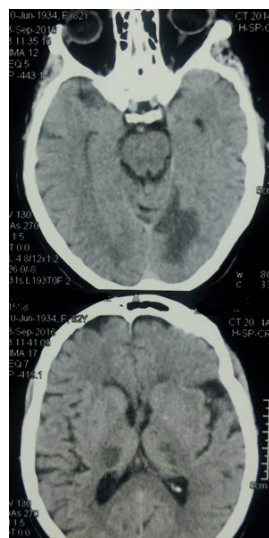
Occipital and bilateral thalamic hypodensities consistent with acute strokes

Results: Transesophageal echocardiography revealed extensive atherosclerotic plaques of the aortic arch, complicated with superimposed floating thrombi. Corroborating all the information we concluded that the most likely source of the stroke was embolism originating at the aortic arch. We decided on double antiplatelet therapy and high dose statin, with very good clinical evolution and significant reduction of the thrombi at two weeks.
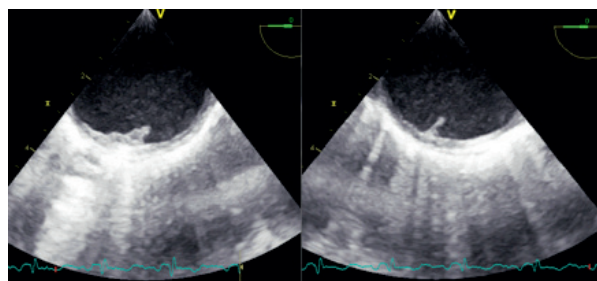
Transesophageal echocardiography showing floating thrombi in the aortia
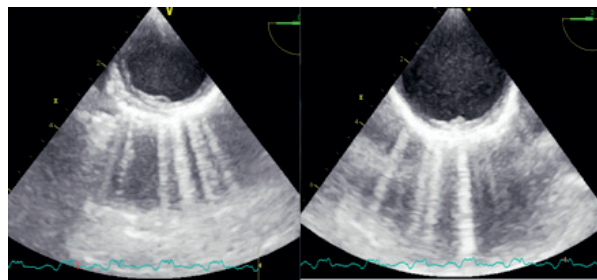
Reexamination after two weeks of double antiplatelet therapy and high dose statin - significant reduction of the aortic plaques and thrombi

Conclusion: Aortic emboli should be considered in stroke patients with no obvious cardioembolic source or significant cervical vessel atherosclerosis. Transthoracic echo-cardiography is a reliable diagnostic tool. Although reports are scarce, data points towards double antiplatelet therapy as being the treatment of choice.

Disclosure: Nothing to disclose

EP1033

Prehospital stroke scale (FAST PLUS TEST) predicts patients with large arterial vessel intracranial occlusion

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Background and aims: Mechanical thrombectomy is indicated for the treatment of occlusions of large cerebral arteries (LVO), it should be provided as quickly as possible, therefore, a test identifying the suspected occlusion in the pre-hospitalisation stage is needed for the patients to be directed to the centre providing mechanical recanalisation. We assume that the patients with clinically severe hemiparesis have a high probability of the presence of large cerebral vessel occlusion. Therefore, the FAST test was modified to the FAST PLUS test. The FAST PLUS has two parts: the first is the well-known FAST test, the second part evaluates only the presence of severe arm or leg motor deficit (scored 0-1) and unilateral occurrence of its motor function deficit (scored 0-1). Prospective multicenter study to determine specificity and sensitivity of the FAST PLUS test regarding the occlusion of major arteries in the anterior cerebral circulation confirmed by CT angiography (CTA).

Methods: Firstly, paramedics trained in conducting the FAST PLUS test via e-learning. Secondly, in all patients, demographic, NIHSS score, brain CT and CTA were recorded. Sensitivity and specificity of the FAST PLUS test were calculated.

Results: During 10 months 2016, 371 patients were enrolled to study. In 125 patients (33%) CT angiography showed the occlusion of intracranial artery. The sensitivity of the test for ICA/MCA occlusion was 93% and specificity 49%, NPV 93%,PPV 48%.

Conclusion: We found high sensitivity of the FAST PLUS test in our work. The test is suitable for prehospital selection of acute patients with suspected ischemic stroke due to LVO.

Disclosure: Nothing to disclose

EP1034

Cerebral amyloid angiopathy - clinical impact of using the modified Boston criteria

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Background and aims: Early identification of patients with cerebral amyloid angiopathy (CAA) is relevant considering the increased risk for cerebral hemorrhage and the frequent use of antithrombotic therapy. A new set of diagnostic criteria for CAA was recently proposed, which include the presence of superficial siderosis. We aimed to assess the impact of applying these criteria regarding use of antithrombotic therapy.

Methods: We reviewed clinical records of consecutive patients admitted to a Neurology Department from 2014 to 2016, with a possible or probable CAA according to the original and modified Boston criteria. Information was collected regarding presentation, imaging findings and concomitant therapy.

Results: Using the modified Boston criteria, 8 patients fulfilled criteria for probable CAA and 14 for possible CAA. When we applied the original Boston criteria to the same patients, only 7 fulfilled criteria for probable CAA and 8 for possible CAA. Among the additional patients identified with the modified Boston criteria, 4 were using antithrombotic therapy.

Conclusion: The use of the modified Boston criteria allowed for the identification of 7 additional patients, more than half of which were taking antithrombotic therapy. Systematic utilization of these criteria could have an important impact in clinical practice. Raising awareness on the different presentations of CAA among clinicians is of the utmost importance.

Disclosure: Nothing to disclose

EP1035

Risk factors for brain vessels's stenosis in young patients with ischemic stroke

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Background and aims: Thrombophilia is defined as a predisposition to form blood clots and is characterized by deficiencies and mutations in endogenous anticoagulants. Thrombophilic polymorphism such as factor VLeiden, MTHFR mutation (A1298C, C677T), prothrombin mutation G20210A, PAI-1mutation, antiphospholipid antibodies, Protein S, Protein C are established risk factors for venous thrombosis, but their role in arterial thrombosis is still controversial.

Methods: We investigated prospectively genetic and acquired risk factors for carotid or vertebral stenosis of 49 young patients (age 18-50 years) with ischemic stroke (32 male, 17 female), 18 in vertebrobasilar system, 31 in carotid system. According to stenosis grade patients were divided in two groups - non clinically significant<50% stenosis and clinically significant >50% stenosis/thrombosis. All patients underwent ECG, clinical cardiological evaluation, colour-coded duplex utrasonography of the cerebral vessels, computed tomography or magnetic resonance imaging of the head and thrombophilia factors examination.
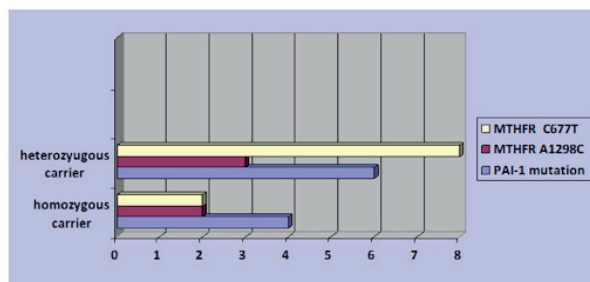
Figure 1 Frequency of thrombophilia in patients with brain vessels thrombosis

Results: The prevalence of acquired risk factors for stroke(arterial hypertension, dyslipidemia, diabetes mellitus, atrial fibrillation, obstructive sleep apnea, smoking, oral contraceptives, family history) are significantly higher in ischemic stroke patients with non clinically significant stenosis. Eleven patients are with thrombosis (5 intracranial and 6 extracranial) and one with severe extracranial stenoses. Ten of these patients have more than one risk factor for thrombophilia plus dyslipidemia. Two patients are only with thrombophilia. The other 37 patients are with ischemic stroke without clinically significant stenosis or thrombosis. Acquired risk factors and hyperhomocysteinemia present in 34 of these patients.
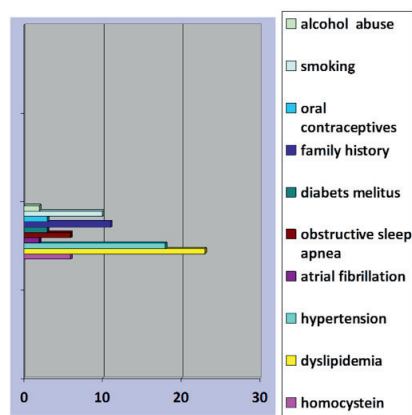
Figure 2 Acquired risk factors

Conclusion: We found that thrombophilia could be a risk factor for severe stenosis or thrombosis in young patients with stroke.
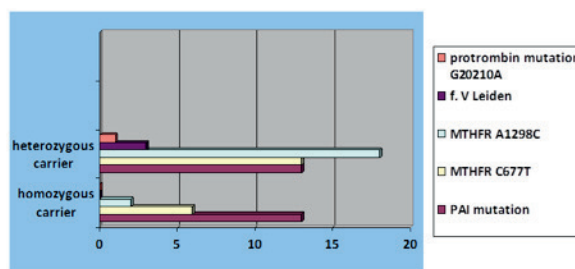
Thrombophilic risk factors in patients without thrombosis

Disclosure: Nothing to disclose

EP1036

Mitochondrial encephalopathy with lactic acidosis and stroke-like episodes (MELAS): A diagnostic challenge

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Background and aims: Mitochondrial encephalopathy with lactic acidosis and stroke-like episodes (MELAS) is a complicated, multi-systemic disorder, known to affect predominantly the brain and skeletal muscles. The early non-specific physical signs, such as short stature, headaches and hypoacusis do not draw sufficient attention until a stroke-like event occurs.

Methods: Case report.

Results: A 19-year-old male presented in our emergency department complaining of numbness and weakness of the left upper limb of abrupt onset. The CT scan revealed an area of hypointensity in the right temporoparietal territory, consistent with an ischemic stroke. On the ward, he experienced a partial seizure. According to his past medical history, he had been thoroughly investigated because of short stature, mild hearing loss, premature adrenarche and features of acromegaly, without reaching a definite diagnosis. He had also received human growth hormone replacement. Karyotype, serum/urine amino acids, as well as enzymes were documented normal. Extensive workout was negative and the stroke was considered of unknown etiology. Four months later the patient experienced an episode of expressive aphasia. Obtaining the family history in detail, we noted that hearing loss and atypical headaches affected at least two generations from the maternal side. That raised suspicion for MELAS, and despite the previously recorded normal electromyography and twice tested normal lactic acid titer, the pathogenic variant m.3243A>G in MT-TL1 was eventually detected in mitochondrial analysis.

Conclusion: MELAS is a diagnostic challenge, worth considering in young patients with vascular incident of unknown etiology. Family history might aid to reach the correct diagnosis.

Disclosure: Nothing to disclose

EP1037

Cancelled

EP1038

Non-traumatic subarachnoid haemorrhage in Malta – are outcomes adversely affected due to lack of a local neurovascular service?

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Objective: The aim of this study was to measure the incidence, treatment and outcome of non-traumatic Subarachnoid Haemorrhage (SAH) cases occurring in Malta during the five-year period between January 2011 and December 2015, in order to determine whether the lack of a local neurovascular service is associated with a poor outcome.

Methods: A retrospective analysis of adult patients (above the age of 16) diagnosed with non-traumatic SAH was carried out. The data collected included a five-year period from January 1st 2011 till December 31st 2015.

Results: The incidence of SAH was estimated at 4.00 cases per 100,000 population per year. An underlying aneurysm was found to be the cause of the SAH in 57.1% of cases investigated with CT angiography or Cerebral Angiography. In these patients, definitive management in the form of coiling or clipping of the aneurysm was carried out in the United Kingdom as part of an agreement between countries, within days. The outcome of these patients measured at 6 months using the Modified Rankin Scale was found to be excellent

Conclusion: Despite our geographical and logistical limitations, outcomes of those patients with initial low Hunt and Hess scores have not been affected by the lack of a local neurovascular service. Results are comparable to those of other international centres. Further studies looking into feasibility of expanding our local services are being carried out

Disclosure: Nothing to disclose

EP1039

Risk factors in young cryptogenic ischemic stroke patients: Findings from the history study

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Background and aims: The cause of ischemic stroke (IS) remains often unclear – cryptogenic, especially in younger patients. Moreover, the presence of known relevant risk factors (RF) is not enough established in this population. Our aim was to assess frequency and spectrum of relevant RF in young CIS patients.

Methods: The study set consisted of young acute IS patients <50 years enrolled in the prospective HISTORY (Heart and Ischemic STrOke Relationship studY) study registered on ClinicalTrials.gov (NCT01541163). In all patients, the brain ischemia was confirmed on CT or MRI. Admission ECG, serum specific cardiac and thrombophilia markers, neurosonology, TEE, 24-hour and 3-week ECG-Holter were performed in all patients to assess CIS.

Results: Out of 1006 patients enrolled in the HISTORY study, 176 (95 males, mean age 40.3 years±8.4 years) were <50 years. 130 (74%) were identified as CIS (72 males, mean age 40.9±7.8 years). In total, relevant RF were present in 88% of CIS patients; 36% of patients had elevated serum cholesterol, 32% of patients were smokers, 30% had detected PFO with right-left shunt, and 28% arterial hypertension. 43% of CIS females used hormonal contraception. Recurrent IS occurred in 5% of CIS patients and all of them had at least one of known RF.

Conclusion: The relevant RF were present in 88% of young CIS patients, hypercholesterolemia and hormonal contraception in females were the most frequent RF.

Disclosure: Study supported by the IGA LF UP_010_2017 and by RVO FNOL 00098892_2017

EP1040

Cancelled

Cognitive neurology/neuropsychology 1

EP1041

Somatoform disorders in neurology

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Background and aims: Functional or medically unexplained symptoms are very common in neurological consultation. In the DSM-IV, these disorders are classified as somatoform disorders. They represent about 30% of the activity of liberal neurologists.

Methods: We report 35 cases of somatoform disorders hospitalized in our general neurology unit over a period of 6 years between 2011 and 2016. The ages ranged from 15 to 80 years. They were 29 women (87.8% of cases).

Results: Psychogenic headaches were the most frequent presenting conditions (42.4%), followed by motor deficits (39.3%), lethargic states (12.1%), ocular symptoms (12.1%), pain (9%), movement disorders (9%), sensory disturbances (6%) and psychogenic nonepileptic seizures (6%). Ten patients exhibited 2 symptoms or more. Anxiodepressive comorbidity was noted in 15% of cases. Eighteen percent of cases had similar episodes in the past. Most of the patients were treated by antidepressants, mainly Amitryptiline, even in the absence of depression. Physiotherapy was used whenever necessary. The evolution was favorable in 57.5% with full recovery before discharge in 42.4%.

Conclusion: 50% of the patients with somatoform disorders are identified by neurologists. The neurologist is faced with the challenge of asserting the diagnosis and making the decision to stop investigations. He should implement an empathetic relation with the patient to announce the diagnosis and during all the follow-up. Some patients should be examined by a psychiatrist because up to two thirds have psychiatric comorbidity. Our series underline the importance for the neurologist to know these disorders in order to establish a comprehensive diagnostic approach and an appropriate medical care.

Disclosure: Nothing to disclose

EP1042

Cognitive impairment in transthyretin-related familial amyloid polyneuropathy

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Background and aims: Transthyretin-related amyloidosis is typically characterized by a progressive neuropathy, cardiomyopathy, nephropathy and ocular disease. More than 90% of amyloidogenic transthyretin is produced by the liver, however this protein is also synthetized in the choroid plexus. Although some patients have transitory neurologic events the impact on cognition is still unknown. The goal of this work was to study the cognitive performance of TTR-FAP V30M patients.

Methods: A prospective observational study of a consecutive sample of patients with 10 or more years of disease duration was conducted. All patients undertook a extensive neuropsychological evaluation.

Results: Sixteen patients were included, with a mean age of 53-year-old and mean duration of disease of 18 years. All had been submitted to liver transplantation. The global status was not incapacitating in the majority, with 75% needing at most a stick to walk in and 38% were still actively working. The neuropsychological evaluation disclosed episodic memory impairments in 31% and executive dysfunction in 25% of patients.

DEMOGRAPHIC AND CLINICAL DATA						
	Mean	Standard deviation		Median	Quartile 1	Quartile 3
Age	53	12	Clinical Staging of TTR-FAP	II	I	II
Education (in years)	12	4				
Disease duration (in years)	18	6	PND disease staging	IIIa	II	IIIa
Years of transplation	14	4				

NEUROPSYCHOLOGICAL DATA BY DOMAIN				
	Attention	Executive functions	Memory	Visucontructive functions
Patient 1		IMPAIRED	IMPAIRED	
Patient 2			IMPAIRED	
Patient 3		IMPAIRED	IMPAIRED	
Patient 4	IMPAIRED	IMPAIRED	IMPAIRED	
Patient 5	IMPAIRED			
Patient 11	IMPAIRED			
Patient 13		IMPAIRED		
Patient 16			IMPAIRED	

NEUROPSYCHOLOGICAL DATA BY TEST						
			Number of patients with deficit			
	Mean	Standard deviation	Mild	Moderate	Severe	Total
Letter cancellation test (A)	-0.55	1.14	2	2	0	4 (25%)
TP - work yield	-1.2	1.81	1	3	2	6 (38%)
TP - inattention index	-0.26	1.58	2	2	0	4 (25%)
Digit-forward test	0.47	1.29	1	0	0	1 (6%)
TMT A	-1.1	1.93	0	3	3	6 (38%)
Digit-backward test	0.12	1.31	1	0	0	1 (6%)
TMT B-A	-1.37	0.92	3	2	1	6 (38%)
Phonological fluency test	-0.76	0.91	4	1	0	5 (31%)
Stroop test - interference	-0.92	0.65	2	0	0	2 (13%)
Raven's matrices test	0.32	1.12	0	1	0	1 (6%)
Pairs of words test	-0.46	1.31	3	2	0	5 (31%)
Logical memory test	-0.2	1.44	1	1	1	3 (19%)
Verbal mem w/ interference	-0.52	0.86	0	2	0	2 (13%)
CVLT - learning	-1.41	0.96	3	5	0	8 (50%)
CVLT - long delay free recall	-1	1.42	1	6	0	7 (44%)
Copy of cube test*	0.96	-0,8 - 1,2	0	0	0	0 (0%)
Clock drawing test*	0.6	0,44 - 0,6	0	1	0	1 (6%)

Demographic, clinical and neuropsychological data
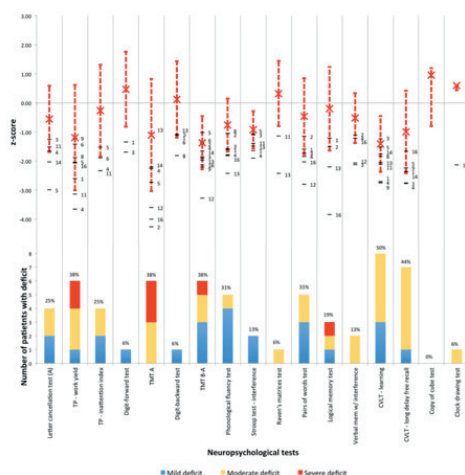
Top – Mean (x) and standard deviation of z scores for each neuropsychological test. Each dash represents an individual with a z-score below -1; different numbers represent different patients. Bottom – Frequency of deficit in each test; different colors represent distinct levels of impairment.

Conclusion: These novel findings suggest that cognitive dysfunction can be a delayed manifestation of Familiar Amyloid Polyneuropathy. The putative relation of cognitive dysfunction with transthyretin-amyloid deposition can provide another model to study the amyloid hypothesis of cognitive impairment.

Disclosure: Nothing to disclose

EP1043
Cancelled

EP1044

Should the Mini Mental State Examination be considered as the best option for screening of cognitive impairment in lower educated individuals?

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Background and aims: Educational level is the most important determinant of performance on Mini Mental State Examination (MMSE) and cultural differences may account for different cutoffs points for each educational level. The Brief Cognitive Battery (BCB) has proven to be more appropriate in our midst. Thus, we aimed to compare the impact of the educational level on both the MMSE and the BCB.

Methods: 112 outclinic patients between 60 and 80 years of age were randomly chosen in a tertiary public hospital to enroll this study. We excluded all subjects who had a previous history of neurologic or psychiatric compromise. Subjects were divided in four groups according to education: illiterates, 1 to 4 years of education, 5 to 8 years and those with >8 years. All subjects were evaluated with both cognitive tests on the same day.

Results: Schooling had an influence on both MMSE scores ($p < 0.0001$) and individual performance on the clock drawing test ($p < 0.0001$). Educational level also had an impact on verbal fluency testing ($p < 0.00035$) of the BCB, but only for those subjects with higher scores obtained in the group with >8 years of education. Conversely, late recall test scores of the BCB were not influenced by educational level ($p = 0.0804$).

Conclusion: Educational level seems to interfere more on overall MMSE than on the BCB in all educational levels. Verbal fluency and the late recall tests of BCB showed impartial results. BCB seems to be a better assessment tool for our population and should be studied in other countries.

Disclosure: Nothing to disclose

EP1045

Cancelled

EP1046

see page 268

EP1047

The effect of high-frequency repetitive transcranial magnetic stimulation of left dorsolateral prefrontal cortex on the motor learning

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Background and aims: Left dorsolateral prefrontal cortex (lDLPFC) plays crucial role in motor learning including working memory and attention. Repetitive transcranial magnetic stimulation (rTMS) may modulate cortical excitability with long-term effects, but effects of rTMS of lDLPFC in healthy volunteers are variable.

The study aimed to assess effects of high-frequency rTMS of lDLPFC on motor learning.

Methods: Ten healthy volunteers (mean age 27.5+/-5.8 years) completed 4-day course of working motor memory trains with mechanotherapeutic device (Fig. 1). In first series kinesthetic stimuli (finger support's movements) were presented one by one randomly, and volunteer had to memorize and repeat the sequence. In second series a combination of visual (finger image on screen) and kinesthetic stimuli was presented. Subjects performed three attempts in each series. Before the third train each subject received one session of navigated rTMS of lDLPFC (20Hz, 80% RMT, 2400 stimuli). Maximum length of sequence, which subject was able to perform, was assessed. We used Schulte test for attention evaluation on Day 1, after rTMS (Day 3), on Day 4.

Mechanotherapeutic device that was used for motor memory trains. Right thumb and fingers tips were attached to the fingers support. Finger support's movements were presented as a kinesthetic stimuli.

Results: High-frequency rTMS of lDLPFC interrupts motor working memory processes in combination of visual and kinesthetic stimuli presentation but not in kinesthetic stimuli presentation alone (Fig. 2). rTMS improves attention efficiency but increases the work warming-up (Fig. 3
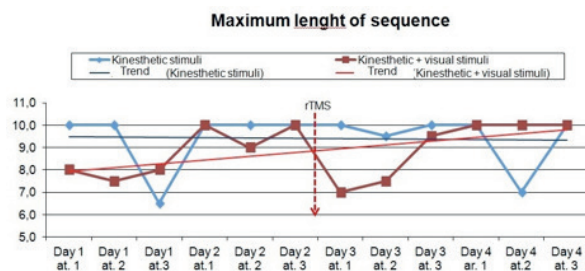
Maximum length of sequence results. rTMS is showed with a red arrow.
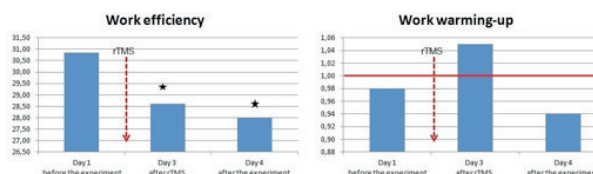
Schulte test results: work efficiency improvement and work warming-up deterioration is observed after the stimulation. rTMS is showed with a red arrow.

Conclusion: rTMS has different effects both on working memory (depending on modality of presented stimuli) and attention.

EP1048

Mental Imagery manipulation in multiple sclerosis

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Background and aims: A mental image is the representation in a person's mind of the physical world outside. Motor imagery (MI) can be defined as "a dynamic state during which a subject mentally simulates a given action" and was recently shown to be a promising tool in neurorehabilitation. However the ability to correctly perform MI may be impaired in patients with neurological dysfunction. Aim of our study is to assess mental images abilities in multiple sclerosis (MS) patients and healthy subjects with a particular attention to MI.

Methods: Patients with Relapsing-Remitting MS (RR-MS) and age, sex and education matched healthy controls underwent a Computer-based Mental Imagery Task (COmit) to assess mental manipulation of visual (letters) and motor stimuli (hands, front and back view bodies). Results were compared using ANOVA, and Bonferroni multiple comparison's test. P values of less than 0.05 were considered statistically significant.

Results: We enrolled 20 RR-MS patients and 20 controls (Table 1). We found different results for group (F=4.91;p=0.033), orientation (F=52.09;p<0.001), task (F=9;p<0.001), and a significant interaction between task and orientation (F=2.68;p=0.005). Patients showed significant differences in reaction times for all tasks (hands and bodies) except for the letter task, suggesting a preserved object analysis in MS and an impaired MI.

	Patients	Healthy Subjects
Age (m, sd)	35 ± 9	33 ± 9
Sex (n, m, sd)		
M	10, 32 ± 9	10, 31 ± 8
F	10, 37.4 ± 9.1	10, 35.2 ±9.9
Education (m, sd)	12.1 ± 3.8	12 ± 4
EDSS (m, sd)	3 ± 1	
Disease duration (m, sd)	10 ± 7.5	

Conclusion: We found a slower information processing speed in MS especially for hands and bodies manipulation. Further studies should investigate correlation between MS features, cognitive performance and MI, and how this influences response to rehabilitation.

Disclosure: Nothing to disclose

EP1049

Baseline characteristics and natural course of Thai patients with dementia

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Background and aims: More than half of patients with dementia lived in countries with low and middle incomes. However, there have been few studies on the natural course of disease in these countries. The purpose of this study was to study the baseline characteristics, natural course, and complications in Thai patients with dementia.

Methods: Patients with dementia who were treated in neurologic and psychiatric clinic from September, 2004 – February, 2016, were included. Data about natural course of diseases, behavioral and psychological symptoms in dementia (BPSD) and complications were studied.

Results: 207 patients were included. Mean age was 77-years-old. Mean Thai Mental State Examination (TMSE) was 17.5. Alzheimer's disease was the most common cause of dementia (55%). With the mean follow-up of 39 months (range from 2-126 months), 64% of the patients had BPSD. Sixty-two patients (30%) had complications required admission. Seven patients died. Fifty-four patients (29%) ended in the advanced stage of dementia. Mean duration from diagnosis to the advanced stage was 49 months. Complications that required admission usually occurred in moderate to severe dementia and were strongly associated with the advanced stage or death (OR 6.1, 95%CI 2.57-14.49, p-value <0.0001).

Conclusion: Alzheimer's disease was the most common cause of dementia in the study. BPSD was also commonly found in the patients. Most demented patients presented in moderate severity of dementia. Mean duration from diagnosis to the advanced stage of dementia was approximate 4-5 years.

Disclosure: Nothing to disclose

EP1050

Transient global amnesia: An altitude sickness?

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Background and aims: Transient global amnesia (TGA) is an episode of acute onset of transient global anterograde memory deficite without other neurologic symptoms. Uncertainty still remains as to the etiology of TGA. The Regional Hospital in Davos reported an unusually high incidence of TGA. As the town of Davos is located at a relatively high altitude of 1560 m.a.s.l we hypothesized that altitude and low temperature may play a role in triggering the onset of TGA.

Methods: Retrospective study on the TGA events documented in the Regional Hospital Davos between 2005-2014. We analysed the following meteorological data: temperature, mean atmospheric pressure at sea level (P), mean relative humidity (RH), mean water vapour pressure (WVP) for all the days - regardles if there were documented TGA cases on those days or not.

Results: The TGA incidence in Davos (12/100'000/year) was higher as compared to the incidence quoted in the literature. We observed a peak of TGA occurrence in the winter. We found a significant relation between the mean day temperature and the incidence of TGA. The mean temperature in days with TGA cases was -1.1°C and in days without TGA cases 6.5°C (p-value <0.0001). There was no significant difference of occurance of TGA in relation to the atmospheric pressure, wind and humidity.

Conclusion: We could illustrate that a peak of TGA cases occurs in winter and it seems the low temperature could be a trigger for TGA. Sympathetic activation due to cold may also play a role in the pathogenesis of TGA.

Disclosure: Nothing to disclose

EP1051

Experience of using meldonium in treatment of mild vascular cognitive impairment

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Background and aims: Neuropathological studies of mild cognitive impairment reveal a large load of vascular ischemic brain lesions. Therefore we have explored effect of antioxidant drug meldonium (Mildronat) in patients with vascular cognitive impairment.

Meldonium (Mildronat) is a licensed medical drug used widely throughout Eastern Europe and Central Asia for a number of cardiovascular conditions and is the basis of much debate in the world of sports doping.

Methods: 120 patients (72 female, 48 male, average age 71.6 years) with vascular cognitive impairment received meldonium 1000 mg i/v for ten days and then continued treatment orally for 6 months. Main clinical manifestations were impaired attention and forgetfulness, psychomotor slowing, impaired executive and visuospatial skills, change in personality, and emotional disturbance. The patient closely followed clinically, with repeated neuropsychological assessment. Results compared with a control group (N=135).

Results: The benefits of treatment began to be apparent within the first months. 46 patients showed stable improvement in cognitive performance measures and in daily life. 40 patients trend back to their baseline. 34 patients had no improvement after treatment. There was no case of worsening disease or bad drug bearing. Statistically significant reduction in cognitive impairment was seen in the treated group in the domains of memory, attention and executive functions.

Conclusion: It is concluded that meldonium may be recommended for the complex treatment of ischemic disorders of the cerebral circulation, include vascular cognitive impairment. The use appears to be effective and safe.

Disclosure: Nothing to disclose

EP1052

Feasibility of individual diagnostic approach for patients with chronic disorders of consciousness

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Background and aims:. Chronic disorders of consciousness (DOC), such as VS and MCS, are diagnosed mostly by clinical examination, that carries high risk of misdiagnosis. New tools may help establish level of consciousness in certain cases, as presented here.

Methods: Case. A clinically VS patient A., male, 48 y.o., 2 years after intracerebral hemorrhage (CRS-R=10) showed only reflex movements to stimulation, no environment contact and preserved sleep-wake pattern. It was reported recently that presence of default mode network (DMN) signal on rs-fMRI was correlates with the degree of clinical consciousness impairment (Vanhaudenhuyse, 2010).

Results: On rs-fMRI (3T) we found activation of DMN areas (mPFC, PCC, LIPC, RIPC) (Fig.1). We also performed TMS-EEG with calculating Perturbational Complexity Index (PCI) - an independently validated promising consciousness metric (Casali, 2014), that allows reliable stratification of unresponsive patients with empirical cutoff level for discrimination between the unconscious and conscious states of 0.31 (Casarotto, 2016). We found out high complexity of the cortical response for the TMS stimuli, with PCI of 0.345 for frontal region stimulation (Fig.2) and 0.424 for parietal region (Fig.3) stimulation which implies the «conscious» state in this patient
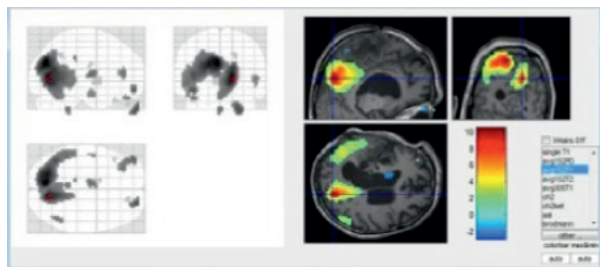
Fig.1. resting state FMRI data.
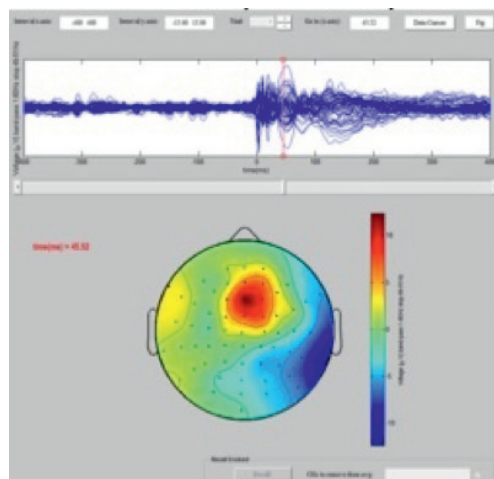
Fig.2. TMS-EEG Frontal stimulation response
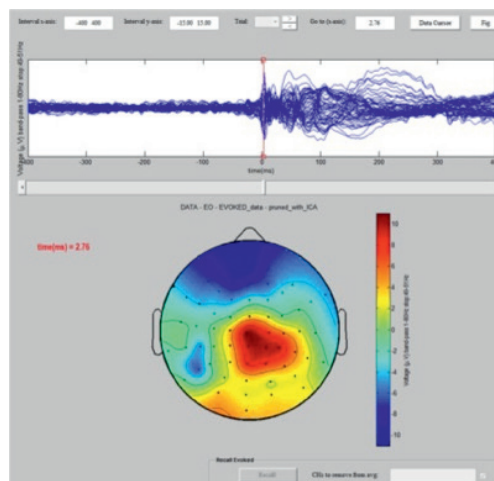
Fig.3. TMS-EEG Parietal stimulation response

Conclusion: novel diagnostic techniques may reveal patients with possible higher level of consciousness than seen clinically. Such patients should become subject for further investigation to find out the cause of discrepancy between clinical and neurophysiological results, as well as for intensive rehabilitation interventions.

EP1053

A challenging case of sporadic Creutzfeldt-Jakob disease: Confounding and evolving findings

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Background and aims: Rapidly progressive dementia poses a diagnostic challenge. We present a case of sporadic Creutzfeldt-Jakob Disease (sCJD) with atypical laboratory features.

Methods: A sixty-four-year-old male presented with a two month history of blurred vision and cognitive impairment progressing over six weeks. Initial examination revealed nystagmus and ataxia. In view of possible autoimmune encephalitis, corticosteroids, plasma exchange and cyclophosphamide were sequentially administered in the setting of new clinical features including myoclonus, pyramidal features, cogwheel rigidity and increasing frontal behaviour. However he deteriorated becoming mute, bedbound and died forty-nine days later.

Results: Vasculitic and infective screens were negative. Cerebrospinal fluid (CSF) examination revealed elevated protein (1.41g/L). 14-3-3 assay was weakly positive but real-time quaking induced conversion (RT-QuIC) assay was negative. Tau protein was markedly elevated. Glycine receptor (GlycR) antibodies were present in serum whilst other antibodies against neuronal surface antigens were negative. Serial MR Imaging demonstrated evolving cortical ribboning and diffusion restriction of the left caudate nucleus. Initial electroencephalogram was consistent with encephalopathy, later demonstrating frontal dominant periodic sharp-wave complexes.

On the basis of treatment-refractory deterioration, radiological and electrophysiological evidence, a diagnosis of probable sCJD was made. Interestingly, the RT-QuIC was positive on re-testing at a different dilution.

Conclusion: In the setting of rapidly progressive dementia, immunosuppression trial may be appropriate, although it is recognised neuronal antibodies can be positive in sCJD. This case is unusual for the presence of GlycR antibodies and markedly elevated CSF protein. This highlights the complex challenge of establishing the aetiology in such cases and interpreting the significance of laboratory findings.

Disclosure: Nothing to disclose

Education, History, Arts & Ethics

EP1054

SONAR identifies registrar research training needs in a clinical training program

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Background and aims: Successful Trainee Clinical Research Networks have been established since 2007 and are primarily run by Surgical and Anaesthetic Trainees. In the southwest peninsula we have set up the first UK Neurology Trainee Audit and Research Collaborative to deliver clinical studies. Ensuring all trainees have appropriate training is a key requirement; we aimed to ascertain the training need of our network members.

Methods: A survey was sent to all 9 neurology trainees in the Peninsula Deanery. It comprised 5 questions to establish trainee clinical research training and experience.

Results: Response rate was 100%. Training level varied from ST3-5; 22% had previously completed higher degrees. 40% of trainees had not been involved in clinical research. One trainee had not had formal good clinical practice (GCP) training and none had formal Informed Consent training. Of those who had been involved in research, there had been limited involvement in project design, ethics approval processes, data analysis, manuscript preparation or findings presentation.

Conclusion: We identified a training need in our Trainee Audit & Research Network. In order to address this, we have organised formal GCP & Informed Consent training; to broaden the research experience of network members, we are planning our first collaborative research project.

Disclosure: Nothing to disclose

EP1055

Integration of international physicians in Germany: An empirical study in the acute-neurological departments in Westphalia-Lippe

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Background and aims: Demographic changes and technical innovations increase the demand for physicians in industrialized countries. Since 1990 medical schools in Germany barely increased capacities, so increasing numbers of physicians are immigrating to fill this gap. The Chamber of Physicians of Westphalia-Lippe, where 8.3 million inhabitants cared by more than 32,000 physicians, hosts a proportion of 15.6% of international physicians. 44% of physicians in specialty training immigrated from non-German speaking countries. Hospitals outside larger cities face increasing difficulties to recruit their physician staff.

Methods: All neurological departments accredited for complete neurological specialty training were included, 30/38 participated in a survey and detailed interview. Data of health economic performance and staff recruitment were collected including anonymized data about all international residents, including professional performance and dismissals.

Results: 27 of 30 neurological departments employed international physicians (range 7 – 92% of all residents). The difference between University-Departments and larger and smaller centers was significant (p=0.009) (figure 1). The same was shown concerning the evaluation of knowledge, skills, language abilities and social competences (figure 2). 220 international residents were individually rated and 56 dismissals analysed: Physicians from Balkan countries had the highest risk (47%) followed by arab-oriental countries (39%).
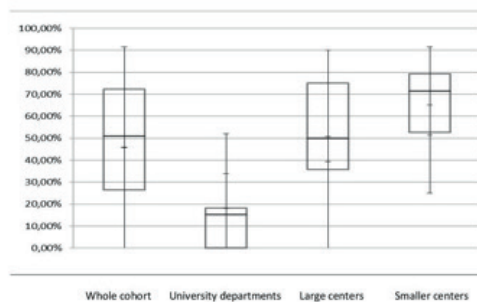
Graph 1: Percentage of international residents among Neurological departments
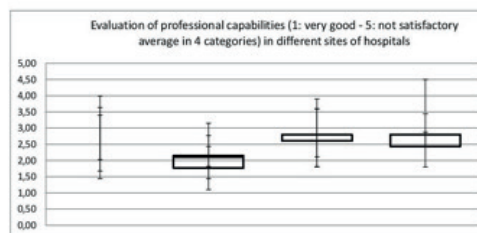
Graph 2:   Whole cohort   University departments   Large centers   Smaller centers

Conclusion: The shortage of German medical graduates leads to marked immigration of international physicians. Neurological departments outside metropolitan areas have immense problems to recruit qualified residents in training concerning to their professional abilities. This leads to high dismissal rates and compromises the quality of care in German neurological departments outside big cities.

Disclosure: Nothing to disclose

EP1056

The Dynamic Dutch Guideline for Epilepsy

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Objective: To develop a Dutch Dynamic Guideline for Epilepsy.

Methods: A clinical practice guideline (CPG) has to be accessible and practical. We developed a modular web-based CPG in which 23 diagnostic and therapeutic modules are listed, with answers to 57 key questions, resulting in 189 recommendations. Questions and recommendations in each module are presented briefly under a first tab. For further reading, other tabs include "summary and grading of the literature"; "references"; "considerations"; "expert opinion" and "information on economics". A reference list with hyperlinks to abstracts is included. Updates, such as studies published after authorization of the latest CPG version, are presented under the tab "new literature", which will then be processed in a subsequent edition. Grading of evidence is made transparent by adding evidence-scoring tables (using GRADE for therapeutic and EBRO for diagnostic studies). Development of this CPG was accompanied by an implementation procedure which included the following actions:

- guideline users are encouraged to submit requests for the development of new modules;
- indicators of good care are formulated and put on the website;
- questions for the obligatory annual exam for Dutch neurologists are retrieved from the guideline;
- annual national courses on epilepsy for residents in neurology and pediatrics are based on knowledge of the CPG.

Results: An exclusively web-based and annually updated Dutch CPG (first edition in 2013). Currently, http://epilepsie.neurologie.nl is accessed 2000 to 3000 times each month.

Conclusion: The development and maintanance of a dynamic guideline with yearly updates is feasible.

Disclosure: Nothing to disclose

EP1057

Incorporating economic evaluations in clinical practice guidelines: A standard approach to increase quality and to reduce workload for guideline developers

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Background and aims: Clinical practice guidelines (CPG's) serve as a roadmap for evidence-based treatment of patients with specific diseases. Although recommended, currently economic evaluations (EE's) are not routinely incorporated in these CPG's. We developed a standard approach to incorporate EE's into CPG's.

Methods: This approach provides an overview of all knowledge and practical information needed to systematically incorporate EE's in CPG's. Specifically, a flowchart containing five steps of the review process: guidance on the development and selection of search strategies, guidance on selection of different databases, information on how to select and use checklists to appraise the methodological quality of the studies, information on how to handle transferability and generalizability issues, guidance on data extraction and data syntheses. In addition, ready to use standard tables for data extraction, a list of existing databases and advice about how to manage references is given.

Results: The five step approach is used to incorporate EE in the Dutch CPG for Epilepsy. This approach facilitates annual actualization of the CPG. Moreover it increases transparency and standardization of performing systematic reviews of with a maximum efficiency for guideline developers.

Conclusion: The use of a standardized approach facilitates the incorporation of EE's in new and existing CPG's. The standardized approach is feasible, ensures reproducibility and minimizes the workload needed. The five step approach is successfully implemented in the Dutch CPG.

Disclosure: Nothing to disclose

EP1058

Health promotion in the field of neurology according to European junior neurologists – an EAN-Resident and Research Fellow (RRFS) survey

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Background and aims: Health promotions (HP) such as exercise, reduced alcohol consumption, smoking cessation, diet may play a role in primary and secondary prevention of different neurological disorders, especially in common conditions such as dementia and stroke, which have an essential global public health and social care burden. Our study focuses on the opinion of European residents and junior neurologists (RJN) on HP.

Methods: An anonymous online survey was distributed among RJN between 1 May 2016 and 31 December 2016. The survey also included a short description about HP.

Results: 98 RJN (66.7% female) from 25 countries completed the survey. The majority (67%) had heard about HP before, but 33% had not. Almost all (99%) agreed on the importance of HP in the management of neurological disorders. However, only a minority of the residency programs offered training on HP (24.5%). The RJN strongly agreed that reduced alcohol consumption (77.6%), smoking cessation (76.5%), diet (52%), exercise (64.3%), stress management (60.2%) and depression treatment (45.9%) can decrease the burden of neurological disorders. Table 1 summarizes which barriers make HP challenging. Despite these difficulties, (99.1%) of RJN would encourage their patients to participate in HP offers.
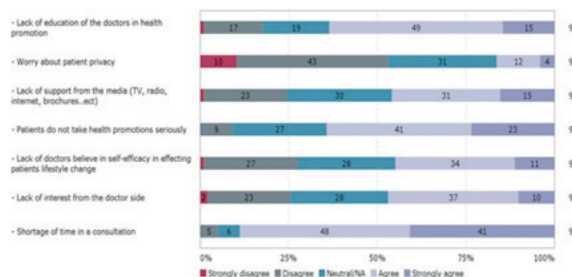
Table 1: Distribution of the answers on "What kind of barriers make health promotion challenging?".

Conclusion: The survey clearly outlines that RJN agree on the importance of HP for the management of neurological disorders. Appropriate training during residency, sharing up-to-date knowledge about HP effect on the neurological diseases, is recommended.

Disclosure: Nothing to disclose

EP1059

Mursili II: First historical primary progressive aphasia case?

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Background and aims: Historical neurology studies usually aim to reach diagnosis by old case information and available additional data.The Hittites were an Ancient people establishing an empire in north-central Anatolia around 1600 BC.Among their kings, Mursili II left the highest number of documents, and a number aspects of his rein(plague, other epidemics and septicemia, religious personality, "wifes of Mursili" etc.)have been studied

Methods: As explained below; Mursili had to live with a language/speech impairment at a certain part of his life. On the documents written he explains this occured after a fear he experienced due to a thunderous storm during his walk. A difficulty/ impairment of speaking occurs, which in time progresses to almost a loss of speech ability. To find the cause of his illness he applied to fortune telling.According to history books, this speech impairment started as dysarthria and gradually progressed.

Results: Basically we do not know the progression time of the illness but probably it is probably not too long.With the present information, nonfluent(Agrammatic) form of Primary Progressive Aphasia(PPA) seems to be the most likely diagnosis. Adults of any age can develop PPA, but it is more common under 65. Patients have a different language symptoms and cases are not same The initial symptoms include slowed/ halting speech, decreased use of language, word-finding hesitations, using words that are incomprehensible, all of which may have been Mursili's original symptoms

Conclusion: Possibly this one of the greatest kings of Hitties was also the first written (cuneiform) described PPA case.

Disclosure: Nothing to disclose

EP1060

Cauterization in the treatment of neurological diseases by famous physicians like Brown-Séquard and Charcot

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Background and aims: Cauterization is one of the oldest means of treatment. The most frequent indication is pain in general. Cauterization is still practiced in folk / primitive medicine in the world.

Methods: During my 12 years of employment in the Kingdom of Saudi Arabia and travelling to many Arab countries, I came in touch with cauterized patients and their healers. Since 1989, I built up an extensive collection of world literature related to cauterization. The Greek and Arab medicine describing the use of cautery for neurological diseases. The 19th and 20th century literature is reporting of cauterization for neurological diseases like paresis, epilepsy by famous neurologists like Charcot and Brown-Sequard. Also the general surgeon Bier was in favour of cautery.

Results: I will present the literature describing the indication for cauterization in neurological diseases by Brown-Sequard and Charcot.

Conclusion: The names of these physicians are world famous and daily used for syndromes. However, most of us do not know that they practised cautery for neurological diseases. I believe it is worth full to report this to the neurological – neurosurgical community

Disclosure: Nothing to disclose

EP1061

Hypercreativity and changes in artistic style as debut of frontotemporal dementia

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Background and aims: The change in artistic style and hypercreativity has been described in frontotemporal dementia (FTD). We present a case of compulsive creation of pieces of arts as the first manifestation of FTD.

Methods: A 65-year-old man, administrative and an amateur artist, was admitted to our hospital with diplopia, ptosis and general weakness. He was diagnosed with Myastenia Gravis, and was discharge. During the admission, the patient showed an amazing compulsive behavior: he created 63 songs with a scatological and erotic theme. Additionally, he changed his pictorial style: he used to paint classical scenes (figure 1) but by this time, he only wanted to paint erotic pictures (figure 2). He had not any other symptoms. A neuropsychological test showed an executive dysfunction and a brain MR showed frontal lobes atrophy.

Figure 1

Figure 2

Results: Five years later, his family advised that he had an abnormal behavior: disinhibition, impulsive actions and euphoria. His compulsive manner of write songs was worsening: he wrote more than 3000 songs of erotic theme, and performed a big sculpture with a lot of scabrous details that he called "pictorial-sculpture" (figure 3).

Finally, the patient was diagnosed with probable behavioral variant FTD, accordingly with the current diagnosis criteria.

Figure 3

Conclusion: The most patients with FTD show a diminution in creativity. However, some patients show a hypercreativity in arts; change their artistic style or even start a new creative ability. This lack of limits or transmodal creativity has been described in FTD.

Disclosure: Nothing to disclose

EP1062

"The metaspirochaetosis is the meningeal process": Neurosyphilis as the driving force of Thomas Mann's Doctor Faustus

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Background and aims: Thomas Mann's Doctor Faustus is one of the undisputed pinnacles of German literature for its insight on the creative process of an artist; at its core, however, lies the influence of neurosyphilis, one of syphilis' most devastating forms. Several classical composers, such as Smetana, Schumann and Donizetti, were victimized by it; in his novel, Mann offers the case of fictional composer Adrian Leverkühn.

Methods: Mann's book, European and American guidelines on syphilis were reviewed.

Results: Disease plays a major role in Thomas Mann's oeuvre, from The Magic Mountain to Death in Venice. In Doctor Faustus, however, the correlation is at its closest. The aspiring composer Adrian Leverkühn comes into contact with a prostitute early in the book and develops a "local infection" afterwards. In chapter XXV, Leverkühn describes his encounter with a Mephistopheles-like entity, perhaps an hallucination from secondary meningo-encephalitis, who reveals his infection by "our livid Venus, the Spirochaeta pallida", giving him 24 years of unmitigated musical genius inspired by the auditive and visual hallucinations of neurosyphilis. After the disease's latent period, he develops Argyll-Robertson pupils, "which always had the same size, (…) were never changed by differences in light", and a prolonged demential period of ten years before his death, paretic and insomniac.

Conclusion: Mann's Leverkühn is a fictional character whose musical brilliance can be attributed to hallucinatory effects of neurosyphilis. Mann's text provides the careful reader clues to the true nature of his aillment, from descriptions of abnormal neurological findings (Argyll-Robertson pupils) to a more florid description of neuropsychological symptoms.

Disclosure: Nothing to disclose

EP1063

The neurological disease as a muse of famous writers

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Background and aims: Some important writers suffered from neurological diseases. We investigated whether their neurological condition could have influenced their artistic production.

Methods: Search for relevant links between neurological diseases and literary output of famous writers.

Results: Friedrich Nietzsche suffered from neurosyphilis that led him into a deep sadness and introspection, what can be easily realized in his works. When Nietzsche became paretic, according to Freud, it "gave him the capacity[…] of seeing through all layers and recognizing the instincts at the very base'. Guy de Maupassant also had neurosyphilis and there is consent that his creativity was changed as the disease progressed. Robert Sherard, in face of Maupassant's literary leap to fame in 1880, became certain that syphilis could take one to new heights. Lewis Carroll had migraine and experienced visual auras. Some studious rigorously affirm that his visual disturbances were the main influence to create the novel Alice's Adventures in Wonderland, that contemplate descriptions of metamorphopsias, distortions and bizarre characters. Gustave Flaubert was diagnosed with epilepsy, when he decided to isolate himself and dedicate more time to literature. Writing became an "outlet", as he once confessed, to his neurological condition that was cause of so much suffering. Charles Baudelaire had a left-hemisphere stroke and once wrote: 'I claim that inspiration is somehow linked to stroke…'. His aphasia would consecrate the expletive Cré nom and made him reinvent his artistic style. **Conclusion:** Neurological disease participated of the creativity process of important famous writers, playing a pivotal role in the genesis of eternal literary masterpieces.

Disclosure: Nothing to disclose

Epilepsy 1

EP1064

Patterns of use of Antiepileptic Drugs (AEDs) in a tertiary neurology clinic in Khartoum City, Sudan

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Background and aims: Patterns of use of antiepileptic drugs (AEDs) differ between developed and developing countries. In the latter, use of second generation AEDs is not common. To study the patterns of AEDs uses in terms of frequencies of use, treatment outcomes, and tolerability.

Methods: This is a retrospective cross-sectional study. A total of 360 adult Sudanese epilepsy patients who attended a tertiary neurology clinic in Khartoum city, Sudan between 2006 and 2010 were included.

Results: 76.1% of patients (274/360) were classified as drug responsive while 23.9% (86/360) were classified to have DRE. Out of 624 prescriptions, the five most frequently prescribed AEDs were carbamazepine (32.7%), sodium valproate (28.5%), phenytoin & lamotrigine (12.5% each) and phenobarbitone (6.2%). 44.1% (275/624) of prescriptions resulted in sustained seizure freedom for their first use whether as monotherapy or in combination, while treatment failure per individual drug was the reported outcome in 41.1% (256/624). In 12.5% (78/624) of the prescriptions, AEDs resulted in seizure freedom in their initial use. The highest rate of achieving seizure freedom during the first use was reported with phenytoin 63.3% (50/79), valproate 48.3% (86/178), carbamazepine 47.6% (97/204) and lamotrigine 21.8% (17/78). Reported treatment failure rates were: lamotrigine 66.7% (52/78), phenobarbitone 64.1% (25/39), valproate 37.6% (67/178), carbamazepine 28.8% (59/204) and phenytoin 24.1% (19/79). Adverse events were reported with 7.4% of prescriptions while AEDs discontinuation was necessary after 2.7% of prescriptions.

Patterns of Uses of Antiepileptic Drugs (AEDs) in A Tertiary Neurology Clinic in Khartoum City, Sudan

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Table 1 Patterns of treatment outcome for individual AEDs [#]

Treatment outcome AEDs	Responsive	Failed	Responsive initially & turned to fail later	Responsive initially and for second time following re-administration*	Failed initially & then became responsive	Total Number of prescriptions
Carbamazepine	97 (47.6 %)	59 (28.9 %)	6 (2.9 %)	21x2 (20.6 %)	0 (0 %)	204 (32.7 %)
Valproate	86 (48.3 %)	67 (37.6 %)	4 (2.3 %)	10x2 (11.2 %)	1 (0.6 %)	178 (28.5 %)
Phenytoin	50 (63.3 %)	19 (24.1 %)	2 (2.5 %)	4x2 (10.1 %)	0 (0 %)	79 (12.7 %)
Lamotrigine	17 (21.8 %)	52 (66.7 %)	0 (0 %)	4x2 (10.2 %)	1 (1.3 %)	78 (12.5 %)
Phenobarbitone	13 (33.3 %)	25 (64.1 %)	1 (2.6 %)	0 (0 %)	0 (0 %)	39 (6.2 %)
Clonazepam	7 (28 %)	18 (72 %)	0 (0 %)	0 (0 %)	0 (0 %)	25 (4 %)
Topiramate	4 (25 %)	12 (75 %)	0 (0 %)	0 (0 %)	0 (0 %)	16 (2.6 %)
Levetiracetam	1 (50 %)	1 (50 %)	0 (0 %)	0 (0 %)	0 (0 %)	2 (0.3 %)
Acetazolamide	0 (0 %)	2 (100 %)	0 (0 %)	0 (0 %)	0 (0 %)	2 (0.3 %)
Gabapentin	0 (0 %)	1 (100 %)	0 (0 %)	0 (0 %)	0 (0 %)	1 (0.2 %)
Total	275 (44.1 %)	256 (41 %)	13 (2.1 %)	78 (12.5 %)	2 (0.3 %)	624

AEDs uses considered in this table were only those which were appropriately used, with adequate trial durations and clinically effective dosage and without withdrawal secondary to adverse drug events.
* As the number of AED prescriptions were considered in this table, the numbers in this column particularly were multiplied by 2 since every prescription to which there was a response has been prescribed in a different occasion and hence considered as a separate prescription

Patterns of Uses of Antiepileptic Drugs (AEDs) in A Tertiary Neurology Clinic in Khartoum City, Sudan

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Figure 1 Percentages of adverse events that led to discontinuation of AEDs when related to the total number of use of individual AEDs
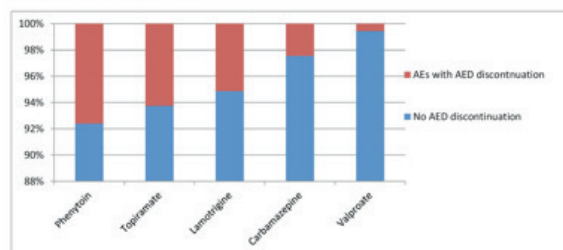
Conclusion: First-generation AEDs are still dominating clinical practice in developing countries with comparable outcomes with second-generation agents.

Disclosure: Nothing to disclose

EP1065

Patterns of drug resistant epilepsy in a cohort of adult epilepsy patients

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Background and aims: Studying patterns of drug-resistant epilepsy enhances understanding its possible pathogenic mechanisms. To study the patterns of drug-resistant epilepsy (DRE) in a cohort of adult epilepsy patients.

Methods: This is a retrospective cross-sectional study. A total of 360 adult Sudanese epilepsy patients who attended a tertiary neurology clinic in Khartoum city, Sudan between 2006-2010 were included.

Results: 23.9% (86/360) of patients were classified to have DRE. Out of these 86 patients, 81.4% were found to have a constant resistant pattern while 18.6% were having an alternating pattern. No significant difference in clinical characteristics was found between the two patterns. When considering covariates related to AED therapy, constant pattern patients were found to have a significantly higher previous history of AED therapy (P=0.046). When tested for the duration of seizure freedom achieved, 35.7% of patients with the constant pattern have never become seizure-free in comparison with 18.8% of patients with the alternating pattern (P=0191). Similarly, 50% of patients with the constant resistant pattern failed to respond to 3 AEDs in comparison with 34.3% of patients with the alternating pattern (P=0.684). Five detailed patterns of DRE were recognized: constant absolute resistant pattern (76.7%), constant partial resistant pattern (4.7%), primary responsive pattern followed by secondary absolute resistance (9.3%), primary responsive pattern followed by secondary partial resistance (2.3%) and primary absolute resistant pattern followed by secondary responsiveness (7%).

Patterns of Drug Resistant Epilepsy in A Cohort of Adult Epilepsy Patients

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Table 1 Characteristics of constant resistant pattern vs alternating patterns using cross-tabulation & Chi-square test

Covariate	Components	Constant resistant pattern (70 cases)	Alternating pattern (16 cases)	P value
Gender	Males	48 (68.6 %)	11 (68.6 %)	0.989
	Females	22 (31.4 %)	5 (31.3 %)	
Age at time of labelling as drug resistant or drug responsive	16 – 25 years	42 (60 %)	11 (68.8 %)	0.390
	26 – 35 years	15 (21.4 %)	0 (0 %)	
	36 – 45 years	7 (10 %)	3 (18.8 %)	
	46 – 55 years	2 (2.9 %)	1 (6.2 %)	
	56 – 65 years	1 (1.4 %)	0 (0 %)	
	> 65 years	3 (4.3 %)	1 (6.2 %)	
Residence	Khartoum	30 (42.9 %)	13 (81.2 %)	0.061
	Central states	20 (28.6 %)	1 (6.3 %)	
	Northern states	9 (12.9 %)	2 (12.5 %)	
	Eastern states	6 (8.6%)	0 (0 %)	
	Western states	5 (7.1 %)	0 (0%)	
Employment	Unemployed	20 (28.6 %)	4 (25 %)	0.668
	Students	22 (31.4 %)	6 (37.5 %)	
	Self-employment	17 (24.3 %)	2 (12.5 %)	
	Formal employment	6 (8.6 %)	2 (12.5 %)	
	Housewife	3 (4.3 %)	2 (12.5 %)	
	Retired	2 (2.8 %)	0 (0 %)	
Age at time of seizure onset	< 1 year	1 (1.4 %)	1 (6.3 %)	0.702
	1 – 12 years	35 (50 %)	7 (43.8 %)	
	13 – 18 years	17 (24.3 %)	3 (18.7 %)	
	19 – 65 years	16 (22.9 %)	5 (31.2 %)	
	> 65 years	1 (1.4 %)	0 (0 %)	
EEG findings	Abnormal	49 (70 %)	12 (75 %)	0.287
	Normal	5 (7.1 %)	3 (18.8 %)	
	Not indicated for diagnosis	15 (21.4 %)	1 (6.2 %)	
	No available data	1 (1.4 %)	0 (0 %)	
Brain imaging	Abnormal	37 (52.9 %)	6 (37.5 %)	0.423
	Normal	29 (41.4 %)	10 (62.5 %)	
	Not indicated for diagnosis	1 (1.4 %)	0 (0 %)	
	No available data	3 (4.3 %)	0 (0 %)	
Seizure type	Focal onset seizures	51 (72.9 %)	11 (68.7 %)	0.741
	Generalized seizures	19 (27.1 %)	5 (31.3 %)	
Aetiology	Genetic	19 (27.1 %)	5 (31.2 %)	0.753
	Structural-metabolic	29 (41.5 %)	5 (31.2 %)	
	Unknown	22 (31.4 %)	6 (37.5 %)	
Duration of epilepsy	1 – 10 years	36(51.4 %)	7 (43.8 %)	0.593
	11 – 20 years	24 (34.3 %)	6 (37.5 %)	
	21 – 30 years	7 (10 %)	1 (6.2 %)	
	> 30 years	3 (4.3 %)	2 (12.5 %)	
Learning disability	Yes	20 (28.6 %)	5 (31.2 %)	0.831
	No	50 (71.4 %)	11 (68.8 %)	
Psychiatric illness	Yes	7 (10 %)	3 (18.7 %)	0.325
	No	63 (90 %)	13 (81.3 %)	

Patterns of Drug Resistant Epilepsy in A Cohort of Adult Epilepsy Patients

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Table 2 Comparison between constant resistant pattern and alternating pattern in relation to treatment related factors

Covariate	Components	Constant pattern of resistance (70 cases)	Alternating patterns (16 cases)	P value*
Previous AED therapy	Yes	56 (80 %)	9 (56.3 %)	0.046
	No	14 (20 %)	7 (43.7 %)	
Seizure freedom has never been achieved even for a single month	Yes	25 (35.7 %)	3 (18.8 %)	0.191
	No	45 (64.3 %)	13 (81.2 %)	
Number of AEDs failed	2 AEDs	24 (34.3 %)	8 (50 %)	0.684
	3 AEDs	35 (50 %)	6 (37.5 %)	
	4 AEDs	7 (10 %)	1 (6.25 %)	
	5 AEDs	4 (5.7 %)	1 (6.25 %)	
Adverse events as a result of AED therapy	Yes	18 (25.7 %)	2 (12.5 %)	0.259
	No	52 (74.3 %)	14 (87.5 %)	

*Significant P values in bolds

Conclusion: These findings indicate that AED pharmacoresistance is a heterogeneous status.

Disclosure: Nothing to disclose

EP1066

Electrical status epilepticus during sleep – a study of 71 Bulgarian patients

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Background and aims: The aim of the study was to analyse the clinical course and the treatment approaches in patients with electrical status epilepticus during sleep (ESES).

Methods: We have retrospectively reviewed the medical data of 51 children with idiopathic ESES and 20 children with symptomatic ESES, treated between 2006 and 2015 in the Clinic of Child Neurology in Sofia, Bulgaria.

Results: The patients with idiopathic ESES showed a later epilepsy onset and more benign disease course than symptomatic cases. A permanent ESES remission was achieved with the initial treatment in 33.3% (15/45) of the children with idiopathic epilepsy, 19 cases showed relapsing and 11 cases – persistent course of ESES, 6 cases were not followed up in the clinic. Good results were achieved with: 1) corticosteroids (CS) (n=21) – permanent ESES remission in 3 and transient – in 14 children, 2) levetiracetam (LEV) (n=20) – permanent ESES remission in 7 and transient – in 3 children, 3) clonazepam (CZP) (n=15) – permanent ESES remission in 5 and transient – in 4 children, 4) ethosuximide (ESM) and sulthiame (STM). The patients with symptomatic epilepsy had more unfavourable evolution as 19 patients had persistent or relapsing course of ESES with only transient improvement with LEV (n=15, transient ESES remission in 9 children), CZP (n=8, transient remission in 3), CS (n=12, transient remission in 9) and ESM (n=5, transient remission in 3).

Conclusion: ESES is characterized by a significant therapeutic resistance, especially in the group of symptomatic epilepsies. The most effective anticonvulsants are CS, LEV, ESM and benzodiazepines.

Disclosure: Nothing to disclose

EP1067

Idiopathic focal epilepsies with occipital paroxysms

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Background and aims: The aim of the study was to analyze and compare the clinical course, EEG and treatment approaches in children with Gastaut (GS) and Panayiotopoulos syndrome (PS)

Methods: We have included 40 patients with PS and 13 – with GS, treated in the Clinic of child neurology in Sofia, Bulgaria.

Results: The children with PS had an earlier age of seizure onset (4y compared to 8y 9m in the cases of GS). Rare seizures (between 2 and 6) predominated in PS (in 65%) while half of the patients with GS had multiple seizures. The seizures were mainly nocturnal in PS (in 80%), while all the children with GS had diurnal seizures and only half of them experienced nocturnal seizures. The most common ictal presentation in PS was nausea and vomiting (in 95% of the cases) while visual symptoms were the main ictal manifestation in GS (visual hallucinations - in 84.6% of the children and visual loss – in 53.8%). The occipital epileptiform activity was the typical EEG feature in GS, but was described in only 57.5% of the patients with PS at the time of the diagnosis.

Conclusion: PS is characterized by a typical clinical presentation with rare, mainly nocturnal seizures with leading autonomic symptoms that show good response to treatment. Unlike PS the typical seizures in GS are brief, mainly diurnal and often multiple. Valproate and Carbamazepine are the drugs of first choice in GS and the treatment is usually long lasting due to the high risk of relapses.

Disclosure: Nothing to disclose

EP1068

Adult phenotype of Dravet syndrome associated with STXBP1 (syntaxin binding protein 1) mutation and good response to cannabidiol treatment

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Background and aims: We present a case of Dravet syndrome: adult phenotype with a STXBP1 mutation and its good response to cannabidiol treatment.

Methods: A 19-year-old woman with history of epilepsy since infancy and poor response to various anticonvulsant therapies. She presented a good psychomotor development until the two years of life, although to the six months had a first crisis which coincided with fever and was followed by motor deficit. Two years later she performed episodes of loss of head tone. From the age of 6, she has generalized seizures more than 10 times a day and from the age of 13 she associates reflexive crises after sound and tactile stimuli. Various genetic-metabolic tests were negative, including the mutation for the SCN1A gene (sodium voltage-gated channel alpha subunit 1). In the last year she has presented marked bradykinesia which impedes walking (FAC 1 according to the gait rating scale - Functional Ambulatory Classifier), mood swings, impulsivity associated with heteroaggressive behavior and visual hallucinosis.

Results: We required whole exome sequencing, finding mutation in the STXBP1 gene. We also suggested to initiate treatment with cannabidiol, achieving a considerable reduction in the number of crises in the day and an improvement in the ability to walk (FAC 4).

Conclusion: The mutation of STXBP1 gene proved to cause Dravet's syndrome in patients with negativity for the mutation of SCN1A. Our case is special because it presents the recent description of the adult phenotype of Dravet's syndrome moreover it is associated to good response to cannabidiol treatment.

Disclosure: Nothing to disclose

EP1069

Determination of social phobia, agoraphobia and depression frequency using clinical scales in epilepsy patients

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Background and aims: Patients with epilepsy can develope psychiatric disorders that decrease quality of life and increase suicide rate. Our study was designed to investigate depression, anxiety, social phobia, agoraphobia of epilepsy patients.

Methods: The study was done between September 2015 - September 2016 in Marmara University Pendik Research Hospital, Turkey, Neurology outpatient clinic, among 150 random patients (18-66 years old) and 70 controls with similar age and gender. Beck Depression Inventory (BDI), Liebowitz Social Phobia Inventory (LSPI) and Panic Agoraphobia Inventory were applied to both groups.

Results: Among evaluated results, 62,7% of the patients were women and their average age was 34.2 ± 10.9, respectively 33.00 ± 10.2 for controls. Fifty percent of the education level of both patients and control group was primary and middle school. The score of BDI for the patients were 15.18 ± 12.25, respectively 10.87 ± 9.06 for controls, that was statistically significant ($p=0.0038$). Both patient and control group were compared according to LSPI and subgroup analysis (for anxiety and avoidance), but no statistical significant result was found ($p>0.05$). Agoraphobia was more common among women and freaquently panic attack occured in closed areas as elevators, tunnels, airplane or subway.

Conclusion: Our results showed that depression and agoraphobia were more common with epileptic patients compared to control group and often seen among women. In epileptic patients, psychiatric deficiencies are frequently ignored and not treated properly. It is very important to identify and treat comorbid factors in order to increase patient's quality of life.

Disclosure: Nothing to disclose

EP1070

Ambulatory EEG: A possible alternative to inpatient video-EEG?

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Background and aims: Ambulatory EEG (AEEG) has been suggested as an alternative to inpatient video-EEG which is particularly useful in assisting the differential diagnosis between epileptic and psychogenic nonepileptic seizures. The aim of this study was to examine the utility of ambulatory EEG (AEEG) in our outpatient clinic.

Methods: We did a retrospective analyses of clinical files and EEG recordings of consecutive patients refered to our neurophysiology department for AEEG studies from January 2011 to December 2015. AEEG recording was performed using a 19-channel recording system and electrodes were applied according to the International 10–20 electrode system. Patients were provided with a clinical diary. Recordings lasting 24 hours. We reviewed clinical files for purpose for the exam and any diagnostic or therapeutic alteration made after the exam.

Results: 58 patient, 30 (52%) male, median age 43 years (7-84 min-max) were included. The primary reasons for the AEEGs were subdivided into three categories: to differentiate between seizures and non-epileptic events (29 patients);to characterize seizure type or localization (20 patients) and to determine the frequency of seizures (9 patients). 84% of the exams had alterations,interictalepilep tiform discharges(IEDs) in 67% and epileptic seizures in 4%. The diagnosis was changed in 12 (21%) patients (non-epilepsy for epilepsy in 9 patients) and 33 patients changed therapeutics.

Conclusion: In our series AEEG was a very usefull tool, particulary in the differential diagnosis between seizures and non epileptic events. As in other studies our data highlights the role of AEEG as an alternative to a more expensive and less available video-EEG.

Disclosure: Nothing to disclose

EP1071

Comparation of corpus callosotomy and vagal nerve stimulation in treatment of pharmacoresistant epileptic encephalopathies

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Background and aims: Corpus callosotomy (CC) and vagal nerve stimulation (VNS) are palliative neurosurgical methods used in treatment of pharmacoresistant epilepsy in patients with unknown, multiple or epileptogenic zones in eloquent brain areas where no resectable surgery is possible.

Methods: We conducted a retrospective research in patients with generalized epilepsy (GE) non responsive to medical treatment in whom either CC or VNS was done. All patients were followed up through one year. The total number of patients was 20, divided in two groups, CC (n=8, mean age 20) and VNS (n=12, mean age 31) group. In the first group all patients, except one who had postencephalitic seizures, had Lennox-Gastaut syndrome (LGS), while in the second one 25% had LGS, 25% had progressive myoclonic epilepsy and 50% had other epileptic encephalopathies.

Results: We observed the effect of CC or VNS on frequency of generalized tonic-clonic seizures (GTCS), atonic seizures (AS) and myoclonic seizures (MS) as they were the predominant types. In the CC group a significant reduction in the frequency of GTCS ($\geq$50%) was noted in 57% of patients, 50% showed significant reduction of AS (half of which were seizure free) and 29% of MS. In the VNS group 82% of patients had significant reduction of GTCS, 73% of AS (9% of which were seizure free) and 60% of MS (20% were seizure free).

Conclusion: Although the patient number in this study was relatively small, according to our results CC is not an inferior method in treatment of pharmacoresistant epilepsy with expecially beneficial results on AS.

Disclosure: Nothing to disclose

EP1072

Frequency of post-stroke epileptiform activity - a systematic review and meta-analysis of observational studies

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Background and aims: Cerebrovascular disease is the most frequent risk factor for epilepsy, and epileptic phenomena following stroke are known to worsen prognosis. Electroencephalography (EEG) is the gold standard biomarker for epilepsy, but it is seldom used, and there is uncertainty about the frequency post stroke epileptiform activity as detected by EEG.

Methods: All studies indexed in MEDLINE, Embase, Web of Science, PsycINFO and OpenGrey (last search on March 2015), which reported the frequency of EEG epileptiform activity after stroke in adults were analysed. Epileptiform activity was defined as ictal activity (electroencephalographic seizures) and interictal activity (non-periodic spikes and sharp waves). Study selection, data extraction and risk of bias appraisal were performed by independent reviewers. Random-effects meta-analysis was used to pool frequencies. Prospero registration number: CRD42015029362.

Results: The electronic search was run on March 2015. A total of 2871 references were retrieved, and 18 studies where included. The pooled frequency of ictal and of interictal activity after stroke was 7% (95%CI 3%-12%) and 8% (95%CI 4%-13%), respectively. The use of continuous EEG did not change the frequency of ictal activity (p=0.55), nor did the management setting (ICU vs. non-ICU, p=0.33). However, studies with continuous EEG showed a greater frequency of interictal activity (p=0.00).

Conclusion: The frequency of ictal and interinctal epileptiform activity was comparable, and consistent with previous analyses of clinical seizures. The former did not change with continuous record or clinical setting, while the latter increased with continuous record. Due to detection bias, it was not possible to correlate clinical and electroencephalographic seizures.

Disclosure: Nothing to disclose

EP1073

New peptide isolated from social wasp venom reduces neuronal cell death and spontaneous recurrent seizures after pilocarpine-induced status epilepticus

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Background and aims: Understanding the pathophysiogenesis of temporal lobe epilepsy (TLE) largely rests on the use of models of status epilepticus (SE), like the pilocarpine model. After several hours of SE, pilocarpine-treated animals remit spontaneously and go into a seizure-free period, known as latent period, before displaying the spontaneous recurrent seizures (SRSs) that characterize the chronic epileptic condition. Based on this, the purpose of our study was to further characterize the capacity of neurovespina (a new peptide similar to one found in a social brazilian wasp Polybia occidentalis) to prevent SRRs and hippocampal neuronal loss.

Methods: During chronic period (fifteen days after SE) animals (swiss mice, n=7) developed a chronic condition determined by SSRs and received daily intraperitoneal injections of neurovespina (doses: 1, 2 or 4 mg/Kg) or saline (control groups) to evaluate the behavioral effectiveness antiepileptic effect. The occurrence of seizures (Racine scale) was evaluated during two weeks (video recorded 9 hours/day).

Results: Our results showed that neurovespina reduced the score, time and number of SSRs in all doses when compared to control group and in the highest dose (4mg/Kg), animals have no seizure in the first 5 hours after treatment during all chronic period. Morphological analysis of hippocampal formation shows no significant loss of selective populations of interneurons in areas CA1 and CA3 and in the hilus.

Conclusion: These data indicate that Neurovespina has potential for the development of novel drugs for neurological diseases, both to reduce the seizures frequency and to minimize the neuronal damage associated with seizures.

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EP1074

Cancelled

EP1075

Continuous thetaburst stimulation for the treatment of refractory neocortical epilepsy

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Background and aims: Repetitive transcranial magnetic stimulation may have anti-epileptic effects, especially in neocortical epilepsy. Continuous thetaburst stimulation (cTBS) seems to be a potent protocol that could optimize safety, tolerablility and applicability based on lower stimulation intensity and shorter duration.

Methods: Patients with refractory neocortical epilepsy are treated with a 4-day accelerated cTBS protocol (figure 1) targeted over the epileptogenic focus. Seizure frequency and adverse events are assessed over a 4-week baseline period and 8 weeks of follow-up. Cognitive and psychological testing is performed at baseline and end of follow-up.
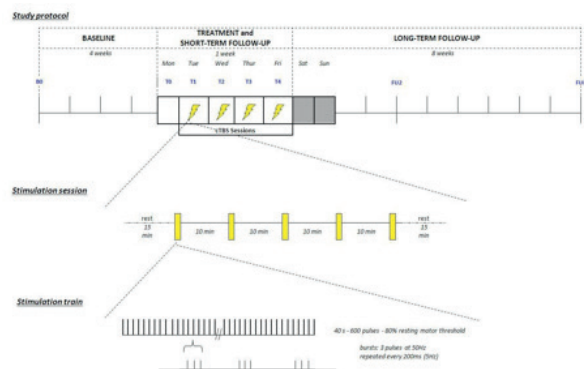
Figure 1: Overview of stimulation protocol

Results: Subject 1 and subject 2 suffer from epilepsy due to a low-grade tumor in the motor cortex causing focal clonic seizures. Subject 1 also experiences myoclonia of the left leg. Subject 3 has epilepsy with auditory seizures following intracranial hemorrhage in the left temporal lobe. cTBS was well-tolerated and did not induce serious adverse events or seizures. Mild headache occurred in subject 3. No negative cognitive or psychological side effects were noticed. Anti-epileptic effects of cTBS varied. Subject 1 experienced a transient reduction in severity of clonic seizures, with complete resolution of myoclonia for 6 weeks. Subject 2 experienced an overall 50% seizure frequency reduction, with most pronounced effect during treatment and initial 4 weeks of follow-up (70% reduction, 3 seizure-free weeks). No marked effect on seizures was identified in subject 3.

Conclusion: cTBS appears safe and well-tolerated, even in seizure-prone subjects. Anti-epileptic effects of variable extent were identified. Extensive parenchymal damage at the target site may have interfered with effective stimulation in subject 3.

Disclosure: Nothing to disclose

EP1076

MERRF presenting with drop attacks due to astatic epileptic crises

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Background and aims: Mitochondrial encephalopathy with ragged red fibers (MERRF) is a progressive mitochondrial disorder characterized by myoclonus, epilepsy, ataxia and myopathy. Drop attacks are seldom recognized as a feature of MERRF.

Methods: A clinical case.

Results: A 50-year-old male presented to our clinic complaining of repetitive drop attacks. He claimed periodic loss of muscle tone in his lower limbs, with loss of orthostatic posture, without impaired consciousness or trigger. The episodes started 10 years earlier and had worsened, occurring now nearly on a daily basis. His previous medical records were remarkable for Wolf-Parkinson-White syndrome, auditory and visual impairment, and surgical removal of neck lipomas. His parents were non-consanguineous. His brother had similar events. His neurological examination was striking for mild cognitive impairment, slow and segmented saccades with limited upgaze, bilateral ptosis, dysarthria, mild proximal muscular weakness, distal hypoesthesia in the lower limbs, diminished reflexes and a wide-based unstable gait. The diagnostic work-up revealed: elevated CK (~1000IU/L); axonal sensory-motor polyneuropathy; bilateral neurosensory hearing loss; generalized cortical atrophy (MRI); abundant bilateral frontotemporal delta rhythm, without paroxysmal activity detected on EEG. Empirical levetiracetam was started, with near-total remission of the astatic crises. MERRF was suspected and a mutation in the MT-TK gene was found confirming the diagnosis.

Conclusion: We describe a case of MERRF presenting with drop attacks due to astatic/atonic epileptic events and excellent improvement with levetiracetam. Multisystemic dysfunction with combination of either: epilepsy, cerebellar, visual or auditory impairment, neuropathy, myopathy, cardiac abnormalities and midline lipomas should raise suspicion of this entity.

Disclosure: Nothing to disclose

EP1077

Cancelled

Headache and pain 1

EP1078

The effects of OnabotulinumtoxinA treatment on the chronic migraine comorbidities of sleep and fatigue

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Background and aims: Chronic migraine (CM) is associated with comorbidities that may exacerbate the condition. This subanalysis of COMPEL addresses effects of onabotulinumtoxinA prophylaxis on comorbid sleep disturbances and fatigue symptoms.

Methods: The 108-week, multicentre, open-label COMPEL Study enrolled adult patients with CM in Australia, Korea and the United States receiving onabotulinumtoxinA 155 U with/without concomitant prophylaxis. Primary outcome was reduction in headache frequency per 28-day period at 108 weeks (9 treatments). Sleep disturbances were assessed using the Pittsburgh Sleep Quality Index (PSQI) and fatigue symptoms using the Fatigue Severity Scale (FSS). Adverse events (AEs) were recorded.

Results: Enrolled patients (N=715) had a mean (range) age of 43 (18-73) years and were predominantly female (84.8%, 606/715). Headache day frequency at week 108 (primary endpoint) was significantly reduced from a baseline mean (standard deviation, SD) of 22 (±4.8) days to 10.7 (±6.4) days (P<0.0001). Patient baseline mean (SD) PSQI score was 13.3 (±3.7), which indicated poor sleep quality. OnabotulinumtoxinA treatment significantly improved PSQI mean scores at weeks 24, 60, 84, and 108 (all P<0.0001; Figure 1). Baseline mean FSS score of 38.1 (±14.5) was also significantly improved at all time points (P<0.0001; Figure 2). Most AEs were mild or moderate in nature; low rates of treatment-related AEs were observed (Table).

Figure 2. Mean Total FSS Scores and Decreases from Baseline by Visit

*P<0.0001
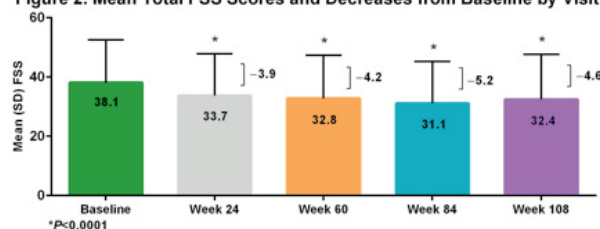
Table. Treatment-Related Adverse Events

Event, n (%)	Overall (N=716)
Neck pain	29 (4.1)
Eyelid ptosis	18 (2.5)
Musculoskeletal stiffness	17 (2.4)
Injection site pain	14 (2.0)
Headache	12 (1.7)
Muscular weakness	10 (1.4)
Facial paresis	9 (1.3)
Migraine	7 (1.0)
Skin tightness	7 (1.0)

Conclusion: Results from the COMPEL Study indicate the effectiveness of onabotulinumtoxinA treatment for reducing headache frequency as well as improving sleep quality and fatigue symptoms up to 108 weeks (9 treatment cycles) in patients with CM. No unexpected AEs were reported.

Figure 1. Mean Total PSQI Scores and Decreases from Baseline by Visit

*P<0.0001

EP1079

SUNCT/SUNA syndrome with cardiac symptoms

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Background and aims: Case report of a short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA) syndrome with transient atrioventricular block during attacks.

Methods: Female, 39-year-old, affected by arterial hypertension and bening familial hematuria, no history of syncopes or headaches, was admitted to the hospital presenting episodes of severe burning facial pain affecting left nasal and maxillar, shorter than one minute, with ipsilateral tearing and nasal congestion, dizziness and one syncope. During her stay in emergency room she suffers new episode, with syncope. Electrocardiography monitorization showed complete atrioventricular (AV) block during attack, nodal rythm at 20 beats a minute, spontaneously recovered to normal sinus rythm. Normal physical exam. The patient was admitted to Intensive Care Unit, persisting attacks with AV block: an external pacemaker was necessary, changed later by a definitive pacemaker.

Results: A cranial tomography (CT) scan showed left cerebellar hemisphere hypodensity, confirmed as chronic left cerebellar infarction by magnetic resonance (asymptomatic). Etiological studies for stroke (CT angiography, hypercoagulability tests, echocardiography) were negative or normal. Indomethacin obtained pain control; lamotrigine rising dose was indicated in order to indomethacin withdrawal, no more episodes with 400mg per day.

Conclusion: SUNA syndrome is a quite unusual headache classified into a group of primary headaches called trigeminal autonomic cephalalgias. Diagnosis features of the group includes unilateral pain and local parasympatethic autonomic symptoms. This is the only case in literature in which pain attacks associate AV block, suggesting hyperactivity of the parasympathetic pathway that exceed local response. Left cerebellar infaction could play an etiological role.

Disclosure: Nothing to disclose

EP1080

Aphasic aura and reversible MRI image in hemiplegic migraine

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Background and aims: Familial Hemiplegic Migraine (FHM) is defined by the occurrence of hemiparesis as part of the aura (ICHD-3 Beta). One of the differential diagnosis is an ischemic stroke. We report a case of FHM that was studied during a prolonged migraine attack.

Results: A 29-year-old woman, developed an intense headache, associated with aphasia and right hemiparesis. She has been diagnosed with FHM type 2 years before with T376M mutation of ATP1A2 gene, localized in 1q21-23 chromosome. Weakness recovered in 24 hours, but she persisted with an atypical aphasia with fluctuating degree of fluency, ranging from periods of almost no speech or difficulty initiating speech to others of fluent speech with paraphasias. Cranial MRI showed a left cortical hypersignal on the temporo-parietal lobe and cingular gyrus on FLAIR but not on DWI. There were no ischemic lesions. EEG showed no paroxysmal activity. The patient recovered from the aphasia in one month, and she repeated the MRI that was normal.

Conclusion: The aura phenomenon has been attributed to cortical spreading depression with vasogenic edema. In this case, the parallel course of symptoms and reversible vasogenic edema supports this pathogenesis. The language disorder was rather atypical for a stroke aphasia, suggesting that the functional impairment is not fixed. This case has unusual features because changes were only observed in FLAIR which is unusual in FHM, where most cases have changes in DWI/FLAIR. The negative DWI excludes ischemic stroke, but FLAIR showed a cortical edema, lead to think in other causes, like FHM.

Disclosure: Nothing to disclose

EP1081

Headache linked to intracranial hypertension and hypertrophic pachymeningitis as the initial and dominant presentation of Granulomatosis with polyangiitis (Wegener granulomatosis)

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Background and aims: Granulomatosis with polyangiitis (GPA, or Wegener granulomatosis) is a rare, systemic disease of unknown etiology, characterized by necrotizing granulomatous inflammation and systemic vasculitis. We are reporting a case of patient with headache as the presenting symptom.

Methods: A 54-year-old male, without any related medical history, developed a non-specific, severe and unresponsive to various treatments headache. In the following 2 months, he gradually developed hoarseness and diplopia affecting the left abducens nerve. An ophthalmological examination revealed bilateral papilledema and diffused flame-like retinal hemorrhages, implying the presence of intracranial hypertension. A brain MRI revealed wide-spread fattening and meningeal enhancement of the left hemisphere, and also mild swelling and inhomogeneous signal at the left half of the nasopharynx. An endoscopy of the pharynx revealed the presence of a tumor-like mass in the left half of the nasopharynx. A biopsy showed inflammation with presence of polykaryocyte Langhans giant cells, implying a specialized granulomatous inflammation. The laboratory testing revealed important albuminuria and microhematuria, positive c-ANCA and negative p-ANCA.

Results: Having fulfilled three out of four diagnostic criteria of the American College of Rheumatology for GPA, we initiated a steroid treatment with a drastic improvement of headache. During the following weeks, the remaining symptomatology resolved gradually whereas a follow-up brain MRI showed a decrease in meningeal enhancement.

Conclusion: Participation of the central nervous system at the initial stage of GPA is an extremely rare condition and occurs in up to 8% of patients. Headache as the sole presenting symptom of GPA is additionally rare and may elude early diagnosis.

Disclosure: Nothing to disclose

EP1082

Migraine and autoimmunity: How often are autoimmune disorders reported by headache patients

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Background and aims: Although the pathophysiology of migraine is not yet totally understood, a possible role of immunological dysfunction and/or autoimmunity has been reported. The aim of this study was to analyse the frequency of autoimmune disease reported by migraine patients and patients with non-migraine headache.

Methods: We review the clinical files of consecutive patients observed in our Headache Ambulatory Clinic between January 2013 and December 2015. Demographic and clinical data, including all the information regarding any diagnostic of autoimmune disorder, were collected. Diagnosis of headache was made based on ICHD3-beta criteria. Migraineurs and patients with headache without migraine features were compared on frequency of the diagnosis of autoimmune disorders. SPSS was used for statistic analysis and a p value of <0.05 was considered significant.

Results: 433 patients, 85% female, median age 43 years (18-92, min-max), 279 (64%) with migraine. Autoimmune disease were reported by 28 (6,5%) patients, 22 (8,6%) migraineurs and 6 (4%) non-migraneurs (p=0,106). Inflammatory Bowel Disease (6 patients), Systemic lupus erythematosus (4) and Psoriasis (4) were the most frequent autoimmune disorders reported. Patients with autoantibodies but without diagnosis were not considered has having autoimmune disease.

Conclusion: In our cohort we didn't find a significantly greater prevalence of autoimmune disorders in migraine patients than in patients with other headache types. Studies with more patients with structured questionnaires regarding autoimmune symptoms and conditions, could help clarify the role of autoimmunity in migraine.

Disclosure: Nothing to disclose

EP1083

Acute Hashimoto's Thyroiditis presenting as worsening of migraine without aura

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Background and aims: The prevalence of hypothyroidism in migraine is significantly higher than in the general population. Hypothyroidism should be considered as one of the variety of migraine comorbidities, even if possible pathophysiologic relationships remain unclear. Presenting an interesting case of autoimmune thyroiditis which was detected during acute phase of migraine.

Methods: Case Study

Presenting young 22-year-old lady, known case of migraine diagnosed 6 years back on regular prophylaxis came with acute headaches, holocranial, throbbing in character, associated with vomitings and nausea and photophobia, no preceeding aura, partially relieved with analgesics. Examination showed conscious cooperative, dull, apathetic, no localising deficit, vitals normal CTSCAN HEAD Normal, blood biochemistry normal, CBC normochromic normocytic anaemia, T4 low, TSH high and anti TPO 1008IU/ml, Patient started on intravenous fluids, analgesics, steroids and thyroxine. Gradually patient improved.

Results: This is the first case report of migraine without aura geting worse secondary to auto immune thyroiditis.

it is proposed that antibodies primary directed against the thyroid gland, "leak" across the blood-brain barrier into the brain parenchyma, inducing an autoimmune lymphocytic response based on shared antigens between brain and thyroid.

Conclusion: Headache disorders may be associated with an increased risk for the development of new onset hypothyroidism. Auto immune thyroiditis can affect from headaches, seizures, and steroid responsive encephalopathy, and early diagnosis helps in managing the patient efficiently.

Disclosure: NO GRANT

EP1084

A systematic literature review and meta-analysis of epidemiologic studies in chronic and episodic migraine

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Background and aims: Despite its public health importance, there is limited understanding on the epidemiology of migraine, especially regarding its demographic or geographic variation. International consensus on the definition of migraine has evolved over time contributing to heterogeneity seen across studies. This study aimed to systematically identify population-based studies that report prevalence and/or incidence of migraine in the past decade.

Methods: A systematic literature review (SLR) was conducted following the 2015 Preferred Reporting Items for Systematic review and Meta-Analysis Protocols (PRISMA-P). The search focused on English publications of population-based studies on the adult prevalence or incidence of migraine, chronic (CM) and episodic migraine (EM), published between 2006−2016. Sources searched were: Medline, EMBASE and conference proceedings (2014-2016) from the American Academy of Neurology, European Academy of Neurology, and International Headache Society. Information was extracted by two researchers independently in parallel and any disagreements were resolved by discussion or independent arbitration by a third reviewer.

Results: 1047 publications were retrieved in total (128 of those were identified from conference abstracts, 915 from database searches and 4 from previously published SLRs or meta-analyses). Overall, 56 publications corresponding to 37 unique studies were retrieved (Figure 1). Fifty-five publications reported prevalence and 1 reported incidence only. The 1-year prevalence of migraine ranged from 4.3% to 45.5%.

Figure 1. PRISMA Diagram for the Systematic Literature Review of Epidemiologic Studies in Migraine

Conclusion: Limited availability of epidemiological estimates in migraine exists. This SLR provides a systematic summary of the available population-based studies reporting prevalence of migraine in the last decade which can form the basis of subsequent meta-analysis for subgroups of interest

Disclosure: This study was sponsored by Novartis Pharma AG, Basel, Switzerland

EP1085

Association of migraines with suicidal ideation among immigrants: Experience of the emergency department of a Greek Tertiary Clinic

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Background and aims: Suicide represents a significant global public health and social concern, and suicide rates have been increased in patients with migraine. Immigrant and ethno-cultural minorities face mental health challenges associated with suicide behaviours,however, data on pain-associated suicidality are lacking. Our aim was to investigate a potential link between migraine and suicidal ideation among immigrants.

Methods: We conducted a retrospective study of all visits in our emergency department between 2014-2016. All immigrants completed the questionnaires, including demographics, headaches characteristics, depression and suicidal ideation (Patient Health Questionnaire9). Diagnoses of headaches were made according to International Classification of Headache Disorders-III beta criteria. Multivariable logistic regression analyses were performed to estimate odds ratios (OR) and 95% confidence intervals (95% CI).

Results: Immigrants represent 22.6% (n=205) of the total number of visits because of headaches (n=5988). Migraineurs reported a higher frequency of suicidal ideation (16.1% [OR]=2.9, 95%[CI] 2.3-3.6; p<0.001), compared of non migraineurs. After controlling for depression score and sociodemographic characteristics, immigrants with migraine had 68% increased odds of suicidal ideation (OR = 1.68; 95% CI: 1.36-2.17) compared with non-migraineurs.Women with migraine and depression were 2fold more likely to report suicidal ideation [OR =2.46, 95% CI (2.55- 4,46)]

Conclusion: Migraine is associated with increased likelihood of suicidal ideation in immigrants after adjusting fordepression. These findings may further support the need to enforce health authorities for outpatient management for this vulnerable population.

Disclosure: Nothing to disclose

EP1086

Stroke-like migraine attacks after radiation therapy (SMART) syndrome with cerebrospinal fluid pleocytosis

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Background and aims: SMART syndrome is a rare syndrome characterized by a remote history of cranial irradiation, severe headache and seizures with prolonged and reversible neurological signs and symptoms referable to a unilateral cortical region. The diagnosis relies on brain MRI and exclusion of alternative diagnoses. Cerebrospinal fluid (CSF) analysis is usually inconclusive.

Methods: Case report

Results: Eighteen-year-old male was diagnosed with glioblastoma of the right frontal lobe in 2008 (age of 10). After the surgery he was treated with chemo- and radio-therapy (59.4Gy) and recovered completely.

In April 2016 he experienced a migraine like headache with numbness and weakness of the left upper limb which spontaneously subsided after 10 minutes. A week later he suffered a severe throbbing headache and paresis of the left upper limb after a night of partying and drinking alcohol. Over 14 days left-sided hemiplegia with left hemispatial neglect and hemianopsia evolved. He suffered several generalized seizures. MRI revealed cortical enhancement over the right hemisphere with spared white matter (Figure 1). CSF analysis revealed pleocytosis (white blood cells count of 12x10^6 with 6x10^6 neutrophils, 4x10^6 lymphocytes and 2x10^6 monocytes). Extensive tests performed to exclude infectious causes were negative. After treatment with verapamil, nimodipine and dexamethasone neurological deficits and headache subsided completely over 8 weeks. Follow up MRI after 7 months showed complete regression. CSF pleocytosis also subsided.
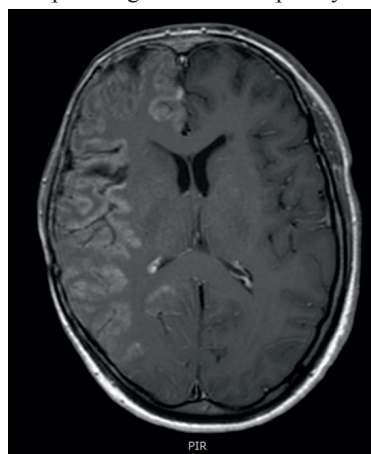
Figure 1: MRI showing vast involvement of the right cerebral hemisphere with no tumor recurence.

Conclusion: This is the first report of SMART syndrome with CSF pleocytosis. Additionally we speculate that ethanol with its effect on endothelial function might provoke development of the SMART syndrome.
Disclosure: Nothing to disclose

EP1087

Psychometric properties of brief pain inventory for assessing hemiplegic shoulder pain

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Background and aims: Hemiplegic shoulder pain (HSP) affects up to 84% of stroke patients and potentially impacts daily functions for stroke patients. However, no scale has yet been developed specifically for HSP. Brief Pain Inventory (BPI) short form is common to evaluate the worst pain intensity (BPI3) and pain interference in daily life (BPI9). The purpose of this study is to investigate psychometric properties of the BPI for assessing HSP.
Methods: Eighty stroke patients were recruited to rate shoulder pain twice, at one-week interval, with BPI and Numerical Rating Scale (NRS). The NRS was used as comparator with BPI to examine concurrent validity using Spearman's rho correlation coefficient (ρ). Test-retest reliability of BPI was analyzed with the intraclass correlation coefficient (ICC) for determining the degree of consistency and agreement between test-retest. The standard error of measurement (SEM), minimal detectable change (MDC), Bland-Altman limits of agreement (LOA) were the absolute reliability indexes used to quantify measurement errors and determine systematic biases of repeated measurements.
Results: Concurrent validity of the BPI was moderate (ρ=0.62-0.72). The ICCs of the BPI3 and BPI9 were 0.88 and 0.86 The SEMs of BPI3 and BPI9 were 0.99 and 0.57. The MDC95 of the BPI3 and BPI9 were 2.74 and 1.58. The Bland-Altman analyses revealed no significant systematic bias between repeated measurements and narrow range of the LOA for the BPI indicated a high level of stability.
Conclusion: The BPI demonstrated good concurrent validity and reliability for measuring shoulder pain in stroke patients.
Disclosure: This work was supported by the Ministry of Science and Technology (104-2314-B-182-035-MY3) and Chang Gung Memorial Hospital (CMRPD3E0331) in Taiwan.

EP1088

Cancelled

EP1089

Cancelled

EP1090

Myofascial pain and musculoskeletal dysfunction

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Background and aims: Myofascial trigger zone [TrZ] are a common cause of musculoskeletal pain. The aim of this study was to evaluate the mechanisms of myofascial TrZ formation and to reveal possible changes in muscle ultrastructure related to myofascial pain syndrome.
Methods: Thirty-six patients with myofascial pain syndrome, mean age 38.4 years (SD 9.7), and 12 age-matched controls were included in this study. The trapezius and brachioradialis muscles were examined by means of single fiber and concentric needle electrodes and electron microscope.
Results: Electrophysiologic studies have revealed significant changes in the shape of the main spike motor unit and endplate potentials: decrease in the duration and amplitude of motor unit potentials, increase in the duration and rise time endplate potentials in myofascial TrZ. The fiber density was increased and mean jitter higher in the TrZ than in control group. The destruction of contractile apparatus involves myofibrils loss and broadened interfibrillar distance. In some parts of muscle we observed total destruction of several sarcomeres. Structure of Z-lines was changed significantly. Autofagosomes in the peripheral part of the cell in sarcoplasma near cellular nucleus were found.
Conclusion: The neuromuscular dysfunction in the immediate vicinity of a motor endplate is the anatomical substrate of TrZ, which produced typical characteristic electrical activity. Divergence of myofilaments and Z-line can be associated with citosceletal protein destruction. The presence of autophagosomes associates either with breach of neurotrophic control or with muscle atrophy after exhausting physical activity. All this can be the basis of effective therapy in patients with myofascial pain syndrome.
Disclosure: Nothing to disclose

EP1091

Cancelled

Infection and AIDS

EP1092

Central nervous system infection with Listeria monocytogenes: 20 years experience in a terciary hospital

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Background and aims: Listeria monocytogenes (Lm) is the third leading cause of bacteria central nervous system (CNS) infection; it especially affects immunosuppressed patients. We present the largest series of patients with CNS involvement by Lm of a Spanish hospital. We analyzed the risk factors for the development of CNS infection, temporal changes in incidence, presentation symptoms, cytobiological features of cerebrospinal fluid, radiological findings, treatment and prognosis.

Methods: Descriptive and analytical research of all Lm isolates collected prospectively by the Microbiology Unit in a tertiary hospital between January 1996 and May 2016.

Results: Lm was isolated in 104 patients, 44 had CNS involvement. There was an increase in the incidence of Listeriosis and CNS infection between 2006 and 2016, compared to the previous decade. CNS infection was associated with treatment with immunosuppressive drugs. The most frequent presenting symptoms were fever and impaired awareness. 27% of patients presented with rombencefalitis. There was a case of brain abscesses. 73% of patients healed without sequelae. Mortality (11%) was only associated with neoplasms. The majority of patients were treated with ampicillin and gentamicin, with no differences in mortality compared to other therapeutic regimens.

Conclusion: The incidence of CNS infection with Lm has increased in recent years, associated with immunosuppressive treatments and neoplasias. The overall mortality rate was low, with no differences according to the antibiotic treatment used.

Disclosure: Nothing to disclose

EP1093

First case reported of cytomegalovirus encephalitis in a multiple sclerosis patient in treatment with fingolimod

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Background and aims: Cytomegalovirus (CMV) encephalitis is an important opportunistic infection that occurs in HIV patients, especially in patients with CD4 <50/mm3, but is rarely recognized in other groups. We present a case of CMV encephalitis in a patient in treatment with fingolimod for multiple sclerosis (MS).

Methods: 22-year-old woman diagnosed of MS since 19-years-old. In treatment with fingolimod with a lymphocyte count always >200mm^3. She has a medical history of Hodgkin lymphoma (in complete remission since 17-year-old) and migraine with aura. The patient presented in the emergency department (ED) with a severe migraine crisis with prolongued aura. Later began with altered level of consciousness, agressive behaviour and altered speech. At examination was afebrile. Brain CT, basic blood test and lumbar puncture were performed,

Results: Blood lymphocyte count was 60mm^3 (previous week 380mm^3). We began treatment with aciclovir, suspended fingolimod and solicitated DNA detection for herpesviridae despite brain CT and CSF composition were unremarkable and no fever. The patient recovered normal status progressively. CMV DNA was detected in CSF and treatment was switched to galanciclovir i.v and then to valaciclovir p.o. Brain MRI didn't show any new alterations. This would be the first case described of CMV encephalitis in patients with multiple sclerosis treated with fingolimod, since we did not find any publication after a bibliographic search. In cases of encephalopathy in an immunocompromised patient (regardless of the cause), CMV encephalitis should be suspected even in the absence of fever, cerebrospinal fluid composition and neuroimaging without alterations.

Disclosure: Nothing to disclose

EP1094

Central nervous system histoplasmosis due to histoplasma capsulatum var. duboisii: First case report and literature review

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Background and aims: Histoplasmosis is a disease caused by the fungus Histoplasma capsulatum whom two differents varieties exist: Histoplasma capsulatum var. capsulatum (American histoplasmosis) and Histoplasma capsulatum var. duboisii (African histoplasmosis). Central nervous system involvement in the Duboisii variety as never been reported yet, we report a case.

Methods: We report a 47-year-old man from Congo, who has lived in France for twenty years and recently travelled to Congo, with a picture of cognitive impairment rapidly installed in a few months. The only localising sign was a left homonymous hemianopsia. There was no extra-neurological sign or symptoms. He was afebrile and laboratory results were normal. Brain magnetic resonance imaging revealed bilateral parieto-occipital ring-enhancing brain lesions. Stereotactic-guide cerebral biopsy was performed and revealed yeasts of Histoplasma capsulatum var. duboisii on direct examination confirmed by polymerase chain reaction-sequencing. The complementary work-up revealed no immunodeficiency and asymptomatic pulmonary and occular localisation. The treatment is ongoing with amphotericin B and switch to oral itraconazole. We searched PubMed® from inception to december 2016 to identify case reports of cerebral histoplasmosis involving histoplasma duboisii.
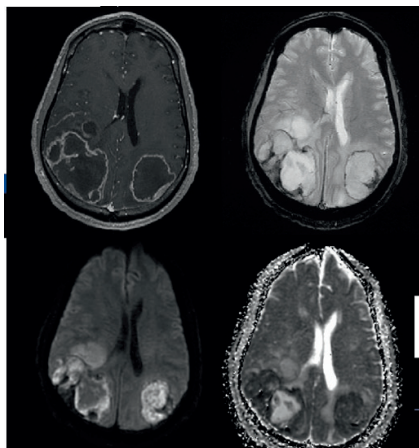
Brain magnetic resonance imaging revealed bilateral parieto-occipital ring-enhancing brain lesions

Results: A total of 105 case reports of histoplasma duboisii infection were identified. Localisations reported were cutaneous, bone, pulmonary, lymphadenic, digestive and one adrenal glands. No cerebral histoplasmosis involving the duboisii variety was reported.

Conclusion: Histoplasmosis is a rare cause of brain tumor-like clinical and radiological picture which has been reported in American Histoplasmosis. Central nervous system involvement in the Duboisii variety has never been reported yet, we report a case.

Disclosure: Nothing to disclose

EP1095

Acute measles encephalitis with an atypical clinical presentation in a vaccinated adult

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Background and aims: Despite the availability of an effective vaccine, measles remains a leading cause of death among children in developing countries. While unvaccinated children are at highest risk of infection and its complications, they can occur even in vaccinated patients. Neurological complications may occur early (acute postinfectious encephalitis) or after years of viral persistence (subacute sclerosing panencephalitis).

Methods: Case report.

Results: A 19-year-old female patient was diagnosed with a right eye retinitis and started treatment with oral methylprednisolone during 20 days. She had no relevant previous medical history and previously received measles vaccination. Five days after the suspension of corticotherapy, she rapidly developed progressive behavioural changes, global aphasia, right hemiparesis and right homonymous hemianopsia. CSF study revealed mild mononuclear pleocytosis. Brain MRI showed bilateral temporal pole and left temporo-parieto-occipital T2 hyperintensities. EEG revealed a pattern of left hemispheric slowing without periodic complexes or paroxistic activity. Metabolic, immunological, bacteriological and viral studies, as well as the search for paraneoplastic syndromes were negative. She continued having a clinical, imagiological and electroencephalographic worsening without response to antivirals or immunotherapies that included high dosage corticotherapy, plasmapheresis and cyclophosphamide. Brain biopsy revealed intranuclear inclusions in oligodendrocytes compatible with paramyxovirus nucleocapsids. The patient became fully dependent and died a year later due to an infectious complication.

Conclusion: This case illustrates a severe atypical presentation of measles encephalitis occurring in a previously healthy vaccinated patient. While the absence of rash history raises some doubts regarding the moment of primary infection, we propose that the retinitis may have corresponded to the primary infection.

Disclosure: Nothing to disclose

EP1096

Cognitive impairment of the frontotemporal profile as a debut of Whipple's disease

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Background and aims: Neurological Whipple's disease without previous systemic involvement is not frecuent but can have different clinical presentations. In this way we present an atypical case with frontotemporal dementia syndrome and pseudotumoral neuroimaging.

Methods: A 71-year-old male with a 3-month history characterized by mnesic failures and deliriform thought that weeks later had dysphasic language with semantic paraphasias, dysnomia, inability to understand complex orders, confusion between right-left, loss of executive skills and apathy. In craneal MRI (magnetic resonance imaging) presented an extensive lesion in the left temporal region that resembles a high grade glioma. Given this finding and the nonspecific nature of the lesion, a cerebral biopsy was performed reporting the presence of intracytoplasmic inclusions and bacilliform structures free in the neuropilo, compatible with the diagnosis of encephalitis by Troppheryma Whipple, confirmed with positive PCR (Polymerase Chain Reaction) in brain tissue.
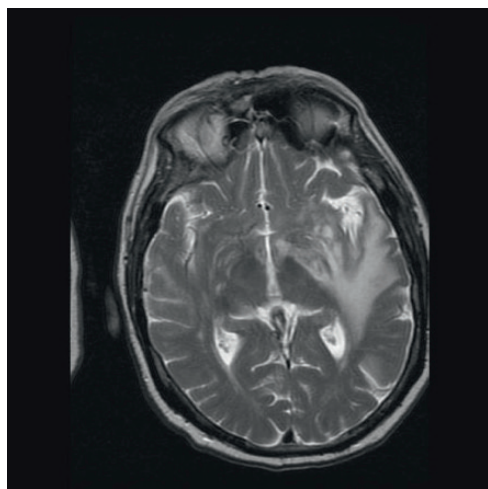
Lesion in the left medial temporal region
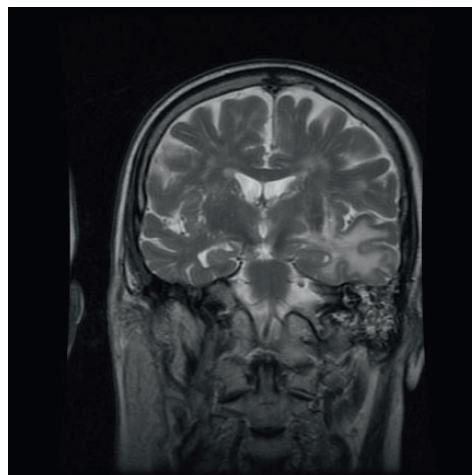
Lesion in the left medial temporal region
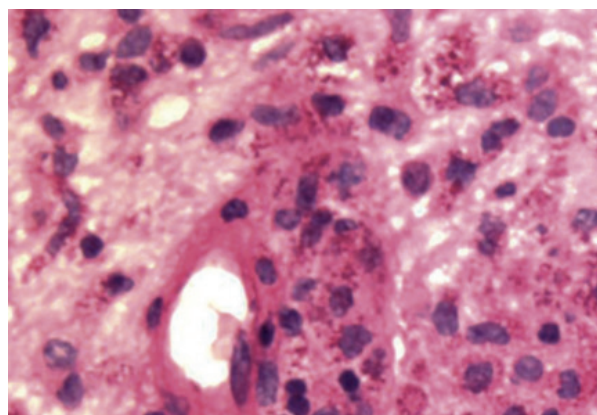
Brain tissue with intracytoplasmic inclusions and bacilliform structures

Results: This clinical case refers a patient with a frontotemporal dementia as a unique clinical manifestation of Whipple's disease, with no prior intestinal involvement, ruled out by duodenal biopsy, which needed three years of antibiotic treatment with ceftriaxone and trimetroprin/sulfametoxazole. He currently presents radiological and clinical stability after five years of follow-up.

Conclusion: Our case is exceptional because it shows a patient with Whipple's disease that begins with cognitive affectation with a pseudotumoral neuroimagen without a history of intestinal or systemic infection.

Disclosure: Nothing to disclose

EP1097

Clinical manifestation and treatment outcome of Parvovirus B19 encephalitis in immunocompetent adults

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Background and aims: Since human parvovirus B19 (PVB19) was discovered from the serum sample of a normal blood donor in the mid-1970s, its infection has been reported to cause a variety of clinical manifestations, such as erythema infectiosum, transient aplastic crisis, non-immune hydrops fetalis, and arthritis. PVB19 has rarely been identified as a cause of encephalitis in immunocompetent adults, in whom clinical information regarding PVB19 encephalitis has remained unclear.

Methods: We reviewed a series of consecutive patients with acute encephalitis who underwent extensive workups for pathogens in the serum and cerebrospinal fluid (CSF) between May 2006 and May 2016 at Seoul National University Hospital. We included patients older than 18 years who had positive PVB19-polymerase chain reaction (PCR) results from their serum or CSF samples.

Results: Although none of the patients showed any distinctive features of PVB19 infection, they showed various clinical manifestations, including one instance of brainstem involvement. Seizure was an especially frequent symptom, which was well controlled with antiepileptic drugs. All the patients showed favorable outcomes at discharge. However, two received immunotherapy due to insufficient recovery from the antiviral treatment; subsequently, these patients showed remarkable improvement.

Conclusion: PVB19 infection should be considered as a possible cause of acute encephalitis syndrome in immunocompetent adults. Since the clinical presentation of PVB19 encephalitis in immunocompetent adults may be non-specific, laboratory tests for PVB19 are critical for a prompt diagnosis. PVB19 encephalitis in immunocompetent adults generally shows a favorable outcome, and immunotherapy can be considered a treatment option, especially in those who are resistant to the initial management.

Disclosure: Nothing to disclose

EP1098

Clinical presentation and diagnostics of Lyme neuroborreliosis in the period of 2005–2015 at the department of neurology in Vilnius, Lithuania

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Background and aims: Lyme neuroborreliosis (LNB) is a tick-borne neuroinfection caused by spirochete Borrelia. Our aim of the study was to analyse seasonal variation, symptoms and diagnostics of LNB.

Methods: The medical records of 91 patients with confirmed LNB, who were hospitalized at the Department of Neurology, Vilnius University Santariškių Clinics, Lithuania, in the period from 4 September 2005 to 4 September 2015 were analysed. The diagnosis of definite/possible LNB was made according to EFNS guidelines on the diagnosis and management of European Lyme neuroborreliosis.

Results: The mean age was 49 ± 17 years, the male/female ratio was 48/43. One third of the patients had a history of a tick bite, only 10% erythema migrans. The mean annual rate of LNB varied significantly (highest rates in 2009, 2010, 2012, 2014). Most of the LNB cases occurred in summer and autumn, but 15% of all cases occurred in winter-spring season. Bannwarth's syndrome was the most common (47%) clinical presentation, meningoencephalitis (24%) and meningitis (21%) were frequent also. Mean cytosis - 174 cells per mm3 (median:104), mean protein concentration 1,22g/l (median: 0,96). 91% of the patients had positive anti-B.burgdorferi (anti-BB) antibodies test from blood serum or cerebrospinal fluid. 12% had positive anti-Tick-borne-encephalitis-virus antibodies.
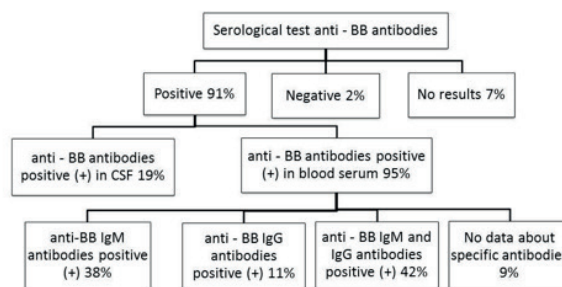
Table 1. Serological test results of anti – BB antibodies.

Conclusion: LNB is highly seasonal disease though some of the cases occur in winter and spring. The most common clinical presentation is Bannwarth's syndrome and meningoencephalitis. The co-infection with Tick-borne-encephalitis virus must be considered.

Disclosure: Nothing to disclose

EP1099

A multi-centre audit of the management of HSV encephalitis in the North West of England

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Background and aims: Herpes Simplex Virus (HSV) encephalitis is a severe, potentially fatal infection of the brain parenchyma affecting between 1 in 250,000 and 1 in 500,000 each year. Prognosis has been historically poor, but the early institution of therapy can improve outcomes.

We audit the management of patients across two hospital trusts; encompassing a Neurosciences centre, Infectious Diseases centre and two District Generals.

Methods: Patients with PCR positive CSF results for HSV-1 and HSV-2 were identified and cross-referenced with those clinically coded as meningoencephaltis within a 1-2 year period. Records were audited according to the 2012 guidance.

Results: A total of 16 patients were included, (n=10 male, n=6 female) with average age at presentation 63 years. Patients presented with decreased GCS (n=10), headache (n=6), seizure (n=5), collapse (n=3) and focal neurology (n=2). Clinical suspicion of encephalitis was documented on average 32 hours after initial presentation. CT brain was completed in 81% of patients, on average 26.5 hours following initial presentation and 69% of patients underwent MRI brain. Lumbar puncture was performed in 93.8% of patients, on average 16.5 hours following documented suspicion. HSV was identified by PCR in 75% of cases. Acyclovir therapy was commenced in 94% of patients, on average 32 hours after initial presentation. Acyclovir was stopped following negative CSF PCR in 69%, due to clinical improvement in 23% and following self-discharge in 7% of patients.

Conclusion: This study continues to identify delays in diagnosis, investigation and the initiation of therapy but also highlights a disparity regarding the decision to stop acyclovir therapy.

Disclosure: Nothing to disclose

EP1100

Neurobrucellosis: A case of reversible rapidly progressive dementia

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Background and aims: Portugal is considered a high risk country for brucellosis. About 5% of the cases develop neurobrucellosis with heterogeneous manifestations, usually accompanied by CSF lymphocytic pleocytosis.

Methods: Case Report

Results: A 81-year-old female was admitted to the neurology ward for rapidly progressive cognitive impairment and frequent falls, causing complete dependency for activities of daily living in 4 months. The patient was afebrile, alert, disoriented with incoherent speech, presented with bilateral extrapyramidal signs and was unable to walk. Head CT and MRI revealed bilateral hippocampal atrophy and moderate leukoaraiosis. CSF analysis showed lymphocytic pleocytosis (25 cells/uL), hyperproteinorraquia and hypoglucorraquia. Despite the absence of relevant epidemiological history, both serum tube agglutination test and CSF polymerase chain reaction (PCR) were positive for Brucella. The patient was started on trimethoprim/sulfamethoxazole, doxycycline and rifampicin and discharged after 2 months, partly improved. Three weeks later, she was readmitted due to persistent CSF pleocytosis and trimethoprim/sulfamethoxazole was changed to ceftriaxone. After 3 months, the patient was discharged on trimethoprim/sulfamethoxazole, doxycycline and rifampicin. After completing 9 months of antibiotic therapy, CSF normalized, extrapyramidal signs disappeared, her gait was normal and she had autonomy for most activities of daily living.

Conclusion: In this case, some clinical and imagiological elements could suggest a neurodegenerative etiology. However, its rapidly progressive course requires exclusion of potentially reversible causes of dementia. Neurobrucellosis is a treatable cause of recent cognitive impairment, requiring prolonged antibiotic therapy, and should be considered in the presence of CSF lymphocytic pleocytosis even without fever or suggestive epidemiological context.

Disclosure: Nothing to disclose

EP1101

Increasing proportion of HIV infection in patients with stroke over a period of 16 years in Spain

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Background and aims: An increase of the incidence of stroke in HIV patients has been reported in recent years. We assessed trends in proportion of HIV infection among patients with stroke in Spain.
Methods: Data were obtained from the national minimum basic dataset. All patients hospitalized between 1997 and 2012 with a diagnosis of stroke at discharge were included. Annual proportion of HIV infection and time trends were calculated, stratifying by type of stroke and HIV stage. Independent predictors of HIV infection were evaluated with multivariate logistic regression. Mortality, stay and cost per patient were also analyzed.
Results: From a total of 857.371 patients with stroke hospitalization, 2.226 had HIV infection. A 2.3% per year increase of the proportion of seropositive patients was observed, exclusively due to an increase of the ischemic strokes (per year-adjusted OR 1.033, CI 95% 1.018–1.046, $p<0.0001$) and the asymptomatic stage of HIV infection (per year-adjusted OR 1.076, CI 95% 1.056–1.096, $p<0.0001$). Factors independently associated with HIV infection were smoking, stimulating drugs consumption and HCV co-infection. HIV infection was associated with a higher mortality (OR 1.81, $p<0.0001$), more days hospitalized (median: 11 vs 9 days, $p<0.0001$) and a higher cost (median: 6.010€ vs 3.781€, $p<0.0001$).
Conclusion: Over the last years, there is an increase in the proportion of HIV-infected patients, mainly asymptomatic, among stroke hospitalizations independently of other vascular risk factors. This finding suggests that HIV infection per se is a specific cerebrovascular risk factor.
Disclosure: Nothing to disclose

EP1102

Silent cerebral small vessel disease in cart well-controlled HIV-infected patients

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Background and aims: Cerebral small vessel disease (CSVD) is defined by white matter hyperintensities (WMHs), silent brain infarction (SBI) or microbleeds (MBs). cART well-controlled persons living with HIV (PLWHIV) are living longer and add conventional and non-conventional vascular risk factors (VRF), all that might act simultaneously to increase the prevalence of CSVD in PLWHIV.
Methods: The ANRS EP51 MICROBREAK (NCT02082574) cross-sectional study, aimed to assess the prevalence of CSVD in treated PLWHIV≥50 years, with controlled viral load for at least 12 months; and to compare this prevalence to that observed in HIV negative controls (HNC). A logistic regression model was used to assess the impact of HIV on CSVD adjusted on traditional risk factors.
Results: 456 PLWHIV and 154 HNC were recruited; median age: 56 and 58 years (p=0.001). All VRF were more frequent in PLWHIV than in HNC (p<0.004), except diabetes. Median CD4 count was 655/mm3. CSVD was detected in 51.5% of PLWHIV and 36.4% of HNC, with an adjusted OR of 2.3 (95% confidence interval: 1.5–3.6). Older age and hypertension were associated with the risk of CSVD. The impact of HIV was different according to age, with ORa of 5.3, 3.7 and 1.0 for age of <54, 54-60 and >60 years, respectively (p=0.022). The proportion of participants with severe CSVD was 19% in PLWHIV and 14% in HNC, with an ORa of 1.6.
Conclusion: Prevalence of CSVD is twice higher in middle-aged PLWHIV. HIV is an independent risk factor of CSVD. Besides age and hypertension, HIV is an independent risk factor of CSVD.
Disclosure: grant from ANRS

EP1103

Respiratory virus-related meningoencephalitis in adults, South Korea, 2012-2015

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Background and aims: The respiratory virus group consists of viruses such as adenovirus; respiratory syncytial virus (RSV) A and B; rhinovirus A and B; coronavirus, influenza A and B; parainfluenza 1, 2, 3; and metapneumovirus. RVs mainly cause upper or lower respiratory tract infections, but they can also cause central nervous system infection, mostly in children. Adult cases of RV-related meningoencephalitis have been reported in only a limited number of patients.

Methods: From March 2012 to December 2015, patients visiting Seoul National University Hospital with clinical suspicion of CNS infection were enrolled in the Seoul Neuroinfection registry. All patients underwent RV multiplex PCR analysis of the CSF and sputum.

Results: Among 661 patients, 10 patients were diagnosed with RV-related meningoencephalitis. Three patients showed positive CSF PCR results, including two with influenza A and one with human parainfluenza 3 virus. The other seven patients showed positive PCR results in the sputum. Six patients had preceding upper respiratory tract infection symptoms before manifestations of CNS infection. Leptomeningeal enhancement was the most frequent finding (70%) observed in MRI. Among the four RV-related encephalitis patients, three were treated with antiviral therapy. All patients completely recovered except one patient who deteriorated despite antiviral treatment
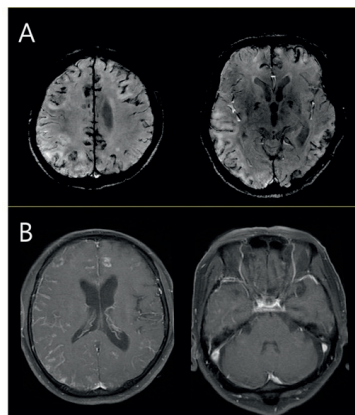
Brain MRI of an RV-related encephalitis patient with poor outcome (patient #3)

Conclusion: This is the first etiological study of adult RV-related meningoencephalitis in a large CNS infection registry. Clinicians should keep in mind that, although rare, RV can cause acute meningoencephalitis in adult patients. We suggest routinely screening for RV by multiplex PCR testing using CSF or sputum in adult encephalitis patients, even in those without URI symptoms.

Disclosure: Nothing to disclose

EP1104

Acute haemorrhagic leukoencephalitis after seasonal influenza vaccination

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Background and aims: To report a case of acute hemorrhagic leukoencephalitis (AHL) following influenza vaccination.

Methods: Case report

A previously healthy 70-year-old man presented with acute headache, fever, confusion, and left hemiparesis four days after influenza vaccination (Alpharix ®).

Results: Brain magnetic resonance imaging showed foci of microhemorrhage and extensive demyelinating lesions in the white matter, extending to the corpus callosum and the posterior part of the brainstem. Cerebral spinal fluid examination revealed a mixed leukocytosis with a high protein content. He was first given intravenous ceftriaxone, ampicilline, and acyclovir. Bacterial culture were negative as well as infectious and autoimmune serologies. Despite high dosis of corticosteroids and plasma exchanges, he developed a deep coma with spastic quadriparesis, decerebration signs, Cheyne-Stokes respiration, bilateral myosis, and absent oculo-cephalic reflexes. He died one month later.
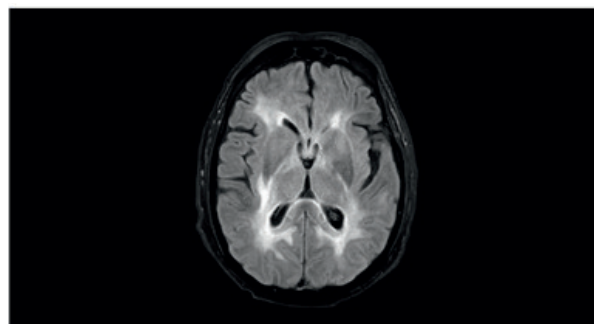
MRI Flair
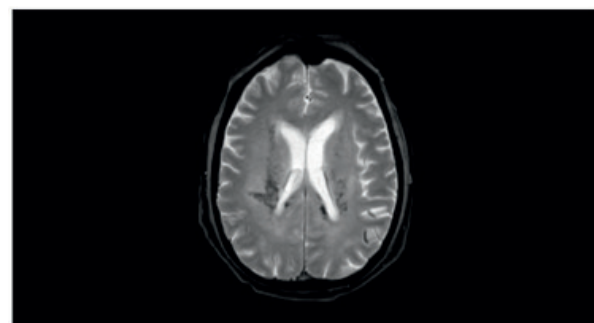
MRI Echogradient
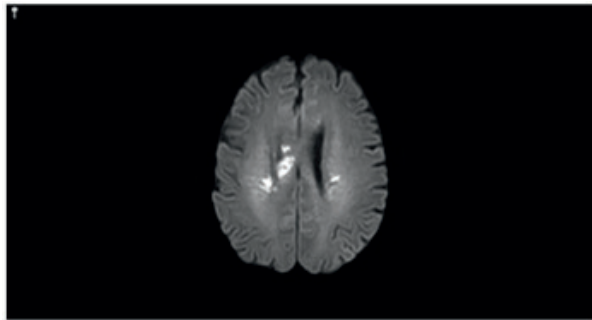
MRI DWI

Conclusion: AHL is a variant of acute disseminated encephalomyelitis (ADEM), an inflammatory demyelinating disease of the central nervous system. The annual incidence of ADEM is estimated to 0.8/100.000. An history of previous vaccine is found in 5% of the cases, including both inactivated or virosomal influenza vaccinations. Our patient fulfilled the WHO causality assessment criteria for a probable diagnosis of AHL due to influenza vaccination. AHL can occur as a very rare complication of influenza vaccination and has a poor prognosis.
Disclosure: Nothing to disclose

EP1105

Central nervous system cryptococcosis in patients with different immunological status – clinical characteristics

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Background and aims: Central nervous system (CNS) cryptococcosis occurs in individuals with HIV or other immunosuppressions, such as autoimmune diseases, malignancies and post-transplantation, and immunocompetent patients. Our objective was to analyse clinical manifestations and prognosis in patients with different immunologic backgrounds, infected by Cryptococcus neoformans or C. gattii.
Methods: We performed a retrospective study of patients with CNS cryptococcosis treated in Hospital de Clínicas - Universidade Federal do Paraná, in southern Brazil, from 1987 to 2013. 247 patients were included and classified in 3 groups: (1) immunocompetent, (2) HIV+, or (3) immunodeficient HIV-. Data were compared using ANOVA and chi-square tests.
Results: 26 patients (10.5%) were immunocompetent, 200 (80.9%) were HIV+, and 21 (8.5%) were immunodeficient by another aetiology (p<0.0001). Most were infected by C. neoformans (n=233, 94.7%), with a higher proportion among groups 2 (n=197, 98.5%) and 3 (n=21, 100%) than in group 1 (n=15, 57.7%), which had association with C. gatti infection (p=0.008). The commonest symptoms were headache (n=195, 78.9%), fever (n=110, 45.6%) and reduced consciousness (n=67, 27.8%). Group 1 had significantly higher age median (46.5 years) than groups 2 (35) and 3 (37), and higher rates of reduced consciousness (n=13, 50%, p=0.04), nuchal rigidity (n=10, 90.9%, p=0.01), ataxia (n=6, 24%, p=0.006) and paralysis (n=12, 48%, p=0.007). Mortality rates had no statistical differences between the groups. Neurologic sequelae were more frequent in group 1 (n=7, 28%, p=0.0003).
Conclusion: In CNS cryptococcosis, immunocompetence is associated with infection by C. gattii, higher age at onset, decreased level of consciousness, nuchal rigidity, motor symptoms, and sequelae.
Disclosure: Nothing to disclose

EP1106

Cancelled

Movement disorders 1

EP1107

Possibilities of gait training of Parkinson's disease treatment

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Background and aims: One of the most significant motor disorders in patients with Parkinson's disease (PD) is gait disorder. It is a decisive factor in determining the severity of the PD patients' condition and their quality of life. Usually, drug treatment not enough for gait disorders. Authors of abstract used self-development method of thempo-rhytmic correction (TRC) of gait (Russian Patent #2281695). The purpose of this study is evaluation effectiveness of TRC for gait correction.

Methods: Essence of TRC is special testing to select the individual frequency of auditory cues. During the gait synchronized with the tempo of the auditory stimulation. Gait trainee with step synchronization to an optimal frequency were held weekly, 3-6 times per day. We have two groups patient: control group (only drug treatment) (n=30) and experimental group (drug treatment plus TRC) (n=30). We assessment step parameters at baseline and 6 months later. We analyzed length of each step, average length of step and a special settlement parameter - the step of variability factor (SVF), which calculated under the formula: (the maximal length of step - the minimal length of step)/average length of step. SVF tend zero for healthy peoples. At Baseline both groups have 3 stage (Hoehn&Yarh) of PD, stable pharmacological treatment, without statistic significant differences.

Results: Results is presented at pic.1.

Time of Examination	Indicators	Group 1	Group 2
		Tempo-rhythmic correction	Control
Initial	Step Variability Factor (SVF)	0.51±0.09	0.52±0.06
	Average Step Length (ASL)	38.00±6.44	36.2±3.96
In 6 months	Step Variability Factor (SVF)	0.27±0.07*	0.40±0.06
	Average Step Length (ASL)	46.85±5.89*	38.21±3.73

*-p 0.05 (vs. control)

Conclusion: TRC method used in the treatment plans of PD patients, proved to be more effective in gait restoration compared to controls. Positive dynamics of the gait parameters (SVC, ASL) exceeded this PD patients whose treatment included only antiparkinson drugs.

Disclosure: Nothing to disclose

EP1108

The role of Clinical Outcome Assessment (COA) data in the drug approval process of medicines for the treatment of Restless Legs Syndrome (RLS): A review of the labels of medicines approved by the FDA and the EMA

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Background and aims: The objectives of this study were 1) to identify the medicines approved for the treatment of restless legs syndrome (RLS) by the Food and Drug Administration (FDA) and the European Medicines Agency (EMA); 2) to find out about the use of clinical outcome assessments (COAs) in the approval process; and 3) to identify the COAs endpoint positioning.

Methods: The EMA and FDA websites were explored to identify all medicines approved for RLS. The PROLabels database was used for labeling claim identification. All corresponding labels were reviewed for endpoint positioning.

Results: The agencies approved nine products with RLS indication (representing four INN, i.e., gabapentin, pramipexole, rotigotine, ropinirole); four products were approved by the FDA; five by the EMA, including one pramipexole generic. All products were evaluated using the same patient-reported outcome (PRO) measure, i.e., the International Restless Legs Syndrome Study Group Rating Scale (IRLS), which assesses disease severity. All had a similar claim, i.e., improvement in baseline IRLS score. The mean change from baseline in IRLS was a co-primary efficacy endpoint. The other COA used to develop a co-primary efficacy endpoint was a clinician-reported outcome (ClinRO) measure, either a Clinical Global Impression scale of Improvement (CGI-I) or a Clinical Global Impression scale of Illness Severity.

Conclusion: The patient's perspective is of paramount importance in the evaluation of medicines approved for RLS. The clinician input is also considered as a valuable endpoint since all evaluations were based on the use of co-primary PRO/ClinRO.

Disclosure: Nothing to disclose

EP1109

Translating the Rapid Eye Movement (REM) sleep behavior disorder screening questionnaire (RBDSQ) into 21 Languages using a standardized methodology

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Background and aims: The rapid eye movement (REM) sleep behavior disorder screening questionnaire (RBDSQ) is a 10-item patient self-rating scale, originally developed in German, using a Yes/No answer, which covers the clinical features of REM sleep behavior disorder. The objectives of this study were to present the method and the challenges of the RBDSQ translation into 21 languages.

Methods: In most languages, the translation process consisted of: 1) Conceptual analysis of the original RBDSQ with its developers; 2) Forward/backward translation step. The forward step (i.e., translation into the target language) used the German original and the UK English version as source versions to create two target versions, which were reconciled into one. This reconciled version was back-translated into English for quality check. For countries using a national variant of the same language (e.g., Australian English vs. UK English), an adaptation was performed.

Results: The translation process did not reveal any major difficulties since most of the behaviors assessed in the RBDSQ are cross-culturally relevant. Most of the issues belonged to the semantic and syntactic fields. For instance, the word "salutieren/saluting" created a range of queries (e.g., use formal vs. informal salute or both?) solved in collaboration with the developers. The translation of "Mücken verscheuchen/shooing away midges" led the translators to choose insects fitting their geographical location or colloquial expressions (e.g., "chasser les mouches" (flies) in French). Other examples are presented.

Conclusion: The multi-step rigorous translation methodology was key in developing 21 translations of the RBDSQ conceptually equivalent to the German original.

Disclosure: Nothing to disclose

EP1110

Cardiovascular autonomic dysfunction in parkinsonian disorders

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Background and aims: Autonomic disorders are the most frequent and severe symptoms of Parkinson's disease and atypical parkinsonism and a part of differential diagnostics.

Methods: Thirty-two patients were enrolled in the study (10 patients with Parkinson's disease (PD), 8 patients with Lewy body dementia (LBD); 8 patients with multiple system atrophy (MSA); 6 patients with progressive supranuclear palsy (PSP) - by clinical criteria). The control group - 10 healthy people without parkinsonism. The Valsalva maneuver was used to evaluate the cardio-vascular autonomic function via blood pressure changes and monitored by photometric method in beat-to-beat mode using NOVA Finapress, Netherlands.

Results: In the control group the systolic blood pressure (SBP) fall was $13.6 + - 2.1$ mmHg ($p > 0.05$); mean in 28 seconds. In PD patients $60.9 + -7.4$ mmHg ($p < 0.05$), in 45 seconds. In PSP patients $56.0 + -5.2$ mmHg ($p < 0.05$), in 25 seconds. In LBD patients $59.8 + -8.1$ mmHg ($p < 0.05$), in 55 seconds. In MSA patients $99.2 + -10.2$ mmHg ($p < 0.05$), in 30 seconds. Clinical manifestations of cardio-vascular autonomic dysfunction were identified in MSA and LBD patients.

Conclusion: The data showed a pathological type of autonomic response to Valsalva maneuver in patients with parkinsonian syndrome by comparison to control group. The pathological responce characterized by the grade of the SBP fall and / or by the length of a cycle, with specific combinations of features for each type of parkinsonism.The clinical manifestations of cardiovascular instability were mainly associated with a length of blood pressure recovery.

Disclosure: Nothing to disclose

EP1111

Genotype may influence the onset of axial signs in early-stage Parkinson's disease

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Background and aims: Heterogeneity exists regarding the onset of axial signs in Parkinson's disease (PD). Dysarthria, swallowing disturbance and respiratory muscles dysfunction can be observed in early-onset PD patients. Due to their impact on the outcome and quality of life, evidencing risk factors of these symptoms is essential to optimize the follow-up of our patients. The aim of our study was to assess the association between the genotype and the axial signs.

Methods: MAPT haplotypes and COMT polymorphism were tested in 31 PD patients (mean age= 61.4 years±6.5) of the Prodigy-Park 1 cohort with a mean disease duration of 1.1 years (±1.1). Neurological, swallowing and voice and pulmonary function testing evaluations were performed.

Results: A valine homozygous polymorphism (n=11) was associated with a significantly higher sniff nasal inspiratory pressure (SNIP) in comparison with methionine homozygous (n=7) and heterozygous polymorphism (n=13) (78%±14.2 vs. 60.9%±19.8 - p=0.02). Regarding MAPT gene, patients with a H1/H1 haplotype (n=21) had a significantly higher severity of their dysarthria assessed by a French adaptation of the Frenchay Dysarthria Assessment (4±2.7 vs. 1.4±2.2 - p=0.02).

Conclusion: In early-stage PD, the onset of dysarthria or inspiratory muscle weakness might be associated with the genotype. Dopamine might impact on the ventilatory function and MAPT H1 haplotype could lead to a pseudobulbar palsy. These preliminary results need to be confirmed in a larger cohort to assess the influence of MAPT haplotypes or COMT polymorphism in the other features of the axial signs (such as the swallowing disturbance).

Disclosure: Nothing to disclose

EP1112

ParkLink Bologna - an Italian record linkage system for Parkinson's disease: Ready, set, go!

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Background and aims: Record linkage systems (RLS), matching data across administrative health databases, help providing information on diseased populations. However, detailed clinical information is often missing. The aim of the project (ParkLink Bologna) is to create a RLS based on clinical diagnosis to perform clinical epidemiologic studies on Parkinson's disease (PD) and parkinsonism (Ps) in a population-based setting (Bologna Health District, Emilia-Romagna Region, Italy).

Methods: Since January 2016, we are inviting neurologists working in private practice or public health service to enroll patients with a clinical suspect of PD or Ps residing in Bologna Health District (870507 inhabitants). Clinical diagnosis, date and type of onset and level of disability of patients who gave consent are linked to different administrative databases.

Results: On December 2016 six databases were linked (drug prescriptions, ER access, hospital discharges, copayment exemption, medical home-care, mortality); 15 neurologists out of 42 joined ParkLink. About 25% (539) of expected prevalent patients were already included (no refusals); 466 had a final diagnosis of PD (73%) or Ps (27%). Compared to Ps, PD were younger, with longer disease duration, lower disability level (Table 1) and a slightly different treatment prescribing pattern (Table 2). Risk of ER access and hospital admission increased with disability level.

Features	Parkinson's Disease N=339 N (%)	Parkinsonism N=127 N (%)	p-value
Age (years): mean (SD)	74.7 (8.7)	78.6 (7.6)	< 0.001
Gender:			0.110
M	215 (63.4)	70 (55.1)	
F	124 (36.6)	57 (44.9)	
Year of onset:			0.012
< 2008	100 (29.5)	22 (17.3)	
2008 – 2010	97 (28.6)	32 (25.2)	
2011 – 2013	96 (28.3)	47 (37.0)	
2014 – 2016	46 (13.6)	26 (20.5)	
Gelb's criteria:			
Possible	107 (31.6)		
Probable	232 (68.4)		
Hoehn and Yahr scale:			< 0.001
1	46 (13.6)	11 (8.7)	
1.5	43 (12.7)	5 (3.9)	
2	107 (31.6)	24 (18.9)	
2.5	47 (13.9)	17 (13.4)	
3	58 (17.1)	27 (21.3)	
4	31 (9.1)	31 (24.4)	
5	7 (2.0)	12 (9.4)	
Type of onset:			< 0.001
unilateral	281 (82.9)	46 (36.2)	
bilateral	58 (17.1)	81 (63.8)	
Type of onset _Tremor:			0.003
yes	223 (65.8)	62 (48.8)	
no	71 (20.9)	44 (34.7)	
missing	45 (13.3)	21 (16.5)	
Type of onset _Bradykinesia:			0.254
yes	233 (68.7)	95 (74.8)	
no	51 (15.1)	19 (15.0)	
missing	55 (16.2)	13 (10.2)	
Follow-up (months): mean (SD)	5.1 (3.7)	5.0 (3.7)	0.664

Table 1. Distribution of demographic and clinical features of patients with diagnosis of Parkinson's Disease and parkinsonism.

Treatment	Parkinson's disease N= 339 N (%)	Parkinsonism N= 127 N (%)	p-value
Levodopa only	105 (31.0)	68 (53.5)	< 0.001
Levodopa + Dopamine Agonists	135 (39.8)	23 (18.1)	< 0.001
Levodopa + MAO B Inhibitors	14 (4.1)	9 (7.1)	0.23
Levodopa + Dopamine Agonists + MAO B Inhibitors	31 (9.1)	3 (2.4)	< 0.001
Dopamine Agonists only	19 (5.6)	7 (5.5)	1.00
MAO B Inhibitors only	4 (1.2)	0 (0.0)	0.58
Dopamine Agonists + MAO B Inhibitors	6 (1.8)	2 (1.6)	1.00
No Levodopa, Dopamine Agonists or MAO B Inhibitors	25 (7.4)	15 (11.8)	0.14

Table 2. Distribution of prescribing treatments in patients with Parkinson's Disease and parkinsonism.

Conclusion: ParkLink is an independent, publicly funded RLS based on clinical diagnosis linked to administrative databases. Neurologists' recruitment is ongoing and a website is published (www.isnb.it/ricerca/parklink). Preliminary findings show that such a system may produce relevant data on clinical epidemiology and burden of disease concerning PD and Ps.

Disclosure: Nothing to disclose

EP1113
Cancelled

EP1114

Persistent L-Dopa responsive hemiparkinsonism after cryptococcal meningoencephalitis in an immunocompetent man

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Background and aims: Secondary parkinsonism due to infectious disorders might present with either generalized or more lateralized symptoms with a acute/subacute evolution. However, documented basal ganglia dopamine depletion in the setting of infectious menincoencephalitis is quite rare. We aim to report the case of an immunocompetent male who had hemiparkinsonism responsive to L-Dopa therapy following cryptococcal meningoencephalitis.

Methods: Case report.

Results: A 43-year-old Caucasian immunocompetent male was admitted to the hospital with a proved diagnosis of meningoencephalitis, with fever, severe headache, mental confusion and somnolence. CSF analysis disclosed Cryptococcus neoformans. Brain MRI showed images on right basal ganglia compatible with Cryptococcal abscesses, which later evolved to encephalomalacia on the right striatum on a follow-up exam after adequate treatment with amphotericin B and ventricular shunt (Figure 1 - a). At the time of hospital discharge from the hospital he had developed with left hemiparkinsonism and mild cognitive decline. A brain SPECT with TRODAT-1 (Figure 1 -b) demonstrated moderate reduction of dopamine transporter binding on the right striatum. The patient was treated with levodopa-benserazide 100/25mg thrice daily, with remarkable improvement of the parkinsonian syndrome.
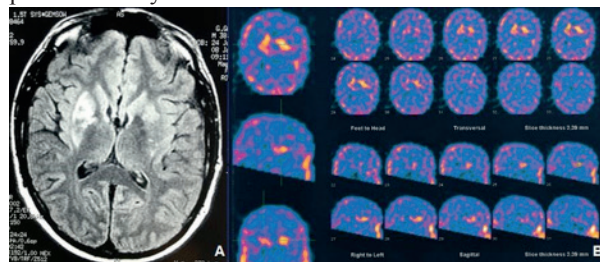
Brain T-1 weighted MRI showing right basal ganglia encephalomalacia secondary to the Cryptococcal abscesses (A). Brain SPECT with TRODAT-1 shows moderate reduction of DTA binding on the right striatum and normal binding on the opposite side (B).

Conclusion: Hemiparkinsonism secondary to Cryptococcal meningoencephalitis leading to striatum encephalomalacia is a rare etiology of secondary parkinsonism, even more so with documented dopamine depletion.

Disclosure: Nothing to disclose

EP1115

Acute restless legs syndrome after liposuction surgery, with hypoxic-Ischemic encephalopathy, associated with Pramipexole-induced kleptomania

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Background and aims: Recently functional neuroimaging studies have suggested that RLS can result from dysfunction of the dopaminergic system in the striatum. Our goal is to report a case of acute RLS following liposuction with hypoxic-ischemic encephalopathy, associated with kleptomania induced by the therapeutical use of pramipexole.

Methods: Case report.

Results: A 40-year-old woman who had previously undergone bariatric surgery underwent liposuction for aesthetical purposes. In the post-operative period of liposuction she presented with somnolence, mental confusion, temporal-spatial disorientation and working memory deficits, later followed by severe and unpleasant discomfort in her lower limbs, which was characterized by pain and severe spasms at rest, particularly at night, with improvement of these symptoms while walking. Brain MRI demonstrated scattered and diffuse nearly symmetrical lesions in the BG and cerebellum suggestive of hypoxic-ischemic insults. A subsequential MRI suggested that most lesions vanished leaving cystic cavitations on the lenticular nucleus and caudate and brain -tractography analysis showed a reduction in fractional anisotropy. Thus, she was diagnosed with acute RLS, following acute hypoxic-ischemic encephalopathy after liposuction, and started on pramipexole 0.5mg qid at bedtime. RLS symptoms subsided with normalization of her sleep pattern. However, after 3 months of pramipexole treatment she developed symptoms of kleptomania. Pramipexole was tritated to a lower dose (0.125mg) with resolution of kleptomaniac symptoms.

Conclusion: The behavioral changes observed in our patient, including kleptomania, most likely arose from failure of inhibitory pathways involving basal ganglia, pre-frontal cortex and limbic structures, and was triggered by the pramipexole treatment, suggesting a impulse control disorder.

Disclosure: Nothing to disclose

EP1116

Tetrabenazine versus deutetrabenazine for Huntington's disease: Twins or distant cousins?

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Background and aims: Tetrabenazine is the only FDA-approved drug for Huntington's disease (HD), and deutetrabenazine was recently tested against placebo. A switching-trial from tetrabenazine to deutetrabenazine is underway, but no head-to-head blinded, randomized controlled trial (RCT) is planned. Using meta-research methodology, we compared these molecules.

Methods: RCTs comparing tetrabenazine or deutetrabenazine with placebo in HD were searched. We assessed the Cochrane risk of bias tool, calculated indirect treatment comparisons, and applied the GRADE approach.

Results: Our evidence network comprised one tetrabenazine and one deutetrabenazine trial, both against placebo. Risk of bias was moderate in both. Tetrabenazine and deutetrabenazine did not differ significantly on motor scores or adverse events. Depression and somnolence scales favoured deutetrabenazine significantly.

Conclusion: There is low-quality evidence that tetrabenazine and deutetrabenazine do not differ in efficacy and safety. Importantly these results are likely to remain the only head-to-head comparison between these compounds in HD.

Disclosure: Nothing to disclose

EP1117

An observational study of the motor and non-motor effects of deep brain stimulation, intrajejunal levodopa infusion, and oral levodopa in advanced Parkinson's disease

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Background and aims: Subthalamic nucleus deep brain stimulation (STN-DBS), continuous infusion of levodopa/carbidopa gel and oral levodopa are effective treatment for both motor and nonmotor symptoms (NMS) of Parkinson's disease (PD). However, the available studies have focused mainly on the effects of STN-DBS and infusion therapies , there are few specific comparative studies.

Methods: In this randomized study, we compared the effect of oral levodopa treated versus intrajejunal levodopa versus subthalamic nucleus deep brain stimulation (STN-DBS) on the different characteristics of NMS in patients with advanced PD.

Results: One hundred and fourteen Parkinson's patients satisfying the UK PD Brain Bank criteria for diagnosis of idiopathic PD participated and assessed using NMS questionnaire (NMSQuest), UPDRS, Hoehn and Yahr classification, Hospital Anxiety Depression Rating Scale (HADs). The results of NMSQ for all three groups were found equal.

Subdomains	Deep brain stimulation	Dopamin agonists or levodopa	Duodopa infusion	*p
	Median (Q1, Q3)	Median (Q1, Q3)	Median (Q1, Q3)	
Urinary tract	2 (1, 2)	2 (1, 2)	2 (1.5, 2)	0.422
Sexual function	2 (0, 2)	2 (0, 2)	1.5 (0.5, 2)	0.641
Sleep	2 (1, 3)	2 (1, 3)	3.5 (2.5, 4)	0.638
Depression/Anxiety	2 (0, 2)	1 (0, 2)	1 (0.5, 1.5)	0.626
Total	14 (10, 16)	13 (9, 17)	15.5 (14.5, 16.5)	0.818

Table : Correlation between three groups.

Conclusion: Several studies have shown that levodopa-based dopaminergic stimulation is beneficial for NMS and health-related quality of life in PD in addition to the reduction of motor fluctuations and dyskinesias.

Disclosure: Nothing to disclose

EP1118

Late-onset levodopa responsive parkinsonism due to POLG mutations

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Background and aims: Polymerase gama (POLG) mutations have been described in association with wide a spectrum of phenotypes. Parkinsonism is unfrequently described and usually a late feature in patients with progressive external ophtalmoplegia.

Methods: Case report.

Results: We describe a 76-year-old gentleman with REM-sleep behavior disorder (RBD) since the age of 61, who developed shuffling gait and stooped posture by 63-year-old, and a year later left-hand resting tremor. Personal/family history were unremarkable. When observed, age 64, he presented hypomimia, left-predominant parkinsonism, camptocormia, short-step shuffling gait and postural instability. He had frontal bossing conferring him a peculiar face, and oversized hands. Levodopa/carbidopa was started with moderate improvement. Brain MRI revealed widespread partially confluent cerebral white matter lesions. An extensive blood/CSF workup was conducted with normal/negative results. Muscle biopsy showed rare ragged-red and COX-negative fibers. EMG excluded myopathy/polyneuropathy. Mitochondrial chain complex activity was normal; however multiple mitochondrial DNA deletions were identified. POLG gene study revealed deletion c.127_132delCAGCAG and point mutation p.G268A(c.803G>C), in compound heterozygosity, already described as pathogenic. Cognitive decline began by 65, and a year later motor fluctuations appeared. Over 12 years there was moderate progression. He now presents cognitive impairment, fragmented pursuit ocular movements (without ophtalmoplegia) and levodopa responsive parkinsonism(video).

Conclusion: The reported patient presents a rare phenotype of POLG mutations: late-onset levodopa-responsive asymmetric parkinsonism, with RBD and motor fluctuations, in the absence of progressive ophtalmoplegia and neuropathy. It was the presence of early gait impairment and postural instability associated with subtle facial dysmorphism, which prompted additional investigation leading to the final diagnosis.

Disclosure: Nothing to disclose

EP1119

Cognitive impairment as FXTAS debut

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Background and aims: Fragile X-associated tremor/ataxia syndrome(FXTAS) is a neurodegenerative disorder caused by a premutation in the fragile X mental retardation 1(FMR1) gene, including as the major clinical criteria tremor and cerebellar ataxia. Retrospective reports show that over 50% of patients have cognitive changes. In fact, those with T2 white matter hyperintensities in the middle cerebellar peduncles (MCP sign)– cardinal radiological sign- are likely to have more severe cognitive deficits.

Methods: We present a 59-year-old man with memory and executive impairment, without previous intellectual disability nor family history, and normal physical examination. In the following 2 years he suffered progressive cognitive deterioration with functional disturbance. In addition, partial seizures, tremor and cerebellar ataxia arose.

Results: Based on the clinical evolution, cranial MRI was reviewed, evidencing the MCP sign, and genetic molecular test for FMR1 gene was performed, confirming the expansion in premutation range. Considering all results, the definitive diagnosis of FXTAS was established.

Conclusion: FXTAS prevalence is estimated about 1 in 3,000 men. Nevertheless, FXTAS is under-recognized and frequently misdiagnosed. Our case is atypical as cognitive impairment without additional features is a rare cause of initial consultation and dementia remained as the predominant feature in early stages. We suggest that this genetic test should be at least considered in cases of unexplained cognitive decline, especially if characteristic white matter lesions on MRI are seen. This case additionally supports that the original diagnostic criteria need to be updated, in order to improve the identification of affected persons due to the expanding phenotypes that are nowadays known.

Disclosure: Nothing to disclose

Movement disorders 2

EP1120

Dopamine transporter imaging and cardiac MIBG in patients with parkinsonism: A case for heterogeneity

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Background: Severe DatScan deficiency is usually correlated with severe motor deficit. Furthermore Parkinson's disease (PD) is characterized by a variety of NMS of which some might be associated with cardiac sympathetic denervation.

Aims: To explore cardiac sympathetic function and clinical non-motor symptoms (NMS) expression in patients with severe DatScan depletion. The relation between the two is unclear.

Methods: Patients who underwent a cardiac MIBG scan, DatScan imaging and completed clinical assessment including the NMSScale were retrospectively reviewed in this going on study. DatScan and cardiac MIBG uptake were classified as normal (>2), or mild (1.5>, <2), moderate (>1,<1.5) and severe (<1) reduction. The NMSburden (NMSB) was assigned according to the NMSScale in mild, moderate, severe and very severe (Chaudhuri et al., 2006).

Results: All nine patients presenting with Parkinsonism had severe dopaminergic depletion in the putamen with an uptake ratio<1.0 (mean putamen uptake right 0.6±0.2 and left 0.8±0.3). Three patients showed a moderately reduced uptake on cardiac MIBG (R1 ratio <1.5), five patients showed a mild reduction (R1 ratio <2) and one patient showed normal cardiac uptake (R1 ratio>2). One patient reported mild NMSB, one reported moderate NMSB, three reported severe NMSB and four reported very severe NMSB.

Conclusion: In spite of the severe putaminal dopaminergic depletion, the patients expressed a very heterogenous presentation of cardiac MIBG scan and NMSB even in this small sample. This highlights the fact that possibly also PD is rather a complex syndromic condition than a disease.

Disclosure: Nothing to disclose

EP1121

Long-term effects of safinamide treatment on pain in fluctuating Parkinson's disease patients

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Background and aims: Safinamide (Xadago ®, Zambon SpA Italy), is a new drug with a dual mechanism of action (dopaminergic and non-dopaminergic). Results of the pivotal trials showed an increase in "ON" time and a decrease in "OFF" time maintained up to two years. This post-hoc analysis investigates the long-term efficacy of safinamide vs placebo on pain in parkinsonian patients with motor fluctuations.

Methods: The effects of safinamide on the reduction of concomitant pain treatments and on the items related to pain of the Parkinson's disease Quality of life questionnaire PDQ-39 were investigated using the data from the pivotal Phase III trial 018.

Results: The percentage of patients with no pain treatments at the end of two years were significantly lower in the safinamide group compared to the placebo group (61.1 vs 50.9%; p=0.0478), with an average reduction of the individual use of pain treatments by 26.2%. Moreover, safinamide significantly improved the PDQ-39 pain-related items.

Conclusion: Safinamide, administered as add-on therapy in fluctuating parkinsonian patient, significantly reduced the number of concomitant pain treatments, maintaining the efficacy up to two years. These results suggest that safinamide may have a positive effect on pain, one of the most underestimated non-motor symptoms of parkinsonism.

Disclosure: Carlo Cattaneo and Ioannis Kottakis are Zambon SpA employees. Erminio Bonizzoni is Zambon SpA consultant

EP1122

Cancelled

EP1123

Autonomic testing in patients with Parkinson-plus syndromes

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Background and aims: Corticobasal degeneration (CBD), multiple system atrophy (MSA) and progressive supranuclear palsy (PSP) consist the Parkinson-plus syndromes. Despite distinct clinical features, differential diagnosis is problematic, particularly in atypical cases or in the early stages of these disorders. The objective of this study was to examine the usefulness of bedside autonomic testing in the differential diagnosis of Parkinson-plus patients.

Methods: A total of 51 Parkinson-plus patients were included (17 CBD, 15 MSA and 19 PSP). Autonomic testing included the heart rate response to breathing (R-R test) and the presence of orthostatic hypotension (reduction of systolic (SBP) and diastolic blood pressure (DBP) within 1 and 3 minutes of standing from the supine position). Analysis of variance, Kruskal-Wallis and ROC curve analysis tests were used as appropriate.

Results: MSA patients differed significantly from the other two groups in the SBP and DBP drop from 0 to 3min and from 0 to 1min when standing from the supine position. There was no difference in the heart rate variability during standing or in the R-R test. SBP difference from 0 to 3min was most potent in discriminating MSA patients (AUC=0.89, p<0.0001, sensitivity 80%, specificity 85.2% for a cut-off point of >20cm H2O BP drop).

Conclusion: SBP drop of >20cm H2O cut-off during standing from a supine position (compared to the more stringent>30cm H2O of the diagnostic criteria) can discriminate MSA patients from other Parkinson-plus patients, with adequate sensitivity and specificity. The R-R test does not differentiate among Parkinson-plus patients.

Disclosure: Nothing to disclose

EP1124

How do Parkinson's disease patients manage Ramadan fasting?

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Background and aims: Although Ramadan fasting is not mandatory for patients suffering from chronic disease, many patients are tied to respect it.To our knowledge, no previous studies have analyzed how PD patients manage Ramadan fasting.

Methods: Twenty four PD patients (60.4 years, 9 females) seen in the outpatients department of Ibn Sina Hospital (Kuwait ciy) having planned to fast during the 2016 Ramadan were included. They underwent a clinical interview and a neurological examination, including the (MDS-UPDRS), the Hoehn and Yahr staging scale, the (NMSS), the (PDQ-39) and the clinical impression of severity index for Parkinson disease (CISI-PD). Assessments were performed 2 to 4 weeks before Ramadan and 2 to 4 weeks after, 20 patients fulfill the whole fasting period.

Results: Mean disease duration was 5.8y with a Hoehn and Yahr score at 1.8. Fourteen patients were treated with a combination of L-DOPA and DA, one patient with DA monotherapy and five patients were treated with L-DOPA monotherapy with a (LEDD) of 820mg (150-1584); 3 patients were treated with subthalamic DBS.6 patients were able to have no drug intakes between dusk and dawn; others patients needed to take 1 or 2 intake of L-DOPA inbetween. Eight patients maintained the same LEDD, 10 decreased it, and 2 increased it .No serious side effects were reported, there were no significant changes after the fasting period in PDQ 39, NMS, CISI.

Conclusion: With some adjustments in the treatment, patients with mild to moderate PD appear to manage Ramadan fasting well without serious damage to their health.

Disclosure: Nothing to disclose

EP1125

Colic fistulisation of jejunal tube in a Parkinson's disease patient under Duodopa® therapy

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Background and aims: In patients with advanced Parkinson's disease (PD), the continuous delivery of levodopa/carbidopa gel (Duodopa) through a percutaneous endoscopic gastrostomy with jejunal extension (PEG-J) allows less variability in levodopa concentrations and results in fewer motor complications compared with oral administration. Over the past years, some severe gastrointestinal complications have been described in patients with Duodopa®.

Methods: We report a serious gastrointestinal complication associated with Duodopa® therapy.

Results: A 53-year-old woman with PD began Duodopa® therapy through a PEG-J due to motor complications, with excellent response to treatment. Three years later she reported loss of Duodopa® efficacy and worsening of Parkinson symptoms, warranting oral levodopa medication with symptom improvement. A gastroscopy revealed gastrostomy tube erosion through the duodenum wall. Contrast-enhanced computer tomography of the abdomen revealed migration of the jejunal tube through multiple downstream entero-enteric fistula with the distal end situated in the ascending colon. Colonoscopy revealed tube tip entrapment by phybezoar with resistance to mechanical pull by endoscopic snare. Removal of the PEG was performed with proximal cut of the jejunal tube, and 2 days later complete anal exteriorization of the remaining tube spontaneously occurred without any complications.

Conclusion: This case illustrates that loss of response to Duodopa® therapy should alert the clinician to some potentially severe complications and should grant prompt endoscopic examination. Unlike some fatal cases published in the literature, our patient spontaneously expelled the jejunal tube without any complication. We believe that in particular cases an expectant attitude should be considered as an option.

Disclosure: Nothing to disclose

EP1126

Isolated dystonia caused by ATP1A3 mutation unresponsive to deep brain stimulation

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Background and aims: Mutations in the ATP1A3 gene are associated with a wide spectrum of neurologic disorders encompassing rapid-onset dystonia-parkinsonism (RDP) and alternating hemiplegia of childhood (AHC). Isolated dystonia has been occasionally reported. The efficacy of deep brain stimulation (DBS) in cases of isolated dystonia with ATP1A3 gene mutations has not been established.

Methods: We reported the outcome, after ten years of stimulation adjustments, in a patient with ATP1A3 isolated dystonia who received a GPi DBS implant and then compared the results to all published cases of ATP1A3.

Results: Our patient bore a heterozygous de novo missense mutation (c.1250T>C, p.L417P) in the ATP1A3 gene, had isolated dystonia and did not respond to GPi DBS. Overall, seven cases with isolated dystonia were reported and four ATP1A3 dystonic patients have received stereotactic surgery in the GPi; no patient has received surgery in other targets. The mutation found in this case of isolated dystonia has been previously observed in one patient with RDP.

Conclusion: We report failure of GPi stereotactic surgery in five patients with ATP1A3, including this observation with isolated dystonia and one case of pallidotomy without mention of parkinsonism. We also confirm clinical and genetic heterogeneity of this condition. ATP1A3 dystonia may possibly represent a case of "surgicogenomics", meaning that such genetic diagnosis may be a negative indication for stereotactic surgery in the GPi. It remains unknown whether DBS in other targets may be efficacious.

Disclosure: Nothing to disclose

EP1127

Monotherapy with perampanel as an alternative for refractory myoclonus

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Background and aims: Myoclonus is a sudden, brief, shock-like, involuntary movement. Cortical myoclonus treat is often refractory and requires the use of polytherapy being the dose occasionally limited by the onset of side effects. The aim of this study is to report three patients with drug-resistantre chronic myoclonus that had not improved with clonazepam, levetiracetam and valproic acid, but improved markedly after onset with perampanel.

Methods: Three case reports. Patients unresponsive for available drugs for myoclonus were started on perampanel in monotherapy. Patients were video-taped before and after achieving therapeutic full dose with perampanel, and change on myoclonus severity was assessed by the Clinical Global Impression of Change (CGI-C) scale.

Results: Two adult patients with myoclonus as a sequelae of hypoxic-ischemic brain injury during the perinatal period, and one young woman with drug-induced myoclonus started treatment with perampanel after conventional politherapy for chronic myoclonus. Global improvement was rated as "much improved" in two patients (CGI-C=2), and "very much improved" in one patient (CGI-C=1). Global improvement was associated with an improvement in daily functionality and recovery of tasks that have been withdrawn because of myoclonus. Two patients experienced improvement at 4mg/day, and one at 6mg/day. During titration phase, three patients experienced dizziness 10-15 minutes after taking the drug, but good tolerance was achieved after 1 month of treatment.

Conclusion: Perampanel appears as a good alternative in patients with drug-resistant myoclonus. Based on these anecdotal cases, clinical trials seem promising for further assessing the efficacy of perampanel for refractory chronic myoclonus.

Disclosure: Nothing to disclose

EP1128

Cancelled

EP1129

Psychiatric disorders and personality traits in patients with essential tremor

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Background and aims: Essential tremor (ET) can have more complex motor features (e.g. ataxia), likewise different non-motor manifestations regarding both cognitive and psychiatic symptoms. The aim of the work was to determine psychiatric disorders and personality pattern in a cohort of ET patients, and to asses relation between motor and non-motor features of ET.

Methods: ET patients (101) were examined for the presence of psychiatric disorders accorrding to DSM IV criteria. All patients were evaluated by standardized psychiatric and neurologic battery of tests. Personality profile was assessed by Millon Clinical Multiaxial Inventory III (MCMI).

Results: ET patients (age 49.6±18.6, disease duration 15.6±14.4) were divided in two groups, early onset ET (EOET) and late-onset ET (LOET). Depression (according to SCID-I), and obsessive-compulsive personality disorder (SCID-II) were was the most prominent psychiatric disorders in both groups. MCMI scores above 75, indicating presence of specific personality trait, were found for paranoid personality trait, and for psychotic depression among psychiatric symptoms. Associations between dominant personality characteristics and main clinical and demographic factors showed that narcissism and anxiety were in correlation with ADL (p=0.039, p=0.007) and social burden (p=0.014, p=0.001), whereas major depression was in correlation with social handicap (p=0.002), severity of tremor (p=0.019), ADL (p=0.006), and social burden (p=0.049).

Conclusion: Our research confirms that ET is more than a disease of motor system. A significant number of patients suffer from psychiatric disorders, with a high frequency of specific personality disorders.

Disclosure: Nothing to disclose

EP1130

The spatiotemporal gait parameters assessment in Wilson's disease patients

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Background and aims: Wilson's disease (WD) is an inherited disorder of copper metabolism. Gait disturbances may present with both extrapyramidal and cerebellar patterns. Our previous study showed that gait abnormalities are observed in almost 60% of WD patients. The most frequent was ataxic gait (45%) characterized mainly by impaired tandem. So far spatiotemporal gait parameters were not established in WD patients. The aim of our study was to characterise basic objective gait parameters.

Methods: We analysed gait parameters in 34 WD patients in comparison with 28 healthy controls. Spatiotemporal parameters: velocity, cycle time, cadence, base of support was assessed using GAITRite walkway system. Clinical neurological assessment was based on Unified Wilson's Disease Score Scale (UWDRS).

Results: We examined 16 neurologic and 18 hepatic WD patients, and compared their results with healthy control group. Velocity of gait was lower in neurologic group (p=0.03), and not differ from control group in hepatic subjects (p=0.15). Cadence was decreased in neurologic patients (p<0.0001) as well as in hepatic (p<0.005). Neurologic group had had statistically significant wider base of support (p=0.002) as compare to control group.

Conclusion: Our study shows in objective analysis, gait disturbances in WD neurologic patients compared to healthy controls. Notably, subjects with WD demonstrated wider base of support than control group. This is in accordance with our previous clinical observation that impaired tandem gait is common. Although neurologic WD patients presented markedly impaired gait, in hepatic patients we observed decreased cadence. Further analysis on larger group of WD patients is needed to provide insight into gait disturbances.

Disclosure: Nothing to disclose

EP1131

Effects of Chronic Pain on Quality of Life, Depression, Anxiety, Fatigue and Sleep Quality in Turkish Patients with Parkinson's Disease

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Background and aims: There are limited researches in literature evaluating the exact relationships between pain, and other comorbid symptoms like mood and sleep in patients with Parkinson's disease (PD). In this study, we aimed to explore the characteristics of chronic pain and its effects on quality of life, anxiety, depression, fatigue, and sleep quality.

Methods: Forty one patients with PD and 21 healthy controls matched for age and gender were included. The Unified PD Rating Scale and Hoehn&Yahr stage were used to assess motor disability and disease severity. Patients examined relating to the characteristics of the chronic pain. All subjects completed Beck Depression and Anxiety Inventories, Parkinson's Disease Questionnaire, Pittsburgh Sleep Quality Assessment, Fatigue Severity Scale questionnaires.

Results: Twenty eight patients (68%) suffered from chronic pain. Of these, 48% had musculoskeletal, 14% radicular/peripheral neuropathic, 9% dystonia related, 4% central parkinsonian, 14% headache, and 2% vascular pain respectively. Nine patients (21%) had two or more types of pain. Comparing PD patients with and without pain and their demographical and clinical features and mean quality of life scores, there were not any statistical differences. We found that mean depression, anxiety and sleep quality scores between PD patients with and without pain and control group were not stastically significant. Furthermore, there was not correlation between pain and depression, anxiety, fatigue and sleep quality.

Conclusion: There are different pain types co-existing in patients with PD. Despite the previous studies, our findings support that pain does not affect patients' quality of lives and other non-motor sypmtoms such as depression, anxiety, fatigue and sleep.

Disclosure: Nothing to disclose

EP1132

Subacute hemichorea associating dopamine depletion in basal ganglia and cerebral hemiatrophy

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Background and aims: There are few ethiologies of subacute hemichorea. Common causes structural lesions or nonketotic hyperglycemia. The association with contralateral dopamine depletion or cerebral atrophy is uncertain.

Methods: Case report

Results: We present a woman aged 57 whose past history included dyslipidemia, diabetes mellitus and depression treated with clonacepam and venlafaxine. She presented to our clinics due to involuntary movements involving right hemibody that appeared gradually over the past 3 months. Neurologic examination disclosed choreic movements affecting right extremities. Movements increased with distraction and disappeared while sleeping. There were neither parkinsonian signs nor limb atrophy. Supraaortic trunk sonography was also normal. Complete blood and cerebrospinal fluid analysis including biochemistry, glucose, immunology and, microbiology were all normal. Genetic analysis of Huntington's disease was negative. MRI showed atrophy of left cerebral hemisphere (figures 1,2). DaTscan (figure 3) was performed disclosing marked reduction of presynaptic nigrostriatal dopamine affecting left caudate and putamen. 10 years after disease onset the patient still has choreic movements affecting right hemibody.
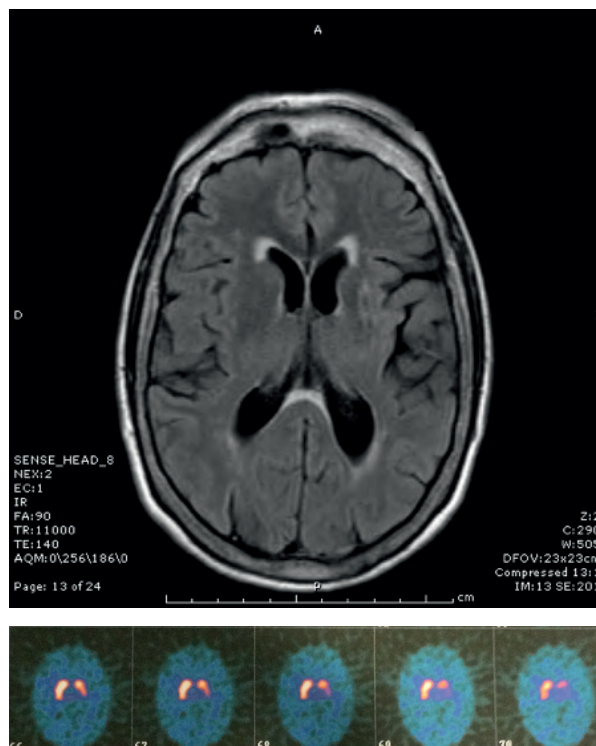
Conclusion: We present a patient with right hemichorea with left basal ganglia dopamine depletion and left hemicerebral atrohy of unknown significance.

Disclosure: Nothing to disclose
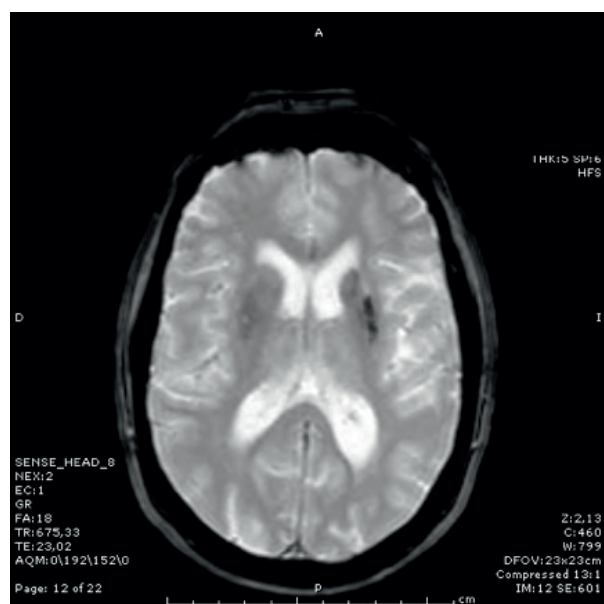
MS and related disorders 1

EP1133

Correlation between retinal nerve fiber layer thickness and presence of IgM oligoclonal bands in relapsing-remitting multiple sclerosis

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Background and aims: Axonal degeneration is related to the development of neurologic disability in multiple sclerosis (MS). We studied the correlation between the presence of IgM oligoclonal bands (OB) in the CSF, a biological marker of poor prognosis, and the degree of axonal degeneration as measured by the thinning of retinal nerve fiber layer (RNFL).

Methods: Fifty-one consecutive patients with a recent diagnosis of RRMS were included ($\leq$ 5 years since first attack) and divided into two groups according to the presence/absence of IgM OB. Sociodemographic and clinical variables were collected and optical coherence tomography (OCT) was performed.

Results: Mean age was 37.14 years, 62.75% were women. Median time from first attack to recruitment was 2.18 years (range 0,35–3.89). One-hundred and two OCT explorations were performed, 52 of them belonging to the IgM OB group. In this group, we found a statistically significant reduction on RNFL thickness on the temporal quadrant (59.30µm, SD 13.19) as compared to the group without IgM OB (64.49µm, SD 11.81), p=0.03.

The examination of those eyes without history of optic neuritis (n=89) showed a thinner temporal quadrant of CFNR in the group with IgM OB (61.88µm, SD 11.81) as compared to the group lacking IgM OB (65.07µm, SD 10.80), without reaching statistical significance (p=0.23).

Conclusion: Patients with IgM OB present a thinner CFNR on the temporal quadrant from early stages. This tendency must be confirmed on follow-up studies (ongoing).

Disclosure: This research has been funded by the Health Department of the Basque Government

EP1134

The expression of matrix metalloproteinase peripheral profile in multiple sclerosis patients treated with natalizumab: Possible additional mechanisms of natalizumab action

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Background and aims: Natalizumab (NAT) is a powerful treatment in multiple sclerosis (MS) patients that was designed with a clear mechanism of action (inhibition of α4-integrine, the key molecule of brain homing). Still, approximately a third of treated patients continue to present disease activity due to blood-brain barrier (BBB) damage. In MS, Matrix Metalloproteinases (MMPs) are involved in BBB disfunction, leading to the perpetuation of neuroinflammation.

Objectives: Evaluation of the evolution of a panel of MMPs during NAT treatment in MS patients.

Methods: 30 RRMS patients (mean MS duration 10.5 years) treated with NAT (mean duration 21.7 months) and 30 healthy subjects were tested using a Bio-PlexPro™ Human MMP Panel (MMP-1, MMP-2, MMP-3, MMP-7, MMP-8, MMP-9, MMP-10, MMP-12, MMP-13) through Multiplex method. The study had a mean duration of 9 months and the patients underwent clinical, MMP and brain MRI evaluation at the inclusion and at the end of the research. Statistical analysis considered significant values: $p \leq 0.05$.

Results: NAT decreased the peripheral values of MMPs (in MMP-9 and MMP-3 statistical significance was found). In patients that had relapses before and during the study, values of MMP-3,8,9,10 were significantly higher compared with patients with NEDA or without relapses. MMPs did not correlate with EDSS variation.

Conclusion: 1) During NAT treatment, MMP-3 and MMP-9 decreased significantly; 2) Patients that continued having relapses had higher MMPs despite NAT treatment; 3) MMPs can be used as biomarkers during NAT treatment, higher values determining the persistence of BBB dysfunction; 4) Further studies are required.

Disclosure: This study was supported by the internal research Grant of The University of Medicine and Pharmacy Targu Mures, Grant Number 18/2015.

EP1135

Low levels of vitamin D in multiple sclerosis patients in geographic areas with higher sunlight levels: Association with quality of life

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Background and aims: Vitamin D status is associated with the incidence and prevalence of a variety of neurologic disorders, including multiple sclerosis. Several studies suggest or support that multiple sclerosis has increased prevalence in geographic areas with lower sunlight levels. We aimed to investigate the correlation between vitamin D level and quality of life in patients with multiple sclerosis who were exposed to sunny seasons within one year in western Turkey.

Methods: Vitamin D status is associated with the incidence and prevalence of a variety of neurologic disorders, including multiple sclerosis. Several studies suggest or support that multiple sclerosis has increased prevalence in geographic areas with lower sunlight levels. We aimed to investigate the correlation between vitamin D level and quality of life in patients with multiple sclerosis who were exposed to sunny seasons within one year in western Turkey.

Results: Of 200 multiple sclerosis patients, 185 (92.5%) had lower vitamin D level. Patients reported no side effects during the study. The increase in Vitamin D level from baseline to 12 months was significant (p<0.0001). The improvements remained significant in all categories of MSQOL-54 after the vitamin D administration (p< 0.001). According to our results, the longer vitamin D use the higher improvement of quality of life.

Conclusion: This study showed that the prevalence of vitamin D level is still low in geographic areas with higher sunlight levels, and also, when vitamin D deficiency or insufficiency was corrected, there was indeed a positive effect on quality of life of patients.

Disclosure: Nothing to disclose

EP1136

Brief paroxysmal attacks as initial manifestation of multiple sclerosis

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Background and aims: Multiple sclerosis (MS) is characterised by a variety of symptoms. Usually these symptoms persist for a longer period.

There are, however, reports of patients suffering from repeated paroxysmal events lasting seconds to a few minutes, which may not be recognised as a manifestation of MS. In the literature they are referred to as paroxysmal symptoms or attacks, transient neurological events, and paroxysmal demyelinating events. They consist of brief, frequent and stereotyped attacks which may continue for days to months. The frequency varies from one to thirty times daily. Paroxysmal symptoms are most common early in the course of the disease and may even be the initial manifestation of MS.

Methods: Four types of attacks are identified in the literature: painful tonic spasms, dysarthria occasionally associated with cerebellar ataxia, sensory symptoms, and paresis. The attacks are thought to be caused by ephaptic activation of axons within a partially demyelinated lesion in fibre tracts resulting in transverse spreading of neuronal conduction to adjacent anatomical structures.

Results: We present the case of a male patient aged 23 years who was seen with a 3-month history of attacks of tingling around his right ear spreading to his neck and sometimes to his right forearm. This was associated with a sensation of loss of use in his left leg. MRI of the brain and cerebrospinal fluid analysis were consistent with a diagnosis of MS. The symptoms quickly subsided after starting a treatment with dimethyl fumarate.

Conclusion: MS should be considered in the differential diagnosis of transient neurological events.

Disclosure: Nothing to disclose

EP1137

Regional efficacy of fingolimod in relapsing remitting multiple sclerosis

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Background and aims: Fingolimod is approved in England as a second line treatment for highly active relapsing-remitting multiple sclerosis (RRMS). We aimed to evaluate the real world effects of fingolimod in a typical NHS clinical setting (relevant to appropriate prescribing, safety profile and cost-effectiveness).

Methods: Retrospective review of the medical records and MRI scans of RRMS patients on fingolimod for a minimum of 1 ear at Brighton and Sussex University Hospitals NHS Trust. Patient demographics, disease duration, Expanded Disability Status Scale (EDSS) and no evidence of disease activity (NEDA) were used as covariates. Findings were compared with FREEDOMS and TRANSFORMS outcomes.

Results: 61 patients, followed-up for a mean of 2.7–years were included. The cohort was slightly older (mean age 43 vs. 36), included a higher proportion of females (85% vs. 65-69%), had longer disease duration (12.5 vs 8 years) and was more disabled (median EDSS 4 vs 3) compared with the trial data. At 1 year 81.35% were relapse-free, similar to the trial data. For the whole follow-up period, NEDA was seen in 57.37% of patients, suggesting some expected waning effect. 14.75% of patients discontinued treatment. Logistic regression was performed to ascertain the effects of age, gender, disease duration and disability on the likelihood of patients responding to treatment. None of these was found to be significant predictors.

Conclusion: The efficacy of fingolimod mirrored the findings from the pivotal trials in a real world cohort with slightly different demographics.

Disclosure: Nothing to disclose

EP1138

Social cognition and quality of life in multiple sclerosis

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Background and aims: A recent meta-analysis outlined that MS patients could experience poor performances in Social Cognition (SC), defined as "the mental operation underlie social interactions" and specifically in Theory of Mind (ToM, the ability to attribute mental states to oneself and to others). This raises the need to evaluate the impact of SC on Quality of Life (QoL). We performed a cross-sectional study aimed at shedding further light on this relationship.

Methods: We collected socio-demographic and clinical data from 37 MS patients. They were tested for neuro-cognition (Brief Repeatable Battery), social cognition (Story-based Empathy Task, further divided in the following subscores: attribution of intentions (SET-IA), emotional states (SET-EA), together with a control condition (SET-CI)), depression, fatigue (Beck Depression Inventory and Fatigue Impact Scale) and QoL (Multiple Sclerosis Quality Of Life-54).

Results: SET global score and SET-IA were not related to any clinic-demographic, cognitive and psychosocial features except for disease duration (coeff. Beta -0.34,p=0.04 and coeff. Beta -0.42,p=0.01 respectively). SET-CI and SET-EA scores were not related to any clinic-demographic, cognitive or psychosocial features. Finally, neither physical composite or mental composite scores were related to SET measures.

Conclusion: Although ToM abilities might be involved in social activities and be related to QoL, this association did not emerge in our sample. Since ToM is the ability to understand others' emotions and intentions and MS patients could have ToM deficits, they could be not completely aware of their emotions and intentions involved in social context making them not impacting on the self-perception of QoL.

Disclosure: Nothing to disclose

EP1139

Translating the Parkinson's Disease Sleep Scale (PDSS-2) into 31 languages using a standardized methodology

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Background and aims: The Parkinson´s Disease Sleep Scale (PDSS-2) is a patient self-rating scale comprising 15 items, evaluated on a 5-point frequency scale, which assesses nocturnal disturbances in Parkinson's disease (PD) patients. The objectives of this study are to present the method and the challenges of the PDSS-2 translation (originally developed and validated in British English and German) into 31 languages, now widely used in various countries.

Methods: In each country, the translation process consisted of: 1) Conceptual analysis of the original PDSS-2 with its developers; 2) Forward/backward translation step; and 3) Test on five PD patients through interviews. An adjusted process was used for countries using a national variant of the same language (e.g., adaptation of the British English version for use in Australia).

Results: The translation process did not reveal any cultural issues since most of the concepts assessed in the PDSS-2 are cross-culturally relevant. Most of the difficulties belonged to the semantic, pragmatics and syntactic fields. For instance, the word "night" in item 2 (Did you have difficulty falling asleep each night?) could not be literally translated in eight languages. For contextual and colloquial reasons, the word "evening" was more appropriate in Czech, Danish, French (Belgium, Canada, France), Italian, Latvian, and Slovak. The distinction between "sometimes" and "occasionally" in the frequency scale created a range of queries, solved in collaboration with the developers. Other examples are presented.

Conclusion: The multi-step rigorous translation methodology was key in developing 31 translations of the PDSS-2 conceptually equivalent to the British English original.

Disclosure: Nothing to disclose

EP1140

Efficacy of cladribine tablets in patients after conversion to clinically definite multiple sclerosis (CDMS): Analysis of the ORACLE-MS study open-label maintenance period

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Background and aims: In the ORACLE-MS study in patients with a first demyelinating event, cladribine tablets (3.5 and 5.25mg/kg) significantly reduced risk of conversion to clinically definite MS (CDMS) vs placebo. If CDMS occurred in the initial double-blind treatment period (DBTP), patients entered an open-label maintenance period (OLMP) and received interferon-beta 1a. Here, annualised relapse rate (ARR) and lymphopenia during the OLMP of the ORACLE-MS study were assessed.

Methods: Participation in the OLMP depended upon the clinical course of the patient's disease in the DBTP. Patients in ORACLE-MS who converted to CDMS during the DBTP entered the OLMP and received subcutaneous interferon-beta 1a (titrated over 4 weeks to 44mcg) 3 times/week.

Results: 109 ORACLE-MS patients converted to CDMS in the DBTP and received ≥1 dose of interferon-beta 1a. Disposition is shown in Figure 1. Median time on interferon-beta 1a was 56.0 weeks. Estimated ARR in the OLMP are shown in Figure 2.
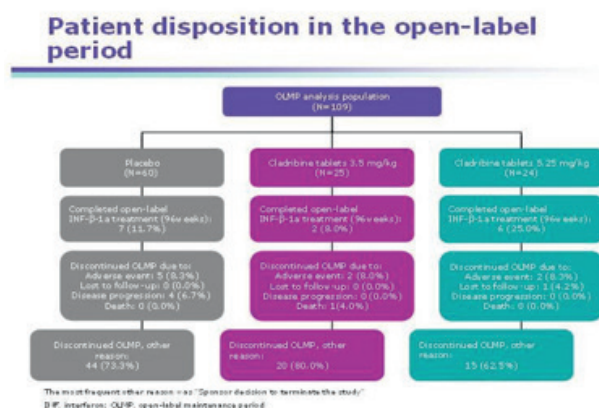
Figure 1
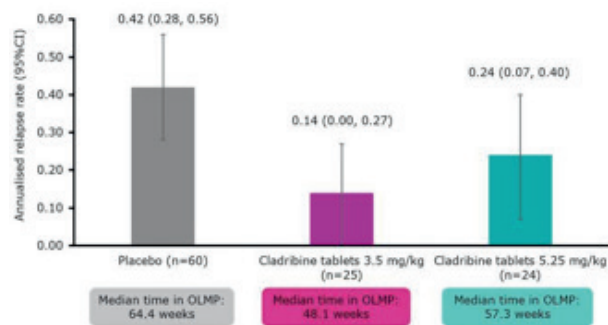
Figure 2

Conclusion: In these exploratory analyses for the open-label maintenance period of ORACLE-MS, treatment effects of cladribine tablets were observed in patients who converted to CDMS and subsequently received sc IFN β-1a. The point estimate of ARR in the open-label period was lower in patients originally randomised to cladribine tablets 3.5mg/kg, compared with placebo. There were no observed differences in MRI activity during the open-label period. The incidence of lymphopenia during the open-label period following conversion to CDMS was low, even if sc IFN β-1a was administered within 10 months of the last dose of cladribine tablets.

Disclosure: This study was funded by Merck KGaA, Darmstadt, Germany. Medical writing assistance was provided by inScience Communications, Springer Healthcare, Chester, UK, and was funded by Merck KGaA, Darmstadt, Germany.

EP1141

Safety of cladribine tablets in the treatment of patients with multiple sclerosis (MS): An integrated analysis from the MS clinical development program

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Background and aims: Efficacy has been demonstrated for cladribine tablets (CT) in patients with early MS and relapsing MS (RMS) in the ORACLE-MS, CLARITY, and CLARITY Extension studies. Adverse event (AE) data from these studies have been reported separately. Pooled safety data for integrated analyses allowing comprehensive characterisation of CT 3.5mg/kg (CT3.5) AE profile are reported here.

Methods: The monotherapy oral 3.5mg/kg cohort comprised 923 patients (3432.65 patient years [PY] exposure) derived from CLARITY, CLARITY Extension, ORACLE-MS and the PREMIERE registry; 641 patients in this cohort received placebo (2025.97 PY; Table 1).

Table 1

Results: The mean study period for patients receiving CT was 194 weeks; 165 weeks for placebo recipients. Adj-AE per 100PY rates for CT3.5 and placebo are reported in Table 2. Concerning known events expected with CT treatment, Adj-AE per 100PY for lymphopenia (preferred term) were 7.94 (CT3.5) and 1.06 (placebo), and for system organ class

of infection and infestations, 24.93 (CT3.5) and 27.05 (placebo); herpes zoster (preferred term), 0.83 (CT3.5) and 0.20 (placebo). Adj-AE per 100PY for the system organ class of neoplasms, benign, malignant and unspecified were 1.14 and 1.01, for CT3.5 and placebo, respectively.

Table 2

Conclusion: The AE profile for CT3.5 as monotherapy has been well-characterised in a pooled population of patients from early to more advanced RMS. Lymphopenia was expected from cladribine tablets' mode of action; herpes zoster was reported more frequently in patients experiencing Grade 3 or 4 lymphopenia; no clustering of types of malignancy, and no malignancies commonly associated with immunosuppression were observed.

Disclosure: This study was funded by Merck KGaA, Darmstadt, Germany. Medical writing assistance was provided by inScience Communications, Springer Healthcare, Chester, UK, and was funded by Merck KGaA, Darmstadt, Germany.

EP1142

Year-by-year lymphopenia rates in patients with relapsing multiple sclerosis (RMS) treated with cladribine tablets 3.5mg/kg in CLARITY and re-treated in CLARITY Extension

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Background and aims: CLARITY and CLARITY Extension demonstrated the efficacy of cladribine tablets (CT) in patients with RMS. The most common adverse event was lymphopenia, consistent with the mechanism of action of CT. Here we evaluate whether lymphopenia persists following treatment with CT.

Methods: Lymphopenia by grade (Common Terminology Criteria for Adverse Events v3.0) for patients who were randomised to CT 3.5mg/kg in the two-year CLARITY study and re-randomised to CT 3.5mg/kg in the two-year CLARITY Extension (N=186) are reported. Patients with Grade 0 lymphopenia ($\geq 1.0 \times 10^9$ cells/L) before the first course and Grade 0/1 ($\geq 0.8 \times 10^9$ cells/L) prior to administration of all subsequent courses in Years 2/3/4 were included in the analysis, according to re-treatment guidelines.

Results: 176 patients were Grade 0 at the start of CLARITY and 167 patients were Grade 0/1 at the start of CLARITY Extension (Table). By Week 13 in Year 1 and Week 12 in Years 2/3/4, 18–55% of patients developed Grade 2/3 lymphopenia. By Week 48 in each of Years 1/2/3/4, Grade 2/3 was observed in 11–14% (Figure). Occurrence of Grade 3 lymphopenia at any time was reported in <18% of patients; no patients had Grade 4 lymphopenia.

Table: Year-by-year lymphopenia by grade in patients that received cladribine tablets 3.5 mg/kg in CLARITY followed by retreatment in CLARITY Extension

	CLARITY				CLARITY Extension			
	Year 1		Year 2		Year 3		Year 4	
	Baseline	End of year	Baseline	End of year	Baseline	End of year	Baseline	End of year
Patients*	176	175	161	154	167	161	136	123
Lymphopenia grade†								
0	176	119	122	97	134	86	85	59
1	0	37	39	39	33	52	51	48
2	0	19	0	16	0	23	0	16
3	0	0	0	2	0	0	0	0
4	0	0	0	0	0	0	0	0

Data shown are number of patients.
* Patients had lymphopenia Grade 0 at the baseline of Year 1, and Grade 0 or 1 at the baseline of Years 2–4; end of year values are the number of patients with laboratory values.
† Lymphopenia graded by National Cancer Institute Common Terminology Criteria for Adverse Events v3.0

Table 1

Figure: Lymphopenia by grade over time in patients that received cladribine tablets 3.5mg/kg in CLARITY followed by retreatment CLARITY Extension
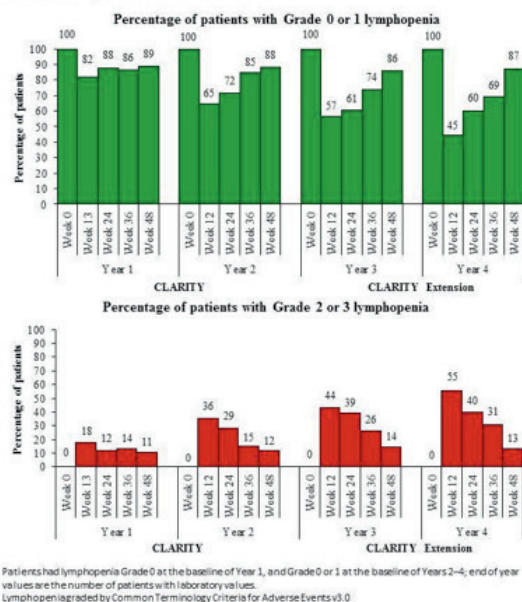
Figure 1

Conclusion: In patients with lymphocyte counts ≥1.0×10^9/L before the first course and ≥0.8×10^9/L before ≤3 subsequent annual courses of CT, no patients experienced Grade 4 lymphopenia at any time. Approximately 86% of patients recovered to Grade 0/1 by the end of each treatment year. There was no reduction in the proportion of patients recovering towards baseline with additional CT courses.

EP1143

Fingolimod 2012 and 2016: How did the profile of patients treated with fingolimod change? A comparison of two non-interventional studies PANGAEA and PANGAEA 2.0

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Background and aims: Over the years the therapeutic options for multiple sclerosis (MS) increased and treatment guidelines changed. How did this change the profile of the fingolimod-treated patients from 2012 to 2016?

Methods: PANGAEA and PANGAEA 2.0 are two non-interventional studies conducted in Germany that recruited patients switching to fingolimod between 2011/12/13 and 2015/16 respectively. Here we compare baseline data from these two studies to demonstrate a change in the profile of relapsing-remitting MS patients that switch to fingolimod.

Results: The mean age of patients enrolled in PANGAEA 2.0 was slightly younger (38.4+/-10.7 vs 38.8+/-10.1 years) compared with PANGAEA and higher proportion of patients were younger than 40 years (59.6% vs. 54.1%). Patients in PANGAEA 2.0 have a shorter disease history (7.3+/-6.6 vs. 8.2+/-6.3 years) a similar number of relapses 12 months before baseline (1.3+/-1.0 vs. 1.5+/-1.2), a lower EDSS (2.2+/-1.6 vs. 3.0+/-1.7) and MSSS scores (multiple sclerosis severity score; 3.5+/-2.5 vs. 5.1+/-2.6). 41.9% of the patients in PANGAEA 2.0 had an EDSS score of ≤1.5 at baseline (PANGAEA: 23.3%). The MSSS score of 50.0% of the patients in PANGAEA 2.0 ranged within the first 3 deciles (PANGAEA: 29.5%). 18.2% of the patients in PANGAEA 2.0 were treatment naïve or without any treatment in the previous 12 months (PANGAEA 5.8%).

Conclusion: Patients enrolled into PANGAEA 2.0 (2015/16) switched to fingolimod earlier from a demographic and clinical point of view in comparison with PANGAEA (2012/13). This might indicate a trend towards optimizing fingolimod therapy early in MS from 2012 to 2016 in Germany.

EP1144

5 years safety of fingolimod in real world: Results from PANGAEA, a non-interventional study of RRMS patients in Germany

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Background and aims: Fingolimod (FTY720; Gilenya®, Novartis Pharma AG) is approved for the treatment of relapsing MS. As of August 2016, approximately 160,000 patients have been treated with Fingolimod.
PANGAEA (Post-Authorization Non-interventional German sAfety study of GilEnyA in RRMS patients) is a non-interventional study, conducted in Germany, to investigate long-term safety, effectiveness and patient reported outcomes in daily practice.
Methods: 4229 patients were enrolled into PANGAEA. By Jan 2017 over 300 patients finished the five year documentation period. Here we present safety and adherence data of fingolimod treatment in daily clinical practice for up to five years.
Results: Over five years, the yearly mean study discontinuation rate was 12%. 67% of patients who started fingolimod treatment between 2011 and 2013 in PANGAEA are still on drug. 79% of patients who discontinued the study also discontinued fingolimod. Most frequent reasons for study discontinuation (multiple answers possible) were patient's decision (33%) and adverse events (28%). Over five years, the safety profile of fingolimod in real world is comparable to that observed in phase III clinical trials. Common adverse events were reductions in lymphocyte counts, increase in liver enzyme values, upper respiratory tract infections (e.g. nasopharyngitis [9.9%]), and MS related adverse events like fatigue (3.4%) and depression (2.6%). Approximately 45% of the patients experienced no adverse events. 3.9% of all adverse events were rated as serious.
Conclusion: The results of PANGAEA support the positive benefit-risk profile fingolimod, demonstrated in clinical trials, with real world evidence data. The frequency/nature of reported adverse events is consistent with previous findings.
Disclosure: This study was supported by the Novartis Pharma GmbH, Nuremberg, Germany.

EP1145

Teriflunomide real-world outcomes in the phase 4 Teri-PRO Study: Results from Europe, Canada, and Latin America

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Background and aims: Teriflunomide is a once-daily oral immunomodulator for relapsing-remitting MS. Teri-PRO (NCT01895335), a global, phase 4 study in patients with relapsing forms of MS, investigated patient-reported outcomes (PROs), effectiveness, safety, and tolerability associated with teriflunomide treatment in routine clinical practice in the US and rest of the world (Europe, Canada, and Latin America; ROW). Here, we report outcomes for Teri-PRO patients enrolled in ROW.
Methods: ROW patients received teriflunomide 14 mg for 48 weeks. The primary outcome was patient Global Satisfaction at Week (W)48, measured using the Treatment Satisfaction Questionnaire for Medication (TSQM-V1.4). TSQM scores were measured at baseline (patients switching from a prior disease-modifying therapy [DMT]), and at W4 and W48/end of treatment. Secondary outcomes included PRO assessments, annualized treated relapse rate, and adverse events (AEs).
Results: For ROW patients (n=455), mean (SD) age was 42.9 (10.1) years; time since first MS symptoms was 11.3 (8.9) years. TSQM Global Satisfaction remained high over the study period (mean [95% CI]: W4, 72.3 [70.4, 74.2]; W48, 68.5 [66.0, 70.9]). In patients switching from another DMT (n=278), mean (95% CI) Global Satisfaction significantly improved from baseline (54.9 [51.9, 57.8]) to W48 (70.4 [67.4, 73.4], P<0.0001). Mean treated relapse rate was low (0.23). AEs were reported in 385 (84.6%) patients, and were mostly mild to moderate.
Conclusion: High levels of treatment satisfaction with teriflunomide were observed in ROW patients, including significant improvements in patients switching from another DMT, consistent with the full study population. Teriflunomide was well tolerated and safety outcomes reflected those observed in other studies.
Disclosure: Study supported by Sanofi Genzyme.

MS and related disorders 2

EP1146
Cancelled

EP1147
Retrospective evaluation of hospitalizations in a cohort of multiple sclerosis patients from a tertiary centre

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Background and aims: There is poor knowledge on current hospitalizations in the multiple sclerosis (MS) population. Our aim is to examine hospitalization causes and outcomes in a MS cohort.

Methods: Retrospective study of MS patients admitted to our Centre between August 2009 and July 2015, excluding admissions to establish MS diagnosis.

Results: There were observed 308 hospitalizations from 155 patients with MS, mainly women (67.5%), with a median age of 47 (IQR 23). Relapsing-remitting MS was present in 51.1%, the overall median Expanded Disability Status Score (EDSS) was 4.5 (IQR 5) and the median MS duration was 12 years (IQR 10). Infection was responsible for 22.1% of hospitalizations and diseases of the nervous system for 21.4% (including 59.1% due to relapses but also epilepsy, tremor and others). They were followed by diseases of the genitourinary (14%) and circulatory systems (9.7%) and neoplasms (6.8%). A total of 23 hospitalizations (7.5%) required Intensive Care (IC) admission. The length of stay and death rate were higher in patients requiring IC. There were no significant differences in age, gender, MS duration, disease subtype, comorbidities or EDSS in those needing IC. Nine admissions (2.9%) resulted in death. IC admission, secondary progressive MS and increased comorbidities index (Charlson index) were statistically related to fatality.

Conclusion: Infections are the most common cause of hospitalizations in our study. Almost 8% of all MS hospitalizations required IC admission. These may be related to longer admission lengths and higher death rates. Mortality may be associated with secondary progressive MS, comorbidities and IC admission.

Disclosure: Nothing to disclose

EP1148
On the possible role of kappa free light chain index (KFLCi) in the initial setting for the diagnosis of multiple sclerosis

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Background and aims: Diagnosis of multiple sclerosis (MS) includes clinical and imaging findings to demonstrate lesions dissemination in space and time and to exclude other diseases. The contribution of biochemical assays of cerebrospinal fluid (CSF) is marginal. However, the kappa free light chain index (KFLCi) has emerged as alternative marker, with high sensitivity and low costs.

Methods: 85 patients were enrolled in this preliminary study: 54 had a suspicion of MS (sMS) and 31 of non MS Inflammatory Disease (sNMSID) within the central nervous system. MS diagnosis was based on the 2010 McDonald's criteria (MD). KFLCi has been measured on serum and CSF by nephelometry.

Results: 34 sMS patients (63%) fulfilled both the MD criteria at clinical presentation and had a KFLCi above cut-off values (5); all of them were diagnosed as MS. Despite 20 sMS patients (37%) did not fulfill MD criteria, a final diagnosis of MS was confirmed in 13 of them (65%). In the 92% of this latter group, KFLCi was indeed above the cut-off value. About 23% of sNMSID patients fulfilled the MD criteria at the time of rachicentesis and had a KFLCi higher than 5; for all of them a final diagnosis of MS has been confirmed. Despite 74% of sNMSID patients initially did not fulfill MD criteria, MS was confirmed in 26% of them, and KFLCi was indeed above the cut-off value in 86% of them.

Groups	Initial suspect diagnosis of MS or NMSID (n)	Final confirmed diagnosis of MS (n)
sMS MD+ KFLCi+	34	34
sMS MD+ KFLCi-	0	0
sMS MD- KFLCi+	13	12
sMS MD- KFLCi-	7	1
sNMSID MD+ KFLCi+	7	7
sNMSID MD+ KFLCi-	1	0
sNMSID MD- KFLCi+	10	6
sNMSID MD- KFLCi-	13	0
Total	85	60

sMS: suspected Multiple Sclerosis
sNMSID: suspected Non Multiple Sclerosis Inflammatory Disease
MD: McDonald Criteria
KFLCi: kappa free light chain index

Suspect and confirmed diagnosis of the patients investigated

Conclusion: These findings strongly suggest that KFLCi must be included in the initial setting to improve diagnosis of MS

Disclosure: Nothing to disclose

EP1149

Time to pregnancy in multiple sclerosis: A case control comparative study

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Background and aims: Multiple sclerosis (MS) is a neurological disease mostly affecting women of childbearing age. The likelihood of spontaneous conception in subsequent cycles is important in MS, mostly because of the indication to withdrawn the disease-modifying treatments due to their unknown effect during pregnancy. We used data on the number of cycles required for a couple to conceive (tine to pregnancy). Time to pregnancy provides a sensitive measure of fertility.

Methods: A prospective, observational study in a clinical-based cohort of MS patients was performed. Clinical and epidemiological data were analyzed. Numbers of noncontracepting cycles until conception were collected. Data were compared with a healthy age-matched control group.

Results: MS cohort: 56 patients. Relapsing-remitting: 87%, primary progressive 6%, secondary progressive 6%. Disease duration: 9.2 years (2-22). Unintended pregnancies 6%. EDSS at pregnancy 1 (0-5). Time to pregnancy 3.77 month. Infertility treatments: 12%. Control group: 64 women. Unintended pregnancies 12.5% ((P<0.05). Time to pregnancy 3.66 month (P>0.05). Infertility treatments: 10%. (P>0.05)

Conclusion: This study reveals that time to pregnancy is similar between MS patients and the control group. A major proportion of unintended pregnancies were found in the control group. The likelihood of conception in subsequent cycles is of major interest to neurologist for a better Disease Modifying Therapies (DMTs) planning.

Disclosure: Nothing to disclose

EP1150

Corpus callosum demyelination associated with acquired stuttering

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Background and aims: Differences have been reported in fractional anisotropy, voxel-based morphology, and white matter integrity in the corpus callosum of patients with developmental stuttering. Adult onset acquired stuttering is uncommon; however, case reports have described callosal infarction and neoplasm associated with acquired stuttering.

Methods: Case Report

Results: A 32-year-old female with polycystic ovarian syndrome presented with fatigue, concentration impairment, and acute headache. Neurological and fundoscopic exam were normal. CSF was normal except for 10 nucleated cells (95% lymphoctyes). Immunological testing was not performed. Opening pressure was 31cm H2O but performed in a flexed position. Non-contrast brain MRI demonstrated multiple ovoid nonspecific T2 hyperintensities in the subcortical and deep white matter. Migraine or possible IIH was suspected and Topiramate initiated. One month later, the patient gradually developed stuttering and stopped Topiramate. Severity of stuttering progressed, and she developed new bilateral lower extremity paresthesias. Severe stuttering and bilateral thigh numbness were noted on neurological exam, but was otherwise normal. Brain and spinal cord MRI demonstrated new T2 hyperintense lesions, including an enhancing 11mm x 8mm lesion in the rostrum of the corpus callosum and a non-enhancing C7-T1 T2 hyperintensity. CSF demonstrated 14 nucleated cells (90% lymphocytes), 10 oligoclonal bands restricted to CSF, elevated IgG index, and normal opening pressure. The patient was diagnosed with MS, started on disease modifying therapy, and speech impairment slowly improved over the following 3 months.

Conclusion: Corpus callosal lesions are a common radiographic finding in multiple sclerosis but uncommonly affect language. In rare cases, callosal demyelination may be associated with acquired stuttering.

Disclosure: Nothing to disclose

EP1151

Evoked potentials and other guiding factors of conversion from radiologically isolated syndrome to definite multiple sclerosis

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Background and aims: Radiologically Isolated Syndrome(RIS) has become a popular subject recently with quite number of follow-up and other clinical studies being done. The aim of our study was to assess the role of VEP and SEP as a guiding factor for the conersion from RIS to MS.

Methods: 49 RIS patients who were referred our Neurology department between 2011-2015. All of the patients fullfillied the Okuda ciriteria. For the VEP examination the p100 latancy and amplitudes, for the SEP examination the p40 latency and mplitude was analysed.

Results: 49 patients were included in this study, the mean time of follow up was 21.8 months. 63% of patients were female. The mean age was 31.2 years. Among the 4 patients with abnormal SEPs, MS developed in 3 of them(75%) over time(p:0.011) VEP and/or SEP was abnormal in 8 patients and MS developes in 4(50%) 8p:0.017). The most important factor for the transformation is the presence of active plaque with increases the risk 8.1-fold. The second important factor seems to be the presence of VEP and/or SEP abnormality, but this factor does not reach statistical significance.

Conclusion: In this conversion to MS risk from RIS, VEP-SEP examinations are important and should take its place in the follow-up of these patients.

Disclosure: Nothing to disclose

EP1152

Characterising immunological properties of dimethylfumarate treatment: Longitudinal data from MS patients

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Background and aims: The mode of action of dimethylfumarate (DMF), an immunomodulatory treatment for relapsing-remitting multiple sclerosis (RRMS), has not yet been fully elucidated. While in-vitro experiments suggest effects on pathways essential for immune cell survival, cytokine secretion and oxidative stress response, a proof from human ex-vivo studies is lacking.

Methods: Blood samples were collected from twenty well-characterized RRMS patients at baseline and after 3 months of DMF treatment and an age- and gender-matched cohort of healthy individuals at 0 and 3 months. Peripheral blood mononuclear cells (PBMC) were separated and cryopreserved for flow cytometry and immunoassays. Lymphocyte subpopulations and cytokine patterns were recorded. PBMC were assessed for their response to oxidative stress induced by hydrogen peroxide, their T cell proliferative capacity as well as activation of NFkB and MAPK pathways.

Results: After 3 months DMF treatment T cell counts dropped by 31 percent with increasing CD4/CD8-ratio, while other lymphocyte populations were not altered significantly. No change in response to oxidative stress was detected. DMF inhibited proliferation of T cells (CD8>CD4), but this anti-proliferative effect decreased over time. Both ex-vivo and in-vitro treatment with DMF resulted in altered cytokine profiles; specifically secretion of interleukin 4 and interleukin 6 was reduced after 3 months. Longitudinal data on NFkB and MAPK activation in lymphocytes will be presented.

Conclusion: This study expands the knowledge on alterations in lymphocyte patterns and translates in-vitro and ex-vivo findings on DMF related immune response and pathway activation into the clinical setting.

Disclosure: This study was supported by an Investigator Initiated Trial grant from Biogen. The institution (University Hospital Basel) received in the last 3 years and used exclusively for research support: steering committee, consulting and speaker fees from Actelion, Addex, Bayer HealthCare, Biogen, Biotica, Genzyme, Lilly, Merck, Mitsubishi, Novartis, Ono, Pfizer, Receptos, Sanofi-Aventis, Santhera, Siemens, Teva, UCB and Xenoport; support of educational activities from Bayer HealthCare, Biogen, CSL Behring, Genzyme, Merck, Novartis, Sanofi-Aventis and Teva; royalties from Neurostatus Systems GmbH; grants from Bayer HealthCare, Biogen, the European Union, Merck, Novartis, Roche, the Swiss Multiple Sclerosis Society and the Swiss National Research Foundation.

EP1153

Antibodies against MOG for patients with neuromyelitis optica and neuromyelitis opticus spectrum disorders

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Background and aims: Neuromyelitis optica (NMO) and NMO-spectrum of disorders (NMOSD) are inflammatory disorders of the central nervous system (CNS).The detection of anti-AQP4-antibodies (AQP4Abs) has become an important part of the diagnosis, but in some patients AQP4Abs cannot be detected even if the patients are clinically similar and the diagnosis is the same. This group of NMO/NMOSD patients is called sero-negative. Myelin oligodendrocyte glycoprotein (MOG) is a surface protein of the myelin sheath in CNS. We investigated if anti-MOG-antibodies may play a role as a diagnostic marker for NMO/NMOSD making it relevant to define a new sero-positive NMO/NMOSD subgroup.

Methods: Systematic searches were performed in PubMed, Cochrane library and Scopus for original articles regarding ON or NMO/NMOSD antibodies against MOG were analyzed.

Results: We found 158 MOGAbs+ accounting for 16% of NMOSD patents. This group distinguished itself phenotypically from AQP4+ patients by being younger, have a more equal gender distribution, more often being monophasic, with fewer and less severe attacks and better disorder resolution. They could, however, not account for all AQP4Ab- NMOSD patients.

Conclusion: MOGAb+ NMOSD patients distinguish themselves phenotypically from AQP4Ab+ patients, but cannot account for all the AQP4Ab- patients with NMOSD. MOGAbs are found in several other demyelating CNS disorders and are thus not specific for NMOSD. It remains to reveal if the presence of MOGAbs is a marker for a distinct underlying mechanism of disorder with phenotypical characteristics comprising multiple of todays established diagnosis. Further research is needed to establish such a potential mechanism, for example to determine the right treatment.

Disclosure: Nothing to disclose

EP1154

Smoking: Effects on the progression of Multiple Sclerosis - a cohort study of patients treated with immunomodulatory therapy

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Background and aims: We investigated the influence of smoking on disease progression measured by Expanded Diability Status Scale (EDSS) in patients with Multipe Sclerosis (MS) treated with immunomodulatory therapy (IMT).

Methods: We conducted a retrospective national representative cohort study on all consecutive treated patients with MS and Glostrup University Hospital. Data on smoking habits was collected on 871 patients (632 women and 239 men). Kruskal-Wallis One Way Analysis of Varians was used and results were adjusted for age at onset, gender, and disease duration.

Results: The results showed no significant association between smoking and disease progression measured as change in EDSS score/years of treatment (p=0.196). Smokers (n=236) tended to have a higher initial and final EDSS score (p-value 0.056 and 0.085, respectively).

Conclusion: We found no correlation between smoking and disease progression in patients treated with IMT. The results contribute to the still open debate whether smoking affects the progression of MS. The results suggest that smoking cessation may be less important for patients treated with IMT, but further studies are needed.

Disclosure: Nothing to disclose

EP1155

Quantitative MRI in daily practice: Assessment of brain volume and lesion load in patients with multiple sclerosis from INSPIRATION study

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Background and aims: To investigate the results of standardised MRI-scans qualitatively and quantitatively, obtained from patients with MS. INSPIRATION, a non-interventional multicentre study conducted in Germany, aimed to validate the feasibility and explore the potential benefits of standardized MRI-acquisition and centralized quantitative MRI-reading in clinical practice for RRMS patients.

Methods: INSPIRATION included 253 patients from 15 centers between 05/2014 and 07/2015. MRI and clinical data will be documented over 3 years. Staff at individual sites underwent expert training and standardized sequence implementation. A centralized quantitative MRI-data analysis was performed. The results were reported to the neurologist and radiologist.

Results: 99.6% of the obtained MRI-scans passed the quality analysis; <0.03% of scans led to site inquiries or data exclusion. The mean number (+/-SD) and volume (+/-SD) of T2-lesions at baseline was $30.1(+/-2.8)/11033.1(+/-1578.9)mm^3$ and that of black holes was $4.0(+/-0.9)/490.3(+/-136.6)mm^3$. The corresponding values after 12 months follow-up were $32.3(+/-3.6)/11479.9(+/-1927.5)mm3$ and $4.1(+/-1.1)/488.9(+/-165.2)mm^3$, respectively. Whole brain volume at baseline was $1,142,397(+/-15,988)mm^3$. Brain volume reduction after 12 months was $3,231(+/-1,944)mm^3$ (0.28%+/-0.1%).

Conclusion: Comparability of MRI-Scans is a central medical need in the management of MS patients. INSPIRATION provides a centralized quantitative MRI-analysis and might improve the comparability of individual MRI-scans in daily clinical routine. The quantification of lesion volumes and visualization of MRI-abnormalities may facilitate neurologists to integrate MRI-data to support patient management.

Disclosure: This study was supported by the Novartis Pharma GmbH, Nuremberg, Germany.

EP1156

High Disease Activity (HDA) definitions in patients with Relapsing Multiple Sclerosis (RMS) receiving placebo in the CLARITY Study

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Background and aims: The 2-year CLARITY study in patients with RMS allows assessment of HDA definitions for identifying patients with a higher rate of relapse or disability progression.

Methods: Placebo recipients in CLARITY (N=437) were retrospectively analysed using two sets of HDA criteria that assessed whether they had experienced high relapse activity ([HRA] ≥2 relapses in the previous year) regardless of prior treatment, or HRA plus treatment nonresponse ([HRA+TNR] ≥2 relapses in the previous year OR ≥1 relapse in previous year while on DMD therapy and ≥1 T1 Gd+ or ≥9 T2 lesions). The ability of these criteria to identify HDA patients among placebo recipients was assessed according to relapse and disability outcomes.

Results: ARR was higher in the placebo HRA and the placebo HRA+TNR subgroups than in the overall placebo population and the non-HRA and non-HRA+TF subgroups (Figure 1). Time to first qualifying relapse was shorter in the HRA and HRA+TF subgroups than the overall placebo population and the non-HRA and non-HRA+TNR subgroups. Time to 6-month confirmed EDSS progression (10% of patients) was 110 days for the HRA subgroup (non-HRA patients=330 days), 162 days for the HRA+TNR subgroup (non-HRA+TNR patients=329 days) and 245 days, overall placebo population (Figure 2). The increased ARR and shorter time to EDSS progression highlights the increased risk in patients identified by these HDA criteria.

Figure 1. ARR in placebo recipients by HDA subgroup

ARR for placebo-treated patients in CLARITY by disease activity subgroup
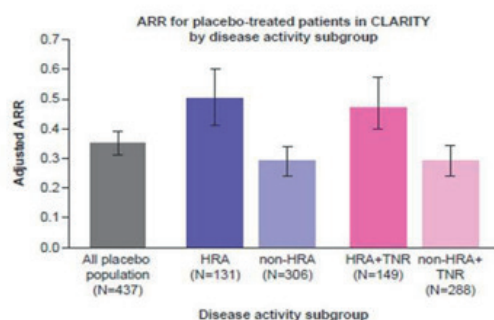
Figure 1

Figure 2. Kaplan-Meier survival curves for time to 6-month EDSS progression by HDA subgroup
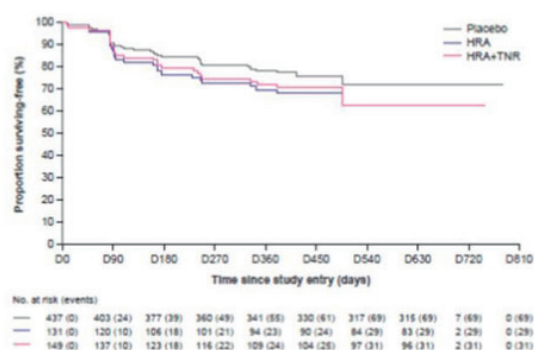
Figure 2

Conclusion: Post-hoc analysis from the CLARITY study showed that HDA criteria based on relapse history, treatment history and MRI characteristics can identify patients with RMS at increased risk of experiencing relapses and disability progression.

EP1157

Cladribine tablets in high disease activity (HDA) subgroups from the CLARITY study of patients with relapsing multiple sclerosis (RMS)

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Background and aims: In the CLARITY study, treatment with cladribine tablets (CT) vs placebo showed strong efficacy in a large cohort of patients with RMS over 2 years. Patients with HDA are at higher risk of relapses and disability progression. This post-hoc analysis compared the effects of CT 3.5mg/kg (CT3.5) vs placebo in subgroups of CLARITY patients selected using two HDA definitions.

Methods: CLARITY patients randomised to CT3.5 (N=433) or placebo (N=437) were retrospectively analysed using two different HDA definitions based on relapse history, prior treatment, and MRI characteristics. Patients were categorised according to whether they had experienced high relapse activity ([HRA] ≥2 relapses in the previous year) regardless of prior treatment, or HRA plus treatment nonresponse ([HRA+TNR] ≥2 relapses in the previous year, or ≥1 relapse in previous year while on DMD therapy and ≥1 T1 Gd+ or ≥9 T2 lesions).

Results: In the overall CLARITY population, CT3.5 reduced the risk of 6-month confirmed EDSS progression by 47% vs placebo (Figure 1). A larger risk reduction for CT3.5 vs placebo of 82% was seen in the HRA subgroup and the HRA+TNR subgroup indicating greater responsiveness to CT3.5 in patients identified by these criteria. ARR was lower with CT3.5 than placebo in the overall population and even lower with for the HRA and HRA+TNR subgroups (Figure 2).

Figure 1. Forest plot of Hazard Ratio of time to 6-month confirmed EDSS progression by HDA subgroup for cladribine tablets 3.5 mg/kg vs placebo
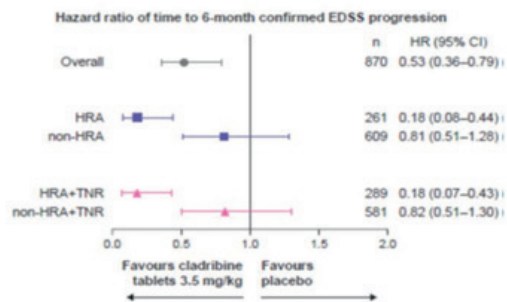
Figure 1

Figure 2. Forest plot of Relative Risk of ARR by HDA subgroup for cladribine tablets 3.5 mg/kg vs placebo
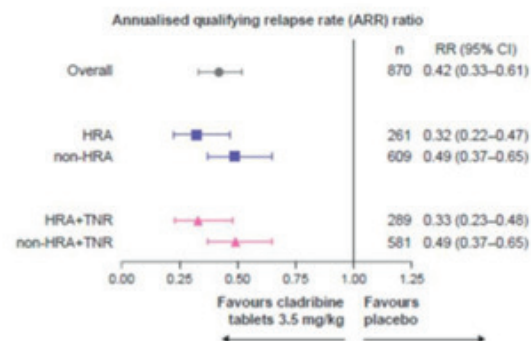
Figure 2

Conclusion: In the CLARITY study, patients identified by HDA criteria showed clinical and MRI responses to CT3.5 that were generally better than, or at least comparable with, the outcomes seen in the overall CLARITY population.

Disclosure: This study was funded by Merck KGaA, Darmstadt, Germany. Medical writing assistance was provided by inScience Communications, Springer Healthcare, Chester, UK, and was funded by Merck KGaA, Darmstadt, Germany.

EP1158

Investigation of demographic and clinical properties of familial multiple sclerosis patients

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Background and aims: Multiple sclerosis (MS) is known as an autoimmune neurodegenerative disease, characterized by familial aggregation. In this study, it was aimed to investigate the familial transition characteristics of MS, thereby contributing MS genetics studies and helping with personalized therapy approaches.

Methods: We investigated 110 patients (admitted to MS outpatient clinic between January 2015 - November 2015) from 50 families - with members that were diagnosed with definitive MS diagnosis according to the 2010 McDonald criteria - in terms of demographical and clinical properties.

Results: Paternal inheritance was observed on the 19 of the patients and maternal inheritance was observed on the 30 of all the patients. When the relatives of the patients with paternal and maternal transition observation was compared, significant difference was found ($\chi2=6.437$, p=0.04). Median EDSS (2015) value was 3.0 (1.5 – 6.0) and median MSSS value was 3.4 (1.6 – 6.4) for all patients involved in the study. Median MSSS value for paternal transition observed patients was determined to be 1.6 (0.6-2.9) and for maternal transition observed patients was 4.5 (2.1 – 6.7); and the difference was significant (p=0.016 ; z=-2.411).

Conclusion: This study shows that clinical presentation and progression is more severe in maternally inherited MS cases compared to paternally inherited MS cases. Thus early diagnosis and treatment is important however, larger and more homogenous patient cohorts, prospective controlled studies would be more helpful in deciding treatment options and management.

Disclosure: Nothing to disclose

Muscle and neuromuscular junction disease 1

EP1159

Ephedrine and 3,4 diaminopyridine responsive myasthenic syndrome in plectin-related epidermolysis bullosa simplex with muscular dystrophy

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Background and aims: Mutations in the plectin gene causes a variety of disorders, namely: epidermolysis bullosa simplex with muscular dystrophy (EBS-MD), EBS-MD with myasthenic features (EBS-MD-MyS), limb girdle muscular dystrophy type 2Q, EBS with pyloric atresia, and EBS-Ogna. We report an unusual patient with EBS-MD-MyS, who displayed a marked suppression of his myasthenic symptoms in response to ephedrine and 3,4 diaminopyridine (3,4-DAP).

Methods: No

Results: A 41-year-old Caucasian male suffered from congenital hypotonia, muscle weakness, delayed motor milestones, and skin and mucous membrane blistering since birth. At the age of 25, he developed progressive symmetrical scapular and peroneal weakness and atrophy. In his early thirties, additional ptosis, diplopia, dysphagia, and fatigue manifested. CK-levels were markedly elevated (2,200-16,000 UI/L). Needle EMG showed a generalised myopathic pattern, and repetitive nerve stimulation studies at 3 Hz depicted a 20% decremental response. MRI showed pronounced fatty replacements of shoulder girdle muscles, the posterior compartment of thighs, and the anterior compartment of his legs. Muscular biopsy revealed severe dystrophic changes and desmin-positive aggregates. Genetic analysis revealed two heterozygous PLEC mutations: one (c.11737del; p.(Arg3913Valfs*30)) leading to a premature translational stop codon, and a second (c.2539-2A>G) residing in the highly conserved splice-acceptor site of intron 21. While pyridostigmine was of no benefit, a combination of ephedrine and 3,4-DAP effectively controlled his myasthenic-related symptoms.

Conclusion: To date, no specific treatment is available for any form of plectinopathy. In EBS-MD patients with additional evidence of myasthenia, a combination of ephedrine and 3,4-DAP should be considered as a symptomatic treatment option.

Disclosure: Nothing to disclose

EP1160

Cancelled

EP1161

Exercise-induced fatigue and measurement of oxidative stress biomarkers in myotonic dystrophy type 1 DM1

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Background and aims: Fatigue, the inability to maintain the expected motor performance over time, can be an acute or chronic status in neuromuscular disorders; a greater fatigability it is reported to be more common in myotonic dystrophy (DM1) (Laberge et al. 2009). Oxidative stress has been proposed to be one of the pathogenic factors (Angelini and Tasca, 2012), although others (Bray et al. 2012) suggested a role for CNS involvement.

Methods: We studied exercise-induced fatigue in a sample of adult-onset DM1 patients (17males, 9females, mean age 41.6yrs,sd±12.7), through an intermittent-incremental-effort-exercise; oxidative stress balance blood biomarkers were collected. Motor disability was assessed using a muscle impairment rating scale (MIRS). To test for possible effects of central fatigue, patients have been administered with clinical scales about fatigue, mood and quality of life.
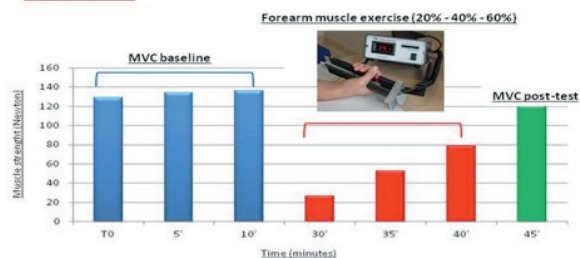
Results: Our exercise protocol proved to be easily deployable and well-tolerated. Statistical analysis revealed a significant increase in AOPP in DM1 patients versus controls but no significant differences between oxidative stress balance markers before and after the effort (Fig.2-3). The occurrence of central fatigue suggests that central activation worsens during motor contractions;central-fatigue score(FSS) was significantly correlated to MVC (r-before: -0.583,p<0.01; r-after=-0.534,p<0.05), and to motor disability (r-MRC =-0.496,p<0.05).
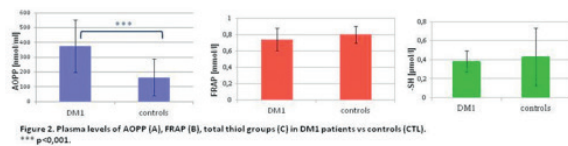
Figure 2. Plasma levels of AOPP (A), FRAP (B), total thiol groups (C) in DM1 patients vs controls (CTL). *** p<0,001.
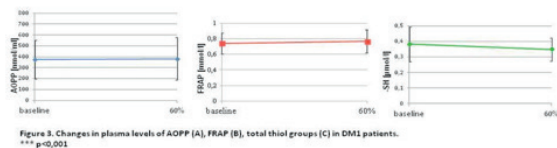
Figure 3. Changes in plasma levels of AOPP (A), FRAP (B), total thiol groups (C) in DM1 patients. *** p<0,001

Conclusion: Biochemical correlates of oxidative stress represent a viable biomarker for clinical use in, although these markers still need to be validated in larger sample sizes;these results also suggest that comparative studies assessing CNS and muscle involvement are useful to define fatigability profile in DM1.

Disclosure: Nothing to disclose

EP1162

Towards a definition of fatigability profile in myotonic dystrophy type 1 (DM1)

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Background and aims: Myotonic dystroph type 1(DM1) is characterized by high fatigability (Kalkman et al. 2005). Oxidative-stress(Angelini and Tasca, 2012) and central mechanisms(Bray et al.(2012) have been proposed to be possible pathogenic factors.Our aim was to investigate the fatigability profile in DM1, looking specifically at the relationship between self-reported fatigue, objective measures of peripheral fatigue, cognitive performance and gross brain structure.

Methods: We studied fatigability profile in a sample of 20 adult-onset DM1 patients (14males, 6females, mean age 41.6 years, sd±12.7) through an intermittent incremental effort(Søgaard et al. 2006). To test for effects of central fatigue, patients have been administered fatigue severity scale (FSS), cognitive tests and 3T magnetic resonance (MR) imaging.

Results: FSS-score was significantly correlated to MVC before and after the effort, (r_before=-0.583, p<0.01,r_post=-0.534, p<0.05), and to motor disability (r =-0.496, p<0.05); moreover we found a strong tendency trend-to-significance in the association with baseline-lactate(r =0.378,p=0.057). Out of the six measures of cognitive performance used, 40% (n=8) of DM1 patients had impairment in two or more scores related to attention processes. MRimaging investigations revealed that DM1patients had reduced gray-matter volume in the bilateral prefrontal cortex, consistently with previous studies reporting this area to play a role in the neural regulation of fatigue.

Conclusion: These data suggest that fatigue in DM1 is a multifaceted entity, also related to the disruption of fatigue-related processes in the brain. The tools used in this study may be used as effective means to define fatigability profile in DM1patients.

Disclosure: Nothing to disclose

EP1163

Clinical, laboratory and anatomopathological evaluation of patients with RyR1 mutations

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Background and aims: Mutations in the RyR1 gene underlie several debilitating and/or life threatening muscle conditions: central core disease, susceptibility to malignant hyperthermia, multiminicore disease and centronuclear myopathy.

To describe the clinical, laboratory, anatomopathological and genetic findings of a group of patients with RyR1 gene mutations followed at the Neuromuscular Disease Unit of the Neurology Department of Coimbra's University and Hospital Center.

Methods: The medical files of patients with confirmed RyR1 mutations were reviewed for demographic, historical and clinical data. Serum creatine kinase, forced vital capacity, electromyography and muscle biopsies were also analysed.

Results: Seven patients, three females, from five unrelated families were included. There was no parental consanguinity. The symptoms began in childhood or the second decade of life and were very slowly progressive. All patients acquired independent ambulation but three had a delayed attainment of motor skills. One patient, son a symptomatic patient, was asymptomatic. Five had proximal upper and lower limb weakness and one only proximal lower limb weakness. One patient presented with malignant hyperthermia. The mean value of CK was 1111.25UI/L. The muscular biopsies showed characteristics of central core disease (two), multiminicore disease (one) and centronuclear disease (one). All patients had a molecular study confirming the existence of a pathogenic variant in the RyR1 gene.

Conclusion: Our study provides further evidence that RyR1 related myopathies are very heterogeneous. Clinical, histopathological and molecular features are essential to better understand genotype-phenotype correlation.

Disclosure: Nothing to disclose

EP1164

20 years clinical follow-up in patients with oculopharyngeal muscle disease (OPMD)

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Background and aims: Oculopharyngeal muscle dystrophy (OPMD) is an autosomal dominant muscle disease. OPMD is clinically characterized by ptosis, eye movement abnormalities, dysphonia and dysphagia. It is caused by an abnormal (GCN) triplet expansion within the PABPN1 gene located on chromosome 14 (14q11.2-q13).

Methods: We present a cohort of 18 patients (12 female and 6 male) with OPMD. We performed quantitative Electromyography in all patients and muscle biopsy in 11 out of 18. We also applied MRC score for muscle strength evaluation as well as the EAT-10 (Eating Assessment Tool) which is a self-administered scale for dysphagia evaluation. All patients were genetically defined for PABPN1 gene variants.

Results: Main results are shown in table 1.

Dysphagia and dysphonia worsened during the course of the disease as well as orbicularis oculi muscle strength; in addition, we observed that either axial muscles or posterior thigh muscles were progressively affected. 10 patients were evaluated with EAT-10 showing a worsening of dysphagia.

table 1

Pt	Sex	Age	Familiarity	Onset symptom	Q-EMG	CK	Muscle biopsy	Orbicularis oculi MRC onset	last	AM MRC	PTM MRC at last visit
1	F	55	no	ptosis, dysphonia	normal	↑	normal	3	4	4	4
2	F	50	yes	ptosis	myopathic	↑	atrophy, some	4	4	4	3
3	M	60	no	ptosis, dysphonia, dysphagia	myopathic	↑	marked atrophy,	4	3	4	4
4	M	55	yes	dysphagia, ptosis	normal	↑	atrophy, some	4	4	4	4
5	F	40	yes	ptosis, OP	normal	↑	normal	4	3	5	5
6	M	50	yes	ptosis, dysphagia, dysphonia	normal	↑	ND	4	3	4	3
7	F	50	yes	ptosis, OP, dysphagia	normal	↑	ND	4	4	4	4
8	M	56	yes	ptosis, dysphagia	myopathic	↑	atrophy	4	4	5	5
9	F	60	yes	ptosis	normal	normal	atrophy, some	4	3	4	4
10	M	44	yes	ptosis, OP, dysphagia	myopathic	normal	atrophy	4	3	4	4
11	F	46	yes	dysphagia	normal	normal	ND	4	4	5	5
12	M	43	yes	ptosis, dysphagia	normal	normal	ND	4	4	5	5
13	F	60	yes	ptosis, OP	normal	normal	atrophy	4	4	5	5
14	F		yes	asymptomatic patient	normal	normal	ND	5	4	5	5
15	F	55	yes	ptosis, OP	normal	normal	atrophy, some	4	4	5	5
16	F	56	yes	ptosis, dysphagia	normal	normal	ND	4	3	4	4
17	F	58	yes	ptosis, dysphagia	myopathic	normal	atrophy,	4	4	5	5
18	F	50	no	ptosis, dysphagia	myopathic	normal	ND	4	3	3	3

Legend Q-EMG= quantitative electromyography; MRC= Medical Research Council; AM= axial muscles; PTM= posterior thigh muscles; OP= ophtalmoparesis; RV: rimmed vacuoles; ND= not done

table 1

Conclusion: Our data confirms that, at disease onset, the weaker mimic muscles are the orbicularis oculi. During the OPMD course, it has been found a worsening of orbicularis oculi weakness and of dysphonia and dysphagia with a progressive involvement of proximal limb and axial weakness.

Disclosure: Nothing to disclose

EP1165

Limb girdle muscular dystrophy due to LAMA2 gene mutations: 5 new Italian cases enlarge the clinical and molecular spectrum of the disease

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Brain MRI - Axial TSE T2 images (A-B) and axial T2 FLAIR images (C) showing diffuse abnormal hyperintensity involving peri- and sovra-ventricular white matter in three different patients.

Background and aims: Mutations in LAMA2 gene, encoding merosin, are generally responsible for a severe Congenital Muscular Dystrophy (CMD type 1A). Since now only few cases with adult-onset and partial merosin deficiency have been reported.

Methods: We describe 5 independent Italian subjects presenting with Limb Girdle Muscular Dystrophy (LGMD), brain white matter abnormalities, merosin deficiency and LAMA2 gene mutations. Patients underwent complete neurological examination, muscle biopsy, brain and muscle imaging.

Results: All patients showed slowly progressive proximal weakness with onset spanning from childhood to adulthood. Creatin-kinase levels were moderately elevated. One patient developed dilated cardiomyopathy. Muscle MRI allowed to evaluate the degree and pattern of muscular involvement in all patients. Brain MRI was fundamental in order to direct and/or support the molecular diagnosis, showing typical widespread white matter hyperintensity in T2-weighted sequences in all subjects; these alterations were associated with signs of central nervous system (CNS) involvement in 3 patients presenting epilepsy (2) and migraine (1). Muscle biopsy showed heterogeneous patterns ranging from dystrophic to myopathic features; misleading patterns were also detected, leading to the suspect of mitochondrial myopathy and polymyositis. Protein analysis displayed partial merosin deficiency. LAMA2 gene analysis detected 7 different mutations, 6 of which are new.

Conclusion: These cases further enlarge the clinical spectrum of LGMD due to mutations in LAMA2 gene. In our opinion this form is an underestimated cause of LGMD and CNS study, which was fundamental to address the diagnosis, should be included in the diagnostic workup of undiagnosed LGMD.

Disclosure: Nothing to disclose

EP1166

Cancelled

EP1167

Congenital myasthenic syndrome with favourable response to 4-aminopyridine

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Background and aims: Congenital Myasthenic Syndromes (CMS) are infrequent inherited disorders, difficult to diagnose, with several clinical features, in which neuromuscular transmission is compromised by different mechanisms. We present a patient with a CMS caused by a mutation in the epsilon subunit of acetylcholine receptor (AChR), who has a surprising clinical response with 4-aminopyridine (4-AP), although not approved in Spain for this use. 4-AP is reportedly effective in refractory cases of CMS.

Methods: A 27-year-old female who was diagnosed a CMS when she was 3. She presented generalized weakness and ophthalmoplegia, and she was treated with pyridostigmine, ephedrine, fluoxetine and salbutamol with incomplent beneficial effects. In 2015, a mutation in gene CHRNE was found, after doing a genetic panel. Because of different treatments inefficacy, she was offered an off-label agent, 4-AP. She was treated with oral 4-AP (20mg/day) for up to 10 months. We supposed it could have some effect in prolonging the action potential by blocking potassium channels, and consequently, increasing calcium entry into the nerve terminal. Similar to 3,4-diaminopiridine, it could have positive effects in structural defects of the AChR subunit.

Results: She obtained a rapid and extremely good clinical response, which is still mantained, improving her quality of life.

Conclusion: MCS have some thoroughly known effective medications, as pyridostigmine or 3,4-diaminopyridine. Nevertheless, in many patients the beneficial effects are incomplet and other therapeutic options are limited because of the abscence of controlled clinical trials. 3-AP could be a symptomatic treatment in some CMS. It is needed to continue researching about such findings.

Disclosure: Nothing to disclose

EP1168

Still looking for predictors for myasthenic crisis occurrence

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Background and aims: Myasthenic crisis (MC) is a complication of Myasthenia gravis (MG), characterized by increase of muscle weakness which results in respiratory failure and requires intubation and mechanical ventilation or non-invasive ventilation. The latest medical strategies are focused on prevention of myasthenic exacerbation/crisis, including evaluation and early managing of the precipitating factors. In this study we evaluate the significance of different precipitating factors for aggravation of MG resulting in MC, describing a cohort of 97 Bulgarian patients with autoimmune myasthenia, of whom 26 presenting crisis. The listed factors were stress, infection, surgery, pregnancy, therapy changing or aggravation of another persisting disease. Since we had discovered that important part of MC are caused by unknown precipitating factor, we evaluated the significance of other concomitant conditions such as depression, thymectomy, presence of hypertension or other autoimmune disease.

Methods: Statistical analysis was performed using two-sided tests at a significance level of $\alpha=0.05$, and for each factor an Odds ratio (OR) was calculated.

Results: The results show that the major precipitating factor for crisis development is infection with OR7.44 (CI95% 2.01-27.54;p<0.05). The factor influence of depression over the crisis development was significant in our group with OR7.181 (CI95% 2.258-22.830;p<0.001), as well as for thymectomy with OR4.297 (CL 1.454-12.699; p=0.001). All other evaluating factors did not show a significant correlation to MC occurrence.

Conclusion: The presence of infections, depressive disorders and thymectomy may exhibit a higher predictive significance for MC occurrence and applying specific preventive strategies is needed.

Disclosure: Nothing to disclose

EP1169

Long-term follow-up and IgG anti rh-GAA assessment in late-onset Pompe disease

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Background and aims: Late-onset Pompe disease (LOPD) is an autosomal recessive metabolic disorder due to deficiency of the lysosomal acid alpha-glucosidase enzyme. On 2006, alglucosidase alfa (rhGAA) was approved as an enzyme replacement therapy (ERT) for Pompe Disease.

Efficacy of ERT in LOPD has been well demonstrated. However, only few studies have assessed ERT effects in long-term treated patients and the role of IgG anti rh-GAA antibodies in modulating efficacy of treatment is still incompletely known.

Methods: We report clinical and functional findings from 9 LOPD patients treated with ERT for a time ranging between 3 and 9.5 years. Serial measurements of IgG anti rh-GAA antibodies were performed in 7 of them.

Results: At the end of observation, respiratory function tests improved or were stable in 66% of cases; the walked distance at 6MWT improved in 75% of the patients up to 54 months, while in the subsequent follow-up (up to 108 months) 63% of them slowly reduced the walked meters. MRC subscore shows stabilization or improvement in 88% of patients.Titers of anti-rhGAA antibodies also in in very long treated patients are only mildly elevated (max 12800). No clear-cut relation between titers of anti-rhGAA antibodies and clinical outcome were observed.

Conclusion: Our results confirm ERT long-term effectiveness, though it appears to be reduced over time compared to the first two years of therapy.

A specific relation between titers of anti-rhGAA antibodies and response to treatment seems not to exist but it deserves further studies on wider numbers of patients.

Disclosure: Nothing to disclose

EP1170

International-DMD (IDMD): A PTC therapeutics-supported diagnostic project to widely identify dystrophin mutations by NGS technologies

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Background and aims: Extensive molecular diagnosis in genetic diseases is vital to confirm clinical diagnosis and to enable genetic counseling and personalized management. Duchenne muscular dystrophy (DMD) is a rare genetic neuromuscular disease affecting 1/5000 males, due to a variety of dystrophin gene mutations. The first signs and symptoms of DMD include delayed milestones such as walking and talking, and enlarged calves. PTC Therapeutics International Ltd. and the University of Ferrara, Italy, have established a collaboration focused on identifying patients affected by rare genetic disorders through increased genetic testing activities, with an initial focus on DMD. Genetic testing is available to patients throughout European countries, potentially expanding to other regions.

Methods: Diagnostic settings include MLPA (MRC Holland) and NGS dystrophin gene sequencing (Multiplicom).

Results: Currently DNA from 57 DMD boys was collected. Patients were from Poland (34), Hungary (10), Lituania (5), Romania (3), Russia (1) and Serbia (4). Among the 30 samples analyzed, 7 deletions, 4 duplications, 11 small mutations (8 nonsense) were identified.

Conclusion: This collaborative project demonstrates PTC's commitment to expanding awareness of the importance of genetic testing for patients with DMD. The early identification of the underlying genetic mutation is critical to potentially affecting the course of a disease such as DMD as well as the choice of treatment and aids in the setup of appropriate and effective care and follow up. Genetic counselling can also be offered to patients and families with important repercussions on reproductive choices and lifestyle planning (full details and contacts at www.ospfe.it/medicalgenetics).

Disclosure: Work supported by PTC Therapeutics International Ltd.

EP1171

Cancelled

Neuroimmunology 1

EP1172

Plasma exchange for neurological disorders in Hungary – an overview of 10 year's data in the NEUROHUN 2004-2013 project

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Background and aims: Plasma exchange (PE) may be the preferred intervention due to financial considerations in some neuroimmunological diseases where intravenous immunoglobulins could also be applied as an evidence-based treatment. We evaluated the use of PE in a 10-year period in Hungary.

Methods: Hungary has a single-payer health insurance system covering the whole population of 10 million inhabitants. In the framework of the Hungarian Brain Research Program we created the anonymized NEUROHUN database from medical reports submitted for reimbursement purposes to the National Health Insurance Fund from all hospitals and outpatient services throughout the country for the ten-year period between 2004 – 2013. ICD-10 codes were used for diagnoses. Clinical diagnoses of the patients with PE treatment were analyzed.

Results: In this 10-year period 8757 persons were treated with PE in Hungary, of these 5127 had some neurological service use and 2586 were given a neurological diagnosis within 10 days of the PE treatment. The vast majority of PE treatments were applied in 3 major diagnostic groups: diseases of the peripheral nervous system (ICD-10 G60–G64, n= 1415), diseases of the myoneural junction (G70–G73, n=836) and demyelinating disorders of the central nervous system (G35-37, n=278).

Conclusion: As in Hungary PE is the preferred method of treatment in Guillain-Barré syndrome (GBS) and chronic inflammatory demyelinating neuropathy (CIDP), the average annual PE treatments in the G60-G64 diagnostic group suggests that the combined incidence of GBS and CIDP may be not less than 1.4/100.000 inhabitants/year in Hungary – corresponding to values reported from other European countries.

Disclosure: Nothing to disclose

EP1173

Hypertrophic pachymeningitis of autoimmune/inflammatory etiology

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Background and aims: Hypertrophic pachymeningitis (HP) is characterized by localized or diffuse thickening of the dura mater, with or without inflammation. Different etiologies are recognized, with autoimmune/inflammatory conditions increasingly reported.

Aims: Describe a cohort of HP patients with probable autoimmune/inflammatory etiology.

Methods: Retrospective study. Patients' identification through a key-word search of MRI reports from July/2008-September/2015. Data collection and analysis of those with an autoimmune/inflammatory etiology.

Results: Forty patients with HP were identified, 8 with an inflammatory/autoimmune etiology. Of these, 6 were female, with mean age at clinical presentation of 49.7±12.4 years. Four patients were diagnosed with IgG4-related HP. The remaining were associated with Wegener's granulomatosis (1), sarcoidosis (1), rheumatoid arthritis (RA) (1) and Tolosa-Hunt syndrome (1). In 6 patients PH was the clinical presentation of the underlying inflammatory disease, being only a late manifestation in the patient with sarcoidosis. Presenting symptoms were cranial nerve palsies (3), headache (2), cognitive deterioration (2), lumbar pain (1). PH was cranial in seven patients and spinal in one. Laboratory findings included hiperIgG4-emia (4), raised ECA (1) and serum positivity for pANCA/MPO (1), FR/anti-CCP (1) and ANA (1). Two patients had brain biopsy. Seven patients were treated with corticosteroids, 3 requiring additional immunossupressants. Overall, outcome was good, with only one relapsing.

Conclusion: In our series of autoimmune/inflammatory PH there was a higher percentage of IgG4-related disease than reported, probably due to increased awareness of this entity. Clinical presentations were diverse, being brain MRI crucial in establishing PH diagnosis. We highlight the importance of laboratory findings in the final diagnosis, and the good outcome of most patients.

Disclosure: Nothing to disclose

EP1174

Thoracolumbar pachymeningitis causing bilateral subacute radicular compression in Wegener's granulomatosis: A case report

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Background and aims: Spinal dural involvement is one of the least frequent neurologic manifestations of Wegener's granulomatosis (WG).

Methods: We report a case of thoracolumbar pachymeningitis in a patient with a 5-year history of WG. A comprehensive search of the English language literature was performed. The differential diagnosis is widely discussed.

Results: A 70-year-old female presented with subacute paraparesis accompanied by severe lumbar pain and moderate biological inflammatory syndrome in the absence of fever. At age 65 she was diagnosed WG based on histopathological proven bilateral retro-orbital granulomas and angeitis. Her disease also included pulmonary, rino-sinusal,uveal and intracranial dural involvement. The serum titer of proteinase 3 anti-neutrophil antibodies was highly positive. Monthly high-dose cyclophosphamide and corticosteroids applications resulted in remission after 6 months. The MRI scan of the spine showed T11-L3 gadolinium-enhancing dural thickening consistent with WG-related spinal pachymeningitis. The L2-L3 vertebral discus and L3 vertebral body appeared to be mildly involved. Surgical biopsy and decompression could not be performed because of an unexpected fatal cardiac complication probably caused by WG.

Sagittal pre- and post-gadolinium T1-weighted spine MRI showing the contrast enhancing spinal dural thickening. Mild signal changes and contrast enhancement are also seen in the cranial region of the L2 vertebral body.
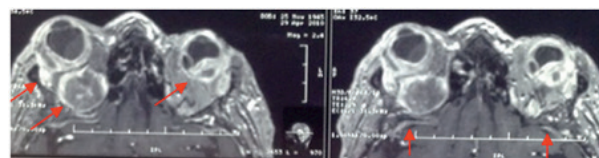
Axial post-gadolinium T1-weighted brain MRI showing intraocular and orbital granulomas as well as temporal dural thickening and contrast enhancement.

Conclusion: Meningeal involvement occurs in less than 4% of people with WG. Though very rarely described, isolated spinal dural involvement may be the first manifestation of a WG relapse. Considering the lack of pathognomonic features an infectious cause should be excluded prior to therapeutic immunosuppression.

Disclosure: Nothing to disclose

Axial T2-weighted spine MRI showing dural thickening at L2 level.

EP1175

Neurexin-3alpha antibody-associated encephalitis after Plasmodium falciparum malaria

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Background and aims: A new form of autoimmune encephalitis associated with neurexin-3alpha antibodies was recently described in 5 patients. One of them had history of malaria a few months before presentation (not reported). We describe a new case that was preceded by Plasmodium falciparum malaria.

Methods: Review of clinical information. Determination of neurexin-3alpha antibodies was performed as reported (Neurology 2016;86:1-8).

Results: A 57-year-old Caucasian man with no clinical history of interest returned to Portugal after a long stay in Angola. Five days later he was diagnosed with P. falciparum malaria (8% parasitemia) and successfully treated with quinine-doxycycline. Two weeks after recovery he developed fever, somnolence, confusion and abnormal behavior. At examination he was disoriented in time and had inattention, acalculia, and visuospatial difficulties without focal deficits; the general exam was normal. The CSF showed 159 cells (91% mononuclear), protein 2.12 g/dL, and normal glucose. The EEG was consistent with a severe subcortical encephalopathy without epileptic activity. Brain MRI showed a mild increase of T2/FLAIR signal in the caudate-capsule-lenticulate regions without gadolinium enhancement. Extensive CSF and serum studies were negative for infectious or systemic autoimmune causes. On the 8th day, a clinical diagnosis of post-malaria neurological syndrome was made and a 5-day course of 1g intravenous methylprednisolone was initiated with progressive clinical improvement. CSF and serum samples were then found to be positive for neurexin-3alpha antibodies.

Conclusion: The case of this patient suggests that the encephalitis associated with neurexin-3alpha antibodies can develop as post-infectious encephalitis. Recognition of this disorder is important because it responds to immunotherapy.

Disclosure: Nothing to disclose

EP1176

Bickerstaff brainstem encephalitis following Chlamydophila pneumoniae infection

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Background and aims: Bickerstaff's brainstem encephalitis (BBE) is a rare entity characterized by acute ophthalmoplegia, ataxia, altered consciousness, and variable signs of central nervous system dysfunction. It is included in the "anti-GQ1b antibody syndrome" along with a spectrum of disorders with a common immunological profile and variable overlapping features. Most patients have a history of preceding infection and several causative organisms have been described.

Methods: We report a case of BBE following Chlamydophila pneumoniae infection.

Results: A 30-year-old patient was admitted to the emergency department with a 24-hour history of gait unsteadiness, ascending weakness and psychomotor retardation. She reported symptoms of an upper respiratory infection a week earlier. Over the next few hours she developed blurred vision, worsening paralysis and became increasingly lethargic. Examination revealed a low-grade fever, drowsiness, bilateral external ophthalmoplegia and facial weakness, dysarthria, and tetraparesis with upper limb hyperreflexia. A diagnosis of BBE was considered and she was admitted to an intensive care unit, requiring assisted ventilation. Cerebrospinal fluid studies showed mild lymphocytic pleocytosis and brain magnetic resonance was normal. Serum anti-GQ1b IgG antibodies were positive, confirming the diagnosis, and a positive C. pneumoniae antigen was detected in bronchial secretions and assumed to be responsible for the respiratory illness. She was treated with intravenous immunoglobulin and doxycycline and slowly improved.

Conclusion: To the best of our knowledge, this is the first report of BBE following C. pneumoniae infection, although this pathogen has been previously reported in cases of MFS and acute isolated ophthalmoplegia. Further studies are needed to clarify a possible causal relationship.

Disclosure: Nothing to disclose

EP1177

Autoimmune limbic encephalitis in an Algerian population: A case series

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Background and aims: Limbic encephalitis (LE) results in the acute or subacute appearance of a clinical syndrome associating memory disorders, epileptic seizures and / or psychiatric disorders. It may be paraneoplastic or not, pure or associated with an extralimbic involvement. To study the clinical, radiological and immunological profiles of autoimmune ELs associated with anti-neural antibodies in a series of 4 patients. Describe the peculiarities of these EL in our patients and confront atypical situations, not or little reported, to the data of the literature

Methods: A monocentric, retrospective study of ALE associated to onconeuronal (ONA) and anti-membrane antibodies. All patients received clinical and neuropsychological evaluation, cerebral MRI, standard EEG, infectious, endocrine and metabolic assessment, ONA and membrane epitope antibody (LGI-1 and Caspr2, NMDA-R and GABAb-R) and finally a primary cancer assessment.

Results: Four patients, all men, aged between 48 and 77 (mean=58.7 years) were included. Clinical, radiological, biological and immunological characteristics are described in Tables 1 and 2

Conclusion: The characteristics of ELAs diagnosed in our patients are:

1. Anti-PNMA 2 LE mimicking Gayet-Wernicke encephalopathy

2. Anti-NMDA-R antibodies following HSV-1 encephalitis

3. LE to anti-Yo in a man, mimicking a Creutzfeldt-Jacob disease

4. The presence of at least one second antibody when the 1st antibody has an intracellular epitope

These descriptions confirm the clinical heterogeneity of ALEs and may contribute, with the discovery of new autoantibodies, to a better knowledge of these encephalitis. This first work in Algeria on ALEs raises the interest of a more extensive study in order to better characterize them.

Disclosure: Nothing to disclose

EP1178

Clinical course of LGI1 and CASPR2-antibodies associated limbic encephalitis

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Background and aims: Seizures, cognitive impairment and memory loss as well as other central and peripheral nervous system characterize limbic encephalitis. In the past years voltage-gated potassium channel antibody (VGKC-) associated limbic encephalitis has been characterized and further distinct into subgroups. To date only few case reports have shed light to course and treatment of this devastating disease.

Methods: We would like to present 8 patients with VGKC associated limbic encephalitis (3 of which have VGKC/LGI1- antibodies, 3 present VGKC/CASPR2-antibodies and 2 are VGKC positive but lack both LGI1/CASPR2 antibodies). We will present the clinical course and evolution under immunomodulatory as well as anti-epileptic and psychoactive therapy backed by diagnostic follow up through serum/CNS -serology, magnetic resonance imaging and video-electroencephalogram-findings, detailed neuropsychological testings and additional electro-physiological testing.

Results: Although the case number is limited we would like to help further differentiate those three VGKC-subgroups formally summarized by VGKC-complex-antibodies.

Conclusion: The three VGKC associated limbic encephalitis have distinct patterns of differentiation both in clinical and in diagnostic evaluation. Awareness in clinical presentation as well as serum/CNS -serology, magnetic resonance imaging, electroencephalography and neuropsychological testing can help in early diagnosis and mangement of this devastating disease.

Disclosure: Nothing to disclose

EP1180

Anti-GAD encephalitis presenting with non-epileptic choreo-dystonic movements and coexisting electric seizures

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Background and aims: Anti-GAD antibodies have been associated with limbic encephalitis, new-onset type 1 diabetes, Stiff-person syndrome, exaggerated startle, cerebellitis, and refractory epilepsy.
Methods: We report a case of a patient with anti-GAD encephalitis including chorea and dystonia.
Results: A 38-year-old woman presented with a 4-month history of involuntary movements of the left hand, slurred speech, and gait instability. On examination, we observed nystagmus and round the houses sign, orofacial dyskinesia, dysarthria, cervical dystonia, choreo-dystonic movements of the left upper limb, and mild gait ataxia. Brain-MRI documented a left temporal hyperintensity in T2 sequence. Anti-GAD title was positive in blood (1/3200) and CSF (1/320). The EEG disclosed nine seizures of left temporal origin in 30 minutes, which showed no temporal correlation with the aforementioned involuntary movements, nor other obvious clinical manifestations. The patient was treated with sodium valproate (1800mg/day), and methylprednisolone, followed by IV immunoglobulin. Upon discharge, she maintained mild orofacial dyskinesia, and choreo-dystonia of the left hand. There were no seizures or interictal epileptiform activity on the EEG and the Jerk-locked back average (JLBA) analysis of the facial movements showed no cortical correlate.
Conclusion: This case of anti-GAD encephalitis presented previously unreported choreo-dystonia, besides electrical temporal seizures. Absence of a cortical correlate of choreo-dystonia on EEG-JLBA, and movement persistence after resolution of the epileptic activity support a non-epileptic origin of those movements. The association of clinical signs of basal ganglia involvement with subclinical electrical seizures expands the spectrum of anti-GAD disorders.
Disclosure: Nothing to disclose

EP1181

Study of inflammation in CSF in NeuroBehçet disease

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Background and aims: NeuroBehçet disease (NBD) is the most frequent vasculitis in our country. In presence of inaugural neurological forms, CSF study is systematic because of diagnosis difficulties.
Our aim was to describe the immunoelectrophoretic and cytokine profile in NBD.
Methods: Criteria of selection: NBD according to the International consensus recommendation (ICR) with definite and probable forms including isolated neurological syndrome suggestive of NBD. Subjects were consecutive patients who referred to Neurological department of Charles Nicolle hospital since 2013. Blood and CSF samples are taken from all patients. Cell counting, protein analysis, immunoelectrophoretic profile with Ig G Index was performed. Cytokines levels were evaluated by PCR.
Results: From 26 NBD recruited 17 had an inaugural neurological form of which 15/17 had a parenchymal involvement. The IgG index was increased in only 2 patients (8%). At the Immunoelectrophoresis, the profile was type 1 in 22 patients (81%), type 2 in 1 patient (3.7%) and type 3 and 4 in 4 patients (11%). The study of lymphocyte populations showed an increase of IL-17, interferon gamma and IL10 levels in more than 80% of patients.
Conclusion: The profile data in CSF of NBD patients in our study are in line with those found in the literature. Given the limited data on CSF levels of cytokines in patients with NBD, our results showed that cytokines make a pivotal role in pathogenesis of NB, as evidenced by the conjoining increase of pro and anti-inflammatory cytokines in our patients.
Disclosure: Nothing to disclose

EP1182

Erythromelalgia and stiff man syndrome: New insights in ion channels pathology

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Background and aims: Erythromelalgia (EM) is a rare vascular peripheral pain disorder in which blood vessels, usually in the lower extremities or hands, are episodically blocked. There is severe burning pain in small fiber sensory nerves and skin redness. Stiff person syndrome (SPS) is a disorder characterized by progressive rigidity, stiffness, which affects the truncal muscles, superimposing by spasms. Chronic pain, lumbar hyperlordosis are common. The Nav1.7 voltage-gated sodium channels antibodies (AB) seems to have a cornerstone effect in EM pathophysiology. Glutamic acid decarboxylase (GAD) AB evidently are a positive SPS sign.

Methods: Under our observation were 6 patients with EM and 3 patients with clinicaly proved SMS. We studied AB against Nav1.7 and GAD in both groups patients and in control group comprising of 34 neurologically healthy donors. Positive labeling by an antibody against the neurofilament protein peripherin was used to identify group IV neurons and axons. Western Blot analysis (WBA) was used to determine comcentration of both AB types in these diseases.

Results: Concentrations of AB to Nav1.7 and GAD were considerably increased in all EM with hyperemic and inflamed extrremities and SPS patients characterized by spasms and postural deformities, correspondingly. These results were confirmed both by WBA and using immunohistochemistry.

Conclusion: In both cases (EM and SPS) appear as autoimmune neurological disorders with evidence of pathgenetic rol of AB to Nav1.7 in EM and anti-GAD AB in SPS. Immunohistochemistry and WBA showed some correlation to clinical picture of both sufferings and could serve as targets for future therapeutic approaches.

Disclosure: Nothing to disclose

EP1183

An unusual brainstem encephalitis associated with anti-glycine receptor antibodies: Clinicopathological description

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Background and aims: Glycine receptor (GlycR) antibodies are most frequently associated with the syndrome progressive encephalomyelitis with rigidity and myoclonus. Previous reports of GlycR-associated syndromes demonstrated a variable response to immunotherapy. Neuropathological reports are few. The current case is of interest in that it was characterised predominantly by brainstem features without rigidity, responded to immunotherapy and proceeded to post-mortem examination.

Methods: A well 64-year-old man presented with external ophthalmoplegia, facial weakness, bulbar dysfunction, hyper-reflexia and myoclonus with onset three days after coryzal symptoms. There was no rigidity, cognitive impairment or seizures. No neoplastic or vasculitic condition was identified. Serum GlycR antibodies were positive. Negative tests included: onconeuronal antibodies; antibodies vs. N-methyl-D-aspartate receptor, voltage gated potassium channel, glutamic acid decarboxylase, and gangliosides; MRI of the neural axis; cerebrospinal fluid analysis; nerve conduction studies.

Results: Despite two courses of intravenous immunoglobulin, he had a respiratory arrest and required prolonged invasive ventilation, complicated by fluctuating tachy-bradycardia with intermittent asystole. Following plasma exchange and corticosteroids, he was weaned from ventilation and began mobilising. Ophthalmoplegia and myoclonus completely resolved but bulbar recovery was incomplete. The patient died following severe pulmonary oedema 110 days after presentation. Detailed post-mortem examinations found no significant abnormalities in the brain, spinal cord or heart and no evidence of a malignancy.

Conclusion: This case illustrates a GlycR-associated brainstem syndrome with significant autonomic involvement as well as the potential for neurological improvement with immunotherapy. The absence of rigidity was unusual.1 The lack of histopathological change supports previous literature arguing against a destructive pathogenesis of GlycR-associated syndromes.1

Disclosure: Nothing to disclose. Please include following as reference for abstract: 1. Glycine receptor antibodies in PERM and related syndromes: characteristics, clinical features and outcomes. Carvajal-González A et al. Brain (2014) 137 (8): 2178-92.

Neurorehabilitation

EP1184

Effect of functional electrical stimulation (FES) on the muscle tone and the motor function of the paretic upper limb in four chronic stroke survivors

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Background and aims: To determine whether FES can contribute to inhibit spasticity in the flexor muscles of the affected wrist and improve the motor function of the paretic upper limb.

Methods: The design of the research was a case study. The four patients included in the current study were evaluated before and after 20 sessions of FES (five days a week, for four weeks). Each patient performed several training tasks in the workstation assisted by the FES device. The following parameters were evaluated: (i) the muscle tone of the flexor muscles of the wrist of the affected upper limb, which was measured according to the Modified Ashworth Scale (MAS); (ii) motor function, measured by the Action Research Arm test (ARAT) , and (iii) the perception of the manual ability of the paretic upper limb by the Manual Ability Measure -16 (MAM-16).

Results: There was a favourable decrease in the MAS scores in the four participants after the FES intervention. Likewise, there was also an improvement in the ARAT scores and a significant increase in the self-perception of the manual ability of the upper paretic limb after FES intervention.

Conclusion: The application of FES can contribute to manage the spasticity of the flexor muscles of the affected wrist in chronic stroke survivors. In addition, 20 sessions of FES are associated with an improvement in the motor function and the self-perception of the manual ability of the paretic upper limb.

Disclosure: Nothing to disclose

EP1185

Effect of hiding view of the starting hand position when using a home-friendly treatment for spatial neglect in healthy participants

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Background and aims: Prism adaptation is an experimental treatment for spatial neglect with limitations preventing its clinical application. Peg-the-Mole (PTM) is a new home-friendly prism adaptation iPad procedure that induced after-effects in healthy participants. The purpose of this study was to examine whether hiding view of the starting hand position during PTM would increase the magnitude of after-effects by reducing self-correction in pointing movements.

Methods: Sixty healthy participants were randomly assigned to one of four conditions (Goggles: Prism/Sham, Starting Hand Position: Visible/Hidden). After-effects were measured using a proprioceptive and visual pointing tasks and a wheelchair obstacle task.

Results: Larger pointing errors were observed in the Prism/Hidden than the Prism/Visible groups during PTM. Significant Goggles x Starting Hand Position interactions were observed on the visual pointing task and the wheelchair task. The difference in after-effects between Prism and Sham groups on the visual task was larger in the Hidden than the Visible groups ($p<0.05$). On the wheelchair task, fewer hits on the right side of the course ($p<0.05$) and a trend for more hits on the left side of the course ($p=0.06$) were found in the Prism compared to the Sham conditions, but only for the Hidden group.

Conclusion: These results suggest that hiding view of starting hand position contributes to induce larger after-effects by reducing self-correction in pointing movements, which is of clinical relevance considering the relation between after-effects and the improvement in neglect symptoms.

Disclosure: Work supported by Harrison McCain Foundation and Atlantic Innovation Funds.

EP1186

Comparative effectiveness research of dual-task and single-task balance training on gait speed and cognition in individuals with stroke

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Background and aims: Decrements in dual-task capacity may predispose stroke survivors to risk of falls. There is a need to explore whether dual-task training would enhance dual-task performance. The purpose of this study is to compare the effect of single- and dual-task training on gait speed and cognition in stroke patients.

Methods: Twenty-six subjects with stroke were randomly allocated to either a single- or dual-task balance group. Both groups received training at progressively increasing task difficulty (60 minutes per session, three times a week, for four weeks). Single-task group undertook balance and gait training. Dual-task group trained balance and gait while simultaneously performing cognitive tasks. All participants were examined walking and cognition under single- and dual-tasking at pretreatment, posttreatment, and 1-month follow-up. Primary outcome measures of walking and cognition were gait speed and composite score of cognitive tasks (serial 3 subtractions, Stroop, and auditory Stroop) under single- and dual-tasking. Dual-task costs were calculated.

Results: Both groups showed statistically significant improvements on gait speed under single- and dual-task walking, and reduced gait costs under walking with serial 3 subtractions. Compared to single-task group, dual-task group was significantly reduced more gait speed cost under walking with Stroop task at follow-up. Only dual-task group significantly improved gait costs under walking with Stroop and auditory Stroop tasks at posttreatment and follow-up. Both groups significantly improved composite scores of single- and dual-auditory Stroop task.

Conclusion: The preliminary results showed a favorable trend toward dual-task balance training with greater reduced dual-task costs on gait speed.

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EP1187

Cancelled

EP1188

Neurotransmitters changes after rTMS treatment in patients with secondary-progressive multiple sclerosis and severe spasticity

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Background: To improve our knowledge about neuroplasticity changes in patients with spasticity we used proton magnetic resonance spectroscopy (H-MRS) of motor cortex before and after navigated repetitive TMS (rTMS) of motor cortex .

Introduction: Our aim was to qualify H-MRS technique in assessment of neurotransmitters changes in patients with secondary-progressive multiple sclerosis (SPMS).

Methods: Twenty three patients (10 males, 13 females, mean age 44.7 ± 11.47 years) with SPMS and lower spastic paraparesis were enrolled in double-blind placebo-control study. Neuroplasticity changes in motor cortex area were investigated before and after two types of rTMS (20 Hz,n=9; intermittent theta birst (iTBS), n=5) or sham stimulation (n=9). We assessed levels of neurotransmitters using simple voxel proton MRS. Voxel was placed in the senso-motorial region. For assessment spasticity level we used Modified Ashworth Scale (MAS),Subjective Evaluation Spasticity Scale (SESS) before and at the end of rTMS sessions, SESS - 2 weeks and 3 months after of rTMS sessions.

Results: We did not recognize significant changes in neurotransmitters level in all groups after rTMS. There was only slight increase of lactate level in 20 Hz group. Patients underwent both types of rTMS showed a reduction of spasticity on MAS and SESS in compare with placebo group.

Conclusion: Our results indicate no significant changes in neurotransmitters level after rTMS session in comparison with placebo. But we noticed a significant reduction of spasticity on MAS and SESS in both treatment groups. Lack of H-MRS changes can be due to strong neuroplasticity changes in patients with SPMS.

Disclosure: Nothing to disclose

EP1189
Correlation between cognitive impairment and early functional rehabilitation outcomes after stroke in elderly patients

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Background and aims: Stroke is among the leading causes of disability and mortality in the elderly and leading cause of hospital admission and prolonged length of stay for patients 65 years and older. Evidence from clinical trials supports the premise that early initiation of rehabilitation influences recovery from stroke. Cognitive impairment, as manifested by low scores in mental status questionnaires, has been correlated with limited functional gains and poor rehabilitation outcome in elderly patients.

Methods: Patients and Methods: Our study was prospective and conducted at Neurological department of General Hospital "Prim.dr A. Nakas" Sarajevo during 01.01.2015.-31.12.2015. We included 50 patients older then 70 years hospitalized because of first ishaemic stroke with significant motor impairment which is defined with NIHSS score at admission and at discharge and all of them were included in early rehabilitation program for 2 weeks at Neurological Department. Cognitive status was assessed with the Mini-Mental State Examination (MMSE).

Results: The majority, 69.2%, exhibited cognitive deficits on admission. There were 9.8% patients with an MMSE score equal or lower then 10 points. Better rehabilitation outcomes were observed in patients with higher admission cognitive status, adjusting for the effect of age, sex and severity of stroke (odds ratio 2.57; 95% confidence interval, 1.2–2.5;p=0,01).

Conclusion: Because many rehabilitation techniques require normal cognition and patient cooperation, cognitive status must be considered when determining the rehabilitation aims, establishing treatment strategies and predicting outcome. Better functional outcomes being achieved in cognitively intact elderly stroke patients.

Disclosure: Nothing to disclose

EP1190
Action observation training effects on brain structural and functional changes in Parkinson's disease patients

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Background and aims: To assess brain functional and structural changes following action observation training (AOT) associated with exercises of balance, gait, transfers and manual dexterity in Parkinson's disease (PD) patients.

Methods: Twelve PD patients were randomized into two groups: AOT-group performed a 4-week training consisting of AO combined with practicing the observed actions; LANDSCAPE-group performed the same exercises combined with landscape-videos observation. At baseline (T0) and week 4 (W4), patients underwent clinical assessments. 3D T1-weighted, diffusion tensor (DT) MRI and functional MRI (fMRI) were acquired. FMRI tasks consisted of hand anti-phase movements and motor imagery of circumstances representing activities of daily living. Clinical evaluations were repeated at 3-month follow-up.

Results: At W4 both groups showed changes of the step frequency. The AOT group had an improvement of quality of life at W4 and velocity during manual activities at 3 months. During the hand anti-phase task, AOT-group showed an increased activity of frontal areas and a decreased recruitment of cerebello-thalamo-cortical network, while the LANDSCAPE-group had an increased activity of the thalamus and a decreased recruitment of parietal areas. During the motor imagery task, AOT-group showed a reduced recruitment of the cerebello-thalamo-cortical network and occipital areas, while the LANDSCAPE-group showed an increased activity of motor areas. Only in the AOT-group, functional plasticity was correlated with clinical improvements. AOT-group showed an increased integrity of cerebellar peduncles correlated to cerebellar functional plasticity.

Conclusion: The combination between physical and cognitive exercises has the potential to stimulate both functional and structural brain plasticity compared to a pure motor training in PD patients.

Disclosure: Nothing to disclose

EP1191
Cancelled

Neurotoxicology & Neurotraumatology & Spinal cord and root disorders

EP1192
Cancelled

EP1193
Cancelled

EP1194

Acute neck pain in mild traumatic brain injury as a predictor of chronic posttraumatic complaints

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Background and aims: The role of acute neck pain as a predictor of persistent posttraumatic complaints after mild traumatic brain injury (mTBI) is unknown. The aim of this study was to describe the characteristics and course of acute neck pain following mTBI and its relation to persistent posttraumatic complaints and functional outcome. We also studied whether demographic and injury related factors were associated with persistent neck pain.

Methods: We analyzed data of 933 mTBI patients (n=162 mTBI patients with acute neck pain and n=771 without acute neck pain) admitted to the Emergency Department (ED), from a prospective follow-up study in three level-one trauma centers (UPFRONT-study). Posttraumatic complaints and resumption of activities were evaluated at six months post-injury using standardized questionnaires.

Results: Patients with acute posttraumatic neck pain were more often female (p=0.002) and younger (41 vs. 46 years p=0.002) compared to controls. No differences regarding CT abnormalities were found. Neck pain correlated with headache, dizziness and nausea in the acute phase (p<0.005). Patients with neck pain had more often motor vehicle accidents (p=0.009) and reported more neck pain pre-injury (p=0.012). Also more neck pain and posttraumatic complaints with lower Glasgow Outcome Scale-Extended scores after six months were present.

Conclusion: Acute neck pain after mTBI is a predictor for the development of persistent neck pain and posttraumatic complaints six months post-injury. Pre-injury neck pain and motor vehicle accidents are factors predisposing for acute posttraumatic neck pain. This suggest that patients at risk for an unfavorable outcome might already be identified at the ED.

Disclosure: This study was funded by the Dutch Brain Foundation (grant no. Ps2012-06).

EP1195

Relationship between a sense of generalized anxiety and occurrence of somatic symptoms in patients after mild traumatic brain injury

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Background and aims: The aim of the study was to investigate the relationship between presence of generalized anxiety at the time of mild head injury and the somatic symptoms occurring 3 months after that incident.

Methods: At the beginning using the Generalized anxiety disorder 7-item scale (GAD-7) we evaluated 97 patients consecutively admitted to the Emergency Department because of mild traumatic brain injury (mTBI) but without pathology in computerized tomography scan and who did not require hospitalization. Based on GAD-7 they were divided into two groups: patients with a high level of anxiety (above 6 points) and patients with a low level of anxiety (equal or less than 6 points). Next, from primary group of 97 patients we assessed 56 of them regarding 7 somatic symptoms by using three points measurement (from "1 - not at all" , 2 - " a little" to "3 - a lot") during neurological control examination conducted at least 3 months after brain injury.

Results: Among the group of patients with a high level of anxiety on admission, 78% of them reported at least one somatic symptom which was assessed on 3 points, from which 50% of them notified at least two symptoms with 3 points. The majority of patients (89%) from the second group with a low level of anxiety did not report the somatic symptoms.

Conclusion: GAT-7 scale could be useful as a prognostic tool to select patients after mTBI who are predisposed to develop somatic symptoms , what could be helpful to manage this group of patients

Disclosure: Nothing to disclose

EP1196

Alcohol-related mild traumatic brain injury and outcome in elderly patients at the Emergency Department

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Background and aims: Acute alcohol intoxication (AAI) is associated with a higher risk of mild traumatic brain injury (mTBI) in the overall population. However, the incidence and impact of mTBI due to AAI in elderly patients is unknown. The aim of this study was to describe the characteristics of alcohol related mTBI in elderly patients and to determine the mechanism of trauma and outcome.

Methods: We analyzed data from 388 mTBI patients with an age of 55 years or older (84 AAI vs. 304 non-intoxicated patients) from a prospective cohort study in three Dutch level 1 trauma centers (UPFRONT-study). Injury mechanism and outcome were compared between groups. Posttraumatic complaints and functional outcome were evaluated after 2 weeks and 6 months using standardized questionnaires.

Results: 22% of the elderly mTBI patients was intoxicated with alcohol. There was no significant difference in intracranial traumatic CT findings, Glasgow Coma Scale at admission, frequency of hospital admission and Glasgow Outcome Scale Extended compared to controls. Injury Severity Score was higher in the non-intoxicated group (8.5 vs 6.6 p=0.036). Falls were the most common trauma mechanism and even more common in the AAI group (94% vs. 72% p=0.000). Patients with AAI mTBI reported less posttraumatic complaints after 2 weeks (p=0.010) and 6 months (p=0.044).

Conclusion: One in five injuries in our aged mTBI patients was alcohol related and most injuries were due to falls. For clinical practice, it might be necessary to focus more on alcohol and fall prevention strategies in the older population to reduce the incidence of mTBI.

Disclosure: This study was funded by the Dutch Brain Foundation (grant no. Ps2012-06).

EP1197

Neurological complications of regional anesthesia: Two cases illustrating a broad spectrum

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Background and aims: Regional anesthesia procedures are associated with a 1-4/10.000 neurological complication rate. Such complications are varied, and include intracranial hypotension, transient Horner syndrome, myelopathy or radiculopathy. We report two cases that illustrate this broad clinical spectrum.

Results: Case 1: A 31-year-old female patient developed, during cesarean section under epidural anesthesia, symptoms indicating rostral spread of local anesthetics (arterial hypotension and left upper limb paresthesiae). After surgery, a left Horner's syndrome was noted. Head CT with CT Angiography was normal. The clinical picture resolved within six hours. Case 2: A 68-year-old female patient submitted to a knee arthroplasty under combined spinal and epidural anesthesia (L3/L4) remained with a flaccid monoparesis and hypoesthesia of the left lower limb with a D7/8 hemisensory level on the left. Spinal MRI revealed an extensive myelopathy, with ischemic features, occupying the left half of the dorsal and lumbar spinal cord. Recovery was poor and the patient maintained the deficits at discharge.

Conclusion: In Case 1 the sympathetic pathway to the eye was transiently compromised because of the rostral spread of the anesthetics. In Case 2 the exact pathophysiological mechanism remains unknown, but imaging features suggest a venous infarction. These two cases remind us that regional anesthesia is not without risk. The pathophysiological mechanism and clinical presentation of its complications are numerous, ranging from self-limited disorders with a very good prognosis (Case 1) to severe ones with major sequelae (Case 2). Neurologists should get acquainted with these complications as they may be called upon to manage them.

Disclosure: Nothing to disclose

EP1198

Polio-like disease: A case report

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Background and aims: Since the introduction of the vaccination against poliovirus, poliomyelitis has become a disease virtually eradicated in developed countries. In 2016, the National Spanish Institute of Epidemiology reported 60 cases of pediatric patients with acute flaccid paralysis or rhombencephalitis, identifying in 5 of them non-polio enteroviruses.

Methods: 63-year-old male patient, consulted with acute onset of occipital headache, fever and general discomfort. Successively, dysphonia, dysphagia and cervical weakness were added. Neurological exploration revealed bilateral ptosis, dysphonia, severe weakness for cervical flexoextension, generalized hypoactive myotatic reflexes, flexor plantar reflexes and normal sensory examination. He presented a rapid progression to severe asymmetric proximal weakness of superior limbs with respiratory distress secondary to bilateral phrenic paralysis requiring admission in the intensive care unit.

Results: Cerebrospinal fluid (CSF) revealed 43 leucocytes/mm3 (68% mononuclear), proteins 85 mg/dl and normal glucose. Gram's stain, CSF culture and neurotropic virus serologies were negative. Polymerase chain reaction for enterovirus in CSF, nasopharyngeal aspiration and feces were negative. Successive electromyographies demonstrated acute denervation in upper extremities. Cerebral and spinal magnetic resonance identified non-enhancing hyperintense lesions in T2 sequences of the anterior horn of cervical (figure A and B), dorsal and lumbar spine. The patient was treated with intravenous metilprednisolone and immunoglobulins with partial recovery of the symptoms.
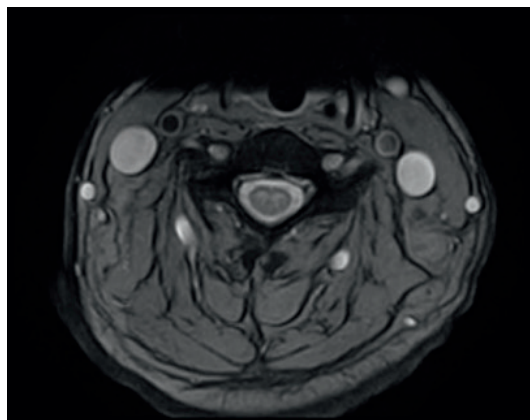
Magnetic resonance. T2 sequences. Non-enhancing hyperintense lesions in the anterior horn of cervical spine in axial (Figure A).

Magnetic resonance. T2 sequences. Non-enhancing hyperintense lesions in the anterior horn of cervical spine in saggital (Figure B).

Conclusion: This is a case report of a patient with polio-like disease. Sometimes it is not possible to identify the etiological agent. Nevertheless, it is an entity to remember in the differential diagnosis of acute flaccid paralysis even in adult patients.

Disclosure: Nothing to disclose

EP1199

The effect of NeuroGelTM with neural crest stem cells implantation on motor function recovery after experimental spinal cord injury

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Background and aims: To examine NeuroGelTM with xenogenic neural crest stem cells (NCSC) implantation on rat's hind limb motor function recovery after experimental spinal cord injury.

Methods: Animals: outbred albino rats. Experimental groups:1— spinal cord injury only (n=16); 2 — spinal cord injury +immediate homotopical transplantation of NeuroGelTM (n=20); 3 —spinal cord injury+analogous transplantation of NeuroGelTM in association with adult mouse NCSC (n=12). Group 3 consisted of 12 animals, respectively, —subgroups 3m and 3f. Model of injury — left-side spinal cord hemisection at Т11; duration of observation —28 weeks; ipsilateral hindlimb function indicator (IHL FI) determination — the BBB scale.

Results: Significant differences between the group 2 and group 1 IHLFI noted during period of 2th–28th week (p<0.001), between IHL FI of the group 1 and group 3 — during the whole observation period (p≤0.02). The maximum prevalence of group 3 IHL I over the group 2 IHLFI pointed at 24thweek (p=0.055). Significantly (p<0.05) difference between IHL FI of the subgroup 3m and group 2 was found at the 5th–16th week, between IHL FI of the subgroup 3m and group 3f — during period of the 1st–6th week. Significant difference between the subgroup 3f and group 2 IHL FI was not observed, the maximum value of its difference was found at the 3rd–4thweek.

Conclusion: NCSC xenotransplantation generally changes the function recovery dynamics, conditioned a trend towards potentiation of the NeuroGelTM positive effect on the course of the spinal cord injury; efficiency of this influence significantly depends on the sex of recipient organism.

Disclosure: Nothing to disclose

EP1200

Soft surfaces provide different effects on walking characteristics spatiotemporal gait modification of ambulatory patients with spinal cord injury who walked with or without a device

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Background and aims: Soft surfaces offer unstable supporting area that may alter walking characteristics of patients with impaired walking ability such as those with spinal cord injury (SCI).Therefore, this study aim to investigate spatiotemporal gait characteristics of 15 ambulatory participants with SCI who walked with (n=8) or without (n=7) a walking device while walking on hard and 3inches thickness soft surfaces.

Methods: The participants were assessed for their demographics, SCI characteristics, and spatiotemporal gait parameters while walking over a 10-m walkway of hard and soft surfaces. Findings of each surface were compared using the paired simple t-test.

Results: Walking on a soft surface attributed obvious effects on step length and cadence of participants who did not use a walking device (p<0.05). However, for those who used a walking device, walking on soft surface significantly affected only in walking cadence (p<0.05).

Conclusion: The different effects of soft surfaces on walking characteristics of those who walked with or without a walking device may suggest the contribution of upper limb functions when they encountered a challenging task as that seen in those who used a walking device. The findings may suggest the risk of falls for these individuals when they participate in a different surface from that commonly used in rehabilitation settings. Thus the incorporation of soft surfaces during walking training may promote rehabilitation outcomes for the patients.

EP1201

Myelopathy chameleons - they're out there!

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Background and aims: Cervical spondylotic myelopathy (CSM) is a common, underdiagnosed and potentially debilitating disorder, with significant clinical heterogeneity. Despite its prevalence, delayed or misdiagnosis of CMS is still frequent nowadays.

Results: Case 1: A 61-year-old female was observed for a right foot drop, with numbness, and was given the diagnosis of diabetic neuropathy. She presented to us one year later having developed a left foot drop plus weakness and numbness in both hands. Neurological examination revealed hyperreflexic quadriparesis with right side predominance, bilateral Hoffmann and Babinski signs, hypoesthesia and hypopallesthesia of hands and lower limbs, with sensory level at D6. Spinal MRI showed severe spinal stenosis with myelopathy at C5-C6 level. The patient underwent cervical laminectomy and, at one-year follow-up, exhibited partial recovery of strength.

Case 2: A 76-year-old male presented with a one-year history of progressive stepwise left limbs weakness, at first confined to the lower limb, and hence attributed to lumbar radiculopathy. Neurological examination uncovered bilateral upper limbs and torso fasciculations and hyperreflexic left hemiparesis with Babinski sign. Cervical MRI revealed spondylotic myelopathy at C3-C6 levels. Six months after cervical laminectomy, there was only a mild left crural paresis remaining.

Conclusion: These two patients' atypical presentation of CSM incited a lengthy diagnosis and late referral to surgery. Given the lack of pathognomonic symptoms, identification of CSM requires a high index of suspicion. It is imperative to keep improving the awareness of the disorder, especially regarding unusual presentations, since early diagnosis and treatment limits disease progression and prevents irreversible neurological impairment.

Disclosure: Nothing to disclose

EP1202

Heterotopic ossification and spinal cord compression: Long-term follow-ups of a patient with implant in the cervical spine after incomplete spinal cord injury

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Background and aims: This case study examines long-term biomechanical changes caused by a total disc replacement in a 34-year-old female patient after traumatic incomplete spinal cord injury C5/C6 and cervical myelopathy, AIS D sub C5.

Methods: 10-year follow-ups. First MRI was done prior to surgery. Clinical, radiological (X-rays, CT, MRI, myelography of the spine), electrophysiological examinations (Somatosensory and Motor Evoked Potentials SSEPs/MEPs, NLG, EMG) were acquired yearly because of fluctuating neurological symptoms.

Results: After implant the patient showed slight problems with bladder function and hypoesthesia in the complete left leg. 9 months later intermittent pain in the cervical spine and a worsening of bladder function occurred. CT scans, X-rays and myelography proved an osteophyte level C5/6. Slight protrusions within presurgical MRI level C4/5, C6/7 became more prominent. Heterotopic ossification in the level of implant and disc protrusions were progressive and finally diagnosed as disc bulging in 7-year follow-up report for MRI. SSEPs were normal, MEPs showed a slight increase of the resting motor threshold of the left leg. NLG/EMG was regular. The 10-year follow-up report showed further aggravation of the clinical parameters.

Conclusion: Heterotopic ossification in the level of implant and disc herniation in the adjacent spine segments were detected at least 9 months post implantation with progression in the further time course. Altered biomechanical stress due to the implant could be responsible to these secondary changes beyond age-related degenerative alterations. Long-term biomechnical effects of implantation should be taken into consideration and should lead to further research implant improvement with regard to material and biomechanics.

Disclosure: Nothing to disclose

EP1203

Spinal arteriovenous fistulas: Critical issues in differential diagnosis and therapy

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Background and aims: Spinal arteriovenous fistula (SAVF) is a rare cause of myelopathy, frequently misdiagnosed as myelitis. Our aim is to describe a case of SAVF, summarizing the main features of this pathology to help future early diagnosis.

Methods: A 57-year-old male was hospitalized for paresthesia and stiffness in both legs: the symptoms started a year before, after he had undergone bone marrow transplantation for an acute myeloid leukemia, successfully treated with fludarabine and busulfan. Over the past two months the symptoms worsened quickly. Neurological examination showed hypopallesthesia, hypertonia and hyperreflexia in both legs, Babinski sign on the left and hypoesthesia under D12 level.

Results: An EMG showed a mild axonopathy in both legs. A longitudinally extensive dorsal myelopathy from D7 to D12 segments was detected at a spinal MRI scan. We first postulated an inflammatory disease, supported by mild increase of CSF proteins. A steroid therapy was started, but after two days the symptoms worsened, resulting in severe gait disturbances. At this point the hypothesis of SAVF was formulated and confirmed by MRA scan, which evidenced a spinal venous congestion, and eventually by a spinal DSA. We promptly started a mannitol therapy to reduce the edema with benefit, while the patient was waiting for surgical intervention.

Conclusion: Although SAVF is a rare condition, it should be considered in the differential diagnosis of longitudinally extensive myelopathies. This is much more worthy as steroid therapy may result in symptoms worsening. Spine MRA scan should be performed in the setting of longitudinally extensive myelopathies.

Disclosure: Nothing to disclose

EP1204

Spinal cord ischemia syndrome due to anterior spinal artery occlusion: A case report

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Background and aims: Spinal cord ischemia is a rrare disease compared to cerebral ischemia because of the rich anastomotic vessels of the spinal cord. Acute spinal cord ischemia syndrome represents <1% of all strokes. Diagnosing the occlusive vascular lesions of the spinal cord is challenging and there is a need to clear the aetiology.

Methods: 60-year-old female presented with severe pain starting from the right hip extending to the right leg spreading to the left leg and abdomen. Her medical history revealed diabetes, hypertension and lomber disc hernia. At the admission she had flaccid paraplegia on both limbs. Analgesia was present under T10 level, plantar responses were indifferent

Results: The cranial, cervical, thoracic and lomber MRI showed no findings of a mass or myelitis. In the thoracal segments increased T2 signals were seen on the anterior spinal cord from T5 to conus medullaris. Thoracal disc protrusion was seen on T3-4 level. The patient was diagnosed with spinal cord ischemia syndrome and was treated with acetylsalicylic acid and LMWH .
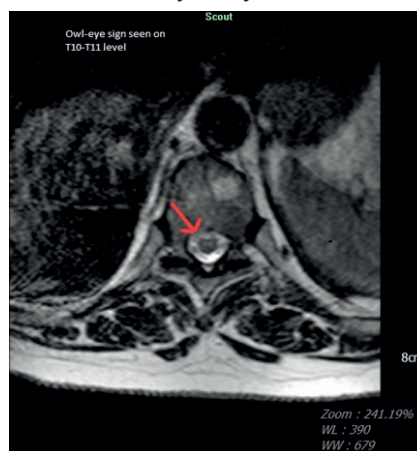
Owl-eye sign seen on T10-T11 level

Thoracal disc hernia seen on T3-T4 level and increased T2 signals seen below T5 level

Conclusion: Spinal cord infarcts are usually present with acute radicular pain, radiating caudally, combined with paraplegia, paresthesia and sphincter dysfunction. The aetiology includes aterosclerotic and aortic pathologies, trauma or emboli. Fibrocartilaginous emboli resulting from a herniated disc is also an important cause of the spinal infarct which is seen in our case. Gold standard diagnostic tool is the spinal MRI. Spinal MRI is also used to exclude other pathologies of the spinal cord. Increased T2 signals in the cord, owl-eye sign on axial sections is typical.

Disclosure: Nothing to disclose

EP1205

Catastrophic arachnoiditis following posterior fossa aneurysmal subarachnoid haemorrhage.

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Background and aims: Arachnoiditis is a rare complication of subarachnoid haemorrhage(SAH) with less than 30 cases reported. It commonly presents following a posterior fossa aneurysm, with haemomyelia being the proposed trigger of the inflammatory response.

Methods: We present a case and review the literature.

Results: A 55-year-old right-handed carpenter, presented with three week history of sudden onset band-like thoracic chest pain, followed by progressive numbness and weakness of both legs and micturition difficulty. Three months prior, he had a spontaneous SAH secondary to two posterior inferior cerebellar artery aneurysms;these were clipped and he made a complete recovery. Examination showed myelopathy with a T9 sensory level and urgent MRI showed extensive arachnoiditis of the cervical, thoracic and lumbar spine with cauda equina compression. He was transferred to a neurosurgical unit and had an attempted laminectomy and drain insertion; weakness worsened significantly post-operatively. Two subsequent courses of IV methylprednisolone had no effect and he was left with spastic paraplegia, incontinence and T6 sensory level.

Conclusion: Post-SAH arachnoiditis is rare, with no consistent approach to treatment and variable outcomes reported. Most cases, as in our patients, follow posterior fossa aneurysms. Given the significant time delay following the initial SAH, this important diagnosis can be missed in the early stages. Unfortunately in our patient, neither surgery or immunomodulatory treatment altered the disease course, however early intervention may lead to better outcomes.

Disclosure: Nothing to disclose

Peripheral nerve disorders 1

EP1206

Optimal treatment in CIDP (OPTIC protocol): Combined intravenous immunoglobulin and methylprednisolone as induction treatment

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Background and aims: Intravenous immunoglobulin (IVIg) and pulsed corticosteroids are both efficacious first choice treatments in CIDP. Each has its own benefits. IVIg has a fast mode of action usually leading to improvement within 6 weeks of treatment. Alternatively, corticosteroids can lead to long-term remission, defined as sustained improvement after stopping treatment. As fast improvement and long-term remissions can both be regarded as equally important, we hypothesized that combining IVIg and pulsed corticosteroids will lead to a higher rate of improvement, faster improvement and more frequent long-term remission in CIDP compared to treatment with IVIg or corticosteroids alone.

Methods: We started a prospective open-label uncontrolled feasibility study with a convenience sample of 20 probable or definite CIDP patients according to the EFNS/PNS criteria. Patients are treated with 3-weekly pulses of IVIg (2g/kg in first week followed by 1g/kg) and 1000 mg intravenous methylprednisolone during an 18-week period. Primary outcome is the number of patients in remission at 1 year after start of treatment.

Results: So far, the OPTIC protocol was initiated in eighteen patients. Thirteen completed treatment period, in two treatment was adjusted because of adverse events (toxicoderma, diverticulitis) and two patients are still being treated. One patient discontinued treatment because of a myocardial infarction. Fourteen of sixteen patients improved to a level that further treatment was regarded unnecessary. During a median follow-up of eight months off treatment, eight patients are currently in remission, five experienced a relapse and one died from a cause unrelated to CIDP or treatment.

Conclusion: Results expected in 2018

Disclosure: Nothing to disclose

EP1207

Paucisymptomatic sensory neuropathy associated with familiar chronic cough and gastroesophageal reflux

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Background and aims: Sensory-motor hereditary neuropathies are a heterogeneous group of neurodegenerative disorders defined by progressive neuropathy. Those with prominent sensory features and autosomal dominant inheritance are classified as Hereditary Sensory Neuropathies I (HSNI). In 2002, Springs described Hereditary Sensory Neuropathies I (HSNIB), characterized by adult onset paucisymptomatic sensory axonal neuropathy, chronic cough and gastroesophageal reflux. Non responsible gene has been identified but linkage to chromosome 3p22-p24 has been notified. We present 3 cases from the same family with hereditary sensory neuropathy with cough and gastroesophageal reflux.

Methods: We identify 3 brothers (2 females, 1 male), aged between 43 and 52 years. All of them refer chronic cough of unexplained etiology beginning in young-adult life and at least one of them symptoms of gastroesophageal reflux without response to proton-pomp inhibitors.
Only the eldest presents paresthesias and painful cramps in lower extremities.

Results: Electroneurogram demonstrates the existence of axonal sensory neuropathy of variable severity in the 3 siblings. A molecular study is performed after obtaining DNA from peripheral blood samples. The technique involves the expansion of 4 microsatellites located on chromosome 3p (D3S2403, D3S2336, D3S2466 and D3S1266). The three patients share a haplotype of 3 of these markers located in the 3p22-p24 region.

Conclusion: We consider of great interest to contribute 3 new cases that share haplotype of 3 of the 4 markers that previously had been associated with HSN1B. Symptoms derived from sensory neuropathy are mild and appear later than cough or gastroesophageal reflux. Therefore it could be an underdiagnosed entity.

Disclosure: Nothing to disclose

EP1208

Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP) associated with peritoneal dialysis

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Background and aims: A rapidly progressive demyelinating polyneuropathy has previously been described in the context of severe renal failure in individuals undergoing continuous ambulatory peritoneal dialysis (CAPD). However, literature searches identified only three case reports demonstrating a clear temporal relationship between commencing CAPD and rapid onset of severe demyelinating polyneuropathy, and none following haemodialysis. We describe another case of polyneuropathy following CAPD that is also supported by ultrasound imaging.

Methods: Case report and literature review. Literature search using Ovid and Pubmed databases.

Results: A 28-year-old male became anuric with end stage renal failure (ESRF) due to staghorn calculi. He was commenced on CAPD but developed severe sensory loss in hands and feet within one month of starting treatment. This was followed by severe proximal and distal weakness affecting all limbs. He became unable to walk or care for himself. Neurophysiology showed absent sensory responses and slowing of motor responses. Cerebrospinal fluid was acellular with raised protein. Ultrasound demonstrated diffuse swelling of the median nerve and nerve roots (Figure.1). To the authors' knowledge, this is the first description of nerve ultrasound findings in such a patient. There was improvement of proximal but not distal weakness, and improved disability following intravenous methylprednisolone, five cycles of intravenous immunoglobulin and switching to haemodialysis.

Figure. 1: An ultrasound image showing swelling around the C5/6 nerve root.

Conclusion: We describe a further case of a severe demyelinating polyneuropathy associated with CAPD, with ultrasound imaging. This may represent a subtype of chronic inflammatory demyelinating polyradiculo-neuropathy (CIDP). We postulate an immune mediated mechanism triggered by a peritoneal reaction.

Disclosure: Nothing to disclose

EP1209

Novel approaches to the treatment of polyneuropathy induced by diabetes type 1

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Background and aims: The aim of the study was to investigate the biomechanical characteristics of skeletal muscle contraction rats with diabetes and exposure to the drug "Cocarnit."

Methods: The study were conducted on 30 white nonlinear laboratory rats, which were divided into 3 groups of 10 animals each. Group 1 rats were used as control. In rats of the second and third groups were induced type I diabetes by administration of streptozotocin (STZ) (65mg/kg, i/p). Rats in group 2 was administered saline, and rats 3rd group – Cocarnit (1mg/kg, i/p, complex of nicotinamide, thiamine pyrophosphate, cyanocobalamin and adenosintriphosphate sodium) (company World Medicine) during 9 days. To determine the basic parameters of the dynamics of skeletal muscle contraction in rats was performed modulated stimulation of isolated nerve bundles on anesthetized rats with simultaneous detection of force reduction tibia muscle with discrete control changes its length under constant external load.

Results: It was established that diabetic neuropathy results in suppression of skeletal muscle contraction dynamic parameters due to time delay realization of muscle efferent stimulation; increasing delay realization of efferent stimulation with increasing time of active muscle; suppression of speed-power parameters muscle contractions within the studied time range; violation of the time correlation between the level of efferent activity flowing to the muscles and their realization in muscle system. Cocarnit restoried biomechanical characteristics skeletal muscle of rats with diabetes.

Conclusion: Obtained results indicates that the consequence of diabetic neuropathy is nerve conduction abuse that cause accurate positional movements violations and Cocarnit restored investigated biomechanical parameters

Disclosure: Nothing to disclose

EP1210

Giant axonal neuropathy diagnosed with Next-generation sequencing technology

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Background and aims: Next-generation sequencing (NGS) or massively parallel sequencing detects the precise order of nucleotides within a DNA molecule. NGS is more effective than traditional sequencing methods, such as Sanger sequencing, when several genes are involved. Targeted NGS is starting to be used in diagnostics for disorders caused by several genes. About 100 genes may cause hereditary neuropathies. Charcot-Marie-Tooth disease (CMT) is the most frequent hereditary neuropathy with a prevalence of 40-80 per 100,000 in Norway. Giant Axonal neuropathy is a rare form of hereditary neuropathy with autosomal recessive inheritance caused by mutations in the gigaxonin gene (GAN).

Methods: A 7-year-old girl with progressive neuropathic features and corkscrew curly hair was investigated. Nerve conduction velocities were in the axonal range. She was previously diagnosed as CMT type 2.

Results: NGS revealed compound heterozygous GAN mutations. Some of her clinical features were also indicative of the diagnosis.

Conclusion: Giant axonal neuropathy is progressive and may cause severe functional deficits, later symptomatology from the central nervous system and reduced life expectancy. One of the GAN mutations was novel.

Disclosure: Nothing to disclose

EP1211

Foot drop of tumoral origin: An unusual etiology

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Background and aims: Foot drop is frequently due to peroneal nerve compression. The nerve is vulnerable to external forces, including persistent postures, because its superficial position at the neck of the fibula. We present two clinical cases of foot drop in which the study revealed a tumoral cause.

Methods: Patient 1: A 55-year-old woman presented with repeated falls, distal hypoesthesia in her lower left limb and progressive left foot drop. She had impaired foot dorsiflexion, weakened plantar flexion, abolition of the ankle reflex, and hypoesthesia in the lateral leg, dorsum of the foot and heel.

Patient 2: A 31-year-old woman presented with a foot drop that had evolved over 3 months. She had severe impairment of left foot dorsiflexion and toe extension, gastrocnemius and peroneal atrophy, and a diminished ankle reflex.

Results: Patient 1: An electroneurogram (ENG) revealed damage of both left common peroneal and posterior tibialis nerves. Magnetic resonance imaging (MRI) of popliteal fossa showed multiple adenopathies suggestive of a lymphoproliferative disorder with extrinsic nerve compression. The final diagnosis was a non-Hodgkin lymphoma.

Patient 2: The ENG revealed damage of the left common peroneal nerve. MRI of the lower thigh showed an area of thickening of peroneal nerve, which was later revealed to be a neurofibroma.

Conclusion: Despite usually having a benign cause, foot drop with atypical features should prompt an adequate work-up. Attention should be paid to findings suggesting associated deficits of other nerves such as decreased ankle jerk. Our cases highlight that tumours should be considered among the possible etiologies.

Disclosure: Nothing to disclose

EP1212

Preserved muscle strength but deterioration in aerobic capacity after discontinuation of regular exercise in patients with chronic inflammatory demyelinating polyneuropathy

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Background and aims: In a previous study we demonstrated that in patients with chronic inflammatory demyelinating polyneuropathy (CIDP), aerobic exercise led to a significant increase in aerobic capacity of 11% and following unilateral resistance exercise muscle strength increased significantly by 14% in trained extremities and 4% in non-trained extremities. In this one-year follow-up study we evaluated whether muscle strength and aerobic capacity was preserved despite discontinued formalized exercise.

Methods: In our previous study, fifteen CIDP patients performed 12 weeks of aerobic exercise on ergometer bike and 12 weeks of unilateral resistance exercise of muscles at the knee and elbow. After participation no scheduled training was initiated. We performed a one-year follow-up test with measurement of isokinetic muscle strength by dynamometry and evaluation of aerobic capacity by determining maximal oxygen consumption velocity.

Results: Ten out of fifteen patients from the initial study participated. Combined isokinetic muscle strength (cIKS) had changed insignificantly with $-3.4\pm17.6\%$ and $-2.9\pm14.7\%$ on the trained and non-trained side, respectively. Aerobic capacity had decreased by $14.8\pm9.5\%$ (p=0.002). Compared to baseline before exercise cIKS had increased $15.6\pm20.5\%$ (p=0.04) on the trained side whereas on the non-trained side the difference was only $3.0\pm12.9\%$ (ns). Aerobic capacity had changed only $1.6\pm13.8\%$ (ns). During the one-year follow-up only two patients had performed regular aerobic exercise, and one patient had performed regular resistance training.

Conclusion: Muscle strength was preserved one year after resistance training despite discontinuation of training whereas aerobic capacity had fallen to a level comparable prior to training.

Disclosure: Nothing to disclose

EP1213

A rare cause of facial asymmetry

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Background and aims: We report a patient presenting with facial asymmetry due to isolated unilateral trigeminal motor neuropathy.

Results: A 40-year-old woman presented with progressive facial asymmetry, left hemifacial numbness and pain for the last month. She denied past history of head or facial trauma, dental procedures, diabetes herpes-zoster or other infections, as well as systemic symptoms. On neurological examination it was disclosed left temporal and masseter muscle atrophy, left deviation of the mandible on opening of the mouth, and mild poorly-defined left hemifacial hypoesthesia. Electrophysiological study confirmed the diagnosis of pure motor trigeminal neuropathy, with chronic neurogenic potentials in the atrophic muscles. Trigeminal sensory fibers were normal on blink reflex and facial laser-evoked potential. Facial and cranial MRI revealed atrophy and fatty infiltration on left masticator muscles (figure 1) and regular thickening of the affected fifth cranial nerve at its origin in the anterolateral surface of the pons, extending to cisternal portion and Meckel´s cave (figure 2), which suggested an inflammatory lesion. Blood and cerebrospinal fluid studies were negative for autoimmune and infectious diseases. Clinical picture remained stable over 9 months of follow-up.

Facial MRI coronal. Fat infiltration on left masticatory muscles

Cranial MRI, T2 3D DRIVE HR, reformatted images along the trigeminal nerves. Thickening and hyperintense signal on apparent origin (white arrows), cisternal segment (black arrows) and Meckel's cavum (gray arrows) of the fifth cranial nerve.

Conclusion: Trigeminal neuropathy is usually characterized by motor and sensory involvement. Reviewing the literature we found that 16 similar cases have been reported. As described in some other patients, sensory symptoms were referred in spite of isolate motor involvement on neurophysiology investigation. There is a wide array of possible etiologies for this neuropathy, however in most of the cases, no apparent cause is found.

Disclosure: Nothing to disclose

EP1214

Bilateral carpal tunnel syndrome as an adverse effect of Pembrolizumab

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Background and aims: Pembrolizumab is a monoclonal antibody approved for treatment of metastatic melanoma and non-small cell lung cancer. We report a case of acute bilateral carpal tunnel syndrome as a possible adverse effect to Pembrolizumab.

Results: A 77-year-old man presented with progressive paresthesia and numbness in fingers and hands for the last month. Five months before he had started treatment with Pembrolizumab 2mg/kg IV every three weeks for metastatic melanoma. He denied similar symptoms on the past. He rejected recent repetitive manual activity, distal edema or arthritis symptoms. On neurological examination it was disclosed bilateral positive Phalen sign and hypoesthesia in median nerve territory. Nerve conduction studies confirmed severe bilateral carpal tunnel syndrome, without signs of peripheral neuropathy. Bilateral carpal infiltration with betamethasone dipropionate and levobupivacaine was performed, with major symptomatic and electrophysiological improvement over the following week. Pembrolizumab treatment was continued and three months later he remains clinically well, with continued neurophysiological recovery.

Conclusion: This is the first report of bilateral carpal tunnel as an adverse reaction to Pembrolizumab. One of the possible mechanisms could be a bilateral tenosynovitis of the wrist, as this condition has been reported as an uncommon adverse reaction to this drug. In our patient we found a segmental demyelization, in a local prone to nerve compression, as the most probable explanation.

Disclosure: Nothing to disclose

EP1215

20-year follow-up of Lewis-Sumner Syndrome with several cranial nerve palsies

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Background and aims: To describe a patient with Lewis-Sumner Syndrome (LSS) characterized by a long follow-up, a relapsing and benign course and atypical cranial palsies.

Methods: A 49-year-old male consulted because of sudden diplopia and right upper limb weakness the previous 6 months acutely worsened. On physical examination he had an incomplete third cranial nerve palsy of the on right side, a subtle proximal weakness and hypoesthesia in that upper limb, the rest of the neurologic exam being normal.

Results: All of the complementary exams and laboratory tests were normal (blood cell count, routine biochemistry, immunology including autoantibodies such as anti-GQ1b, GM1, infectious serology and cerebrospinal fluid. The thorax film revealed a new right diaphragmatic elevation that resolved with time. The electrophysiological study showed persistent multifocal conduction block. The patient had a spontaneous complete recovery after two weeks. During his evolution he suffered six relapses coinciding with fever and different infectious diseases.

In some relapses he showed new cranial nerves involvement: right reversible diaphragmatic elevation, right hypoglossal palsy, right facial palsy and right trigeminal involvement. After all episodes the recovery was complete.

Conclusion: LSS is an asymmetric sensorimotor neuropathy, considered as a variant of chronic inflammatory demyelinating poliradiculopathy. Clinically, it is characterized by predominant upper limb impairment and electrophysiologically it shows a persistent multifocal conduction block. We present a patient with 20 years follow-up LSS characterized by multiple cranial nerve involvement, among which, X and XII nerve palsies have not been described in the literature yet.

Disclosure: Nothing to disclose

EP1216

Subacute polyradiculoneuropathy: Is vitamin deficiency a cause? About 3 cases

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Background and aims: Peripheral neuropathy due to vitamin deficiency may have a misleading clinical presentation and mimic Guillain-Barré Syndrome. We present 3 cases of rapid onset peripheral neuropathies with potential vitamin deficiency context.

Methods: We identified 3 patients aged from 28 to 31 years old presenting with subacute 4 limbs sensorimotor peripheral neuropathy with potential vitamin deficiency context : a woman who had gastric by-pass with post-surgery vomiting and 65kg weight loss, a woman with depression, anorexia and 25kg weight loss, and a man with alcoholism, recent vomiting and 3kg weight loss.

Results: Electroneuromyography showed 4 limbs sensorimotor non length dependent neuropathy, with demyelinating features without official criteria. Cerebrospinal fluid study was normal. Immunologic and infectious study were negative. We found B1 and B9 vitamins deficiencey for 2 of 3 cases, which was considered as a cause with clinical and electrophysiological slow improvement after supplementation. For the third case, only B9 vitamin deficiency was found and we considered it as an acute demyelinating polyneuropathy complicating an old axonal polyneuropathy. Slow improvement was observed after intravenous immunoglobulins treatment. These 3 cases have a common history of potential vitamin deficiency. We discussed both inflammatory and carential etiologies but neither electroneuromyography nor cerebrospinal fluid study brought a clear answer.

Conclusion: B1 vitamin deficiency is a cause of rapid onset neuropathy needing quick treatment. It is important to know when to think about it but also search for other diagnosis with specific treatment.

Disclosure: Nothing to disclose.

EP1217

Predicting factors of clinical outcome in chronic inflammatory demyelinating polyneuropathy

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Background and aims: Chronic inflammatory demyelinating polyneuropathy (CIDP) represents a heterogeneous group of symmetric classical sensorimotor, pure motor, sensory ataxic and Lewis Sumner form. The aim was to exame relationship between different factors (gender, age at disease onset, course and severity of disease, CSF protein level, comorbidities and treatment procedure) and clinical outcome of different forms.

Methods: This retrospective study included 48 CIDP patients classified in 4 groups in relation to clinical form.

Results: The classical form had 39 patients, pure motor 5, Lewis Sumner 3 and one had sensory ataxic form. Majority of patients with classical form had relapse remitting course (69.7%), while 30.8% of patients had progressive course. Stable remission in this group was achieved in 61.5% cases, improvement in 30.8%, and in 7.7% of patients disease continued to progress. Logistic regression analysis showed that all risk factor included in the study are in correlation (positive or negative) with clinical outcome of classical form, but none of this correlation was statistically significant. Highest predictive value had disease severity (r=-0.285), treatment with IVIG (r=0.27) and CSF protein level (r=-0.228). Only one patient with motor form had progression after treatment onset, this was female patient with MGUS IgM, high CSF protein level, progressive course and most severe form of the disease.

Conclusion: Considering all risk factors through specific score based on predictive value of each factor, we can predict clinical outcome of classical form of CIDP with high statistical probability (88.5%).

Disclosure: Nothing to disclose

EP1218

Cancelled

EP1219

Descriptive study of an Algerian cohort of anti-ganglioside antibody neuropathies: Clinical, electrophysiological and immunological aspects

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Background and aims: Anti-ganglioside antibody (AGA) neuropathies are dysimmune, rare and heterogeneous neuropathies. These AGAs are attracting increasing diagnostic interest, especially since the emergence of the concept of "nodo-paranodopathies" To study the association between neuropathic syndromes and AGA in our patients and to analyze these results in the light of recent concepts.

Methods: A retrospective, descriptive monocentric study in the EHS Ait-Idir neurology department in collaboration with the immunology department of Pasteur Institute of Algeria. All patients had acute or chronic peripheral neuropathy, associated with, at least, one anti-ganglioside antibody.

Results: Ten patients were included. Multifocal motor neuropathy was the most frequent phenotype. The others phenotypes were pure axonal and motor forms of the Guillain-Barré syndrome, sensory ataxic neuropathy, an "overlap syndrome" between MMN and MADSAM and an ALS syndrome. The most frequent AGAs were anti-GM1 (80%) and anti-GD1b (70%). The most frequent association was anti-GM1 and anti-GD1b. An association between AGA and onco-neural antibodies was encountered in one patient. Our series includes characteristic forms, rarer and exceptional phenotypes. Undetectable antibody levels are the likely consequence of the involvement of different epitopes of nodal and paranodal region. The concept of "nodopathies" seems, at present, more appropriate to characterize these neuropathies and thus explain some "misleading" aspects.

Conclusion: This first study in Algeria highlights the phenotypic and immunological heterogeneity of neuropathies associated with AGA. The recent discovery of new antibodies targeting the antigens of the Ranvier node allows us to solve certain nosological difficulties.

Disclosure: Nothing to disclose

EP1220

An Italian multicenter database for the diagnosis and therapy of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) and its variants

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Background and aims: Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a chronic disabling disease that often improves with immune therapy. Several variants of CIDP were reported but their frequency and relation with CIDP remains unclear.

Methods: We implemented a web-based database to collect data from Italian patients with CIDP to determine the frequency and characteristic of these variants, the diagnostic criteria used, the possible evolution into typical CIDP, and their response to therapy.

Results: By January 2017 we included 319 patients with CIDP and variants (197 men, 122 women), aged 18-86 years (median 58) with a mean disease duration of 7.8 years (range 0.5-38). Based on clinical symptoms, CIDP was defined as typical in 88% and atypical in 12%. The diagnosis of CIDP fulfilled EFNS/PNS criteria in 81% of the patients while nerve conduction studies (NCS) were not diagnostic in 12% or available in 7%. CSF studies were diagnostic in 81% of the patients, nerve biopsy in 50% and imaging (US or NMR) in 56%. Two supplementary diagnostic criteria including a relapsing course were present in 77% of patients with non diagnostic NCS (clinical CIDP). Improvement after one or more therapies was reported by 88% of treated patients with a positive response to IVIg in 74%, steroids in 51%, plasma exchange in 60% and immune suppressant in 36% without differences according to the fulfillment or not of EFNS/PNS diagnostic criteria.

Conclusion: This multicenter study provided useful information on the natural history, course, diagnosis and response to therapy in patients with CIDP and variants.

Disclosure: Kedrion Biopharma srl, Italy supported the cost of the Database. I received travel supports to attend Scientific Congress from CSL Switzerland and Kedrion Italy.

Sleep disorders 1

EP1221

Excessive daytime sleepiness as first symptom of adult Pompe's disease

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Background and aims: Pompe's disease is a clinically heterogenic disorder of autosomal recessive inheritance caused by an alpha-glucosidase (acid maltase) deficiency. There are 3 age dependent phenotypes; a rapidly progressive infantile form that is usually fatal within the first year of life, and a slowly progressive juvenile and adult variant. Onset at adult age may vary from the second to sixth decade. Patients may present with a proximal myopathy of the limb girdle type and fatigue. In a later stage a considerable number of patients develop respiratory failure.

Methods: We report on a 61-year-old patient suffering from severe hypersomnolence since 6 months.During the night he would wake up several times. His wife noticed that his breathing was slow when asleep. He had no complaints of breathlessness or exercise intolerance

Results: A polysomnography showed frequent awakening, reduced baseline oxygen saturations, and periods of hypopnoea. Following a bronchoscopy he developed acute respiratory failure with severe hypercapnia. He needed mechanical ventilation for a month and was finally discharged from the hospital with nocturnal non-invasive ventilation. Extensive investigations were normal except for a mildly increased creatine kinase and an alpha-glucosidase deficiency. Pompe,s disease was confirmed by DNA testing.

Conclusion: The diagnosis of adult onset alpha-glucosidase deficiency must be considered in patients with unexplained respiratory insufficiency. In our patient this was masked by excessive daytime sleepiness due to nocturnal hypoventilation.

Disclosure: Nothing to disclose

EP1222
Cancelled

EP1223

Sleep disturbances in systemic lupus erythematosus

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Background and aims: There are few studies that evaluate sleep disturbances and especially restless legs syndrome (RLS) in patients with systemic lupus erythematosus (SLE). The aims of this study were: 1.) to assess sleep disturbances in SLE 2.) to determine the prevalence of RLS 3.) to assess the clinical characteristics of RLS.

Methods: This is a case-control study of consecutive SLE patients. Assessment instruments included RLS Rating Scale, RLS Quality of Life Instrument, Pittsburg Sleep Quality Index, Epworth Sleepiness Scale, Hospital Anxiety and depression scale. For this study were recruited 26 consecutive patients with SLE and 26 patients in the control group.

Results: There were 23 females (88.46%) in the study group; the mean age was 52.35±10.76 years.

There were 9 patients that met RLS criteria (34.62%) in the study group and 2 patients (7.69%) in the control group (p<0.05). In the study group, the severity distribution of RLS was: mild - 1 case, moderate - 8 cases. In the control group there was one case with mild severity and one with moderate severity.

There was no excessive daytime sleepiness in any of the patients. However, 69.23% of the patients from the lupus group had the ESS score between 6-10, in comparison with 46.15% in the control group (p<0.05). Higher global PSQI scores were found in the study group.

Conclusion: This study confirmed the poorer sleep quality and higher prevalence of RLS in SLE patients.

Disclosure: Nothing to disclose

EP1224

A deficit in visual processing for both insomnia and obstructive sleep apnoea patients overcomes the effect of age

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Background and aims: To test perceptual processing in two sleep disorders, both a group of 23 insomnia disorder (ID) and a group of 19 obstructive sleep apnoea (OSA) patients were compared with 19 age-matched healthy controls (HC).

Methods: All the participants performed a visual search task in which they had to detect the presence/absence of a target (letter T) embedded in the 50% of trials into a set of distractors (letters Os, Xs, or Ls). Target's salience and distractors' numerosity were manipulated as independent variables, whereas accuracy and reaction times (RT) were recorded as dependent variables.

Results: Data generally confirmed the typical effects of visual search. Moreover, both ID and OSA patients reported significantly slower RT in comparison with HC. Interestingly, RT increased as expected with age in HC, whereas no correlation between age and RT was found for both ID and OSA patients.

Conclusion: Our results demonstrate the existence of a perceptual deficit occurring in both ID and OSA patients, consisting in a harder extraction of relevant visual information from noise. Finally, for both clinical groups the effect of age is hidden by the overwhelming effect of the disorder.

Disclosure: Nothing to disclose

EP1225

Impaired neurocognitive functions in patients with disorders of arousal

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Background and aims: Sleepwalking, sleep terrors, and confusional arousals are non-REM sleep parasomnias grouped under the category of disorders of arousal (DOA), resulting from incomplete arousals from slow wave sleep. Frequently DOA patients exhibited excessive daytime sleepiness leading to abnormal functioning during the day. Therefore, cognitive impairment might be observed in this subjects, but a comprehensive evaluation of this patients has not been performed. Accordingly, the aim of this study is to assess neurocognitive functions in DOA patients through a complete neuropsychological evaluation and to compare their performance with that of healthy controls.

Methods: 69 patients (62.3% male and 37.7% female, mean age 32.8 ± 14.1) with a diagnosis of DOA and 31 healthy controls matched for sex, age and education have been evaluated by means of a complete neuropsychological assessment battery.

Results: A significant impairment in Corsi block tapping test and Attentive Matrices (which respectively investigate visuo- spatial short term working memory and visual selective attention) was found in DOA patients in comparison to healthy controls. Additionally, significant correlations between percentage of N1 and Corsi block tapping performance ($r=-0.418$, $p<0.022$), Attentive Matrices and number of awakenings ($r=-0.403$, $p=0.027$) and sleep efficiency ($r=0.374$, $p=0.042$) were found.

Conclusion: A deficit in visuo-spatial working memory and in selective visual attention have been found in DOA patients. Moreover, our results suggest that sleep disruption, objectively assessed by PSG recordings, could explain the neurpsychological deficits.

Disclosure: Nothing to disclose

EP1226

Non-24-hour sleep-wake syndrome and melatonin secretion impairment in a patient with pineal cyst

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Background and aims: Non 24-hour sleep-wake syndrome is a circadian rhythm sleep disorder (CRSD) characterized by the inability to maintain a stable circadian rhythm that became progressive longer; this lead to impossibility to fall asleep at the desired time. The majority of cases remain idiopathic, while few studies demonstrated CRSD associated to hypothalamic lesions. The role of melatonin and pineal gland on sleep structure is still debating, since sleep disorder as well as lack of consequences on sleep structures has been reported after pinealectomy. We present the case of a 14-year-old girl with a wide pineal cyst and severe CRSD.

Methods: Prolonged polysomnographic recording, brain MRI, actigraphy, 24-hour melatonin serum curve and endo-rectal temperature measurement were collected.

Results: Brain MRI examination disclosed a 20mm pineal cyst without evidence of acqueductal or mesencephalic compression. The prolonged actigraphy demonstrated a free-running disorder with total inversion of sleep-wake cycle. Polysomnographic recording and endo-rectal temperature profile were within the normal. Melatonin curve showed blunted nocturnal peak (max 82ng/L, mean nightime 68.5), normal total quantity of melatonin secretion (AUC 1118.5ng*h/L), and a shape suggesting higher morning levels of melatonin. Evening administration of melatonin up to 14 mg was able to restore the normal sleep-wake cycle.
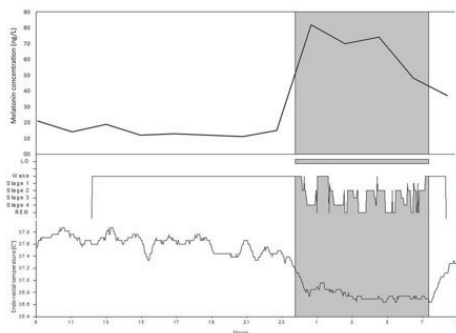
Figure 2: Melatonin curve plotting with hypnogram and rectal temperature. Note the Dim Light Melatonin Onset (DLMO) occurs 2 hours before sleep onset, while melatonin peak is anticipated and lower than normal subject. The graphical show dissociation between melatonin peak and lowest value of rectal temperature.
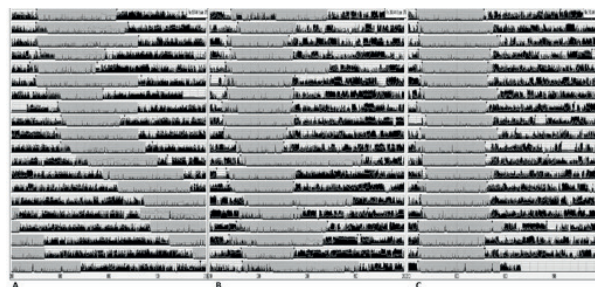
Figure 1: Homemade actigraphy. A: From the 6th day melatonin administration was discontinued. B: partial efficacy of 7 mg of melatonin at bedtime. C. Restoration of wake-sleep cycle after administration of 14 mg of melatonin.

Conclusion: The CRSD associated to melatonin secretion impairment were restored in our patient after melatonin administration. We speculate that the compression on the normal pineal parenchyma exerted by the cyst, may decelerate melatonin secretion with a slower return to basal concentration, leading to progressive sleep cycle advance.

Disclosure: Nothing to disclose

EP1227

Cancelled

EP1228

The Bern sleep database: A valid tool for clinical sleep research

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Background and aims: Multidisciplinary Bern Sleep-Wake-Centre was founded in 1982 and is a tertiary sleep-centre. Database is a useful tool in rare diseases for a better characterisation, evaluation, treatment, and research in the field. For over 25 years, patient data are collected in the Bern sleep database (BSD). In Bern, one of the main research and clinical areas always has been narcolepsy.

Aims: We aimed to set-up a new tool for sleep research including the development of predictive models to further assist clinicians in their diagnosis or treatment decisions.

Methods: BSD has been transferred into an application designed to support data capture and management for research studies. New BSD contains 13 forms/instruments with 720 potential items in total. Descriptive statistics has been executed.

Results: Patients: The total number of patients was 8543. Mean age was 49.0 years. Annual inclusion of new patients is continuously increasing since 2011 from 600/year to 1050/year in 2015.

Diagnosis: Diagnosis included sleep apnoea (N=5537), insomnia (N=476), narcolepsy (N=157) and excessive daytime sleepiness not otherwise specified (N=590). The annual number of new narcolepsy diagnosis maintained stable from 2000 to 2015 (10 to 15/year).

Tests: Data from 6500 polysomnographies, 1445 MSLT, 1823 "Bern sleep-wake-questionnaires", and 2375 actigraphies are included. Data about narcolepsy and narcolepsy-borderland are currently under evaluation and will be presented.

Conclusion: The BSD is a unique database, including long-term data and will serve as a research tool for clinical sleep studies, validation of (new) diagnostic criteria or questionnaires, and the development of predictive models.

Disclosure: Nothing to disclose

Sunday, 25 June 2017

Ageing and dementia 2

EP2001

COMAJ (Early-Onset Alzheimer's disease cohort): Two-year follow-up

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Background and aims: Before 60, Early-Onset Alzheimer's disease (EOAD) is still the first cause of dementia. Atypical phenotypes are more frequent than in the elderly and disease course may be faster, and remains misunderstood. We aimed to describe clinical, neuropsychological, medical-social, autonomy and imaging courses of EOAD (onset before 60) patients on two-year follow-up.

Methods: All the patients of the prospective cohort COMAJ between the 01/06/09 and the 01/05/14 with probable or certain EOAD according to the NIA and IGW criteria were included, except those with autosomal dominant AD. Demographic data, vascular risk factors, APOE4 status, history, neuropsychological, medical-social, autonomy and MRI data were collected, according to a standardized protocol.

Results: 94 patients were included (women: 62%, mean age: 57.4±3.3 years, diagnostic delay 3.8 (2.2) years); 56% of the patients showed a typical amnestic phenotype, 44% were depressive, 62% were APOE4 carriers. APOE4 carriers were significantly more amnestic than the non-carriers (75.5% vs 36.3%, p=0.0007). Mean MMSE was 19.7 (5.7) at diagnosis, 14.1 (7.8) at inclusion and 9.8 (7.8) /30 on two-year follow-up. Mean Scheltens score was 1.8 at baseline and 2.5 two years later. Loss of autonomy was severe: only 8.5% (n=8) of the patients were working at baseline, none on follow-up. A daily help was required in 76% (n=71) of the patients at baseline, in 91% on two-year follow-up, with 26% living in institution at this time.

Conclusion: This large cohort provides information on the progression of the disease at early age, highlighting the severe and fast cognitive impairment.

Disclosure: Fund : Labex DistALZ

EP2002

Asymptomatic carotid stenosis might worsen cognitive functions in hypertensive patients

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Background and aims: Systolic arterial hypertension (SAH) in midlife is a risk factor for cognitive impairment (CI) but the relationship of asymptomatic carotid stenosis (ACS≥50%) to CI is still a matter of debate. The aim of this epidemiological study is to estimate the significance of ACS≥50% for CI in hypertensive and non-hypertensive persons without signs and symptoms of stroke or TIA.

Methods: A total of 500 volunteers, aged 50-79 years, were enrolled and followed-up for cognitive performance. CI has been defined as a score between 24 and 27 of MMSE. A battery of additional neuropsychological tests has also been conducted.

Results: Multiple logistic regression analysis has shown that ACS≥50% attributes to CI (OR=10.7; 95%CI: 3.36-34.14; p=0.0001) only in hypertensive patients with SAH but not in normotensives. Logistic regression analysis has revealed that the abnormal scores of neuropsychological tests (MMSE, DFS, DBS and VF) are significantly associated with ACS≥50% (OR 2.121; 95%CI: 1.048-4.292; p=0.036). The strongest relationship has been established between ACS≥50% and DBS (OR 10.818; 95%CI: 1.165-100.439; p=0.037). CI has presented as an executive dysfunction and decline of attention, verbal fluency and working memory.

Conclusion: ACS≥50% might be attributable to CI in patients with SAH. This suggests a complexity of a large and small artery dysfunction, caused by both atherosclerosis and hypertension, underlying the CI pathogenesis.

Disclosure: Nothing to disclose

EP2003

Alzheimer's disease environmental, biological and clinical risk factors in a Tunisian population

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Background and aims: Late-Onset Alzheimer's disease (LOAD) is a multifactorial idiopathic pathology caused by clinical, environmental and genetic factors. Hence its etiology is still unkwown. We aimed to evaluate the main environmental, clinical and biological factors associated with this disease.
Methods: We enrolled 97 LOAD patients (diagnostic criteria: DSMIV and NINCDS-ADRDA) and 284 controls. Data concerning clinical and biological parameters, life style and dietary habits were collected. Biostatistical analysis were conducted on SPSS.v20.0.
Results: After binary logistic regression, we noted that factors significantly associated with LOAD risk were hype rhomocysteinemia(OR=5.47;p=0.001), high total cholesterol levels (OR=6.78, p<0.001), high chlorine levels (p=0.034), decreased C-reactive protein and total thyroxine (T4) levels (p=0.042;p=0.046, respectively) hypocalcaemia (OR=2.6,p=0.038), hypovitaminosis-B12 (OR=5.4, p<0.001), hypovitaminosis-D (OR=5.48,p=0.001) smoking (OR=4.49;p=0.001), hypertension (OR=6.78, p=0.002), Diabetes (OR=4.89, p=0.003) and Chronic Kidney Diseases (OR=4.69, p=0.001). We also noted that high education level(OR=0.10, p=0.002), urban habitat(OR=0.30;p=0.032), currently or formerly active professional life (OR=0.20; p=0.016), consumption of fish (OR=0.21;p=0.012), olive oil (OR=0.18; p=0.015), curcuma (OR=0,10; p=0,026), coffee(OR=0,20; p=0,021) and black chocolate (OR=0.10; p=0.015) seem to decrease LOAD risk.
Conclusion: Our results support the hypothesis of cognitive reserve, which stipulates that the brain with cognitive reserve, ensured by an active social life and a high level of education, may protect against cognitive decline. It seems that a healthy life style and dietary habits mentioned above are recommended to prevent LOAD.
Disclosure: Nothing to disclose

EP2004

Antibodies against glial derived antigens in Alzheimer disease may reflect hippocampal demyelination and memory loss

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Background and aims: Alzheimer's disease (AD) is known to exhibit well characterized pathologies including the extracellular accumulation of amyloid plaques, intra-axonal presence of neurofibrillary tangles and glial hypertrophy. Nevertheless the nature of myelin pathology in AD has not been well studied. Recent studies on animal models of AD, revealed however focal demyelination within beta amyloid plaques in hippocampus. Thus we decided to assess humoral response against proteins of myelin sheath in AD, in hope to find an early biomarkers of memory loss and neuropathological process characteristic for the disease.
Methods: We assessed antibodies levels against proteins of myelin sheath: myelin oligodendrocyte glycoprotein (MOG), myelin basic protein (MBP), myelin-associated glycoprotein (MAG), proteolipoprotein (PLP) in sera of 26 AD patients and 26 healthy controls, using commercially available ELISA system (Mediagnost, Germany).
Results: In the AD patients subgroup significantly higher titers were observed for all types of assessed IgG autoantibodies compared to healthy control subjects (anti-MOG, anti-MAG, anti-MBP, anti-PLP). For IgM antibodies, among AD patients we observed higher titers for majority of investigated autoantibodies (p<0.05), with exclusion of anti-MAG IgM antibodies (p>0.05).
Conclusion: The study provides the evidence for the significantly increased production of autoantibodies against proteins of myelin sheath in AD. These results can be of importance in the light of emerging data from animal models of AD, indicating early demyelination of hypocampal region. Further studies on larger population are necessary to confirm whether these autoantibodies could serve as early biomarkers of AD in humans.
Disclosure: Nothing to disclose

EP2005

Apolipoprotein E ε4 allele frequency in Korean patients with Parkinson's disease dementia

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Background and aims: It has been well known that the apolipoprotein E(ApoE) ε4 allele is a strong risk factor in Alzheimer's disease and occurs at an increased frequency in dementia with amyloid pathology. However The clinical significance of the ApoE ε4 allele in Parkinson's disease dementia(PDD) with synucleinopathy has been a subject of debate. PDD is one of the second most common subtypes of dementia in Korean population. The ApoE allele frequencies were evaluated in Korean patients with probable PDD diagnosed by the MDS task force criteria for the diagnosis of PDD in this study.

Methods: Forty patients (20 PDD and 20 age matched healthy controls) participated in the study. The ApoE genotype was determined by the polymerase chain reaction (PCR) and allele specific hybridization using the ApoE typing test kit. (DNA extraction: Wizard Genomic DNA purification kit (Promega), Polymerase chain reaction : Commercial INNO-LiPA (Line Probe Assay) ApoE test kit)

Results: The ApoE ε4 allele frequency in the PDD group was 35% and was significantly higher than those of normal controls (15%) (p< 0.05). The ApoE ε4 carrier frequency in the PDD group was was 60%, and also significantly higher than those of normal controls (30%) (p< 0.05). The ApoE ε3 allele was the most frequent genotype in Korean population generally in this study.

Conclusion: These results that the elevated ApoE ε4 frequency in the PDD with synucleinopathy in which the overall brain neuritic plaque burden was low, indicates that ApoE ε4 might contribute to neurodegeneration through mechanisms unrelated to amyloid processing

Disclosure: Nothing to disclose

EP2006

Cancelled

EP2007

SORL1 mutations in familial Alzheimer's disease

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Background and aims: The sortilin-related receptor 1 gene (SORL1) encodes a protein involved in the trafficking of amyloid precursor protein. Some SORL1 variants have been associated with increased risk of Alzheimer's disease (AD), and potentially pathogenic mutations have been reported in a few early-onset autosomal dominant AD cases. We report screening for SORL1 mutations in a Spanish cohort of cases with dementia of the Alzheimer type (DAT).

Methods: We screened for SORL1 mutations in 124 familial (44 early- and 80 late-onset) and in 15 early-onset sporadic DAT cases recruited from a referral memory clinic. Mutations found were reviewed in genomic databases, further screened for in a control population of 200 elderly subjects, and analyzed for potential pathogenicity with prediction programs (PolyPhen2 and SIFT). We also searched for segregation in the families with available siblings.

Results: Nine different potential pathogenic changes were found in ten probands (7%). Four changes had not been previously described: Trp848Ter, Arg1702Met, Gly1871Val, and splice site variant. Another five were considered very rare or rare variants (Glu270Lys, Gly852Ala, Asn1809Ser, Asp2065Val, and Ala2173Thr). After screening for these changes in the control population and available siblings, correlation with the disease (presence in at least 1/200 controls and/or no segregation) was ruled out in seven of the mutations. The change Trp848Ter and the splice-site change remained potentially pathogenic, although the study of segregation was very limited.

Conclusion: SORL1 mutations are present in 7% of our familial DAT cohort but in most cases could not be correlated with the disease process.

Disclosure: Nothing to disclose

EP2008

Cancelled

EP2009

Cancelled

EP2010

The relationship between white matter lesions and clinical features in Alzheimer's disease

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Background and aims: The purpose of this study was to determine whether in patients with Alzheimer's disease (AD), white matter lesions (WMLs) are associated with cognitive dysfunctions and the behavioral and psychological symptoms of dementia (BPSD) at initial presentation.

Methods: We retrospectively selected 73 patients with probable AD without medical history of clinical stroke. As WMLs, periventricular hyperintensity (PVH) and deep and subcortical white matter hyperintensity (DSWMH) were rated using the Fazekas scale (range, 0 to 4) on MRI imaging at initial visit. We analyzed the relationships between WMLs and clinical features including the presence of silent brain infarcts (SBIs) in basal ganglia, complication such as hypertension and scores of the Mini Mental State Examination (MMSE) and the Neuropsychiatric Inventory (NPI).

Results: Of all patients, PVH $\geq$ 2 (severe PVH) was found in 13 patients and DSWMH $\geq$ 3 (severe DSWMH) was found in 23 patients. Using multivariate analysis, severe DSWMH (OR 41.8 ; 95% CI 6.9-100< ; p<0.001) was independently correlated to severe PVH. Hypertension (OR 5.9 ; 95% CI 1.4-33.1 ; p=0.014), severe PVH (OR 26.2 ; 95% CI 4.7-219.4 ; p<0.001) and delusion subscale of NPI (OR 1.3 ; 95% CI 1.1-1.5 ; p=0.014) were independently correlated to severe DSWMH.

Conclusion: In AD, the presence of PVH did not influence clinical features, whereas the presence of severe DSWMH might show potentially serious of BPSD, especially delusions.

Disclosure: Nothing to disclose

EP2011

Age adjusted, MRI-derived normalized brain volume as a predictive biomarker of cognitive decline

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Background and aims: The objective of our study is to determine whether MRI-derived anatomical features of brain atrophy can predict cognitive impairment as measured by the Mini Mental State Examination (MMSE) scale.

Methods: In this study, we employed longitudinal data available from the Open Access Series of Imaging Studies (OASIS), (Marcus DS et al, 2009). Employing a cut-off value of 24 for the baseline MMSE, we divided the study population into the (A) normal cognition vs. (B) mild cognitive impairment groups. Subsequently, we employed derived anatomic volumes available in the OASIS dataset, namely 1. Estimated total intracranial volume (eTIV) (mm3) (Buckner et al., 2004), 2. Atlas scaling factor (ASF) (Buckner et al., 2004) and 3. Normalized whole brain volume (nWBV) (Fotenos et al., 2004) along with baseline age in order to produce a multivariate model. Multivariate analysis was performed via stepwise discriminant function analysis (DFA. Finally, curve estimation was used to determine whether a linear association existed between the DFA score and MMSE at baseline and visit 3.

Results: Stepwise DFA produced a single discriminant function, including Age and nWBV as predictors of cognitive impairment, (Wilk's lambda=0.888, $\chi 2$=16.553, P<.0001) achieving an overall 76% predictive accuracy. Curve estimation determined a statistically significant association between DFA score and both baseline and visit 3 MMSE score P<.05).
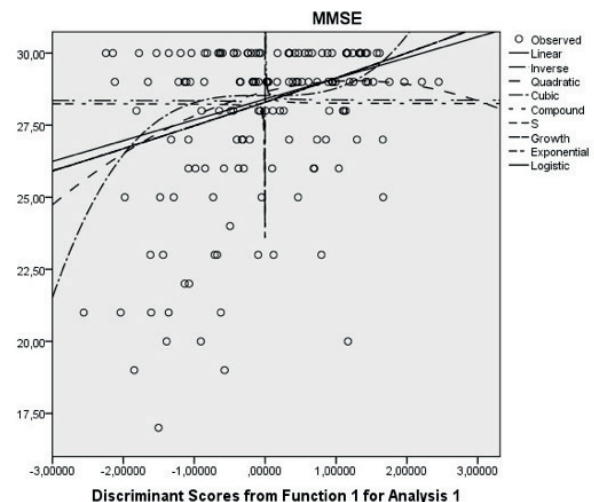
Curve estimation for the association between baseline MMSE and DFA Score
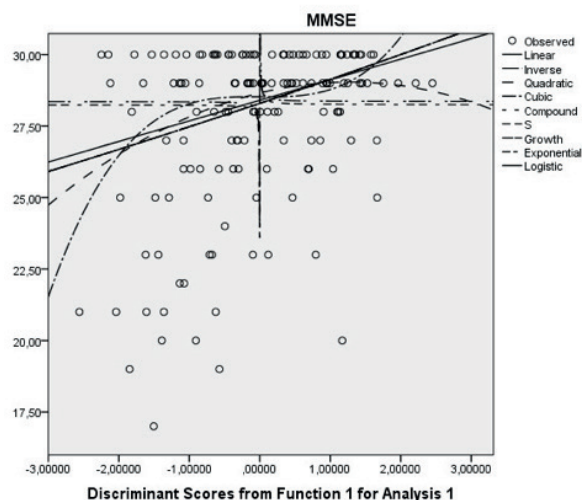
Curve estimation for the association between visit 3 MMSE and DFA Score

Conclusion: DFA derived age adjustment on nWBV provides an easy to use biomarker predictive of cognitive impairment; the DFA predictive accuracy may be further enhanced via incorporating measurements regarding regions of interest (ROIs) into the stepwise model.

Disclosure: Nothing to disclose

EP2012

Subjective cognitive complaints in nondemented older adults relates to hippocampal atrophy as well as objective memory testing

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Background and aims: Subjective cognitive complaints (SCC) and hippocampal atrophy are potential markers of early-stage Alzheimer´s disease (AD). The aim of this study was to assess the relationship between hippocampal volumes and specific SCC and to compare it to standard, routinely used memory tests.

Methods: Ninety seven non demented older adults (30 with amnestic mild cognitive impairment, 8 with non amnestic mild cognitive impairment and 59 cognitively healthy older adults) underwent comprehensive neuropsychological testing, 1.5T brain MRI scans with quantitative volumetry using FreeSurfer package to measure estimated total intracranial volume (eTIV) along with adjusted right and left hippocampal volumes, and were administered a 10-item yes/no questionnaire to evaluate SCC in the last 6 months. Spearman's correlation was used to correct for non-normal score distribution. Subjects with significant vascular changes or depression were not included.

Results: We found significant correlations of both hippocampal volumes with with the total SCC score (rR=-.19 and rL=-.22) and several items: "Difficulties with recalling past events" (rR=.-31and rL=-.34), "Feeling of memory change" (rR=-.25 and rL=-.24) items. Left hippocampal volume correlated with "Worse memory in comparison to peers" (r=-.18) and "Subjective limitation in daily activities" (r=-.21) items. Auditory Verbal Learning Test - learning (trials 1 to 5) and delayed recall correlated with left hippocampal volume (both rs=.21). All ps' were <.05.

Conclusion: Specific SCC reflect hippocampal atrophy equally well as standard memory tests in non demented older adults and should be taken into account when identifying individuals in early-stage AD.

EP2013

Age- and sex-specific parental family history of dementia in relation to subclinical brain disease and risk of dementia: A population-based study

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Background and aims: Family history is an important risk factor for dementia, but the importance of age at onset and sex of the affected parent, as well as underlying mechanisms, are uncertain.

Methods: From 2000-2002, we assessed parental history of dementia in 2087 non-demented participants of the population-based Rotterdam Study (mean age 64 years, 55% female). We investigated risk of dementia (until 2015) in relation to family history, adjusting for demographics, cardiovascular risk factors, and known genetic risk variants. We furthermore determined the association between parental history and markers of neurodegeneration and vascular disease on MRI.

Results: During a mean follow-up of 12.2 years, 142 participants developed dementia. Parental history was associated with risk of dementia independent of known genetic risk factors (hazard ratio, 95% confidence interval: 1.67,1.12-2.48), in particular when parents were diagnosed at younger age (HR,95%CI <80years: 2.58,1.61-4.15 versus ≥80years: 1.01,0.58-1.77). Accordingly, age at diagnosis in probands was highly correlated with age at diagnosis in their parents <80 years (r=0.57,p=0.001), but not thereafter (r=0.17,p=0.55). Among 1161 non-demented participants with brain MRI, parental history related to lower cerebral perfusion, and higher burden of white matter hyperintensities and microbleeds. Dementia risk and MRI markers were similar for paternal versus maternal history.

Conclusion: Parental history of dementia increases risk of dementia, primarily when age at parental diagnosis is <80 years. Unexplained heredity may in part be attributed to cerebral hypoperfusion and small-vessel disease. We found no evidence of preferential maternal compared to paternal transmission.

Disclosure: Nothing to disclose

Cerebrovascular diseases 3

EP2014

Prevalence of spasticity in patients with ischemic stroke in the internal carotid artery territory – pilot results of the national SONAR registry

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Background and aims: The main aim of the study was to provide estimate of the incidence and prevalence of spasticity following stroke in the internal carotid artery territory for the regional stroke centers in the Czech Republic; the secondary goal was to identify predictors for the development of spasticity.

Methods: In a prospective cohort study, 256 consecutive patients with clinical signs of central paresis due to a first-ever stroke were examined in the acute stage. All of the patients had primary stroke with carotid origin and paresis of the upper and/or lower limb present longer than 7 days after the stroke onset. All patients were examined between 7-10 days after IS. The degree and pattern of paresis and muscle tone, the Barthel Index, baseline characteristic, and demographic data were evaluated. Spasticity was assessed using the Modified Ashworth Scale (MAS).

Results: Out of the 256 patients (157 males; mean age 69.9±12.4 years), 115 (44.9%) patients developed spasticity during the first 10 days after stroke onset. Eighty-three (32.5%) patients presented with mild neurological deficit (modified Rankin Scale 0 – 2) and 69 (27.0%) patients were bedridden. -024.

Conclusion: Spasticity was noted in 44.9% patients with neurological deficit due to first-ever stroke in carotid territory in the first 10 days after stroke onset. Severe spasticity was rare.

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EP2015

Associations of common carotid artery intima-media thickness with risk factors for stroke in the population of Republic of Moldova.

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Background and aims: Increased common carotid artery intima-media thickness (CCA-IMT) is associated with an increased risk of stroke. We studied the relationships between CCA-IMT and stroke risk factors in the population of Republic of Moldova. Here we present preliminary results of the National State Programme joined to International Project "Primary Stroke Prevention".

Methods: The included subjects were examined according to a pre-established International Protocol of risk factors' estimation, which included non-invasive measurements of average CCA-IMT from left and right side (B-mode ultrasonography), questionnaire, clinical and laboratory examination.

Results: In this study were enrolled 300 subjects, among which 180 (60%) were women and 120 (30%) men (age 49.91±14.5 years). We found significant associations between CCA-IMT and several clinical and laboratory variables. CCA-IMT significantly correlated with systolic (r=0.43, p=0.00) and diastolic (r=0.34, p=0.00) blood pressure, body mass index (r=0.40, p=0.00), abdominal circumference (r=0.46, p=0.00), glycated haemoglobin (r=0.24, p=0.00), total cholesterol (r=0.14, p=0.01), LDL-cholesterol (r=0.20, p=0.00), HDL-cholesterol (r=-0.18, p=0.00) and fibrinogen (r=0.24, p=0.00).

Conclusion: Increased thickness of intima-media of the carotid artery is associated significantly with other traditional risk factors for stroke. Thus, CCA-IMT can be considered an early common integrator of the effects of multiple risk factors on the arterial wall.

Disclosure: Nothing to disclose

EP2016

Addenbrooke's cognitive examination in nondemented patients after stroke

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Background and aims: The aim of study is compare cognitive functions in nondemented stroke patients 3-6 month after stroke, with sex and age matched nonedemented and nonedepressed controls, by Addenbrookes' Cognitive Examination.
Methods: Totally 156 respondents, 72 healthy controls (19 men, mean age 64.5±12.4 years) and 84 patients after stroke (54 men, average age 62.2±9.0 years) were tested.
Results: Statistically significant difference between healthy controls and stroke patients in total score of Addenbrookes' Cognitive examination (Stroke patients' score 86.2 points, Healthy controls' score 91.2 points, p<0.01), Verbal Production domain (stroke patients'score 9.8 points healthy groups' score 11.5 points, p<0.01) and Memory domain (stroke patients' score 19.5 points, healthy groups'score 21.7points, p<0.01) were demonstrated. The difference was statistically significant also between the both stroke patients subgroups: A/ patients with right-sided brain lession and healthy controls in the total score (88.3 vs. 91.3points, p<0.05) and Verbal Production (9.9 vs. 11.5 points, p<0.01) were demonstrated and B/ left-sided brain lession and healthy controls in total score (83.9 vs. 91.3 points, p<0.01), domains Memory (18.6 vs. 21.7 points, p<0.01) and Verbal Production (9.6 vs. 11.5 points, p<0.01).
Conclusion: This study showes the decline in cognitive functions tested using Addenbrookes' Cognitive Examination in stroke patients 3 – 6 month after stroke.
Disclosure: Supported by institutional support NO. 1 RVO-FNOs/2012 1.7.2012 - 1.7.2015.

EP2017

The role of contralesional motor areas in the first days after stroke – an fMRI-guided TMS-study

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Background and aims: Neuroimaging studies have demonstrated that after stroke a number of areas in the contralesional hemisphere show increased activity when patients move their affected hand (Rehme et al., 2012). While some studies suggest a supportive role of these regions during stroke recovery (Lotze et al., 2006), others point to a maladaptive role (Nowak et al., 2008).
Methods: We here tested the functional relevance of activation changes in contralesional M1, dorsal premotor cortex (dPMC) and anterior intraparietal cortex (aIPS) in early subacute stroke patients. Activity was assessed by fMRI and subsequently disturbed using trains of 10Hz rTMS time locked to hand motor tasks. Motor performance was measured using a 3D motion analyser system. Imaging data were analyzed using SPM8.
Results: Online-TMS over the individual fMRI maxima led to differential effects on motor performance. TMS interference with contralesional M1 and dPMC normalized movement fluency in patients showing higher activation during paretic hand movement. Moreover, TMS-interference with contralesional aIPS led to an increase of tapping amplitude and peak velocity across the patient group.
Conclusion: In conclusion, online-TMS over higher activations of M1 and dPMC improved patients' motor fluency, whereas online-TMS over aIPS improved spatial aspects of movements. Thus, the present results suggest a disturbing influence of all examined regions on different features of movement kinematics already during the first days after stroke in mildly to moderately affected patients.
Disclosure: Nothing to disclose

EP2018

Posterior Reversible Encephalopathy Syndrome (PRES): A disease with a broad clinical and radiological spectrum

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Background and aims: PRES is a disease related to specific entities that affect the cerebral blood flow regulation. The aim of this study is to analyze the epidemiological and clinical features, as well as the outcome of patients diagnosed with PRES in our institution.

Methods: Retrospective observational study of patients diagnosed with PRES and assessed by neurologist in our hospital between the years 2010-2016. Demographics, medical background and previous treatments, clinical features at income, diagnostic test results and clinical outcome were recorded.

Results: Among the 14 patients included, 50% (n=7) were woman, with an average age of 52.7 years old (range 3-80). In the medical background found as trigger were high blood pressure in 43% (n=6) of cases (BP at income 183/95mmHg, SD 53/30mmHg) and immunosuppressive therapy, 43% as well. The main clinical manifestation was epileptic seizure, 71% (n=10): 50% (n=5) generalized tonic-clonic type and 10% (n=1) epileptic status. 60% (n=6) required ≥2 antiepileptic drugs and 10% required iv sedation. The second most common manifestation were visual alterations, 43% (50% (n=3) had binocular blindness). Among de imaging findings 86% (n=12) were atypical (unilateral, asymmetrical and non parieto-occipital). 43% of patients experienced some complication, 33% (n=2) of them neurological (hemorrhage and epileptic status). In the outcome 86% were fully recovered by 3 months and only 14% (n=2) were dead (of non-neurological causes).

Conclusion: PRES affects patients of any age and gender with wide clinical and radiological features, being epileptic seizures and "atypical" images the most common ones. It´s not always reversible, exclusive of white matter or posterior.

Disclosure: Nothing to disclose

EP2019

What would happen if all stroke patients arrived within the therapeutic window for thrombolysis?

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Background and aims: In the last years, many efforts have been made to increase thrombolysis rates. Media campaigns, prenotification systems and hospital reorganization have been developed with varied success. Anyway, thrombolysis rates are still low. Studies addressing elegibility in patients excluded from reperfusion therapies because of exceeded therapeutic window are scarce.

Methods: Patients attended in the Emergency Department with a final diagnosis of stroke or TIA from November 2013 to January 2015 were included. Data on PD, treatment applied and exclusion criteria for thrombolysis (if present) were recorded. A descriptive analysis of the reasons for exclusion from thrombolytic treatment was performed

Results: 382 patients were included. 197 (51.57%) had a PD>3h. One received rt-PA (0.51%). 196 were excluded. 104 of them (53.06%) were asymptomatic or paucisymptomatic at arrival, 22 (11.22%) became asymptomatic before treatment decision, 18 (9.18%) were excluded because of CT findings, 13 (6.63%) because of poor functional status and 3 (1.53%) showed INR>1.7. 36 patients (18.36%) would have been eligible if the therapeutic window hadn't been exceeded. 29 (14.8%) had a PD>4.5h, 6 (3.06%) because of inhospital delays and one (0.51%) because of unknown onset.

Conclusion: Most patients arriving after the first three hours do it asymptomatic or paucisymptomatic, or symptoms resolve spontaneously before thrombolitics are administered, but some of them would have been treated – with prognostic implications – with a sooner arrival, as would some of those excluded because of CT findings. Still many patients remain untreated only because of an exceeded therapeutic window. They should be the target for future campaigns.

Disclosure: Nothing to disclose

EP2020

Pelvic deep venous thrombosis in patients with cryptogenic stroke and patent foramen ovale

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Background and aims: Paradoxical embolism from pelvic deep vein thrombosis (DVT) has been suggested in several studies as a mechanism of ischemic stroke in patients with patent foramen ovale (PFO) and cryptogenic stroke. Performing a pelvic magnetic resonance venography (MRV) as part of an inpatient diagnostic evaluation has been recommended.

Methods: Adult patients with ischemic stroke and PFO who underwent pelvic MRV and lower extremity (LE) duplex ultrasound as part of the diagnostic evaluation were included in this single-center retrospective observational study, between 2006-2015, to determinate DVT prevalence as a possible source of paradoxical embolism.

Results: Of 81 patients with ischemic stroke and PFO (male sex 57%, median age 55 years), 49 were diagnosed with cryptogenic stroke (male sex 55%, median age 50 years). Deep vein thrombosis imaging study was performed in 80% of patients, 95% with LE duplex ultrasound and 51% with pelvic MRV. DVT prevalence in cryptogenic stroke patients was 8.2% (4 patients), 3 of them had LE thrombosis (6.1%) and 1 had pelvic DVT (2.0%). All these patients had a normal hypercoagulability testing. There was no significant difference in the prevalence of pelvic DVT in patients with PFO and non-cryptogenic stroke.

Conclusion: Our results differ from those of the PELVIS Study (20% pelvic DVT prevalence) and are similar to more recent studies which find a lower prevalence of pelvic DVT in patients with PFO and cryptogenic stroke. We think routine inclusion of pelvic magnetic resonance venography in the diagnostic evaluation of this subtype of patients cannot currently be recommended and needs further investigation.

Disclosure: Nothing to disclose

EP2021

Endovascular treatment of cerebral venous sinus thrombosis

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Background and aims: Anticoagulation is the standard treatment for cerebral venous sinus thrombosis (CVST). However, neurological condition may worsen during anticoagulation especially in cases with extensive thrombosis. Endovascular treatment (ET) may be considered in these selected cases. The aim of this study was to report our experience with ET in severe cases of CVST.

Methods: In this retrospective case series, we report the clinical and radiological outcomes of 11 CVST patients treated with endovascular methods at our institution between July 2010 and February 2016.

Results: The mean age (10 female, 1 male) was 28 years (17-45). All patients received intravenous heparin initially. The most frequent indication requiring ET was worsening or no improvement in mental status despite treatment. Mean GCS before ET was 11.2±0.6. Balloon venoplasty was used in six patients, suction thrombectomy in five and stent-retriever thrombectomy in one. All patients received local intrasinus thrombolytic therapy with t-PA (5-40 mg). Clinical stabilization or rapid clinical improvement observed within 1-3 days of ET. Patients' mean GCS reverted to 15 at discharge. Discharge modified Rankin scale (mRS) scores were 1 in seven patients, 2 in one and 3 or over in three. Eight patients scored below 2 at one month and nine patients scored below 1 at long-term follow-up (6-48 months).

Conclusion: Although there are no randomized controlled trials, ET may be considered in carefully selected cases with more severe clinical condition, with worsening or no improvement despite anticoagulation. Randomized controlled trials are required to provide the evidence of endovascular treatment effect in CVST patients.

Disclosure: Nothing to disclose

EP2022

Polymorphisms of platelet von Willebrand factor receptor gene in patients with atherothrombotic and lacunar stroke

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Background and aims: Receptors to von Willebrand factor (vWFR) are on second place according to density on platelets. Experimental vWFR inhibition demonstrated promising results for cerebral ischemia manifestation prevention on animals.

Aim of study - reveal association between vWFR polymorphisms and age of atherothrombotic stroke (ATS) and lacunar infarction (LI) occurrence.

Methods: We examined patients with uncomplicated ATS and LI. Type of stroke in all patients was verified by clinical, neuroimaging and laboratory investigation. Patients were distributed on 2 subgroups: I –18-60 years in men, 18-55 years in women, II–from 61 years in men/55 years in women till 74. Genetic tests to detect c.3550C>T and T(-5)C polymorphisms into gene coding vWFR alpha-chain were performed. Confidence interval (CI) of frequencies was detected using angular transformation, relative risk (RR) was calculated by usual formula.

Results: Polymorphism frequencies are shown in tables 1 and 2. Presence of c.3550C>T mutation predispose to stroke in younger age – RR for ATS was 2.1 (95%CI 1.6–2.9), RR for LI – 2.0 (95% CI 1.1–3.6). Such mutation results in vWFR activity increasing. Presence of T(-5)C polymorphism predispose to ATI in younger age with RR 2.1 (95%CI 1.5–2.9) and there was no frequency difference in LI subgroups. T (-5)C polymorphism is connected with increased density of vWFR upon platelet surface.

Table 1. Frequency of mutant allele for c.3550C>T

Group	Age subgroup	
	I	II
ATS	24,7% (95% CI 18,1–32,0) n=73	6,0% (95% CI 2,9– 10,1) n=83
LI	14,1% (95% CI 7,8–21,9 n=46	4,3% (95% CI 2,0–7,5 n=104

Table 2. Frequency of polymorphisms for T(-5)C

Group	Age subgroup	
	I	II
ATS	21,9% (95% CI 15,6–29,0) n=73	6,6% (95% CI 3,3–10,9) n=83
LI	22,8% (95% CI 14,9–21,9) n=46	24,1% (95% CI 18,5–30,1) n=104

Conclusion: Presence of abnormalities into gene, coding alpha-chain of Ib platelet receptor, predispose to younger age of stroke occurence. Further investigation is required to reveal influence of hereditary changes in platelet vWFR to different stroke variants.

Disclosure: Nothing to disclose

EP2023

GLA p.A143T variant Fabry disease may result in a severe phenotype with extensive microvascular cerebral involvement at a young age

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Background and aims: Fabry disease (FD) is a rare inborn error of glycosphingolipid catabolism that results from the deficient activity of the lysosomal enzyme alpha-galactosidase A (AGAL-A). Genetic screening studies have revealed over 600 variants in the galactosidase alpha (GLA) gene. The p.A143T variant is a genetic variant of unknown significance (GVUS), with its associated phenotype ranging from classical FD to healthy unaffected patients. Some authors however deem this variant non-pathogenic.

The aim of this case report is to describe the case of a 16-year-old male with multifocal white matter lesions on brain MRI performed in the diagnostic workup for episodic headaches, who was diagnosed with Fabry disease.

Methods: Available demographical, clinical and ancillary investigations were reviewed.

Results: A 16-year-old male presented with episodic headaches and an MRI that showed multifocal punctate to patchy white matter lesions (Figure 1, 2 and 3). Past medical history revealed a period of absence-like episodes at the age of 10, with normal EEG. The diagnosis of FD was suggested upon the finding of significantly reduced plasma AGAL-A activity (0.62µmol/L or 13% of normal; normal range ≥1.65µmol/L) and genetic investigation confirmed the presence of a hemizygous missense variant in the GLA gene (p.A143T). Baseline assessment of systemic involvement showed only a discrete proteinuria.
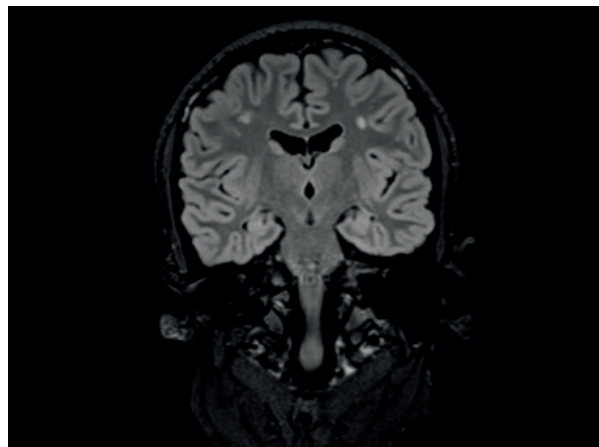
Figure 1
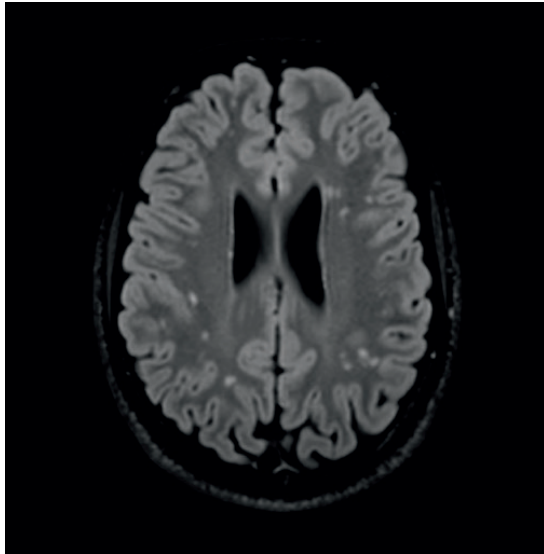
Figure 2
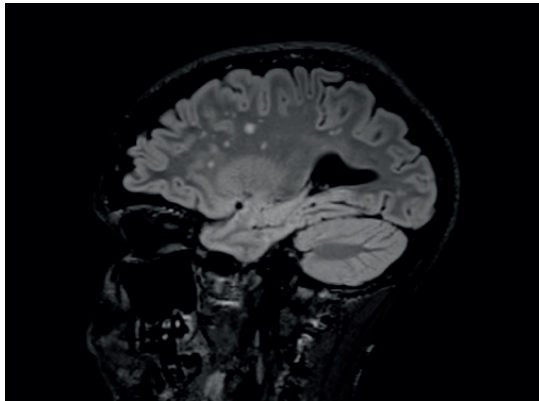
Figure 3

Conclusion: A diagnosis of FD should be considered when finding asymptomatic extensive cerebral white matter lesions in a young patient. Furthermore, the causative p.A143T mutation can be associated with a more severe subclinical phenotype than has been reported to date.

Disclosure: Nothing to disclose

EP2024

Dural arteriovenous fistula with transient memory loss and cognitive decline treated with endovascular embolization

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Background and aims: Dural arteriovenous fistula (DAVF) is an uncommon intracranial vascular malformation, which is accompanied by significant morbidity and mortality. Though true incidence of DAVF is unknown, reported incidence is approximately 10-15% of all intracranial vascular abnormalities. Clinical manifestations of intracranial DAVF are various including pulsatile tinnitus, orbital congestion, headache, intracranial hemorrhage or infarction. However, there have been little reports about DAVF manifested as rapidly progressive dementia.

Methods: A 43-year-old male presented daytime sleepiness at work and indifferent behavior like never before. Two weeks later, he had episodic memory loss with well preserved remote memory. Brain MRI showed thrombus and dural arteriovenous fistula in right lateral transverse sinus with bilateral thalamic venous infarction. Cerebral angiography confirmed right transverse sigmoid dural arteriovenous fistula with feeding artery of right occipital artery and left posterior meningeal artery.

Results: Multiple transarterial embolization was done successfully and patient returned back to his daily life.

Conclusion: Recently endovascular treatment have become one of the main therapeutic options to obliterate the fistulous site. They have led rapid diagnostic approach and management of DAVF with high curative rates. We report a rare case of dural arteriovenous fistula which caused rapidly progressive dementia successfully treated by endovascular approach.

Disclosure: Nothing to disclose

EP2025
Cancelled

EP2026

Long-term outcome and secondary prevention of cardioembolic stroke in severely disabled patients

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Background and aims: Unfavorable functional outcome after stroke is considered a reason not to antiocagulate patients for secondary stroke prevention.

Methods: A score of 4-5 in modified Rankin scale is considered a bad functional stroke outcome. A prospective study included 167 severely disabled cardioembolic stroke survivors discharged from P. Stradins Clinical University Hospital, Riga, Latvia in 2015. Patients or their relatives were interviewed by phone 365 days after leaving the hospital. Standardized questions were asked about patient abilities. The results were compared in patient groups according to prescribed medication.

Results: The average one-year mortality was 52,08%. The functional outcome according to prescribed medication is shown in table below.

mRs	Outcome 90d after discharge			Outcome 365d after discharge		
	0-3	4-5	6	0-3	4-5	6
No antithrombotic (n=15)	0,0%	13,3%	86,7%	0,0%	13,3%	86,7%
Antiplatelet agents (n=79)	10,1%	26,6%	63,3%	12,7%	8,9%	78,5%
VKA (n=17)	29,4%	29,4%	41,2%	41,2%	11,8%	47,1%
NOACs (n=56)	57,1%	19,6%	23,2%	57,1%	12,5%	30,4%

Conclusion: One-year mortality of severely disabled patients is high. But as the functional outcome is improving in one year after the stroke and mortality rate is significantly lower in patient groups started on oral anticoagulants, these patients with unfavorable stroke outcome at time of discharge should not be denied oral anticoagulants for secondary stroke prevention.

Disclosure: Nothing to disclose

Cerebrovascular diseases 4

EP2027

Cerebral venous thrombosis associated with use of erythropoietin as a performance-enhancing drug: A case report

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Background and aims: Central Venous and Sinus Thrombosis (CVST) is a rare and under-diagnosed type of cerebrovascular disease which is more prevalent in young women and often correlated with a pro-thrombotic state; only three case reports have correlated it with use of erythropoietin, two of which as treatment for chronic kidney disease. Our aim is to report a second case of erythropoietin use as doping as contributing factor for CVST.

Methods: Case report, with review of the pertinent literature.

Results: A 38-year-old female professional cyclist without prior history presented to the emergency room after two episodes of seizure in the same afternoon. Her physical examination was unremarkable. The head CT scan without contrast showed no abnormalities. As blood analysis demonstrated a globular volume of 50.35% and hemoglobin of 17.39g/dL, cerebral venous thrombosis was suspected and brain MRI was performed, which showed thrombotic occlusion of the superior sagittal sinus and superficial cortical veins, such as the left vein of Trolard. She admitted to the use of erythropoietin as doping, which was associated with her hemogram alterations. Treatment with warfarin was initiated while in the hospital, and follow-up consultations showed complete clinical recovery. A new MRI performed six months after the initial presentation showed recanalization of the venous structures.
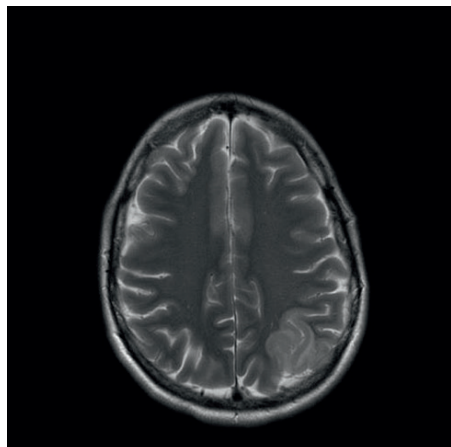
T2-weighted brain MRI demonstrating the area of venous infarction caused by the thrombosis
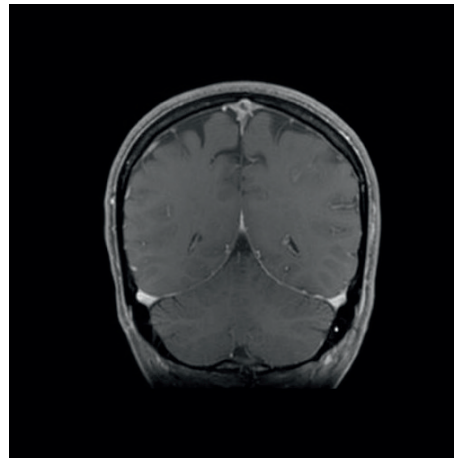
Coronal slice of a T1-weighted brain MRI demonstrating the occlusion of the superior sagital sinus after the injection of gadolinium-based contrast
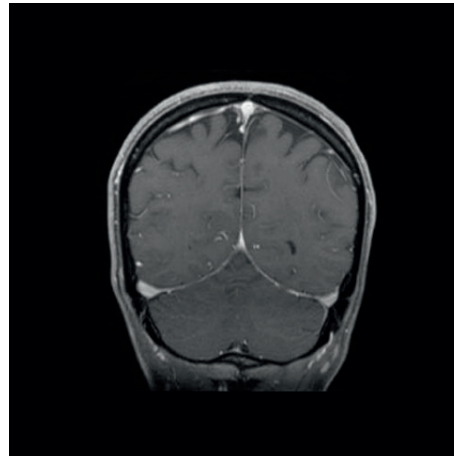
Comparative coronal slice of a T1-weighted brain MRI performed five months afterwards demonstrating recanalization of the superior sagittal sinus

Conclusion: In the investigation of patients presenting with seizures and pro-thrombotic states, such as use of erythropoietin, cerebral venous thrombosis should always be considered.

Disclosure: Nothing to disclose

EP2028

Memory impairment due to bilateral fornix infarction: Characterisation and follow-up

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Background and aims: The fornix is an important structure regarding consolidation of new data into long term memory.
Methods: We report the case of a patient with bilateral fornix infarction, and the results of a 7-month follow-up with neuropsychological evaluation.
Results: A 68-year-old woman had a scheduled, endovascular intervention on a non-ruptured aneurysm of the anterior communicating artery. There were no immediate complications. On the next day, topographic disorientation, repetitive, and digressive speech were noticed. Brain-MRI showed an acute infarction of both anterior fornix pillars, more pronounced on the right side, with a below-centimetre parietal injury. Neuropsychological evaluation documented a severe anterograde memory deficit, involving verbal, visual, and topographic components, with normal working, autobiographic and remote semantic memories testing. Seven months later, the patient maintained a considerable functional impairment (examples, not being able to memorize new routes, unable to read books due to difficulty in remembering elements of the story line), but a substantial improvement in verbal and visual anterograde memory tests.
Conclusion: To our knowledge, a single case with a similarly extended and detailed cognitive follow-up was published, referring to a patient with subarachnoid, intraventricular and intracerebral haemorrhages. In our case, MRI showed a clear anatomical and etiologic definition of the fornix injury, which allowed a more accurate cognitive assessment, and follow-up. These revealed a significant improvement regarding verbal and visual episodic memories.
Disclosure: Nothing to disclose

EP2029

The effect of alpha-lipoic acid supplementation on anthropometric indices and food intake in patients experienced stroke: A randomized, double blind, placebo-controlled clinical trial

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Background and aims: Stroke as a devastating condition is a major cause of death worldwide and accountable for long time disability with high personal and social cost in adults. Metabolic syndrome and obesity are well known risk factors of coronary artery disease, stroke, and mortality. Alpha-lipoic acid (ALA) is an eight-carbon, sulfur-containing compound with antioxidant properties which reduces body weight, changes other anthropometric indices and regulate food intake by suppressing appetite and increasing metabolism This study was designed to evaluate the possible effects of ALA supplementation in patients with stroke.
Methods: In this randomized, double blind, placebo-controlled clinical trial, sixty-seven patients with stroke were randomly allocated to two groups (taking a 600 mg ALA supplement or placebo daily for 12 weeks). Weight, waist circumference, energy, carbohydrate, protein and fat intake were meatured and body mass index was calculated before and after intervention in this study. Dietary intake and statistical analyses were carried out using N4 and SPSS16 software, respectively.
Results: Primary features were similar in the intervention and placebo groups (p<0.05). After the intervention period, waist circumference (p<0.001), energy, carbohydrate, protein and fat intake (p<0.001) decreased significantly in ALA group compared with placebo. While and no differences were observed in weight (p=0.26) and BMI (p=0.56) in ALA supplementation group compared with placebo.
Conclusion: Results of this trial indicated that 12 weeks supplementation with 600 mg alpha-lipoic acid has beneficial effects on anthropometric indices (weight, body mass index, waist circumference) and food intake (energy, carbohydrate, protein, and fat)) in patients with stroke.
Disclosure: Isfahahn university of Medical sciences supported this research.

EP2030

Remote symptomatic intracerebral haemorrhage post intravenous thrombolysis

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Background and aims: Intracerebral hemorrhage (ICH) after treatment with intravenous recombinant tissue-type plasminogen activator (rtPA) for ischemic stroke can occur in local relation to the infarct, as well as in brain areas remote from infarcted tissue.Remote intracerebral haemorrhage (rICH) is ICH post thrombolysis in brain regions without visible ischaemic changes. To date, it is proposed possible influence of cerebral amyloid angiopathy which may contribute to rICH.

Methods: We report a case of 67-year-old gentleman, with history of metastatic non small cell lung cancer to bone, unknown cerebral metastasis, presented with sudden onset of slurred speech and mild hemiparesis. Clinical evaluation revelaed Left Middle Cerebral Artery infarct with aphasia and mild right hemiparesis. Urgent CT Bran and CT Angiogram of the Circle of Willis and Carotid Arteries showed Left M1/ M2 junction occlusion. Patient was given intravenous rtPA at the dose of 0.9mg/kg and he underwent endovascular therapy. The procedure was uneventful.

Results: Noted dropped in Glasgow Coma Scale from 15 to 3 after 1 hour post procedure. Urgent CT Brain done showed large right cerebral haematoma with midline shift and early hydrocephalus. Patient eventually passed away.
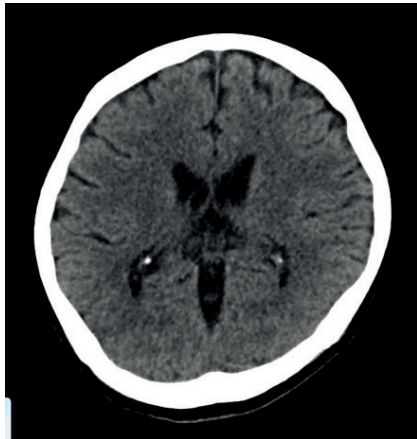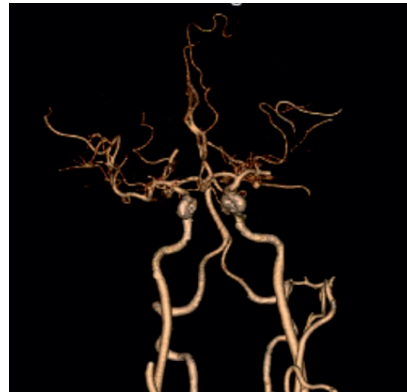
CT Angiogram
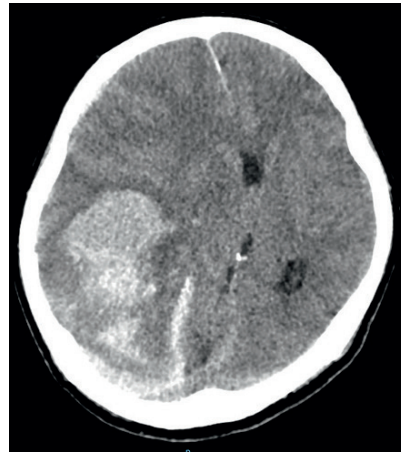
CT Brain post IV Thrombolysis

CT Brain on admission

Conclusion: rICH is an uncommon complication of intravenous thrombolysis that increases the risk of poor neurological outcome and mortality. In this case, in view of relatively young patient with no significant cardiovascular risk factors (diabetes mellitus, hypertension, hyperlipidaemia), there maybe a possibility of micro-cerebral metastasis that was not seen in the plan CT Brain done on admission, which potentially may account for rICH.

Disclosure: Nothing to disclose

EP2031

Abdominal diameter index as a predictor of early neurological deterioration in acute ischemic stroke

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Background and aims: Early neurological deterioration (END) occurs frequently in acute ischaemic stroke. The abdominal diameter index (sagittal abdominal diameter/thigh circumference, ADI) has been shown to predict the cardiovascular disease related with visceral obesity and insulin resistance. To determine the ADI as a predictor of END in acute ischaemic stroke.

Methods: We analyzed 657 consecutive patients with acute ischaemic stroke within 24 hours of symptom onset using a single center registry of maintained clinical data including abdominal diameter index. Major stroke etiologies were divided into cardioembolic, large vessel, small vessel, other, and unknown origins. END was defined as a worsening 2 or more points deterioration on the National Institutes of Health Stroke Scale(NIHSS) during 5 days of hospitalization. Stepwise regression models were generated to associate clinical factors with END.

Results: Of the included 657 patients (median age 68 years, 54% male), 211(32%) experienced END. END was associate with lower NIHSS score on admission (P<0.01), higher glycemia (P=0.04), larger mismatch volume (P=0.01), and proximal artery occlusion (P=0.03). Stroke with large vessel disease were associated with a twofold higher odds of END in stepwise regression models (OR 2.0, 95% CI 1.2-6.4, P=0.001). In a logistic regression analysis controlling for other cardiovascular risk factors including age, smoking, total cholesterol, high-density lipoprotein cholesterol, triglycerides, blood pressure and glucose, ADI were significantly associated with END in large vessel disease (p<0.04).

Conclusion: ADI may be an anthropometric predictor for END in acute ischemic stroke patients with large vessel disease.

Disclosure: Nothing to disclose

EP2032

Cancelled

EP2033

Pre-stroke depression symptoms are not associated with an increased risk of delirium in the acute phase of stroke

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Background and aims: Delirium is an acute cognitive disorder that affects between 10% and 48% of patients after stroke and it associated with worse outcome. Depression can precede, coexist or follow the episode of delirium. It was suggested that these two syndromes could share common pathophysiological mechanisms including monoamine transmission and inflammatory reaction. The link between delirium and depression can be seen only in certain populations such as postoperative patients. We aimed to determine association between pre-stroke depression symptoms and risk of post-stroke delirium.

Methods: We recruited patients with stroke or transient ischemic attack admitted within 48 hours from symptoms onset. We assessed delirium on a daily basis during the first 7 days of hospitalization. Diagnosis of delirium was based on DSM-5 criteria. We assessed pre-stroke depression symptoms using depression item from Neuropsychiatric Inventory.

Results: We included 606 patients (median age: 73, 53% female). We diagnosed delirium in 171 patients (28.2%). In logistic regression, we compared upper quartile of depression score to other quartiles. On univariate analysis, higher score of depression was associated with increased risk of delirium (OR 1.58, 95%CI: 1.04-2.40, P=0.03). However, after adjustment for possible confounders: age, atrial fibrillation, diabetes mellitus, stroke severity, pre-stroke cognitive decline, pre-stroke disability, pneumonia and urinary tract infection, this relation did not remain significant.

Conclusion: Pre-stroke depression symptoms are not an independent predictor of delirium in the acute phase of stroke.

Disclosure: The Leading National Research Centre of Medical Faculty of Jagiellonian University funded the collection of data for the study.

EP2034

Pre-stroke cognitive impairment and the course of post-stroke delirium– analysis of delirium duration, symptoms severity, fluctuations and change in cognition

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Background and aims: Cognitive impairment is a wildly recognized risk factor for delirium. Patients with impaired cognition might have more severe delirium due to diminished cognitive reserve. However, it is not clear how pre-existing cognitive impairment is related to other features of delirium including duration, symptoms fluctuations and change in cognition. We aimed to determine association between pre-stroke cognitive impairment (PSCI) and features of post-stroke delirium: symptoms severity and fluctuations, duration and change in cognition.
Methods: We assessed delirium on a daily basis during the first 7 days of hospitalization. Diagnosis of delirium was based on DSM-5 criteria. To assess PSCI we used Informant Questionnaire on Cognitive Decline in Elderly. We used measures based on Cognitive Test for Delirium and Delirium Rating Scale-Revised-98 to assess severity and fluctuations of delirium symptoms. Severity measures included: mean score, peak score, sum of scores. Fluctuations were measured as a change in delirium scores. We calculated change in cognition as a difference between two Montreal Cognitive Assessment scores (done on day 1-2 and day 7-10).
Results: We included 610 patients with stroke or transient ischemic attack. We diagnosed delirium in 171 patients (28%). Among them 60 (35.1%) had PSCI. Patients with PSCI scored worse in all delirium severity measures. There was no difference in delirium duration, symptoms fluctuations and no difference in change in cognition during delirium episode between patients with and without PSCI.
Conclusion: Pre-stroke cognitive impairment is associated with the severity of post-stroke delirium but not with delirium duration, symptoms fluctuations and change in cognition.
Disclosure: The Leading National Research Centre of Medical Faculty of Jagiellonian University funded the collection of the data for the study.

EP2035

The effectiveness of acupuncture treatment on cerebral vasospasm after aneurysmal subarachnoid haemorrhage

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Background and aims: The purpose of this study is to assess the effectiveness of acupuncture treatment on cerebral vasospasm after aneurysmal subarachnoid hemorrhage (aSAH).
Methods: A double-blind, randomized placebo-controlled trial of acupuncture was conducted. Thirty-two patients with aSAH who had undergone aneurysm clipping or coil embolization within 96 hours of onset were enrolled. Participants received combined therapy consisting electroacupuncture and intradermal acupuncture or sham acupuncture, once a day for 2 weeks. The incidence of delayed ischemic neurologic deficit (DIND), angiographic vasospasm, TCD vasospasm and vasospasm-related cerebral infarction were evaluated for 2 weeks. After 2 weeks or at discharge, mortality and rate of subjects who recovered mRS were also examined. Serum nitric oxide (NO) and endothelin-1 (ET-1) concentration were measured.
Results: The incidence of DIND was not significantly different between two groups. The incidence of angiographic vasospasm in the treatment group was lower than the control group. The incidence of vasospasm-related cerebral infarction in the treatment group was lower than the control group. The percentage of subjects who recovered as mRS $\leq$ 2 at 2nd flow up (4 weeks or discharge) was higher in the treatment group than in the control group.
For both serum NO and ET-1 level, there was a significant difference during 2 weeks only in non-vasospasm group, not in vasospasm group. After 2 weeks' intervention, there was a significant increase in the level of NO in the treatment group.
Conclusion: Acupuncture had a tendency to improve the incidence of DIND, angiographic vasospasm, vasospasm-related cerebral infarction and functional recovery.
Disclosure: Nothing to disclose

EP2036

Cancelled

EP2037

Stroke and TIA mimics in patients referred to a neurological emergency department by outpatient physicians, ambulance physicians and paramedics

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Background and aims: Our aim was to compare the structure and management of conditions mimicking acute cerebrovascular events (ACE, stroke or transient ischaemic attack) between patients referred directly to neurological emergency department (ED) by outpatient physicians, ambulance physicians and paramedics.

Methods: We analyzed consecutive patients referred to a Polish urban neurological ED with suspicion of ACE between 1st January 2014 and 31st December 2014.

Results: There were 128 ACE mimics referred by outpatient physicians, 61 by ambulance physicians and 67 by paramedics. Compared to the other groups, patients refereed by outpatient physicians were significantly younger (median age 66 vs 72 and 73 years), more often female (70.3% vs 54.1% and 56.7%) and with negative history of ACE (80.5% vs 63.9% and 74.6%). We found no significant differences in the history of epilepsy, type of ACE stated on referral, need for neuroimaging in ED, and ratios of neurological to non-neurological ACE mimics (35:93, 22:39, 28:39). However, patients referred by outpatient physicians had a distinct structure of final diagnoses within both neurological (frequent headaches) and non-neurological (frequent very high blood pressure) mimics. The proportion of admissions to a neurological ward despite having ACE mimics in referrals from ambulance physicians was higher than from outpatient physicians (42.6% vs 20.3%, p=0.001) and tended to be higher compared to paramedics (26.9%, p=0.061).

Conclusion: The structure of ACE mimics differs between referrals from outpatient physicians and ambulance physicians or paramedics. However, the need for urgent neurological admission appears to be high only in patients referred by ambulance physicians.

Disclosure: Nothing to disclose.

EP2038

Cancelled

EP2039

A benign presentation of inflammatory cerebral amyloid angiopathy

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Background and aims: Inflammatory cerebral amyloid angiopathy (CAA-ri) is a rare form of meningoencephalitis, presenting with encephalopathy in the majority of patients (74%). Even with imunossupressive therapy, the mortality rate is 33%. We present a case that had a benign presentation with transient symptoms and a full spontaneous recovery.

Results: A 62-year-old-man with a history of hypertension presented in the emergency room with a transient episode of spreading left hemisensory disturbance lasting few minutes. Brain CT scan disclosed a right temporoparietal hypodensity. Brain MRI showed a right temporoparietal white matter lesion, hyperintense on T2- weighted sequences and multiple bilateral corticosubcortical microbleeds in T2*. ApoE genotype was ε4 /ε4. A diagnosis of probable CAA-ri was assumed. Given that the patient remain assymptomatic since admission, a conservative approach was adopted, and steroid therapy and biopsy was postponed. One month later, the patient remained assymptomatic and the MRI showed an almost complete reversion of the temporoparietal lesion while the microbleeds were stable. He remained assymptomatic the following year.

Conclusion: The presented case is consistent with a probable CAA-ri. The presentation with mild, transient and reversible symptoms suggests that this entity might be underdiagnosed.

Disclosure: Nothing to disclose

Cerebrovascular diseases 5

EP2040

Elaboration of new model for predicting early clinical deterioration in patients with acute spontaneous supratentorial intracerebral hemorrhage and secondary intraventricular hemorrhage

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Background and aims: Predicting early clinical deterioration (ECD) in patients with acute spontaneous supratentorial intracerebral hemorrhage (ASSICH) and secondary intraventricular hemorrhage (IVH) is a very important and relevant in modern angioneurology, that can help the practicioners choose optimal treatment approaches to improve its efficacy. The aim was elaboration new statistical model for predicting early clinical deterioration (ECD) in patients with ASSICH and secondary IVH.

Methods: 69 patients (mean age 64.4±1.5 years) were studied during first 24 hours after clinical onset of the disease. Clinical examination included vital signs verification and evaluation by National Institute of Health Stroke Scale, Glasgow Coma Scale, Full Outline of UnResponsiveness (FOUR). Early clinical deterioration was verified in patients with decrease FOUR score ≥1 during 24 hours from the beginning of the disease. Severity of IVH was verified by IVH score (IVHS) using parameters of computer tomography. Secondary IVH volume (IVHV) was calculated by formula: IVHV (mL)=e^(IVHS score/5). Elaboration of prognostic model was made by logistic regression and ROC-analysis.

Results: Out of 69 patients, 19 (27.5%) had ECD. The model with the largest AUC (0.98) was: β=0.04*(systolic blood pressure after 1 hour from admission (mmHg))+0.17*(IVHV(mL))+0.87*(dislocation of transparent partition of the brain (mm))-15.94 (fig.1). Percent Concordant=94.8. The cut-off value of β>-1.06 predicts ECD with sensitivity=87.5% and specificity=95.2%.
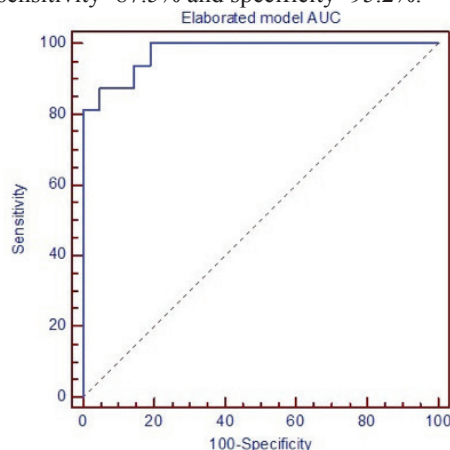
Fig. 1. Elaborated model AUC.

Conclusion: Elaborated prognostic model might be a powerful tool for predicting ECD in acute period of ASSICH and secondary IVH and improving efficacy of treatment.
Disclosure: Nothing to disclose

EP2041

New multivariate prognostic model for predicting early lethal outcome after acute period of spontaneous supratentorial intracerebral hemorrhage with secondary intraventricular hemorrhage

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Background and aims: Identification of vital prognosis in patients with acute spontaneous supratentorial intracerebral hemorrhage (ASSICH) with secondary intraventricular hemorrhage (SIVH) is a very important and relevant in modern angioneurology that can help the practicioners to improve treatment approaches. Therefore the aim was elaboration of new multivariate statistical for predicting ELO after ASSICH with SIVH using clinical and paraclinical parameters.

Methods: 69 patients (mean age 64.4±1.5 years) were studied during the acute period of disease. Clinical examination included evaluation by National Institute of Health Stroke Scale (NIHSS), Glasgow Coma Scale (GCS), Full Outline of UnResponsiveness score (FOUR). Severity of SIVH was verified by the different scores: IVH, Hemphill-ICH, mICH-A, mICH-B, ICH-GS using clinical parameters and parameters of computer tomography. Intracerebral hemorrhage volume (ICHV) and secondary IVH volume (IVHV) were calculated by formulas: ICHV=(a*b*c)/2 and IVHV (mL)=e^(IVHS score/5). Elaboration of prognostic model was made by logistic regression and ROC-analysis.

Results: Out of 69 stroke patients, 13 (18.8%) had died. The model with the largest AUC was: β=-0.09*age (years)+0.17*(NIHSS score at admission)+0.13*(IVHV (mL))-1.37. Percent Concordant=95.6. Elaborated model characterized by higher AUC (0.99) (fig. 1), than used in routine clinical practice standard scores: Hemphill-ICH (0.74), mICH-A (0.81), mICH-B (0.74) and ICH-GS (0.60). The cut-off value of β>-2.18 predicts ELO with sensitivity=91.7% and specificity=92.9%.
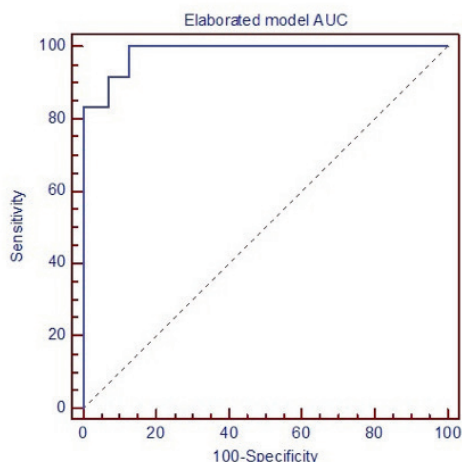
Fig. 1. Elaborated model AUC.

Conclusion: Elaborated prognostic model might be a powerful tool for predicting ELO in ASSICH with SIVH and improving efficacy of treatment.
Disclosure: Nothing to disclose

EP2042
Cancelled

EP2043
Stuttering as stroke presentation

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Background and aims: Acquired stuttering is a rare and poorly understood condition, the majority being of ischemic etiology. It has been described in both dominant and non-dominant hemispheric lesions and in all lobes except the occipital.
Methods: We describe a case of an acquired stuttering as stroke presentation.
Results: 38-year-old right-handed woman, recently diagnosed with hypertension, without history of development stuttering, presented in our hospital with sudden and recurrent episodes of speaking difficulty, with progressive worsening in the past two weeks. Repetitions and prolongations were noted, occurring on grammatical as well as on substantive words, in all positions of the words in the sentence, consistent across every speech tasks (reading, singing), and rarely paraphasias. The remaining neurological examination was unremarkable, except for mild attention deficit. Brain CT was described as normal. Electrocardiogram was unremarkable. Cervical and transcranial ultrasound was compatible with distal middle cerebral artery occlusion. Blood and cerebrospinal fluid investigations were normal, as well as the echocardiogram. Cerebral MRI and MR angiography revealed an acute ischemic lesion affecting the left fronto-parieto-temporo-occipital cortex and lenticulocapsular region, terminal internal carotid and anterior cerebral arteries stenosis, and middle cerebral artery occlusion. Conventional angiography confirmed the previous described and showed evidence of collateral circulation, compatible with a unilateral moyamoya pattern.
Conclusion: We describe a case of a large ischemic lesion presenting only with acute stuttering and rare paraphasias, with the further investigation revealing a moyamoya syndrome. Although frequently attributed to functional disturbances, we emphasize the need to investigate a structural cause in acquired stuttering.
Disclosure: Nothing to disclose

EP2044
Cancelled

EP2045
Cancelled

EP2046
Cancelled

EP2047
Cancelled

EP2048
Cancelled

EP2049
Cancelled

EP2050

Predictors of 3-months functional outcome in nontraumatic intracerebral hemorrhage

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Background and aims: Outcome in patients with intracerebral hemorrhage (ICH) is commonly predicted as 30-day mortality. There are less data concerning factors affecting the long-term and functional outcome. The aim of our study was to determine the prognostic value of ICH baseline parameters for 3-month functional outcome of ICH.
Methods: 89 patients with nontraumatic ICH were included in the study. Evaluated parameters were age, neurological status characterized by National Institute of Health Stroke Scale (NIHSS), hematoma volume measured using 3D Slicer, presence of intraventricular hemorrhage (IVH) and hematoma location categorized as lobar, deep brain (including basal ganglia and thalamus), brainstem and cerebellar. The outcome of interest was 3-months functional outcome classified as good (modified Rankin Scale (mRS) 0-2) and poor (mRS 3-6).
Results: A binomial logistic regression was performed. Of the imputed variables were only NIHSS and age statistically significant. Increasing age and NIHSS score were associated with poor outcome. HR for poor outcome was 1.284 (95% CI 1.159-1.422, p<0.001) for NIHSS and 1.055 (95% CI 1.026-1.084, p<0.001) for age.
Conclusion: Age and the severity of neurological deficit are the crucial baseline parameters for predicting 3-months functional outcome in patients with nontraumatic ICH.
Disclosure: Nothing to disclose

EP2051

Decompressive craniectomy in middle cerebral artery malignant ischemic stroke: 11 years of experience

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Background and aims: Middle cerebral artery (MCA) ischemic stroke has high morbidity and mortality related to cytotoxic edema mass effect. RCT favored better functional and mortality outcome with decompressive craniectomy (DC) in a selected group of patients. We describe the experience of our center.
Methods: Retrospective analysis of clinical charts from every patient with MCA ischemic stroke who underwent DC at our center from January/2006 to October/2016.
Results: Thirty-seven patients were included (average 49 yo): 57% with DC until 48h of symptoms. At 12 months, mRS distribution was: 1 - 2.9%; 2 – 5.7%, 3 – 22.9%, 4 - 40%, 5 – 5.7%, 6 – 22.9%. The 31% who could walk unassisted were younger (40 vs. 53, p=0.034) and had lower GCS score at admission (11±3 vs. 13±2, p=0.038). Mortality was lower for those with smaller infarction area at admission (68% of survivors had <1/3 MCA territory vs. 44.4% of those who passed away, p=0.046). Only younger age was a positive predictor of mRS≤3 [OR=1.07 (IC95% 1.003-1.133)]. Prognosis was not different according to time from symptoms to surgery (average 54h) or incidence of surgical complications.
Conclusion: Our DC patients had the prognostic benefit described in previous studies of DC vs. best medical therapy, with lower mortality and 31% walking unassisted at 12mo. Surgical complications did not impact outcome, favoring the safety of the procedure.
Disclosure: Nothing to disclose

EP2052

Genome-wide association study reveals a distinct locus associated with early neurological status after acute ischemic stroke

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Introduction: Post-event pathophysiological processes are known to influence neurologic status after acute ischemic stroke (AIS) but it is uncertain if genetic factors affect early outcome.

Hypothesis: Early neurological change after AIS is influenced by genetic variants.

Methods: AIS patients were prospectively enrolled at Jagiellonian University in Krakow, Poland. Early change in neurological status was assessed by NIHSS scores taken within 6 hours of stroke onset, and after 24 hours, using ΔNIHSS24h=NIHSS6h–NIHSS24h. Genotyping was generated for common variants, imputing up to 4 million SNPs. A GWAS was performed using the model: ΔNIHSS24h =ΔNIHSS6h-NIHSS24h, age, sex, SNP, PCA1-2. The population was analyzed through overall statistical analysis taking into account population mixing (MANTRA).

Results: 111 patients (ages 32-95, 47% female) were found to have an NIHSS6h score of 6 (IQR 10) and ΔNIHSS24h score of 2 (SD 5). One novel locus influenced ΔNIHSS24h with genome-wide significance (Figure): rs11670808 in an intron of NLRP11 (chromosome 19) was identified. NLRP11 encodes NLR family pyrin domain containing 11; a part of a subfamily of proteins called NALPs. NALPS are a subset of the CATERPILLAR protein family, a large family of inflammation regulators. NLRP11 is involved in cell signaling by inflammasomes, complexes that activate caspase 1 and in turn pro-inflammatory cytokines IL-18 and IL-1β.
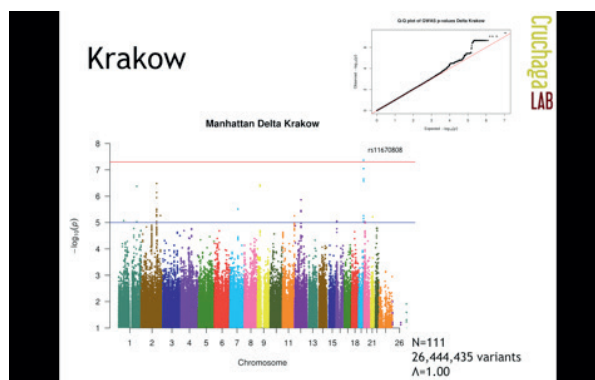
GWAS for Delta NIHSS

Conclusion: In our population of AIS patients, we found a genetic locus that influences early neurological change after AIS. This gene has been shown to be implicated in inflammatory processes, particularly in activation of pro-inflammatory cytokines. Replication in an independent cohort is ongoing.

Disclosure: This study is funded by a grant from the NIH, and also a training grant from the American Heart Association/American Stroke Association.

Clinical neurophysiology

EP2053

Neurophysiological characteristics of restless legs syndrome in Parkinson`s disease

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Background and aims: Restless legs syndrome (RLS) in patients with Parkinson`s disease (PD) occurs more frequently than in general population. It is caused by hypofunction of diencephalic-spinal dopaminergic tracts leading to changes in excitability of the spinal segmental apparatus with development of sensory-motor disorders.
Aim: To investigate the neurophysiological features of RLS in PD.
Methods: We investigated somatosensory evoked potentials (SEPs), blink reflex (BR) and sympathetic skin response (SSR). 82 patients with PD aged 40-70 years were examined: 36 with RLS (1st group) and 46 -without RLS (2nd group). 30 healthy individuals were included in the control group.
Results: SEPs study revealed that in the 1st group, the interpeak intervals (IPI) N9–N13, N11–N13 were significantly shorter and the IPI N13-N20 was longer as compared with 2nd group. A significant increase in the amplitudes N20-P23 and N13-P18 was also revealed in the 1st group, which reflects sensitization processes in patients with RLS. SSR study revealed prolonged latent period and an increase in the peak amplitude in the 1st group and positive correlation between the severity of RLS (according to International RLS Severity Scale) and SSR latency. Trend to hyperexcitability answers of BR was observed, which reflects insufficiency of the inhibitory mechanisms at the segmental level and deficiency of suprasegmental descending control in PD patients with RLS.
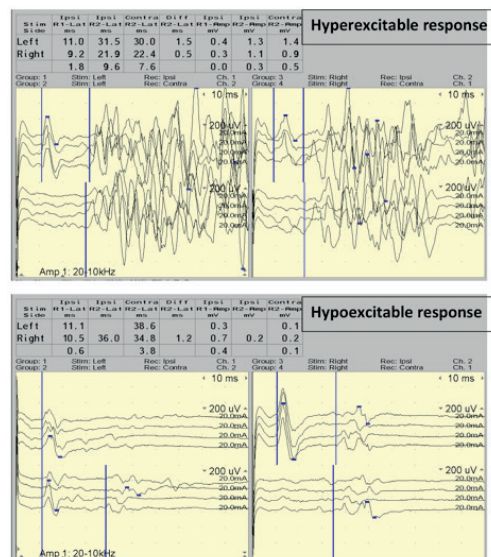
Fig. Examples of the BR registration

Conclusion: A change in the complex interaction between the peripheral, spinal and cerebral divisions of the nervous system was revealed in RLS. Somatosensory disturbances and changes in brainstem and spinal reflexes probably determine the clinical features of RLS in PD.
Disclosure: Nothing to disclose

EP2054

Navigated transcranial magnetic stimulation in differential diagnosis of amyotrophic lateral sclerosis (ALS) and ALS mimic syndromes

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Background and aims: Signs of upper motor neuron involvement are often difficult to elicit in patients with ALS, especially at the early disease stages. The present study aims at investigating diagnostic possibilities of navigated transcranial magnetic stimulation (TMS) in patients with ALS and ALS mimic syndromes.
Methods: A total of 28 patients with pure lower motor neuron syndrome, suspected ALS or possible ALS were recruited into the study. Navigated TMS (NBS eXimia Nexstim) included measurement of resting motor threshold (MT), central motor conduction time (CMCT), cortical silent period (CSP) duration and paired-pulse stimulation with measurement of short-interval intracortical inhibition (SICI) and intracortical fascilitation (ICF). Also we mapped cortical representation of musculus abductor pollicis brevis and analyzed the size of muscle representation and the weighted size.
Results: After extensive investigations and clinical follow-up during 6-12 months 9 patients were diagnosed with ALS mimic syndromes (multifocal motor neuropathy, Kennedy's disease, Hirayama's disease), 19 patients were eventually diagnosed with ALS. There was a significant reduction in SICI (p<0.001) and CSP duration (p<0.001) in ALS patients compared to patients with ALS mimic syndromes. The weighted size of muscle representation was significantly smaller in patients with ALS (p<0.05), although the size of muscle representation was not significantly different. There was no significant difference in CMCT, MT and ICF across the groups.
Conclusion: A reduction in SICI and CSP duration (indicative of motor cortex hyperexcitability) and decrease in the weighted size of muscle cortical representations may be considered as diagnostic biomarkers that distinguish ALS from mimic syndromes.
Disclosure: Nothing to disclose

EP2055

Shaky legs: The clinical spectrum and treatment of primary orthostatic tremor; a systematic overview

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Background and aims: Orthostatic tremor (OT) is characterized by a high-frequency tremor of the leg muscles during stance, resulting in an unsteady feeling. Although an increasing number of publications on OT reflect a growing scientific interest in the disorder, pathophysiology is still not understood. Treatment options are limited and often not satisfactory. A systematic literature search on primary OT is lacking the literature.

Methods: Here we review data of a total of 617 primary OT-patients, retrieved after a systematic search in Pubmed (583 individual patients from 45 case reports, 20 case series, and 7 therapeutic trials) and from a questionnaire-based study in Dutch OT-patients (n=34).

Results: Overall, 67% of primary OT patients is female; mean age at onset is 57 (17-81) years. Six percent (22 of 390 cases) has a positive family history for OT. Mean delay to diagnosis is 7.7 years (n=268). A substantial number of patients reports falls. Quality of life is affected. Clonazepam is the most prescribed drug, but is not always effective. Trials report a possible positive effect of gabapentin. Deep brain stimulation (DBS) has shown a positive effect in 6 out of 7 patients.

Conclusion: Primary OT can be disabling and is under-recognized. The most effective treatment remains uncertain, with some evidence for gabapentin and clonazepam. DBS provides an alternative for drug-resistant and disabling OT, although long term effects are still uncertain. Increasing attention for OT will probably shorten the delay in time to diagnosis and possibly lead to development of better treatment options.

Disclosure: Nothing to disclose.

EP2056

Cancelled

EP2057

Somatosensory evoked potentials (median SEP) in multiple sclerosis: Influence of montage on latency, amplitude and central conduction time and implication for multicentre trials

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Background and aims: To determine comparability of two recommended recording montages of median somatosensory evoked potentials (SEP), as SEP are part of multimodal EP which may becomean outcome measure in multicentre clinical trials.

Methods: 81 patients with relapsing multiple sclerosis (MS)(mean age: 37.5y, median EDSS: 2.0) and 49 healthy controls (HC) had median SEP recordings with high-resolution EEG. Two standard montages were extracted : M1 (C3'/C4'-Fz, C7-Fz) and M2 (C3'/C4'-C4' /C3', C7-EP contralateral). N20 and N13 latency, N20-P25 amplitude and central conduction time (CCT) were independently evaluated by two neurophysiologists (VB, MH) blinded to diagnosis using EPMark. Nine artifactual curves (4%) were excluded.

Results: To determine the physiological effect of montages and not the effect of uncertainty in rating, 12 curves (5%) with a N20-latency difference >2 msec between montages were excluded. In HC, N20 and N13 latencies in M1 were significantly ($p<0.05$) longer than in M2 (mean difference: 0.17 and 0.39msec). In MS patients, only N20 latency differed (0.21msec). Differences in CCT (HC: 0.19, MS: 0.21 msec) were not significant. Amplitudes were 40% and 41% smaller in M2 compared to M1 ($p<0.001$).

Conclusion: N20-latency is significantly later in Fz-compared to ipsilateral C'-reference independent of group, most likely due to injection of a frontal positivity. This difference is 2-6x smaller than variability in HC and thus clinically not relevant. The much higher amplitude favours Fz-reference. However, in clinical trials both montages may be employed in parallel as the technicians' routine is important in achieving standardized follow-up assessments.

Disclosure: VB received a travel grant from the European Academy of Neurology (EAN). The study was supported by the Swiss National Science Foundation (SNF; grants 33CM30-140338 and 326030_128775).

EP2058
Cancelled

EP2059

Small fiber neuropathy in neurological diseases: Contribution of laser-evoked potentials

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Background and aims: Many studies documented the presence of small fiber neuropathy (SFN) in different neurological diseases, such as Amyotrophic lateral sclerosis (ALS) and Fabry disease (FD). Laser-evoked potentials (LEPs) are an emerging neurophysiologic technique to evaluate small fiber involvement, even if no clear data are available concerning their sensitivity, compared to skin biopsy.
Methods: We recruited 34 patients (age 56.2±13.2): 10 ALS patients (5 M, 5 F), 10 FD patients (10 F) and 14 patients with diagnosis of acquired small fiber neuropathy (6 M, 8 F), in order to evaluate LEPs sensitivity. All patients had previously undergone skin biopsy (from thigh and lower leg, using a 3mm punch), disclosing decreased epidermal nerve fiber density. LEPs were carried out using a Nd-YAP laser (1340nm) by stimulating hand, foot and face skin surface.
Results: 74% of patients showed abnormalities of LEPs, respectively 80% in ALS, 60% in FD and 79% in other SFN, with absent LEPs (40%), decreased amplitude (33%), increased latencies (20%) or both (7%). Comparing face, hand and foot, A-δ LEPs were more often abnormal recording from foot (41%). Interestingly, C fibers in the trigeminal territory showed the highest abnormalities (50% of patients).
Conclusion: LEPs showed a good sensitivity in evaluating SFN. Our findings of a higher involvement of C fibers rather than A-δ in SFN deserve a better characterization. However, this study needs to be extended to a larger number of patients, before drawing any definite conclusion.
Disclosure: Nothing to disclose

EP2060

Electromyographic study of thoracic paraspinal and rectus abdominis muscles in the diagnosis of ALS

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Background and aims: The diagnosis of definite Amyotrophic lateral Sclerosis (ALS) requires the presence of upper and lower motor neuron involvement in three spinal regions. The aim of this study was the comparison of active denervation (fibrillation and /or positive sharp wave potentials) in Thoracic paraspinal muscles (T- PMS) with those in Rectus abdominis (RA) in patients with definite ALS.
Methods: Needle electromyographic study (EMG) with concentric needle electrode was performed in T-PSM at T8-T10 level and in RA of 95 patients with ALS.
Results: 95 patients with definite ALS were investigated, 50 men and 45 women, of median age 61.2 yrs (30-83). Active denervation was found more frequently in T-PSM than in the RA (80% vs 65%, p<0.05). Increasing age was related to more severe denervation in the RA (p<0.01). Duration of symptoms, Creatine Kinase levels, sex, initial symptoms (upper limb, lower limb or bulbar), degree of denervation and Revised ALS Functional Rating Scale score were not associated with RA and T-PSM denervation.
Conclusion: T-PMS EMG is recommended for the detection of active denervation in patients with ALS. In case of normal EMG in RA, T- PSM must also be tested. On the contrary, absence of active denervation in T-PSM is rarely associated with active denervation in RA.
Disclosure: Nothing to disclose

EP2061
Cancelled

EP2062

Segmental contact heat-evoked potentials in healthy controls and diabetic polyneuropathy patients

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Background and aims: Contact heat-evoked potentials (CHEPs) provide a means of assessing functional impairment of small nerve fibres and the spinothalamic pathway. The aim of this study was to investigate the impact of physiological and test variables on CHEPs latency and amplitude parameters, and to determine the applicability of the method for diabetic neuropathy (DN) patients.

Methods: In 30 DN patients and 70 healthy subjects, standard CHEPs were tested at wrist and ankle (C6, C8, L4 and L5 dermatomes) using two algorithms: "basic" with temperatures ranging from 35º to 50ºC and "intensive" from 42º to 52ºC). Latencies and amplitudes of N2/P2 response, together with tolerability of the thermal stimuli were (semi-quantitatively) evaluated.

Results: CHEPs were largely well-tolerated and responses could be evoked in most of the individuals tested. Latencies were shorter and amplitudes higher at the wrist compared to the ankle, as they were when applying the intensive algorithm compared to the basic one. The differences between the C6 and C8 dermatomes (as well as between L4 and L5) were not significant. Amplitudes decreased with age, while latencies increased slightly with age and height. At group level, reduction of amplitudes constituted the major difference between healthy controls and DN patients.

Conclusion: CHEPs are an efficient and well-tolerated method of functional testing of pain-related tracts both in healthy controls and DN patients. Age, height, testing algorithm and the area tested need to be considered in the interpretation of the results. Reduction of amplitudes appears to be the most prominent abnormality in DN patients.

Disclosure: Nothing to disclose

EP2063

Tibial somatosensory evoked potentials predict walking speed in early multiple sclerosis

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Background and aims: We aimed to to evaluate somatosensory evoked potentials of the tibial nerve (SSEPt) in correlation with timed 25 foot walk test (T25FW) and MRI findings in patients with first symptom of multiple sclerosis (MS).

Methods: In 120 MS patients (mean age 32.2±8.7 years, 84 females), EDSS, T25FW, brain and spinal cord MRI and SSEPt were performed. P40 latencies and N22a-P40 interlatency were analyzed and zscore for each latency was calculated and combined into SSEPt zscore. MRI was analyzed for the presence of brainstem and cervical spinal cord lesions.

Results: Walking speed measured with T25FW significantly correlated with SSEPt zscore (rs=0.211; p=0.021). When looking each component of the SSEPt separately, T25FW significantly correlated with left P40 wave latencies (rs=0.223; p=0.014) and N22a-P40 interlatencies (rs=0.241; p=0.008). There were no significant correlations for other SSEPt parameters. Furthermore, patients who presented with transverse myelitis (N=41) and patients who had spinal cord lesions on the MRI had significantly higher SSEPt zscore compared to other patients (0.07 vs. -0.28, p=0.019 and -0. 02 vs -0.38 p=0.023; respectively). A linear regression was calculated to predict T25FW based on SSEPt zscore, age, gender and cervical spinal cord MRI lesions. Significant regression equation was found (F(4,87)=6.815, p<0.001), with an R2=0.239. SSEPt zscore corrected for age, gender and cervical spinal cord MRI lesions is statistically significant predictor for T25FW (B=0.268, p=0.023).

Conclusion: In MS patients SSEPt is a potential marker of walking speed and indicates presence of functional impairment at the level of the spinal cord.

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EP2064

Sensory fibers in Martin-Gruber anastomosis: An electrophysiological study

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Background and aims: Anatomical variations in the innervations of intrinsic hand muscle are well known as Martin-Gruber anastomosis (MGA), spread from the median to the ulnar nerves in the forearm. This anastomosis predominantly consists of motor axons, with rare sensory contribution. Although anatomical studies have shown that a crossover of sensory fibers is not rare in Martin-Gruber median-ulnar anastomosis, it has been electrophysiologically described only in rare subjects. The aim of our study was to investigated the frequency of sensory fibers in MGA.

Methods: In order to demonstrate the presence of sensory fibers in MGA, we stimulated the median nerve at the elbow and recorded the antidromic sensory potential from ulnar innervated digit (5th finger), using surface electrodes.

Results: A total of 113 arms were analyzed with presence of motor MGA. Sensory MGA were present in 35 arms (30.9%). There were 59 left hands with motor MGA, of which 15 (25.4%) were with sensory MGA, and 54 right hands with motor MGA, and 20 (37%) of them had sensory MGA. There was no a significant difference between the presence of sensory fibers depending on the right or left hand (p=0.56), or the sex (p=0.49).

Conclusion: The presence of sensory fibers in MGA median-ulnar anastomosis by electrophysiological study is not rare. Knowledge of the anatomical variations relating to the innervation of the hand has great importance, especially with regard to physical examination, diagnosis, prognosis and surgical treatment.

Disclosure: Nothing to disclose

EP2065

Self-rated health and sense of coherence in multiple sclerosis patients

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Background and aims: Multiple sclerosis (MS) is a chronic disease with psychosocial ramifications. Sense of coherence (SOC) refers to the extent to which life is perceived as comprehensible, manageable, and meaningful. It might play role in self- rated health (SRH), which lowly scored, predicts poor health outcomes. The aim of this study was to examine the association between SOC and SRH in MS patients.

Methods: 134 patients completed a socio-demographic questionnaire, the first item of the Short Form-36 Health Survey, and Short form-13 Orientation to Life Questionnaire. Physical disability was assessed using Expanded Disability Status Scale. SRH was dichotomized into poor health- and good health- group (cutoff score 25). T-test and chi-squared test were used to estimate the differences between the groups. Logistic regression was performed to investigate the effect of SOC on SRH when adjusting for sociodemographic and clinical variables.

Results: The good SRH patients were younger (p< 0.001), with relapsing- remitting MS (p< 0.001), less disabled (p< 0.001), with higher SOC (p=0.002), employed (p= 0.002), and on immunotherapy (p= 0.01). The logistic regression analysis showed that, after adjusting for other variables, an incremental change of SOC by one unit, increases the odds of reporting good SRH by 10.5% (Odds Ratio 1.05; 95% Confidence Interval 1.02-1.09).

Conclusion: This study shows the positive effect of higher SOC on perceived health in MS patients. Strategies oriented to enhance SOC may promote health and reduce poor outcomes.

Disclosure: Nothing to disclose

EP2066

A neurophysiological study of small-diameter nerve fibers in the hands of hemodialysis patients

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Background and aims: The prevalence of uremic polyneuropathy varies between 60 and 100% and remains a major disabling feature in the life of uremic patients. The aim of the present study was to evaluate the function of small-diameter A-delta nerve fibers, in the hands of hemodialysis patients.

Methods: A total of 38 randomly selected patients treated three times weekly with hemodialysis were evalueted. The control group consisted of 38 age-matched healthy subjects. The mean age of hemodialysis patients and healthy subjects did not diffeer significantly.

The function of A-delta nerve fibers was measured by cutaneous silent period (CSP). CSP was elicited by nociceptive electrical square pulse stimulation using bipolar electrodes at the palmar distal tip of digit II, stimulating median nerve fibers. Recording electrodes were placed over thenar muscles in the standard the position as for median nerve motor conduction study. CSP onset and end latency, and the difference between the two latencies – duration of CSP (muscle acttivity suppression), were calculated.

Results: The mean CSP onset latency in hemodialysis patients with and without arteriovenous fistula was markedly longer compared with the control group (p<0.0001). The same relationship was found for CSP end latencies. CSP duration did not demonstrate any difference between the two groups. CSP onset latency was obseerved in 12/38 (32%) hemodialysis patients.

Conclusion: The evaluation of CSP is a useful method for detecting the function of A-delta fibers. The delayed CSP onset latency observed in 1/3 of hemodialysis patients reflects the impairment of the afferent conduction of A-delta fibers.

Disclosure: Nothing to disclose

Cognitive neurology/neuropsychology 2

EP2067

A descriptive analysis of behavioural and psychological symptoms in logopenic variant of primary progressive aphasia

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Background and aims: The logopenic variant of primary progressive aphasia (lvPPA) is a distinctive variant of PPA, in which recent evidence shows that Alzheimer disease (AD) might be the most common underlying pathology. Our goal is to evaluate the frequency of behavioural and psychological symptoms (BPS) in lvPPA.

Methods: This is a descriptive study that prospectively recorded data of 20 consecutive patients who met lvPPA criteria: word retrieval and sentence repetition deficits, phonologic paraphasias, sparing of single word comprehension and motor speech, absence of frank agrammatism and predominant left posterior perisylvian or parietal atrophy on MRI and/or hypoperfusion or hypometabolism on SPECT or PET (Gorno-Tempini ML et al, 2011) at the Hospital Universitario de Salamanca, Spain (mean age at onset 73.1±4.9 years, mean duration of dementia 3.8±2.3 years, 55% women). The Neuropsychiatric Inventory (NPI) was used to assess BPS.

Results: At least one BPS occurred in 100% of lvPPA participants, the median NPI score was 34 (range:10-86), with a median number of 5 symptoms per patient. The most frequent symptoms were anxiety (80%), depression (70%), apathy (70%) and sleep disturbances (60%), followed by agitation (50%), disinhibition (50%), appetite/eating abnormalities (45%), irritability (40%), aberrant motor behaviour (40%), hallucinations (35%), delusions (25%) and euphoria (10%). It is remarkable that 7 of 9 patients with appetite/eating abnormalities showed hyperphagia.

Conclusion: BPS are frequent in lvPPA. New investigations are required to better evaluate the relationship between histopathologic evidence of specific neurodegenerative pathologies in lvPPA (e.g. AD, frontotemporal lobar degeneration [FTLD]-TDP, other) and different BPS profiles.

Disclosure: Nothing to disclose

EP1046

Complex visuo-constructive deficits in subjective memory complaint: A combined quantitative and qualitative study

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Background and aims: Subjective Memory Complaint (SMC) is a possible prodrome of Alzheimer's disease (AD) dementia. Objective impairments in SMC may be revealed by in-depth neuropsychological evaluations. Hereby, we analysed in SMC subjects complex visuo-constructive performances and their relationship with basic cogntiive functioning in order to detect subtle impairments and possible correlation with working memory and executive performances.

Methods: Thirty-seven SMC subjects (10 male; age=67.27±5.53 years; education=12.86±3.29) were enrolled. All participants completed a detailed neuropsychological battery. A combined quantitative and qualitative scoring approach was used to analyse Clock Drawing Test (CDT) and Rey-Osterrieth Complex Figure (ROCF) performances. Correlations between CDT/ROCF and other cognitive scores were explored.

Results: Twenty-five subjects presented with a subjective memory disorder (i.e., no objective cognitive deficit), while 12 subjects showed objective impairments at memory, executive and/or visuo-constructive tasks. Statistical analyses highlighted significant correlations between the number of "omitted elements" at both CDT and ROCF tasks and working memory abilities (i.e., Digit Span backward). Additionally, the number of "distortion" (i.e., element incomplete but placed properly) at the ROCF task was correlated with attentional/executive (i.e., Trial Making Test B) performances.

Conclusion: In this study, we provided evidence in SMC subjects of impairments at non-memory tasks including complex visuo-constructive tests. These were crucially affected by working memory and attentional/planning deficits. Our results suggest the importance of a careful cognitive assessment of non-memory domains in case of SMC in order to obtain a better diagnosis and make prediction of the possible evolution.

Disclosure: Nothing to disclose

EP2068

Brain wave entrainment using alpha frequency binaural beats on adolescent swimmers

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Background and aims: Binaural beats combined with music therapy and mental training skills were more effective in increasing α waveswas suggessted to improve anxiety in swimmers.

Aim: The effect of brain wave entrainment in swimmers using binaural beats set at alpha range was investigated. EEG and reaction time were measured before and after sessions of relaxation techniques, music therapy and mental training with and without binaural beats.

Methods: 11 adolescent elite swimmers(4 females , 7 males) were subjected to 18 sessions of mental training skills including relaxation techniques, positive thinking and imagery. 7 swimmers were randomly assigned to group I and received sessions of binaural beats and music therapy and the other 4 to group II receiving just music therapy.(both groups were blind to the music type)EEG and reaction time was measured pre and post the sessions. A written conscent was taken from the parents prior to the study.

Results: There was a significant EEG waves change during the relaxation time (p=0.05) and positive thinking phase (p=0.05) The EEG frequencies significantly decreased (both qualitativly and quantitiativly) in swimmers included in group I(with the beats) than those in group II. In addition to this statistically significant improvement in the reaction time in their performances observed in group I, which was significantly shorter (p=0.01) compared to group II.

Conclusion: Relaxation techniques and binaural beats added to music may have a positive effect on atheletic performance of swmmers

Disclosure: Nothing to disclose

EP2069

Cancelled

EP2070

Motor aspects of daily living are inversely associated with anxiety and dysphoria in Parkinson's disease dementia but not in dementia with Lewy bodies

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Background and aims: Lewy body dementia syndromes present motor impairment and neuropsychiatric symptoms among their main manifestations. It is unclear how motor experiences are associated with behaviour in these patients.

Methods: Participants with Parkinson's disease dementia (PDD) or dementia with Lewy bodies (DLB) were screened with the Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS) and the 12-item Neuropsychiatric Inventory. All tests were correlated with each other by way of linear regressions, significance at $\rho<0.05$.

Results: We included 50 patients - 14 patients with PDD (28.0%) and 36 patients with DLB (72.0%); 23 (46.0%) had mild dementia, 17 (34.0%) had moderate dementia, and 10 (20.0%) had severe dementia; 21 (42.0%) used Levodopa (12 with PDD, 9 with DLB), 34 (68.0%) used cholinesterase inhibitors (9 with PDD, 25 with DLB), 25 (50.0%) used anti-depressants (9 with PDD, 16 with DLB), and 24 (48.0%) used anti-psychotics (6 with PDD, 18 with DLB). For PDD, MDS-UPDRS Part II (Motor Experiences) was inversely associated with anxiety ($\rho=0.0372$) and dysphoria ($\rho=0.0162$) total scores, but not with other symptoms ($\rho>0.07$). Also for PDD, MDS-UPDRS Part III (Motor Examination) was inversely associated with anxiety ($\rho=0.0339$) and dysphoria ($\rho=0.0157$) total scores, but not with other symptoms ($\rho>0.07$). No behavioural symptoms were associated with MDS-UPDRS scores for patients with DLB ($\rho>0.10$).
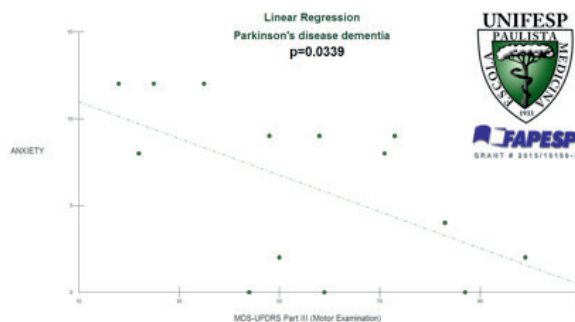
Association of anxiety scores with MDS-UPDRS Part III in Parkinson's disease dementia.
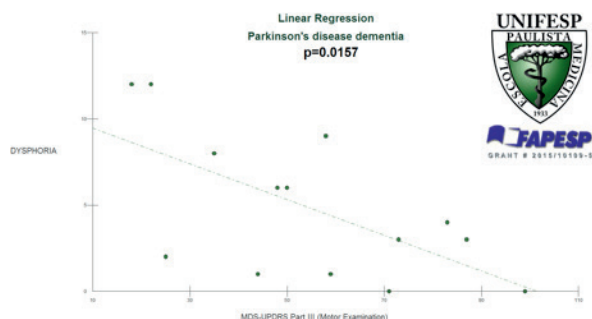
Association of dysphoria scores with MDS-UPDRS Part III in Parkinson's disease dementia.

Conclusion: Anxiety and dysphoria usually occur when motor signs and symptoms involved in experiences of daily living are less burdensome in PDD, but not in DLB.

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EP2071

Foreign accent syndrome: Functional or structural cause?

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Background and aims: Foreign accent syndrome (FAS) is a rare motor speech disorder where the affected person speaks in an accent different from their mother tongue. FAS may be organic, with or without structural lesions, or functional and the distinction might be difficult.

Methods: We report two similar FAS cases with presumed different etiologies.

Results: A 27-year-old Portuguese woman presented with an acute motor aphasia and right motor deficit secondary to a left M1 occlusion. She was treated with thrombectomy, maintaining distal M2/M3 occlusion. After the procedure, she gradually recovered all deficits. Her speech was normal beside presenting a foreign spanish accent. The patient had recently started having spanish lessons. Head-CT after 24 hours revealed a left insular and lenticular/capsular infarction. The foreign accent spontaneously resolved after a week. A 36-year-old Portuguese woman presented with a facial asymmetry mimicking a left peripheral facial nerve palsy after spending a week at London. She gradually developed a left motor deficit with gait impairment, visual symptoms and started talking with a foreign accent perceived as english. She also presented a left hand postural tremor that disappeared with distraction maneuvers. Brain MRI and CSF study was normal. Assuming a functional cause, she started sertraline, speech therapy and psychotherapy with partial improvement. During follow-up she had a normal speech for a year while on homeopathic medications. Recently she reappeared at consultation with a minor foreign accent, evident when on stressful situations.

Conclusion: These two cases highlight different features of functional and organic causes of foreign accent syndrome and possible treatment approaches.

Disclosure: Nothing to disclose

EP2072
Cancelled

EP2073

Neuropsychological disorders in early Parkinson's disease and vascular parkinsonism: Experience in Kyrgyz Republic

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Background and aims: Neuropsychological disorders accompany Parkinson disease (PD) and Vascular Parkinsonism (VP) on every stage of development, in clinical semiology, causing a great impact on patients' life-quality.
Objective: investigate existence and evidence of neuropsychological disorders in PD and VP patients.
Methods: 31 patients were studied (18 females, 13 males), where 23 suffered from PD, and 8 – VP. Average age – 64.42±1.1, disease severity Hoehn and Yahr average stage – 2.5±0.8. Patients were studied by clinical, bedside examination, somatic and neurological status check, global cognitive function: Mini-Mental State Examination and Montreal Cognitive Assessment (MMSE and MoCA), Zung Self-Rating Depression scale, and Spielberger anxiety scale; instrumental examination (ECG, brain MRI). Statistical analysis is done by SPSS.
Results: Average depression level – 52.7±7.3 of all patients: mild and moderate depression in 82.6% with PD, and 37.5% with VP. 64.5% of all patients suffered increased level of anxiety: PD 78.2%, VP 25%. Cognitive disorders analysis (MMSE, MoCA): mild and moderate cognitive disorders in 30.4% of PD, when 75% of VP patients had moderate and severe cognitive disorders. 64.5% of all patients suffered sleep disorders, insomnia and daytime sleepiness: PD 82.6% and VP 37.5%.
Conclusion: Severe cognitive disorders were observed in Vascular Parkinsonism more often, while mild cognitive disorders were observed in patients with Parkinson Disease. Neuropsychological disorders such as depression, anxiety, and sleep disorders are more frequent in PD patients, though still observed in VP, which suggests a common development mechanism for these disorders.
Disclosure: Nothing to disclose

EP2074

Neuropsychological assessment in initial Hoehn and Yahr clinical stages of Parkinson's disease

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Background and aims: To compare cognitive performances in newly diagnosed patients with Parkinson's disease (PD) at Hoehn and Yahr (HY) stage I or stage II at their first medical evaluation.
Methods: Forty-four drug-naïve patients with newly diagnosed PD at HY Stage I and 40 patients at HY Stage II, matched for all variables but UPDRS total score and its sub-scores, completed a standardized neuropsychological battery. A one-way multivariate analysis of variance (MANOVA) was used to compare cognitive scores of the groups, complemented by Bonferroni corrected univariate analysis of variances (ANOVA). Finally, the prevalence of mild cognitive impairment (MCI) was estimated for patients classified in HY stage I or II.
Results: A general significant difference was found between patients at HY stage I or stage II on neuropsychological performances ($^=.645$, $F_{(16, 67)}=2.31$, $p=.009$), with patients at HY stage I showing higher scores than patients at stage II. Moreover, univariate ANOVAs revealed significant differences between HY stages on Rey's auditory verbal learning test-immediate recall ($p<.0001$), prose recall test ($p<.002$), 10 points Clock Drawing Test ($p<.002$), and, Rey-Osterrieth Complex Figure Test-copy ($p<.002$). PD-MCI occurred in 5 of 44 (11.36%) patients in the HY stage I, and in 15 of 39 (38.46%) patients in the HY stage II.
Conclusion: In drug-naïve, newly diagnosed PD patients, motor disability is associated with cognitive deterioration and higher rate of prevalence of mild cognitive impairment at the first medical evaluation (HY stage).
Disclosure: Nothing to disclose

EP2075

Primary progressive aphasia: A case study

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Background and aims: Primary Progressive Aphasia (PPA) is a selective and progressive form of neurodegenerative disease characterized by declining language function. The disease starts with word-finding disturbances (anomia) and frequently proceeds to impair the grammatical structure (syntax) and comprehension (semantics) of language. The clinicopathological correlations in PPA emphasize the contributory role of dementia with Pick's bodies, other taupathies, and TDP-43 proteinopathies. PPA affects five general linguistic skills: oral and written naming, reading, repetition and general comprehension. Standardized language testing and Neuroimaging is important to diagnose and follow the course of the disease.

Methods: A 83-year-old Caucasian right-handed male first presented in July 2005 with progressive speech difficulty for 4 years. We followed-up the patient over the course of 9 years in the Memory Clinic with Neuropsychological evaluation and radiological imaging. His recent visit demonstrated progressive deterioration of speech and language function with intact comprehension. Neuropsychological evaluation demonstrates Expressive aphasia without paraphasias or comprehension problems. He possesses Normal naming capabilities but abnormal repetition.

Results: SPECT Perfusion studies show severe perfusion reduction in the left temporal lobe with mild perfusion reduction extending into the left frontal and parietal cortex. Right temporal lobe perfusion uninvolved. Posterior cingulate perfusion preserved
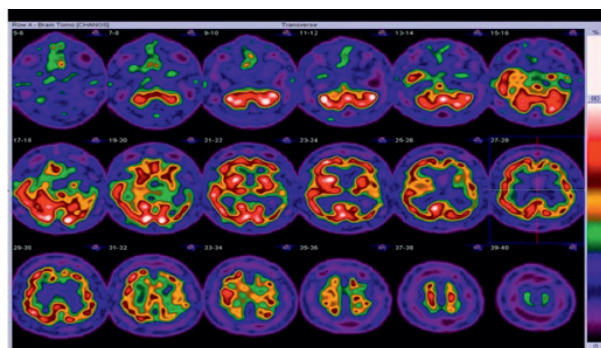
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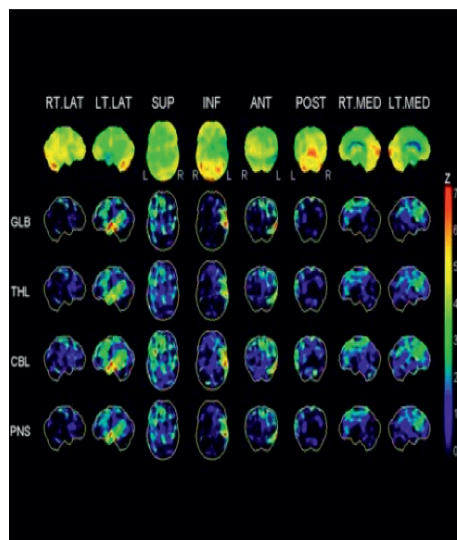
SPECT Perfusion study
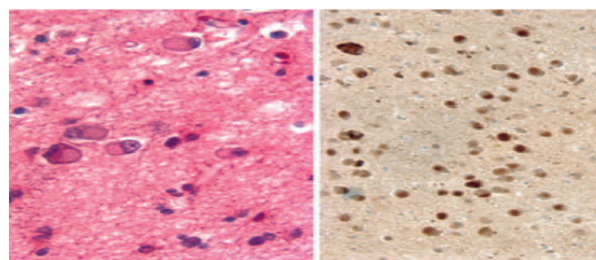
Presence of Pick bodies on immunohistochemistry

Conclusion: Approximately 10 percent of dementias present as primary progressive aphasia.The disease is progressive and unfortunately, no precise treatment modality is present to halt the progression. Speech and occupational therapy is the mainstay of management. High-frequency repetitive Transcranial Magnetic Stimulation (hf-rTMS), applied to the left prefrontal cortex, may improve the linguistic skills in Primary Progressive Aphasia (PPA).

Disclosure: Nothing to disclose

EP2076

Cognitive dysfunction in six patients with anti-NMDA receptor encephalitis

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Background and aims: Anti-NMDA receptor (anti-NMDAr) encephalitis is a recognized cause of rapid onset encephalopathy with wide phenotypic variability. The clinical presentation includes psychiatric manifestations, memory impairment, seizures, movement disorders, autonomic instability and somnolence. The cognitive profile of these patients is yet to be clarified.

Methods: We performed a retrospective review of clinical and neuropsychological data (Dementia Rating scale-2, DRS-2) of six patients with anti-NMDAr encephalitis followed at Centro Hospitalar do Porto.

Results: Three males and 3 females were included. The first manifestation of the disease occurred between age 8 and 26. None of the patients had an underlying neoplasm. The cerebral MRI had persistent lesions in two patients. Five patients had cognitive evaluations at two different time points (the gap between evaluations varied from 4 months to 4 years). In the acute/subacute phase, one patient scored 135 on DRS-2, while the remainder 4 scored between 63 and 120. Affected domains included attention, language, memory and executive functions. The 4 patients with severe cognitive impairment presented with severe acute psychosis (n=2) and seizures (n=2). Two of these patients were younger than 18 years. In 3/4 patients a follow-up evaluation was performed that showed significant cognitive improvement (DRS-2 125 to 134).

Conclusion: This case series confirms the presence of significant dysfunction in different cognitive domains in the acute/subacute phase of anti-NMDAr autoimmune encephalitis. All patients with follow up evaluation showed substantial cognitive improvement, although some deficits persisted. Cognitive dysfunction was more frequent in patients presenting with psychiatric symptoms or seizures.

Disclosure: Nothing to disclose

EP2077

Possible decline of social cognition in amnestic mild cognitive impairment

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Background and aims: Theory of Mind (ToM) refers to the ability to attribute mental states to other people behavior; it can relate to people feelings (affectiveToM) or intentions (cognitiveToM). Several studies showed an impairment of ToM abilities in neurodegenerative diseases, with conflicting results in patients with Mild Cognitive Impairment (MCI). Our study aims to investigate ToM in MCI.

Methods: We enrolled 36 subjects: 16 with amnestic MCI (aMCI) and 20 healthy controls (HC), matching them for sex, age and educational level. Neuropsychological evaluation included tests to evaluate cognitive status, memory, reasoning, visuo-spatial, attention and executive functions. Two test were used to investigate ToM: the "Reading the Mind in the Eyes" (RME), to evaluate affectiveToM, in which subjects had to guess the emotion or thinking of a person whose eyes are shown in a picture; the "Faux Pas Recognition Test", to evaluate both cognitiveToM and affectiveToM, through the presentation of stories containing faux pas.

Results: In RME we observed lower scores in aMCI than in HC. In the other tests, aMCI showed performances below normal only in memory tasks.

Conclusion: Available data regarding the impairment of ToM in patients with MCI are inconsistent: some studies show a generic dysfunction, rather than a specific deficit of cognitiveToM or affectiveToM; others studies exclude alterations. The results of this study show that a deterioration of affectiveToM is possible in aMCI; this assumption requires further confirmation on a larger sample because it could have important clinical and prognostic implications.

Disclosure: Nothing to disclose

EP2078

Clinico-immunological features patients with limbic encephalites

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Background and aims: Limbic encephalitis (LE) is a heterogeneous group of disorders caused by autoimmunity directed against components of the central nervous system involved in cognition and behavior.

Methods: We present the clinical, immunological, imaging and neurophysiological characteristics of 11 patients that presented to the cognitive neurology clinic with complaints regarding memory impairment and/or behavioral changes and were diagnosed with definite or suspected LE during the years 2012- 2016.

Results: Median age was 57 years (42-69), 100% women. Initial manifestations included subacute cognitive decline (9), seizures (4), depression and behavioral disorders (4). The median MMSE score was 24/30 (range 19-30). Auto antibody seropositivity was depicted in 7 patients. The immunological profile included: VGPC (1), GAD 65 (1), LG1 (1), NMDA (2), anti-Yo and anti Ri (1), anti TPO (2) and anti-amphiphisin (1) antibodies. MRI depicted characteristic findings in 4 patients. Six patients had normal MRI and in one patient a lacunar strokes were depicted. CSF with lymphocytic pleocytosis was found in 4 patients. Eight patients were treated by immunotherapy (IV steroids, plasmapheresis, Imuran). Four patients underwent complete recovery or partial improvement following therapy. The treatment course of one patient was complicated by perforation of the lower esophagus. She eventually died from sepsis.   One patient was diagnosed with adenocarcinoma of lung. Her symptomatology resolved following surgery.

Conclusion: LE has to be considered in patients with atypical presentation of cognitive deterioration as early diagnosis and treatment may improve the cognitive outcome. Nevertheless, as the experience with these patients is relatively scarce, treatment should be closely monitored.

Disclosure: Nothing to disclose

EP2079

Cancelled

Epilepsy 2

EP2080

EEG findings in temporal lobe epilepsy and outcome of anterior temporal lobectomy

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Background and aims: To establish if EEG findings are associated with seizure outcomes in patients who undergo anterior temporal lobectomy for temporal lobe epilepsy.

Methods: This was a retrospective data analysis of adult patients who underwent anterior temporal lobectomy at a tertiary neuroscience centre between 2008 and 2015. Demographic and clinical data were collected by review of records. 12 month outcome was categorised based on Engel classification. Fisher exact testing was used to test association between EEG findings and surgical outcomes.

Results: 43 patients were included, with a median age of 41 years (21-63). 22 were female and had left sided lobectomies. 18 (42%) had history of febrile seizures, 41 (95%) had MRI abnormalities, most commonly hippocampal sclerosis (34, 79%). Good (Engel class I) outcome was observed in 29 (69%) patients at 12 months. Video-telemetry was available in 38 (88%) patients. Interictal epileptiform discharges (IED) were present in 35(92%), 25 (71%) of whom had a good outcome; all 3 patients with non specific interictal activity had good outcome (p=0.55). 22 of 35 (71%) of those with ipsilateral IED had good outcomes, compared to 3 of 4 with bilateral IED (75%, p=1.00). Features of the ictal rhythm including dominant frequency (theta versus delta), lateralisation (ipsilateral versus non lateralised and bilateral), timing (early versus delayed) and localisation (anterior temporal/ sphenoidal versus mid or posterior temporal) did not show significant association with outcomes

Conclusion: In this population of lesional temporal lobe epilepsy, interictal and ictal EEG findings did not show significant association with surgical outcomes.

Disclosure: Nothing to disclose

EP2081

Long term follow-up of recurrent status epilepticus and stroke-like episodes in a MELAS patient.

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Background and aims: Mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes (MELAS) is a disorder commonly caused by the A3243G/tRNALeu mutation of mitochondrial DNA (mtDNA). MELAS patients are considered at high risk of epilepsy and status epilepticus (SE) during stroke-like episodes (SLEs). SLEs in MELAS show a predilection for the occipital lobe, which also correlates with the localization of focal epileptic activity on EEG.

Methods: We describe the long-term follow-up of a patient with A3243G/tRNALeu mutation presenting with recurrent focal SE, mostly occurring during SLEs. Neuroimaging, EEG and SLE treatment are discussed.

Results: This 29-year-old patient carries the mtDNA A3243G/tRNALeu mutation. The mother died at 40 years during SE associated with SLE. The patient suffered photosensitive epilepsy since 17 years. Since 23 years he presented recurrence of 7 episodes of occipital SE (elementary visual hallucinations, oculo-clonic seizures) with hemianopia mostly associated with lactic acidosis and stroke-like occipital lesions. SE was refractory to iv lorazepam, diazepam, phenytoin and levetiracetam. SE was effectively treated with iv high-dosage Midazolam. In one episode Propofol was used during SE and the patient suffered multiple organ failure (Propofol infusion syndrome-PRIS).

Conclusion: We report a MELAS patient with recurrent occipital SE and SLEs. SE recurred with an increasing frequency over the years. Midazolam infusion is a first-line drug in SE treatment. Based on the occurrence of PRIS in our patient and evidence of mitochondrial toxicity induced by Propofol this drug should be avoided in patients with mitochondrial encephalopathy.

Disclosure: Nothing to disclose

EP2082

Falls in temporal lobe epilepsy

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Background and aims: The main aim of this study was to evalute the association of sudden, unexpected falls and temporal lobe epilepsy

Methods: We have retrospectively analyzed data of all patients who underwent presurgical evaluation for drug-resistant temporal lobe epilepsy in our center since 2005. The patient was included only if (1) there was anamnesis of sudden, unexpected falls, (2) patient underwent long-term ECG monitoring, which did not reveal cardiac arrhytmia, (3) patient underwent surgery and was categorized as completely seizure-free after surgery, (4) the falls dissapeared after surgery completely.

The interictal and ictal ECGs of these patients were compared to ECG of control group. There were age- and gender-matched patients in control who underwent surgery for drug-resistant epilepsy and were seizure-free since surgery.

Results: We identified 15 patients (7 females, 8 males) treated with temporal lobe epilepsy who reported sudden unexplained falls which completely disappeared after surgery. When analyzing ictal EEG, we identified higher tendency to ictal tachycardia in comparison to control group. No patient had ictal asystolia. No statistical significant differences were found when analyzing interictal EEG.

Conclusion: It seems that suden unexplained falls could be rarely associated with temporal lobe epilepsy.

Disclosure: Nothing to disclose

EP2083

Cancelled

EP2084

Knowledge, attitude and practice of primary school teachers towards epilepsy in Omdurman, Khartoum state 2016

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Background and aims: Epilepsy has become a rising problem and usually the first signs of epilepsy are shown in school, and hence teachers are usually the first to notice it. Objectives of tihis study was to assess the knowledge attitude and practice of primary school teachers on Epilepsy in Omdurman, Khartoum

Methods: This is a cross-sectional descriptive institutional study. Over a period of a week 152 questionnaires were distributed among 15 schools in the area of Abu Siid and South Omdurman, with 10 questionnaires in each school

Results: All the teachers who took part in this interview had heard of epilepsy before. The overall knowledge evaluation of teachers concerning epilepsy was reasonable with 47% having good knowledge, 50% having satisfactory knowledge, and only 3% having poor knowledge. Sadly only 15% had taken a training course on how epileptic kids should be managed. Thankfully around 75% acknowledged that epilepsy wasn't contagious and 70% would allow their kids to play with epileptic kids, reflecting positive attitude towards epilepsy. Around 40% had good management skills
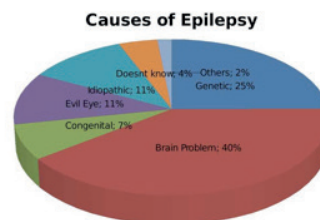
Results of causes of epilepsy by the teachers

Symptoms of epilepsy

Behavioural Changes; 5%   Others; 1%
Seizures; 40%
Transient loss of consciousness; 38%
Abnormal eye and tongue movement; 16%

Type of treatment

Traditional; 3.70%; 4%
Surgical; 2.80%; 3%
Medical; 93.50%; 94%
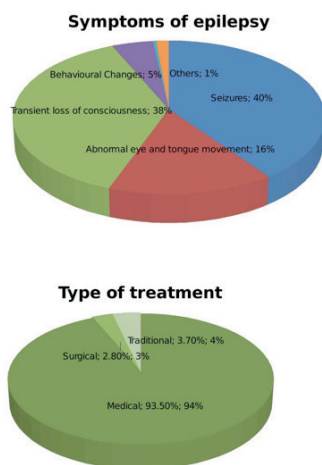
1)Symptoms of epilepsy   2)Type of treatmemnt

Conclusion: While many teachers had positive views about epilepsy, some negative views still persist. Furthermore, most teachers received no formal training on epilepsy. Given the potential impact that teachers' practice and knowledge can have on children with epilepsy, further research in this area is needed. Overall, there was a generally positive attitude towards epilepsy and good knowledge on epilepsy but there were also significant deficiencies in terms of epilepsy management

Evaluation

Poor; 2%
Good; 47%
Satisfactory; 50%

Overall Knowledge Evaluation

Disclosure: University of Khartoum, Faculty of Medicine, Community Medicine department

EP2085

A retrieval-related evoked potential in the parahippocampal gyrus by a short-term memory task

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Background and aims: Working memory (WM) is conceived as short-term memory (STM) applied to cognitive tasks, as a multi-component system that holds and manipulates information, and as the use of attention to manage STM. Different models of WM suggest a mechanism by which a persistent spiking at cellular level could be used to hold various items. Some of these models focus on WM in the medial temporal lobe (MTL). Our purpose is to present the case of a retrieval-related evoked potential (RREP) in the parahippocampal gyrus after Gamma Knife (GK) radiosurgery and its implication on WM.

Methods: We performed this study in a patient with seizure since 2 y.o. In 2006 she was received GK for left temporal lobe epilepsy (TLE), it was not favorable. 3 years later we performed intracranial electroencephalography (iEEG) and surgery (left transsylvian selective amygdalohippo-campectomy). Wada test showed right dominance (memory function). We used trapezoid electrode-sheets ("T" shape), inserted on the parahippocampal gyri (Fig 1). The patient performed two tasks whereas we recorded electrocorticogram (ECoG), picture naming task and memory task. We confirmed diagnosis of MTLE by video EEG, ECoG, MRI, CT scan, PET and SPECT.

Number of Subdural electrodes implanted

32 electrodes on basal cortex
44 electrodes on left hemisphere
8 electrodes on right hemisphere

- 32 electrodes on basal cortex
- 44 electrodes on left hemisphere
- 8 electrodes on right hemisphere

Figure 1. Subdural electrodes implanted.
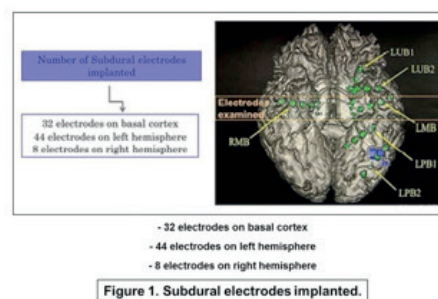
Subdural electrodes implanted

Results: There was a large negative deflection ranging from 400 to 700ms (Figure 2).
The peak latency was around 600ms.
Currently 6 years later she is seizure free (Engel I).

Retrieval: Patient indicated via button press whether the picture matched one of these seen during the encoding period.

Figure 2. Retrieval ERP (left and right parahippocampal gyrus).
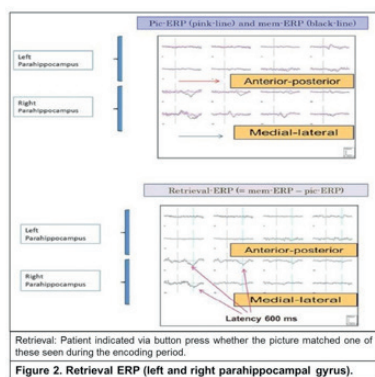
Retrieval ERP (left and right parahippocampal gyrus)

Conclusion: We have seen the activation (ERP) of the right parahippocampus and the absence of activity in the left parahippocampus gyrus (Figure 3); this lateralization is strongly suggested by the effect of Gamma Knife radiosurgery.
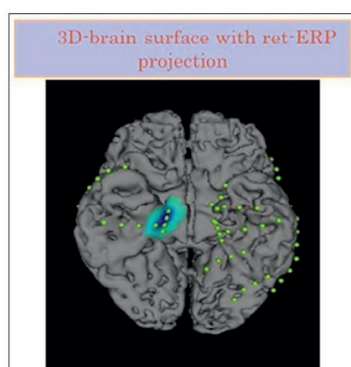
Figure 3. Activation (ERP) of the right parahippocampus

Activation (ERP) of the right parahippocampus

Disclosure: Nothing to disclose

EP2086

Sleep disorders: Clinical features and impact in epileptic patients

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Background and aims: Epileptic patients usually suffer sleep disorders (SD), that can affect negatively in seizure control and quality of life. Our aim is to analyze clinical features, antiepileptic therapy, symptoms, polysomnographic findings and sleep disorder in patients with epilepsy (those who were under suspicion of SD).

Methods: Retrospective descriptive observational study. We included patients that underwent monitoring in the Refractory Epilepsy Unit from January 2014 to April 30th 2016 under clinical suspicion of sleep disorder. We analyze: personal medical background, epileptic syndrome, anti-epileptic drug (AED) used, SD type, video-polysomnogram results, need of treatment and response to it, reduction of number of seizures after SD treatment.

Results: 57 patients: 30 women (54.5%). Medium age: 53 years (22-77). Non-smokers 59.3%. Obesity 21.8% (type 1 obesity 10.9%). Temporal lobe epilepsy in 45.5% (25 patients). 41.8% non-structural epilepsy. 50.9% treated with 1 AED. 46.3% seizure-free in the last year (prior to SD diagnosis). SD diagnosis: 54.38% (31). SAS (Sleep Apnea Syndrome) 45.6% (26): 42.1% OSA (Obstructive Sleep apnea). AHI (apnea-hypopnea index) 14.1 (2.7-51.8). Motor SD 15.8% (9): RLS (Restless Legs Syndrome) 33.3%, PLMD (Periodic Limb Movement Disorder) 66.6%. After treatment of SD: seizures-free 8.7% (5). Reduction >50% 7% (4)
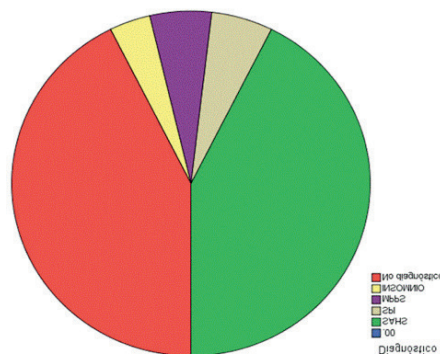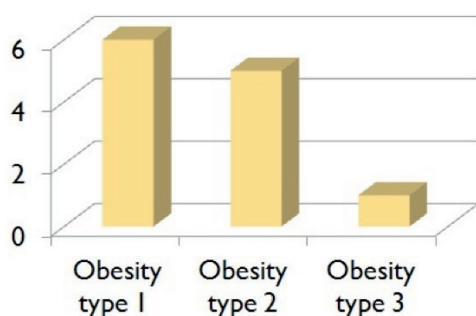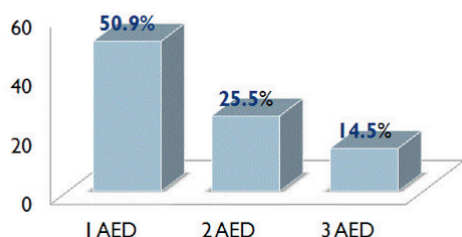
Conclusion: Sleep disorders are a very frequent comorbidity in epileptic patients and cause an inappropiate control of seizures. Diagnosis of SD and proper treatment can affect favorably in seizures control and improve quality of life.
Disclosure: Nothing to disclose

EP2087
Cancelled

EP2088

Concept of epilepsy in Cameroonian health providers: Should we start by education?

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Background and aims: Epilepsy is a stigmatized condition Worldwide, particularly in developing countries. We aim to evaluate the general knowledge about the disease and how to manage epileptic patients in care providers of Cameroon, identifying which topics should be reinforced in their education.
Methods: We conducted an anonymous survey with demographical, social and clinical questions about epilepsy and its management to all the care providers of three Cameroonian hospitals.
Results: 38 care providers participated in the survey, 42.1% of who were female. Mean age was 40.1 y (rank 22-62). Among the causes of epilepsy, 68.4% thought that it is a psychiatric condition, 34.2% a degenerative disease, 28,9% an hereditary condition and a 21.1% secondary to an infection. About how to diagnose a patient, just a 23.7% considered that the anamnesis could be enough to set the diagnosis, being more likely in those who attended more patients (p=0.05). Only 60.5% considered history important for the diagnosis and a 52.6% considered necessary a positive EEG. 28,9% considered important the laboratory exams. Only a 36,8% recommended adding folic acid to pregnant woman and only 39.5% considered possible breast-feeding. The mean number of drugs known were of 2.08, being phenobarbital the most recognized.
Conclusion: The main areas that needed to be addressed in the education of care providers are the origin of epilepsy and its causes, how to diagnose a patient and how to proceed during pregnancy and patient education.
Disclosure: Nothing to disclose

EP2089

The challenge of managing epilepsy in a developing country

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Background and aims: Epilepsy is one of the most frequent conditions in developing countries. The higher frequency is associated with infections, perinatal complications and traumatic brain injury. Its management is harder because of the difficult access to complementary exams and the low availability of drugs.

Methods: Two neurologists evaluated 150 patients complaining about possible seizures in five different hospitals of the West region of Cameroon among 6 days in December 2016. We registered epidemiological and clinical data.

Results: We included 93 patients, 52.7% of whom were female. Mean age was 23.6 years (range 0-78). The relevant prior medical history was: cognitive delay 18.5%, prior CNS infections 15.2%; febrile seizures: 8.6%; perinatal complications 7.6%. Mean age of onset of seizures was 11.9 years old. Frequency of seizures was daily 5.1%, weekly 14.1%, monthly 31.1% and free of seizures 26.9%. The type episodes suggested a focal onset in 35.6%. We performed EEG to 21.5% with positive findings in 41.7%, which change treatment in 47.8% of cases. Initial treatment was phenobarbital 53.8%, carbamazepine 38.9%, phenytoin 6.4% and valproate 3.8%. We started a treatment in 15.8%, increased in 29.0%; changed in 13.2%, decreased in 5.3% and stopped in 3.9%.

Conclusion: We succeeded in making a diagnosis in a high percentage of the patients despite the lack of resources. The management is complicated and the very few diagnostic and therapeutic resources represent a challenge to the clinician.

Disclosure: Nothing to disclose

EP2090

Cancelled

EP2091

Visual illustration supporting patient-physician communication in epilepsy: A validation and reliability study of 24 seizure images, first analysis

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Background and aims: The semiological description of seizures is complicated to comprehend in words. To improve the communication between epilepsy patients and providers, 24 seizure images were developed by experts. This tool can be used during obtaining the patient's history. The objective of this study was to validate 24 seizure images before implementing into practice.

Methods: We included patients with epilepsy, persons who witnessed seizure episodes such as family members of epilepsy patients, care givers, and participants without pre-existing knowledge of epilepsy. Participants completed the questionnaire evaluating 24 seizure images twice within 36 hours. The participants were explained to choose one of the 2 items that best described each seizure image. The validity was assessed using one proportion z-test. Test-retest reliability was assessed by interclass correlation coefficient (ICC).

Results: For the initial analysis, 32 participants were included in the study. Beside two images, the proportion of correctly recognized seizure images was significantly higher than 0.7. The proportions of the two seizure images (image 9: dystonia and image 17: myoclonus) were 0.78 (95%CI 0.63-1.00) and 0.56 (95%CI 0.40-1.00). ICCs for seizure images are also high (range from 0.86 to 1.00) except for the images 9 and 17.

Conclusion: The seizure images were proved to be valid and have a high test-retest reliability. However, two images (images 9 and 17) should be revised in order to improve the validity of this tool.

Disclosure: Nothing to disclose

EP2092

The etiology of symptomatic partial epilepsy in childhood and adolescence in the Siberian region

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Background and aims: Epilepsy is polyetiology disease. The significance of various etiological factors varies in different age periods. The most important etiological factors of symptomatic partial epilepsy are brain dysgenesis, mesial temporal sclerosis, brain tumors, vascular malformations, neurocutaneous syndromes (Tuberous sclerosis, angiomatosis entsefalotrigeminalny), trauma, Rasmussen's Syndrome.

Objective: To study the etiology of symptomatic partial epilepsy in childhood and adolescence in the Siberian region.

Methods: The study and dynamic observation involved 882 patients (463 boys and 419 girls) with epilepsy and epileptic syndromes. The form of epilepsy and epileptic syndromes and the etiology of symptomatic epilepsy refined during neuroimaging (magnetic resonance tomography of the brain) and functional methods of investigation (EEG with standard functional tests, video monitoring).

Results: Among the etiological factors of symptomatic partial epilepsy was a statistically significant superiority (p <0.05), perinatal hypoxic-ischemic lesions (26.4%); second place is occupied by congenital abnormalities of brain development (15.9%); 8.96% were head injuries, almost the same (8.46%) - perinatal traumatic injury - Intracranial hemorrhage. Prenatal and other infectious brain damage amounted to 6.22%; hydrocephalus occurred in 3.73%; vascular pathology - 2.24% of cases. Less incidence of brain tumors (1.49%), chromosomal abnormalities (1%), hereditary neurocutaneous syndromes (0.75%) and congenital errors of metabolism (0.5%). In 14.2% of cases, the etiology of symptomatic partial epilepsy are not verified.

Conclusion: Among the etiological factors of symptomatic partial epilepsy in the Siberian region in childhood dominated by perinatal hypoxic-ischemic injury in adolescence - head injuries, mesial temporal sclerosis, and infections of the central nervous system.

Disclosure: Nothing to disclose

EP2093

The predictive value of quantitative electroencephalography (QEEG) for late-onset seizures in cobalamine mildly deficient elderly patients

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Background and aims: Cobalamine's (B12) importance for maintaining healthy nerve cells is well known. Though wide-ranging references study neuro-psychiatric complications caused by B12 deficiency, only a very few focus on EEG abnormalities and their involvement in late-onset seizures.

Purpose: Brain rhythm analysis of B12 mildly deficient elderly patients and correlation with seizures.

Methods: We evaluated the QEEG of 186 patients (mean age 73 years) with B12 gray zone levels 200-400pg/ml for the last two years. A matching healthy control sample was included. All the patients were submitted to brain imaging and EEG follow-up every 3 months.

Results: QEEG parameters of 72 (38.7%) patients were characterized by pronounced theta rhythms in the fronto-temporal regions and alpha3/alpha2 frequency ratio reduction. An increased of paroxysmal activity was observed in 26 patients and 4 of them presented seizures. After B12 supplementation EEG abnormalities subsided.

Conclusion: Mildly B12 deficiency in elderly patients causes EEG rhythm alterations. Late onset seizures occur in 5.5% of them. Considering that treatment necessity of mildly deficiency is usually underestimated, QEEG analysis is a reliable method for epileptiform activity evaluation

Disclosure: Nothing to disclose

Headache and pain 2

EP2094

Idiopatic intraorbital neuralgia: A rare cause of facial pain

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Background and aims: Infraorbital Neuralgia (IN) is an uncommon disorder, not included in the International Classification of Headache Disorders III Edition (ICHD-III, beta version). It is defined as pain in the distribution of infraorbital nerve (ipsilateral cheek, upper teeth and upper jaw), tenderness over the infraorbital notch and relief of pain by local anesthetic blockade or ablation of the nerve. We aim to analyse clinical characteristics in a consecutive series of 4 cases.

Methods: We included patients with IN attended in a headache outpatient clinic in a tertiary hospital over a 9-year period (January 2008 to January 2017). Characteristics of one of them have already been published. We prospectively gathered demographic and clinical characteristics.

Results: We identified 4 patients (2 females, 2 males) out of 4742 (0.08%) attended during inclusion period, with diagnosis of IN. Mean age at onset was 35.7±17.4 years (16-58). All of them presented tenderness over the infraorbital notch. Possible secondary causes were appropriately ruled out. Three patients suffered a burning or dull background pain, that was rated as moderate (6.3±1.5 (5-8)) on a verbal analogical scale (VAS). In two cases, lancinating exacerbations with variable frequency and rated as severe (8-9 on VAS). Regarding temporal pattern, in two patients we observed spontaneous remissions, one of them achieved a sustained response to pregabalin, and the last case has been refractory to multiple therapies.

Conclusion: Idiopathic Infraorbital Neuralgia is a quite uncommon disorder. Temporal pattern and response to treatment are variable in our series.

Disclosure: Nothing to disclose

EP2095

Case report of a patient affected by migraine with aura

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Background and aims: Migraine is a common, multifactorial, disabling, recurrent, hereditary neurovascular headache disorder. Attack often begin with warning sign (prodromes) and aura (transient focal neurological symptoms) whose origins thought to involve the hypothalamus brainstem and cortex.

Methods: We present the clinical case of a 46-year-old man suffering from childhood by migraine with aura. He had a family history of migraine and was not affected by chronic disease. He reported too memory impairment and loss of attention at work. So we planned blood tests, EEG, MRI with contrast and angiography sequences, neuro-psychological and thrombophilia screening tests. Our patient had never performed neurological finding.

Results: The thrombophilic tests showed polymorphism with mutations in heterozygous, precisely FIIG20210A, MTHFR (C677T), MTHFR(A1298C) and the haplotype e2/e3. Neuropsychological tests performed (MMSE, MOCA, Frontal Assessment Battery, ADL, IADL). They showed slight deficit of short term memory and semantic memory evocation. B-vitamin biomarkers, routine blood test, EEG, and MRI scan were normal.

Conclusion: Migraine with aura is more common in women than in men. Our case is interesting because it raises questions that are important for future research. There is a difference between men and women affected from migraine with aura for the risk of ischemic stroke? The study of thrombophilic polymorphisms is useful in patients with migraine with aura? Mild memory disorders in patients with migraine with aura are predictive of cognitive decline in elderly? In this aspect, there may be a difference between men and women?

Disclosure: Nothing to disclose

EP2096

Single Pulse Transcranial Magnetic Stimulation (sTMS) for migraine: The Plymouth experience

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Background and aims: Migraine can result in economic, social, and educational losses for sufferers, as well as long term health service costs. Randomised clinical trial evidence suggests single pulse Transcranial Magnetic Stimulation (sTMS) is an effective migraine therapy. The UK National Institute of Clinical Excellence encourages the evaluation of sTMS treatment for migraine under specialist supervision. We evaluated self directed sTMS therapy for migraine on an anonymous cohort of patients in Plymouth, UK.

Methods: An anonymous questionnaire was sent to patients in receipt of the eNeura Spring Total Migraine System (TMS). The questionnaire was administered by our pharmacist. Patients were informed about the device from the headache clinic. Patients contacted eNeura Inc. to provide therapy. The device was not prescribed and was loaned by eNeura for a three month free trial period.

Results: 20% (8/39) had a significant response to sTMS therapy over 3 months. 6/8 (75%) were able to return to everyday activities with sTMS therapy. Median length of migraine history was 6-7 years receiving a median of 6 treatments prior to sTMS. 70% (27/39) did not respond to sTMS therapy over 3 months. Side effects were reported in 15% (6/39) and were headache and neck pain, as validated in sTMS safety publication.

Conclusion: sTMS does not appear to be effective for the majority of migraine sufferers in our study (70%). However for 8/39 (20.5%) of patients, sTMS was found to be of significant benefit. Identifingy factors that predict response to sTMS and a local cost benefit analysis require further work.

Disclosure: Patients received a three month free trial of the eNeura Spring Total Migraine System (TMS) from eNeura Inc.

EP2097

Pseudotumor cerebri related to Behçet's disease

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Background and aims: The association of pseudotumor cerebri (PS) and Behçet's disease (BD) is extremely rare. Herein, we present the clinical and laboratory features of five patients with BD who were diagnosed as having PS.

Methods: We retrospectively reviewed 448 patients with Neuro-BD who were managed at Istanbul Faculty of Medicine between 1985 and 2015. Patients who fulfilled the diagnostic criteria for BD and PS were identified.

Results: Five patients fulfilled both criteria. The presenting symptom was headache in four of the patients. Only one patient presented with blurred vision. Four patients had papillary edema. There were no other pathologic findings in the neurologic examination. None of the patients had any parenchymal lesions. The cerebrospinal fluid (CSF) pressure was high in all patients. CSF cell counts, protein and glucose levels were normal. Only one patient had oligoclonal bands in the CSF. After the diagnosis of PS, three patients were treated with high-dose and two patients with low-dose methylprednisolone. All of the patients were treated with azathioprine, two with acetazolamide, and one with topiramate. Starting from the 15th day of treatment, all of the patients showed clinical improvement. In the long-term follow-up, one patient had headache with recurrent oral aphthous ulcers. A relapse with parenchymal involvement was observed in one patient 16 months after PS.

Conclusion: PS should be considered in patients with BD who present with elevated intracranial pressure in addition to cerebral venous sinus thrombosis and aseptic meningitis. Physicians should keep in mind that the pattern of neurologic involvement in patients with BD may change.

Disclosure: Nothing to disclose

EP2098

Patient-completed screening tools have poor diagnostic accuracy for neuropathic orofacial pain in a hospital-based cohort.

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Background and aims: Patient-completed screening tools may aid diagnosis of orofacial pain in non-specialist centres. We aimed to evaluate the diagnostic accuracy of patient-completed screening tools in a hospital-based cohort of patients referred for orofacial pain.

Methods: Prior to first appointment at a hospital facial pain clinic, patients were prospectively assigned Oregon Health & Science University (OHSU, n=152) or painDETECT questionnaires (PD-Q, n=254). The main outcome was the diagnostic accuracy of the OHSU and PD-Q compared to clinical diagnosis made by senior staff; blinded to questionnaires and validated by an independent clinician.

Results: 88 / 139 (63%) patients were correctly diagnosed by the OHSU, and 172 / 251 (69%) were correctly identified by the PD-Q to have neuropathic pain components. The OHSU had sensitivity of 0.48 (95% CI, 0.33-0.63) and specificity of 0.86 (95% CI, 0.78-0.93) to diagnose temporomandibular joint disorder, and sensitivity of 0.84 (95% CI, 0.69-0.93) and specificity of 0.59 (95% CI, 0.48-0.69) to diagnose trigeminal neuralgia. The PD-Q had an area under the receiver operating characteristics curve of 0.65 (95% CI, 0.58-0.73). Patients with a second clinical diagnosis were more likely to be diagnosed incorrectly by the OHSU (p=0.006) and PD-Q (p=0.002).

Conclusion: The OHSU and PD-Q have poor diagnostic accuracy when applied to a hospital-based cohort of patients with orofacial pain. Such patient-completed screening tools should be revalidated in non-specialist centres, prior to research or clinical applications.

Disclosure: Nothing to disclose

EP2099

Cerebral venous sinus thrombosis complicating traumatic intracranial hypotension

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Background and aims: Cerebrospinal fluid leaks may cause intracranial hypotension and associated headache. Cerebral venous sinus thrombosis (CVST) has been described as a rare complication.

Methods: A 31-year-old woman developed severe orthostatic headache with nausea within one day after a minor head trauma. After several days, she additionally experienced headache while lying down. The patient was on an ethinylestradiol vaginal ring and was smoking for 6 months. There was a family history of venous thromboembolism.

Results: Initial brain CT was normal. After the patient started experiencing headache while lying down, a cerebral MR venography demonstrated superior sagittal and left transverse sinus thrombosis (fig.1). Contrast-enhanced brain MRI also demonstrated signs of severe intracranial hypotension (fig.2). A prothrombotic disorder could not be identified. Anticoagulation with low molecular weight heparin was started and a lumbar epidural blood patch was performed. Although the headache in the recumbent position improved, the orthostatic headache remained present. A full-spine MRI with intrathecal gadolinium demonstrated an epidural CSF collection from C6 to D9 level, most prominent at level D7-D8 (fig.3). A targeted blood patch was performed at this level after which the headache subsided. MRI after 4 months demonstrated complete resolution of the CVST and signs of intracranial hypotension.
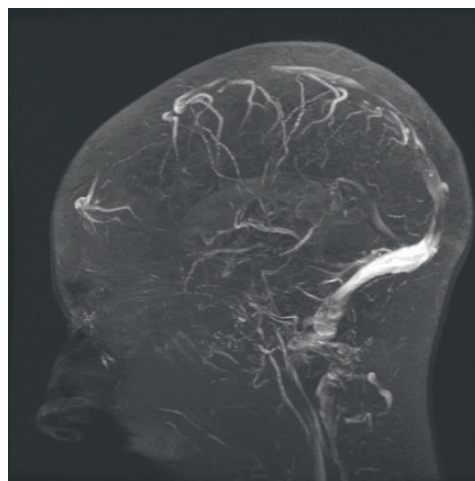
MR venography demonstrating thrombosis of the superior sagittal sinus. A coronal projection also demonstrated thrombosis of the left transverse sinus (not visible in this image).
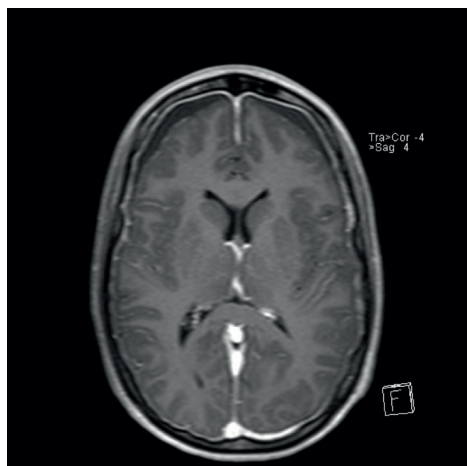
Contrast-enhanced brain MRI demonstrating the signs of severe intracranial hypotension with meningeal enhancement and bifrontal hygroma.
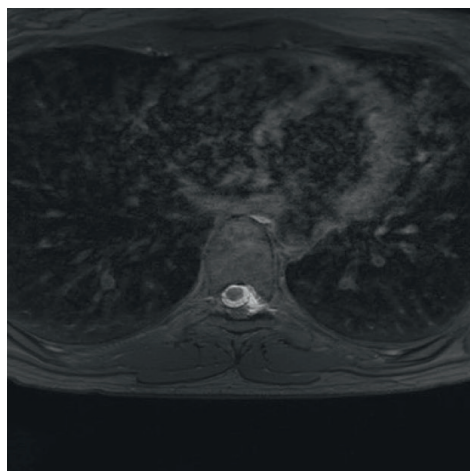
Transaxial section the full-spine MR obtained after intrathecal gadolinium contrast administration. Gadolinium contrast is clearly visualized left posterolaterally to the intradural space, demonstrating a cerebrospinal fluid leak.

Conclusion: This case demonstrates the pitfalls in diagnosing intracranial hypotension with CVST. Orthostatic headache progressing into headache on lying down as well is a red flag. Imaging should be performed urgently to rule out subdural haematoma and cranial venous thrombosis.
Disclosure: Nothing to disclose

EP2100
The knowledge of residents in neurology about management of headache

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Background and aims: Headache is so common in the general population that most physicians should have a good knowledge about the management. While most patients are self-managed or managed in primary care, the most complicated patients are often referred to neurological out-patient clinics. Thus, all physicians working with neurology should have a good knowledge about headache. There is limited focus on headache in the curriculum at the four medical schools in Norway. Furthermore, approximately 50% of all residents in Norway have graduated from abroad. The national five-year training program in clinical neurology has no mandatory headache program. Therefore, knowledge and expertise in headache management must be acquired during the everyday clinical neurology training.

The objectives of this survey were to investigate whether residents acquire the necessary knowledge about headache, and to evaluate experience in, and attitudes towards headache management.

Methods: The study was conducted as a questionnaire survey among all residents in neurology at all the 17 neurological departments in Norway. A contact person at each department had the responsibility for distributing and collecting the forms.

Results: All the 17 neurological departments participated, and the responder rate was over 70%. Residents answered questions about knowledge, attitudes and experiences related to headache management. Barriers to adequate headache treatment were investigated. The use of treatment guidelines and the International Classification of Headache disorders were examined. Finally, a comparison of the status of various neurological diseases was done.

Conclusion: The results are currently being analysed and will be presented at the meeting.
Disclosure: Nothing to disclose

EP2101

Cancelled

EP2102

Quality of life after withdrawal treatment in medication overuse headache: A pilot study

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Background and aims: Medication overuse headache (MOH) affects 1-2% of the population, and 30% of the patients in tertiary headache centers. It most commonly affects people with a previous primary headache disorder, most commonly migraine or tension type headache. Medication overuse results in the chronification of the primary headache, causing further disability and decreased quality of life. MOH represents a therapeutic challenge and even after successful treatment recurrence rates can be as high as 40%.

Methods: A comprehensive treatment program, consisting of acute medication withdrawal, preventive pharmacological treatment and lifestyle intervention was applied to 18 patients (15 women; mean age 40.8±14.2 years) suffering from MOH. The clinical characteristics of the headaches were recorded. Headache-related quality of life was measured using the Comprehensive Headache-related Quality of life Questionnaire (CHQQ) before and after the treatment program.

Results: After the treatment a significant reduction of the number of headache days, headache severity and analgesic consumption was observed. The CHQO score of MOH patients, which was somewhat lower at baseline than in episodic migraine, also showed a significant increase.

Conclusion: We found significant improvement of the headache characteristics and quality of life of MOH patients completing the treatment program. Further investigations are necessary to evaluate the long-term efficacy on a bigger sample size to evaluate, if in-, or outpatient withdrawal is more effective, and follow the patients for a longer period to examine, if the results remain stable over time.

Disclosure: Nothing to disclose

EP2103

Cancelled

EP2104

Orthostatic headache? Think about intracranial hypotension

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Background and aims: Headache is a frequent clinical entity in neurology attesting to various pathologies. His postural character is almost pathognomonic of intracranial hypotension (ICH), a rare cause of chronic headaches often misdiagnosed. Thinking about it is necessary in order to avoid severe outcomes. The aim of this case illustration is to emphasize the severity of this pathology due to her multiple complications.

Methods: We report a case of a patient with ICH diagnosed twelve years after the beginning of his symptoms, after developing several complications of his disease.

Results: This MJ patient was 51 years old. He suffers from nasal polyposis operated with ethmoidectomy. One year after his operation, his started complaining about orthostatic headache and developed epileptic seizures leading to status epilepticus twice. His MRI shows diffuse pachymeningitis with negative etiological investigations. MJ had an intractable epilepsy despite antiepileptic drugs. He was operated five years later of chronic subdural frontal hematoma without traumatic context. Finally, MJ had recently a third status epilepticus due to a cerebral venous sinus thrombosis. The diagnosis of ICH with all his complications was then retained. In front of this case and knowing the clinical history of endonasal surgery of our patient, we realized a CT of facial bones was performed. It showed an old ethmoidal breach. A surgical treatment is planned.

Conclusion: Our case shows the importance of considering ICH as an etiology of uncommon headaches in order to avoid harmful complications. Endonasal surgery may be the alarm sign leading to thinking about it.

Disclosure: Nothing to disclose

EP2105

Therapeutic use of cannabinoids - dose finding, effects and pilot data of effects in chronic migraine and cluster headache

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Background and aims: Aim was to verify therapeutic effect of 19% THC (bedrocan) + <0.4% THC, 9% CBD (bedrolite) in both prophylaxis and acute treatment of chronic cluster headache (CH) and migraine (M).

Methods: Step 1- we performed a dose finding observations in 48 chronic M volunteers, during 4 test--retest of THC+CBD. Starting dose was 10mg/orally. Step 2– M (n=370) and CH sufferers (n=190) volunteered the prospective observation. Entry criteria were: normal examines, normal elctrocardiogram. After a 10-days washout period, M sufferers were randomly assigned to a 3 months-treatment with 25mg/day amitriptyline or THC+CBD 200 mg/day in 200 ml 50% fat emulsion. CH received THC+CBD or 480mg/day verapamil. One-month follow-up was provided. Two hundred mg THC+CBD were also administered as acute treatment. Rescue treatment was 6 mg/s.c. sumatriptan.

Results: Therapeutic dose was 200mg THC+CBD inducing 55% pain decrease. Doses lower than 100mg induced 0% relief. Pilot data refer to 79 M and 48 CH. In M THC+CBD prophylaxis induced 40.4% benefit versus 40.1% amitriptyline-evoked pain relief. In CH, THC+CBD prophylaxis induced scant decrease of severity and number of attacks. Acute THC+CBD decreased attack pain -43.5% in both M and CH who had an history of M when children. Relief was 0% in CH without M history. Adverse effects were drowsiness and inattention. These effects and decrease (range -70%-100%) of stomach ache, colitis and musculo-skeletal pain strictly related to female sex, p>0.0001.

Conclusion: Discussion Cannabinoids may be a prophylaxis for M and an acute treatment for CH in case M occurred during childhood.

Disclosure: Nothing to disclose

EP2106

Chronic pain in patients with Parkinson's disease (PwPD): Quality of life and neuropsychiatric disturbances

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Background and aims: Psychological factors influence clinical picture, health related life quality in PwPD. Anxiety, depression are treatable, so early diagnosis and treatment improve life quality (QoL) in PwPD [Ayla Fila, 2012]. Objective was assessing neuropsychiatric profile in PwPD with chronic pain in Siberian region.

Methods: 798 PwPD are registered in movement disorders electronic database of the Siberian region. 348 non-demented PwPD were included (mean age: 65.2±6.3 years; PD mean duration: 6.8±5.8 years; H&Y stages 1–4, women:men=167:181), divided into two groups (homogeneous by gender, stage, age): I–176 PwPD with chronic pain, II–172 without. Clinical assessments were conducted using the UPDRS, H&Y Scale, MoCA-test, Beck depression inventory II, Hospital anxiety and Depression Scale(HADS-A), Apathy Scale, PD Sleep Scale, Epworth Sleepiness Scale, Parkinson's disease Questionnaire 39(PDQ-39). Chronic pain was analyzed by structured interview questionnaire.

Results: Pain was reported by 176(50.6%) participants, with 128(72.7%) reporting moderate severity or worse. The majority of PwPD had musculoskeletal pain(129 cases or 73.2%), 2(1.1%)- radicular pain, 46(26.1%)- dystonic pain, 24(13.6%)- headache. PwPD with chronic pain had higher values anxiety vs. without pain(6(4;8) vs. 10(9;12),p<0.0001), the same in depression (15(11;20) vs. 20(16;27),p<0.0001). Pain intensity correlated statistically significant with anxiety(r=0.56, p<0.001), Beck depression score(r=0.52, p<0.001), apathy (r=0.51, p<0.001) and health related QoL(r=0.49, p<0.001), but not with measures of disease severity(H&YS). Moderate correlation was between pain intensity and L-dopa equivalent daily dose(r=0.39, p<0.001), UPDRS(r=0.46, p<0.001), lower sleep efficiency (r=0.43, p<0.001).

Conclusion: Musculoskeletal pain is the most common type of pain in PwPD. Disrupted sleep continuity, mood disorders, low QoL are associated with pain in PwPD.

Disclosure: Nothing to disclose

Motor neurone diseases

EP2107

Co-occurrence of ALS and LHON: Is mitochondrial dysfunction a modifier of ALS?

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Background and aims: Mitochondrial dysfunction in the pathogenesis of neurodegenerative diseases is widely investigated and mounting evidences support its contribution in early phases of amyotrophic lateral sclerosis (ALS). Here we present the unprecedented association of ALS and Leber's hereditary optic neuropathy (LHON), a maternally inherited mitochondrial disease due to complex I dysfunction.
Methods: We describe two Caucasian women affected by a sporadic form of ALS both carrying the m.11778A>G mitochondrial DNA mutation.
Results: Case 1 was affected by LHON since 26 years of age. At 73 she developed progressively worsening hyposthenia of the right lower limb, rapidly spreading to the right arm and then to the left lower limb. Bulbar signs occurred in 10 months and the patient died 18 months after onset.
Case 2 was an asymptomatic carrier of the LHON mutation. At 71 years of age she presented a bulbar onset of disease with progressive dysphagia and dysarthria. At 72 she developed proximal paresis predominant on the left side. She died 22 months after onset. A complete clinical work-out confirmed the diagnosis of ALS. Genetic testings (FUS, SOD1, TDP43 and c9orf72) were negative. El Escorial criteria for definite ALS were fulfilled for both.
Conclusion: This is the first report on a clinical association of ALS and LHON. While this association is most probaly due to a chance co-occurrence of two rare diseases, the particularly aggressive course of ALS may suggest a synergistic interaction and further support the role of mitochondrial dysfunction as key in the pathogenesis of ALS.
Disclosure: Nothing to disclose

EP2108

Psychological and neuropsychological profile of ALS patients participating in a clinical trial with foetal stem cell transplantations, Phase I

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Background and aims: Intraspinal stem cells transplantation represents a new therapeutic experimental approach for Amyotrophic Lateral Sclerosis (ALS). We present the results from the psychological and neuropsychological profile of ALS patients participating to a phase I clinical trial with human neural stem cells transplantation.
Methods: 18 ALS patients with normal cognitive and behavioural profiles were recruited (years 2012 to 2015) and evaluated at the time of recruitment and followed monthly for at least one year after treatment. Patients were tested with SEIQol-DW, Profile of Mood State, POMS and MMPI-2 questionnaires, and for cognitive functions (Cognitive Estimation CET, Raven's coloured progressive matrices, Digit span backward and forward, Verbal fluency, Verbal Judgments and Short Story tests).
Results: No cognitive or behavioral deficit emerged during the follow-up period, and quality of life main value (SEIQoL) remained high (73%, range: 69%-77%). Patients did not develop clinical depressive or anxious symptoms during time, except one subject who manifested depression mood in the post-surgery period as a reaction to the paucity of assistance received from the family.
Conclusion: Psychological and cognitive profiles remained non-problematic through time independently of the progression and severity of the disease. The surgical procedure and the lack of clear functional benefits did not affect the patients' perceived Quality of Life which remained high. In our opinion, this result can be explained with the strict clinical follow-up and psychological support given to the patients who felt especially involved in a research project and particularly cared by the specialists involved in the project.
Disclosure: Nothing to disclose

EP2109

Neurophysiological and neuroimaging techniques to monitor the safety of intraspinal foetal stem cell transplantations in Amyotrophic Lateral Sclerosis patients, Clinical Trial Phase I

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Background and aims: Intraspinal stem cells (SCs) transplantation represents a new therapeutic experimental approach for Amyotrophic Lateral Sclerosis (ALS). Given the potential iatrogenic risk and the high costs, SC clinical trials usually recruit a small number of patients; hence, objective measures of safety and effectiveness are mandatory. We present the results obtained from our neurophysiological and neuroradiological protocol applied during a phase I clinical trial with human foetal neural Scs transplantation.

Methods: Spinal cord MRI (1.5 Tesla) with fiber tracking study, and transcranial magnetic stimulation derived from the bilateral FDI and tibialis anterior muscles were performed pre and post-surgery in 18 ALS patients recruited in a phase 1 clinical trial with hNSCs transplantation into the cervical and spinal cord. Central motor conduction time (CMTC), Motor Evocated Potential (MEP) amplitude and CSP duration, were calculated. In addition, we applied during the surgery a standard neurophysiological protocol including Somatosensory Evoked Potential obtained by stimulation of posterior tibialis and median nerve, and MEP with transcranial electrical stimulation.

Results: No patient manifested any clinical side effects during or after surgery. Amplitude and onset of cortical and radicular MEP such as CMTC did not change during and following surgery. MRI showed no modification of spinal cord morphology and DTI values.

Conclusion: The results obtained from neurophysiological and neuroimaging techniques are equally reliable to monitor the possible short-term side effects by surgery. Therefore, we believe future Phase II Clinical Trial could make use of neurophysiological tests only in the short-term monitoring of surgery because easier to perform, and cheaper.

Disclosure: Nothing to disclose

EP2110

The CSF values of advanced oxidation protein products and total thiol content in ALS patients

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Background and aims: Oxidative stress (OS) is considered as one of the most challenging hypothesis in pathogenesis of ALS. The aim of this study was to contribute to the understanding of what extent there is involvement of OS in ALS.

Methods: We assessed biomarkers of oxidative stress - Advanced Oxidation Protein Products (AOPP) and total thiol content (SH) in CSF of 24 ALS patients and 20 controls. Thirteen patients presented with the spinal form of the disease, while the remaining eleven patients had bulbar form.

Results: CSF AOPP levels were higher than those in control group (CG), while SH groups showed lower values compared to CG (p<0.001). When different clinical presentations were compared, AOPP values were higher in patients with bulbar compared with patients with common spinal manifestation (p<0.001). There were no differences in SH group's levels among different clinical forms. Significant negative AOPP and the SH group correlation was confirmed in ALS patients (p<0.01), especially in bulbar group (p<0.01). Significant mild correlations between tested parameters and functional rating scale and index of disease progression were recorded for both of tested parameters in spinal form of ALS (p<0.01), and were more pronounced for the levels of SH groups.

Conclusion: The data support that OS is involved in the patophysiology of ALS. CSF AOPP level may serve as useful biomarker of damage to the brain stem motor neurons. Neither AOPP nor SH groups in CSF of ALS patients can be used as certain biomarkers to assess disease progression.

Disclosure: Nothing to disclose

EP2111

Early-onset Hirayama disease in a female

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Background and aims: Hirayama disease(HD) is a rare myelopathy, occurring predominantly in males with onset in the teens.

Methods: Case report

Results: Here we present a 17yo Caucasian female patient who developed the first signs of HD at 10.5y of age. Prior to onset she had experienced a growth spurt and grew about 8 cm. At the age of 12y more obvious weakness of the hands, predominately on the left side, developed. Weakness increased in cold weather and the hands were often cold and sweaty. No sensory deficit was noticed. Neurological examination at age 13y revealed marked weakness (MRC 2 to 3-) for extension of the index and middle fingers bilaterally and for abduction of the left thumb. Additionally, there was weakness (MRC 3+ to 4) for extension of the ring and little fingers bilaterally, for abduction of the right thumb, and for abduction and adduction of the left fingers II-V, and flexion of the left fingers II-V. Postural tremor and poly-mini-myoclonus of the fingers on extension could be seen. There was marked wasting of the right thenar and mild wasting of other intrinsic hand muscles. The disease further progressed over the next years and the typical clinical, electrophysiological and neuroimaging signs of HD were found. After this period - and achievement of her final height, no further progression was noticed.

Conclusion: Pediatric neurologists should be aware of HD, which can also occur in girls in early adolescence. Prognosis of HD in females is fair and not at variance from males.

Disclosure: Nothing to disclose

EP2112

Mitochondrial disorder may mimic amyotrophic lateral sclerosis at onset

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Background and aims: Mimicry between mitochondrial disorder (MID) and amyotrophic lateral sclerosis (ALS) fades away with disease progression and development of mitochondrial multi-organ-disorder-syndrome. If the arising multio-organ involvement is mild, MID still may be misinterpreted as ALS.

Methods: Case report

Results: A 48 years old male developed slowly-progressive weakness, wasting and fasciculations initially on the left upper limb, which spread to the shoulder-girdle and the lower limbs. Since he additionally developed tetraspasticity, bulbar involvement, and electrophysiological investigations were indicative of a chronic neurogenic lesion, he was diagnosed as ALS. Re-evaluation by muscle biopsy because of features incompatible with ALS, such as hyperhidrosis, thyroid dysfunction, hyperlipidemia, and sensory involvement, revealed morphological features indicative of a MID and a combined complex-II/III defect. A MID was suspected since combined complex-II/III defect has not been reported in patients with ALS.

Conclusion: MID may mimic ALS at onset of the disease and may start as a mono-organ disorder to turn into a multi-organ disease after long-term progression. A combined complex-II/III defect may manifest with bulbar involvement.

Disclosure: Nothing to disclose

EP2113

Rehabilitation in ALS patients: Effects on circulating microRNAs

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Background and aims: Amyotrophic lateral sclerosis (ALS) is a rare, progressive, neurodegenerative disorder caused by degeneration of upper and lower motoneurons. The effects of exercise and rehabilitation in patients with ALS are still debated. A moderate and regular exercise is supported in the treatment of many neuromuscular diseases. We previously conducted microRNAs studies in ALS patients and we observed differences in myomiRNAs levels in spinal versus bulbar onset. In this study we analysed the role of circulating myomiRNAs after physical rehabilitation

Methods: We measured muscle specific microRNAs (miR-1, miR-206, miR-133a, miR-133b) by Real Time PCR in 19 ALS patients (12 male, 7 female). We analysed the levels of these microRNAs in serum collected before (T0) and after (T1) a period of 6-8 weeks of rehabilitation

Results: We observed a general down-regulation of all miRNAs studied after rehabilitation. In our population myomiRNAs decreased in a similar manner in male and female patients, therefore no gender effect was found. On the contrary the age of patients under study was found to be relevant: patients under 55 years old have a more marked decrease in myomiRNAs levels than patients with older age.

Conclusion: We have found that microRNAs are an important tool to monitor rehabilitation in ALS patients and suggests a positive effect of the treatment. There seems to be a more pronounced decrease in myomiRNA levels in patients with younger age in this motoneuron disease after physical rehabilitation. Further study are needed to correlate circulating microRNAs with muscle atrophy and to confirm age differences.

Disclosure: Nothing to disclose

EP2114

Granulocyte colony-stimulating factor for Amyotrophic Lateral Sclerosis: A randomized, double-blind, placebo-controlled study of Iranian patients

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Background and aims: The aim of this study was to determine the efficacy and tolerability of granulocyte colony-stimulating factor (G-CSF) in subjects with amyotrophic lateral sclerosis (ALS)

Methods: Forty subjects with ALS were randomly assigned to two groups, which received either subcutaneous G-CSF (5 μg/kg/q12h) or placebo for 5 days. The subjects were then followed up for 3 months using the ALS Functional Rating Scale-Revised (ALSFRS-R), manual muscle testing, ALS Assessment Questionnaire-40, and nerve conduction studies. CD34+/CD133+ cell count and monocyte chemoattractant protein-1 (MCP-1) levels were evaluated at baseline.

Results: The rate of disease progression did not differ significantly between the two groups. The reduction in ALSFRS-R scores was greater in female subjects in the G-CSF group than in their counterparts in the placebo group. There was a trend toward a positive correlation between baseline CSF MCP-1 levels and the change in ALSFRS-R scores in both groups (Spearman's $\rho=0.370$, $p=0.070$).

Conclusion: With the protocol implemented in this study, G-CSF is not a promising option for the treatment of ALS. Furthermore, it may accelerate disease progression in females.

Disclosure: Nothing to disclose

EP2115

Cancelled

EP2116

Brain white matter demyelinating lesions and amyotrophic lateral sclerosis in a patient with C9orf72 hexanucleotide repeat expansion

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Background and aims: A hexanucleotide repeat expansion in the C9orf72 gene has been associated to amyotrophic lateral sclerosis (ALS) and frontotemporal dementia. The association of multiple sclerosis (MS) and ALS with C9orf72 expansion was described before in four subjects. However, C9orf72 is not associated with increased risk of MS. Inflammatory pathways related to NF-κB have been linked to ALS and MS, and appear to be important in C9orf72-ALS patients.

Methods: Case Report

Results: A 42-year-old woman presented with progressive bulbar symptoms for 9 months. Past familial and personal medical history were unremarkable. Neurological examination disclosed severe spastic dysarthria, atrophic tongue with fasciculations, brisk jaw and limb tendon reflexes, and bilateral Hoffman sign. Brain MRI revealed bilateral, multiple periventricular and juxtacortical changes, configuring a MS-like pattern. Some of them showed gadolinium enhancement. Needle EMG sampling confirmed chronic neurogenic changes involving cranial-innervated muscles. Blood tests were unremarkable. CSF was normal, with no oligoclonal bands. Visual and somatosensory evoked potentials disclosed no abnormalities. Six months later, brain MRI was performed and no new demyelinating or gadolinium-enhancing lesions were identified. Genetic screening revealed a C9orf72 expansion.

Conclusion: This sporadic bulbar-onset ALS, with C9orf72 expansion, revealed white matter abnormalities on brain MRI suggestive of MS. As no clinical manifestation of MS was identified, a diagnosis of radiologically isolated syndrome would be considered. We speculate that these demyelinating lesions might facilitate expressivity of C9orf72 expansion, through NF-κB activation. This plausible association may lead to the identification of a therapeutic target in this subgroup of C9orf72-ALS patients.

Disclosure: Nothing to disclose

EP2117

Amyotrophic lateral sclerosis (ALS) in patient with dermatomyositis

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Background and aims: ALS causes the fast degeneration of both upper and lower motor neuron. Many mechanisms have been hypothesized to participate in pathogenesis while concurrent presence of ALS and other diseases including multiple sclerosis, frontotemporal dementia and myasthenia gravis has been described.

Methods: We present a case of ALS in a patient who had already dermatomyositis diagnosis.

Results: A 69 years old man was admitted to our department with a five-month history of dysarthria and swallowing difficulty. The patient had a dermatomyositis diagnosis established fifteen years ago, based on both clinical features and biopsy. He was treated with MTX and methylprednisolone initially. The last two years MTX dose was 5mg weekly as patient was asymptomatic. After clinical deterioration MTX dose increased to 25mg weekly. On first assessment to our department he presented right foot drop, fasciculations in arms and legs, bilateral Hoffman sign and hyperreflexia. MRI brain showed no signs of intracranial pathology. Blood tests were normal, while lumbar puncture revealed increased neurofilament. Electrophysiological studies showed presence of fibrillations, positive sharp waves and fasciculations. New clinical control further revealed muscle weakness, unilateral positive Babinski sign and tongue fibrillations. Biopsy didn´t show any signs of active inflammatory myopathy. Eventually ALS diagnosis was set and the patient started treatment with riluzole.

Conclusion: To our knowledge this is the first time that dermatomyositis and ALS are present to the same patient. Further studies are required to establish a potential connection between inflammatory myopathies and ALS.

Disclosure: Nothing to disclose

EP2118

Five cases of motor neuron disease associated with a neoplastic process

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Background and aims: Motor Neuron Disease (MND) and neoplastic processes association is rarely described.

Methods: We retrospectively analyzed 35 patients with MND followed in our Hospital since 2013.

Results: A neoplastic process was found in five patients. Case1: 54 years old (y/o) female, had breast tumorectomy and radiotherapy in 2005 due to invasive ductal breast cancer (IDBC), BRCA2 mutation-related. The IDBC relapsed in 2015 implying bilateral mastectomy. After one month, develops symptoms of upper and lower (U+L) MND affecting bulbar, cervical, dorsal and lumbosacral (B+C+D+LS) segments. Onconeuronal antibodies were weakly positive for anti-PNMA2. Case2: 52 y/o female with U+L MND signs in C+D+LS segments in 2013. A thymoma was diagnosed in December 2016. Onconeural antibodies and anti-VGKC (anti-CASPR2 and anti-LGI1) were negative. Case3: 47 y/o male developing lower MND signs affecting B+C+D+LS segments starting in 2015. Onconeural antibodies were positive for Anti-Yo. A Hürthle cell follicular thyroid carcinoma was diagnosed in 2016 being submitted to hemithyroidectomy followed by two cycles of IVIg. Case4: 74 y/o female diagnosed with IDBC in 2014, submitted to mastectomy, radiotherapy and hormonotherapy. In 2016 initiates rapidly progressive symptoms of U+L MND affecting B+C+D+LS segments. Onconeural antibodies not performed. Case5: 71 y/o male presented with U+L MND affecting B+C+D+LS, in 2010. Diagnosed with lung adenocarcinoma in 2011 and submitted to chemo and radiotherapy. He died in 2016. Onconeural antibodies not performed.

Conclusion: In our cohort, 14.3% of MND patients were diagnosed with a neoplastic process. Treating the neoplastic process may potentially halt or reverse the progression of MND.

Disclosure: Nothing to disclose

EP2119

Possible contribution of NO system in the pathogenesis of spinal muscular atrophy, type 2, in in vitro experiments

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Background and aims: Investigate the effect of the substance - RSPU-260 - that increases the activity of endothelial NO-synthase in the condition of organotypic cultivation of spinal ganglia in the medium containing plasma of the patients SMA type 2.

Methods: Objects of the study were the plasma of 12 patients of SMA type 2 and 1200 sensory ganglions of 10-12-day chicken embryos cultivated for 3 days. Control explants were cultivated in a nutrient medium of standard composition. We have added blood serum of 2 type SMA patients to cultural medium in 600 test dishes.The agent RGPU-260 in concentration 10-7 or 10-5 M was added to the culture medium on the plates together with blood serum in a part of experiments. The data were processed with STATISTICA 68.0 and Student's t-test at p=0.05.

Results: The blood serum of 12 patients with SMA, type 2, at dilutions of 1:2, 1:10, 1:50 completely blocked the growth of neurites of sensory ganglia. With further dilution of 1:100, the blood serum did not affect the growth of neurites. The cultivation of explants of spinal ganglia in the growth medium containing the blood serum at a dilution of 1:70 and RSPU-260 (10-5 M), revealed positive elimination of inhibition of neurites by the serum.

Conclusion: There was no inhibition of neurites by the blood serum with RSPU-260, which increases the activity of endothelial NO-synthase, in concentration (10-5M). Thus, the model conditions revealed neuroprotective effects of NO system, apparently mediated by the change of activity of endothelial NO-synthase.

Disclosure: Nothing to disclose

EP2120

Hirayama disease as an ALS-like syndrome

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Background and aims: Hirayama disease (HD) is a slowly progressive benign motor neuron disease that affects the distal upper limb. The gradual onset, progressive course of the disease, and isolated motor neuron involvement may mimic early stage of the amyotrophic lateral sclerosis (ALS).

Methods: Clinical case

Results: A 25-year-old woman presented with evident weakness and hypotrophy in her left arm (more pronounced in the hand) with muscle cramps caused by cold temperature, which slowly progressed for 8 years (Fig. 1). Nerve conduction study revealed signs of damage of the left ulnar nerve with velocity reduction at the elbow joint. Needle electromyography revealed signs of moderate active denervation and fasciculation potentials only in the muscles innervated by the ulnar nerve. Signs of reinnervation were also found at the cervical segments, which are typical for anterior horn disfunction. MRI of the cervical spine was unremarkable. ALS was diagnosed. Later MRI revealed spinal cord flattening and T2-hyperintensity at the C5-C6 levels in neutral position (cervical lordosis was normal and epidural space was not enlarged); in flexion position, displacement of the posterior dura was visualized (Fig. 2). T2-hyperintensity focus was revealed intramedullary at the same level in the left anterior horn (Fig. 3). Thus HD was diagnosed.

Fig. 2. MRI of the cervical spine in neutral and flexion position
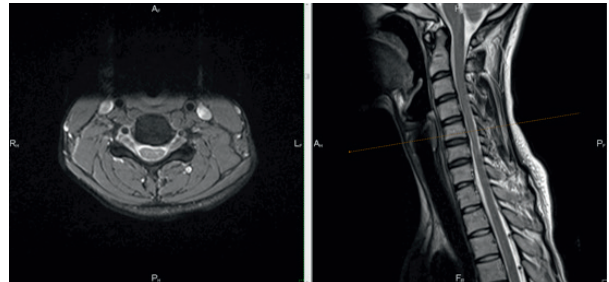
Fig. 3. MRI - T2-hyperintensity myelopathy focus

Conclusion: HD is a rare condition with clinical presentation similar to ALS, however it has specific signs described by K. Hirayama. The neurologists and MRI-specialists should be more informed about HD given the importance of its early diagnosis.

Disclosure: Nothing to disclose

Fig.1. Hypotrophy of left hand

Movement disorders 3

EP2121

Speech and voice response to levodopa in late-stage Parkinson's disease patients: Report from an acute levodopa challenge

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Background and aims: Parkinson's disease (PD) patients are affected by hypophonia, dysprosody and dysarthria that worsen with disease progression. The influence of levodopa on the quality of speech is inconclusive, and no data are available for late-stage PD (LSPD).

Methods: LSPD patients (Schwab and England ADL Scale (SE) ≤50 or Hoehn Yahr (HY) Stage >3 (MED ON)), underwent a levodopa challenge with a supra-maximal dose (150%). Before and after levodopa intake, each participant performed several vocal tasks selected from the European Portuguese version of the Frenchay Dysarthria Assessment version 2 in order to assess: respiratory support for speech, voice quality, voice stability, voice variability and speech rate. Motor performance was evaluated by the MDS-UPDRS part III. All voice samples were recorded using a tabletop unidirectional microphone and analyzed by a speech and language therapist blinded to patients' therapeutic condition using the Praat 5.1 software.

Results: Twenty-four of the twenty-seven LSPD patients included in the study succeeded in performing the voice tasks. Clinical characteristics are detailed in Table I. A positive correlation was found between disease duration and voice quality (R=0.8; p<0.05) and variability (R=0.793; p<0.05). Levodopa significantly improved the MDS-UPDRS-III score (20%), with a beneficial effect on axial signs with the exception of speech, but no improvement was found by means of automated analysis (Table II).

Patients data	LSPD (n= 24)	LSPD MALE (n=14)	LSPD FENALE (n=10)	p-value
Age (yrs)	79 [71.5-81.7]	77.5 [70.7-81.2]	79 [73.5-85]	ns
Age at disease onset (yrs)	64.5 [54.5-69.5]	62.5 [55-67]	65 [51-71.5]	ns
Disease duration	14.5 [11-15.7]	13.5 [8.7-17]	15 [11.7-17.2]	ns
Education (yrs)	4 [4-11]	4 [4-12]	5 [4-10.5]	ns
S&E (ON/OFF)	40/35 [40-40.7 / 22.5-40]	40/30 [40-40/ 40-40]	40/30 [27-50 / 17.5-50]	ns
HY (ON/OFF)	4 [2-4] / 4 [2-4.75]	3 [2-4] / 3 [2-4]	4 [4-5] /4 [4-5]	ns
PDD (n (%))	14 (58%)	10 (71%)	4 (40%)	ns
MMSE MMSE (demented/non-demented)	22.5 [21.2-25] 22 [17-23.7] / 25 [23-26.7]	22.5 [22-24.2] 22 [21.7-24.2] / 23 [22.2-25.2]	22.5 [16-27.2] 17 [13-19.5] / 27 [25-28.5]	ns
LEDD (mg)	1037 [902-1272]	1100 [990-1303]	905 [742-1257]	ns
MDS-UPDRS-II	31 [27-38]	32 [29.2 – 38.5]	30 [20.5-38]	ns
MDS-UPDRS-III (MED ON/MED OFF)	50 [40-54]/64 [52-77]	50 [42.5-55.2]/61[53-76]	50 [37.5-62.5] /64 [48-79.5]	ns
Axial sign (MED ON/MED OFF)	8 [6-13] /10 [7-13]	8 [6-13]/10 [7-13.2]	8 [6.5-12]/ 10 [7-13.5]	ns
MDS-UPDRS-IV	4 [2-9.5]	5 [2-8.5]	4 [0-11.2]	ns

Table I. Values are presented as median [IQR, 25th–75th percentile] if no otherwise specified; ns: not significant. LEDD: L-dopa equivalent daily dose; PDD: Parkinson's disease with dementia; MMSE: mini mental state examination. S&E: Schwab and England scale, HY: Hoehn Yahr Stage. P value is the results for male vs. female scores's comparison.

Table.I

LSPD patients (No 24)			
	MED OFF	MED ON	p–value
MDS-UPDRS-III	64 [52-77]	50 [40-54]	<0.001
Speech	2 [1-3]	2 [1-3]	0.8
Freezing of gait	3 [1-4]	2 [0-3]	<0.05
Postural Stability	3 [2-4]	3 [2-3]	<0.05
Gait	3 [2-4]	3 [2-3]	<0.05
Axial Signs	10 [7-13]	8 [6-13]	<0.05
HY	4 [2-4.75]	4 [2-4]	0.7
Voice Respiratory support for speech Vowel duration (sec)	5.8 [4.4-11.5]	7 [3.6-10.6]	0.6
Voice stability			
Pitch break time	1.2 [0.2-2.4]	0.8 [0.17-3.5]	0.9
SDF0	2.4 [1.6-4]	2.3 [1.3-5.1]	0.8
Jitter	0.8 [0.5-1.1]	0.7 [0.4-1]	0.3
Voice quality F0_ranges	154 [125-200]	162 [147-203]	0.2
Voice variability SemitoneSD±SD	31 [18-51]	29 [20-40]	0.3
Speech rate	3 [1.6-5.6]	3 [4.2-1.7]	0.2

Table 2. Values are presented as median [IQR, 25th–75th percentile]. Statistical significant results are in bold. Axial Signs: sum of item 3.1, 3.10-3.12 of the MDS-UPDRS-III. P – value is the results of MED OFF versus MED ON scores.

Table.II

Conclusion: Speech is severely affected among LSPD patients. Although levodopa still had some effect on motor performance, no improvement was found on speech neither by means of a clinician rating scale nor by automated analysis.

Disclosure: Nothing to disclose

EP2122

Fatigue assessment and risk factors in Parkinson's disease

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Background and aims: Fatigue is a frequently encountered non-motor symptom in Parkinson's disease (PD). There are several scales designed to assess fatigue.

Objectives: the aim of this study is to evaluate the severity of fatigue in patients with Parkinson's disease as well as possible risk factors and the impact on quality of life.

Methods: Prospective study on 52 patients with PD. Fatigue was assessed using Fatigue Symptom Inventory (FSI).

Results: The study included 30 males (58%), with mean age of 61.7 years. For the first part of the scale (questions 1-4), most of the patients rated a moderate level of fatigue (5 out of 10 points on the rating scale). Regarding the perceived interference with quality of life, most of the patients rated a mild-to moderate impact of fatigue (mean of 3.6 out of 10 points for males). Most of the patients (36.3% males, 27.2% females) felt fatigued during three out of seven days, considering the previous week as the reference interval. The patients felt the fatigue mostly during evening. Levodopa equivalent dose and depression are independent risk factors for presence and degree of fatigue.

Conclusion: Fatigue is an important symptom reported by the patients with PD and it impairs quality of life to various degrees.

Disclosure: Nothing to disclose

EP2123

Autoimmune haemolytic anaemia related to apomorphine

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Background and aims: Case report of autoimmune haemolytic anaemia (AIHA) secondary to apomorphine. Well-Known entity related to L-dopa and rarely cause by apomorphine.

Methods: A 62-year-old patient with idiopathic Parkinson disease (IPD) of 10 years of evolution treated with L dopa/carbidopa/Entacapone (375/93,75/600mg per day) and continuous subcutaneous infusion of apomorphine began in June of 2015 (6.5 mg/h during 12 h; total daily apomorphine: 78 mg) maintaining low disability in Schwab & England Scale (90%). In November 2016 was admitted to hospital by hemodynamic angina secondary to severe anaemia (haemoglobin 6.9mg/dl). The haematological studies conclude that presents an AIHA. After ruling out autoimmune diseases, infections or neoplasms associated, the aetiology was interpreted as pharmacological, withdrawing levodopa/carbidopa/entacapone, and starting therapy with methylprednisolone, immunoglobulins, and rituximab. Three weeks later a severe anaemia persisted requiring transfusion; consequently, we finally removed apomorphine and added levodopa/carbidopa, with what the haemoglobin level improved.

Results: Haemoglobin levels after 3 months since the withdrawal of apomorphine were normal so that we attach to this drug cause AIHA. The literature reviewed, shows only 1 case secondary to apomorphine after 6 months of treatment, in our case the AIHA occurred after 17 months.

Conclusion: The apomorphine infusion is a therapy used for EPI, with favourable clinical outcome and safe use, even though there are described range of adverse effects. In spite of the rarity of this complication, it must be recognized, because of may compromise the patient's life. The apomorphine in this case should be suspended valuing other therapies for advanced IPD.

Disclosure: Nothing to disclose

EP2124

Myoclonic dystonia (DYT11) responsive to insulin therapy. A case-report

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Background and aims: A 44-year-old male has been followed for myoclonic dystonia (DYT11) due to a heterozygous pathogenic mutation in the epsilon-sarcoglycan gene (SGCE, NM_003919.2:c.1114C>T). At the age of 44, the patient developed diabetes mellitus type 1, and therefore insulin regimen was started. At each administration of subcutaneous rapid insulin, he reported symptoms' relief, which persisted throughout the insulin effect. We wondered whether the symptom improvement were due to either the reduction of glucose levels or to an insulin-mediated effect.

Methods: After insulin injection and for the next 3.5 hours, a videotape of clinical symptoms along with capillary blood glucose determinations was carried out. Myoclonus was evaluated with the Unified Myoclonus Rating Scale (UMRS).

Results: As reported in Figure1, symptoms clearly improved few minutes after insulin injection. Symptoms remained stable for about three hours, when myoclonus progressively reappeared. We did not find any correlation between UMRS total score and capillary blood glucose levels, while the correlation with time from insulin injection resulted significant (Spearman's rho=-0.629, p=0.038).
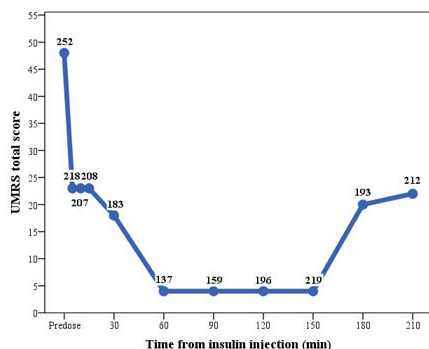
Conclusion: At our best knowledge, insulin-mediated improvement of myoclonus has never been reported. Even though the brain has been considered a former non-classical insulin responsive tissue, it is now recognized as an insulin sensitive organ. In the brain, insulin might exert neuromodulating effect. Albeit these considerations are theoretical, this is the first report arguing for a possible direct insulin effect on myoclonic symptoms. This intriguing association could open new perspectives for treatment of myoclonus or, at least, for myoclonus due to SGCE mutations.

Disclosure: Nothing to disclose

EP2125

Features of speech in Wilson's and Parkinson's diseases revealed by spectral analysis

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Background and aims: Speech impairment occurs in Wilson's and Parkinson's diseases (WD and PD) and may manifest as dysphonia (due to worsening of larynx muscles control) and dysarthria (due to worse control of airways and oral cavity resonance qualities). In the «source-filter» model human speech apparatus is considered as consisting of independent sound source (larynx), linear filter (oro- and nasopharynx, nasal passages, oral cavity), and emitter (mouth). The objective of the research was to study speech impairment in PD and WD, utilizing digital spectral voice analysis.

Methods: Speech was recorded digitally with 16kHz quantization rate while counting from 1 to 30. Calculations were performed using scripts in R language. Spectral analysis was performed on 50ms samples, with step between samples being 10ms; samples which contain speech were detected automatically. For each sample we estimated voice fundamental frequency (FF) using cepstral analysis, and evaluated results for presence of irregular fast FF changes, voice interruptions, and periods of absent FF while vowel pronunciation. Using conventional spectral density estimation, we calculated frequencies F25 and F75, for which intervals [200Hz;F25] and [200Hz;F75] contain 25% and 75% of power in the range [200Hz;4000Hz] respectively.

Results: We studied 29 PD and 35 WD patients. Disturbances of voice production were found in 20 PD patients (69.0%) and 25 WD patients (71.4%). Number of F25-F75 clusters less than 5 (which reflect disturbance of articulation) was found in 8 PD patients (27.6%) and in 18 WD patients (51.4%).

Conclusion: Spectral analysis is a useful tool for speech assessment in PD and WD.

Disclosure: Part of the research on Wilson's disease was done while the visit to the Institute of Psychiatry and Neurology (Warsaw, Poland), which was funded by the EAN Clinical Fellowship program.

EP2126

The Prevalence of Restless Legs Syndrome in Edirne and its districts: concomitant comorbid conditions and secondary complications

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Background and aims: We aimed to determine the prevalence and riskfactors of restless legs syndrome in Edirne and its districts, located in Western Thrace, which is the most western part of Turkey.

Methods: In this study, 4003 individuals who could communicate and agreed to participate in the study were evaluated. To obtain the data from the applicants in 30 Family Health Centres in Edirne and its districts, a face-to-face questionnaire that consisted of 54 questions was prepared by the researchers.The questionnaire included general information, questions to evaluate potential concomitant comorbid conditionsand questions regarding the symptomatology used inrestless legs syndrome (RLS) diagnosis, as well as questionsto evaluate insomnia and tension-type headache secondary to insomnia according to the ICD-II Criteria (InternationalClassification of Sleep Disorders-II Criteria).

Results: Of 4003 individuals, 282 were diagnosed with RLS according to the questionnaire results from Edirne and its districts, and the prevalence of RLS was 7%. Approximately, 47.9% of the patients with RLS were male, and 52.1% were female, which was not significantly different (p[0.05). Anaemia was identified in 41.1% of the cases and control group was detected in 19.4%, which was significantly different (p\ 0.001). Secondary insomnia was identified in 64.2% of the cases with RLS and was not detected in 35.8%, which was significantly different (p\0.001).

Conclusion: RLS prevalence studies will increase the awareness of the community and provide early diagnosis and treatment, as well as serve as a basis to reduce morbidity and improve the quality of life.

Disclosure: Nothing to disclose

EP2127

A case of hereditary tyrosinemia type 3 in an adult patient with atypical parkinsonism

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Background and aims: Tyrosine is an aromatic amino acid important in the synthesis of catecholamines, thyroid hormones and melanin. Hereditary tyrosinemia type 3 is a rare autosomal recessive disorder caused by deficiency of 4-hydroxyphenylpyruvate-dioxygenase (HPD), the second step in the tyrosine catabolism pathway that may result in elevated plasma tyrosine concentrations. The affected patients have neurologic dysfunction: ataxia, tremor, seizures, mild psychomotor and mental retardation. Treatment consists of a diet low in tyrosine and phenylalanine.

Methods: 54-year-old man with arterial hypertension and obstructive sleep apnea who presented from childhood cephalic, lips and limbs tremor. His parents were consanguineous. His father was diagnosed with essential tremor and his brother had mental retardation and general tremor. In the last years our patient presented hypersomnia, generalized slowness of movement, ataxia and worsening tremor. He also had decreased verbal fluency and apathy. Clinical signs and symptoms were compatible with a tremoric hypokinetic syndrome with cognitive impairment and depression.

Results: Tests showed: elevated tyrosine concentrations (plasma: 553 micromol/L, urine: 0.91 mmol/g), moderate cognitive impairment (neuropsychological-tests) and mutation in homozygosis in exon 8 of the HPD gen (c.479A>G)(p.Try160Cys). Cranial magnetic resonance imaging and DaTSCAN were normal. We started diet and symptomatic treatment.

EXCRECION DE AMINOACIDOS FISIOLOGICOS E

GLUTAMICO	0,02	mmol/g creatinina	(0,00-0,11)
HIDROXIPROLINA	0,02	mmol/g creatinina	(0,00-0,11)
SERINA	0,20	mmol/g creatinina	(0,00-0,42)
ASPARRAGINA	0,09	mmol/g creatinina	(0,00-0,38)
GLICINA	0,56	mmol/g creatinina	(0,00-2,40)
GLUTAMINA	0,33	mmol/g creatinina	(0,00-0,81)
TAURINA	1,05	mmol/g creatinina	(0,00-1,50)
HISTIDINA	0,62	mmol/g creatinina	(0,00-1,10)
CITRULINA	0,01	mmol/g creatinina	(0,00-0,10)
ALANINA	0,23	mmol/g creatinina	(0,00-0,51)
ARGININA	0,01	mmol/g creatinina	(0,00-0,04)
PROLINA	0,01	mmol/g creatinina	(0,00-0,12)
3-METIL-HISTIDINA	0,32	mmol/g creatinina	(0,00-0,35)
TIROSINA	0,91	*mmol/g creatinina	(0,00-0,14)
VALINA	0,04	mmol/g creatinina	(0,00-0,10)
METIONINA	0,00	mmol/g creatinina	(0,00-0,03)
CISTINA	0,03	mmol/g creatinina	(0,00-0,15)
ISOLEUCINA	0,01	mmol/g creatinina	(0,00-0,02)
LEUCINA	0,01	mmol/g creatinina	(0,00-0,06)
FENILALANINA	0,02	mmol/g creatinina	(0,00-0,16)
TRIPTOFANO	0,03	mmol/g creatinina	(0,00-0,09)
ORNITINA	0,00	mmol/g creatinina	(0,00-0,05)
LISINA	0,03	mmol/g creatinina	(0,00-0,35)

Image 2: Tyrosine concentrations urine

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        PERFIL DE AMINOACIDOS

ASPARTICO          32  *umol/L   (6-22)
GLUTAMICO         139  *umol/L   (25-110)
ARGINO-SUCCINICO    5   umol/L   (4-13)
HIDROXIPROLINA      9   umol/L   (5-30)
SERINA            129   umol/L   (60-180)
ASPARRAGINA       101   umol/L   (40-120)
GLICINA           250   umol/L   (105-350)
GLUTAMINA         578   umol/L   (300-675)
TAURINA           128  *umol/L   (30-125)
HISTIDINA          67   umol/L   (40-90)
CITRULINA          27   umol/L   (15-40)
TREONINA           84   umol/L   (60-175)
ALANINA           455   umol/L   (200-500)
ARGININA           98   umol/L   (50-170)
PROLINA           162   umol/L   (100-320)
TIROSINA          551  *umol/L   (35-100)
VALINA            262   umol/L   (150-325)
METIONINA          28   umol/L   (15-45)
CISTINA            15   umol/L   (15-55)
ISOLEUCINA         73   umol/L   (35-90)
LEUCINA           162  *umol/L   (70-160)
FENILALANINA       62   umol/L   (30-80)
TRIPTOFANO         52   umol/L   (30-70)
ORNITINA          105  *umol/L   (20-80)
LISINA            216   umol/L   (80-225)
```

Image 1: Tyrosine concentrations plasma
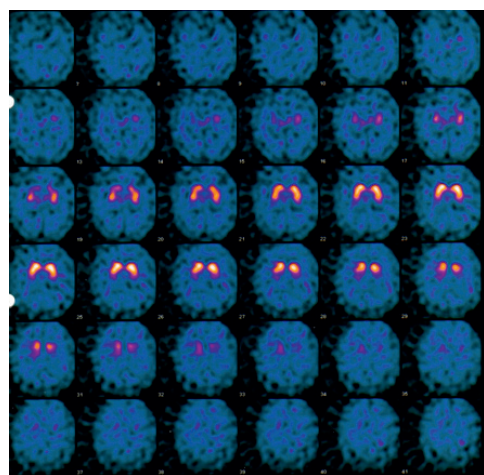
Image 3: DaT-SCAN SPECT

Conclusion: We present the first described case of hereditary tyrosinemia type 3 that was presented clinically as an atypical parkinsonism syndrome. We emphasize the importance of thinking in this disorder if we have a patient with essential tremor and parkinsonism symptoms, especially if they were started from infancy and there are other family members with these symtoms.

Disclosure: Nothing to disclose

EP2128

Depression and anxiety symptoms in dystonic patients

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Background and aims: To study depression and anxiety symptoms in patients with dystonia.

Methods: We treated 223 patients with dystonia (age 44.1±5.0 years, duration of diseases 9.3±0.49 years, the ratio of men and women 1.4:1). The control group consisted of 65 healthy volunteers. We used Hospital Anxiety Depression Scale (HADS), Beck and Spielberger scales and calculated the rate of reactive (situational) anxiety (RA) and personal anxiety (PA).

Results: The average anxiety index on HADS in patients with dystonia was 8.03±3.56, in control group - 2.56±2.08 (P>0.05). The average level of RA in patients with dystonia was 43.9±6.5 marks, in control group - 20.8±8.7 marks (P<0.01), the average level of PA in dystonia was 51.5±5.7 marks, in healthy volunteers - 43.6±8.1 marks (P<0.01). The average level of RA and PA in patients with dystonia means high anxiety. The average deression index on Beck scale in patients was 11.94±6.4 marks, in control group - 6.7±5.2 marks (P<0.05). Generally, 142 (63.7%) patients with dystonia and 8 (12.3%) healthy volunteers had symptoms of depression (P<0.01).

Conclusion: Patients with dystonia had a higher level of anxiety and depression. We have eatablished a high level of PA which prevailed over RA on Spielberger scale. Psychologists and psychotherapists should be involved in treatment and rehabilitation of patients with dystonia.

Disclosure: Nothing to disclose

EP2129

Cancelled

EP2130

Use of the neuropsychiatric inventory to characterize the course of neuropsychiatric symptoms in progressive supranuclear palsy

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Background and aims: Several studies analyzed behavioral and neuropsychiatric symptoms of PSP and emphasized depression and/or apathy as the most prevalent. We aimed to determine the neuropsychiatric profile in our cohort of PSP patients and their dynamic changes over a follow-up period of one year.
Methods: A total of 59 patients were assessed at baseline, while 25 of them were accessible after one year of the follow-up. The detailed demographic and clinical interview was performed and appropriate motor and cognitive scales were applied. The presence of psychiatric symptoms was assessed using the Neuropsychiatric Inventory (NPI). In addition, depressive and anxiety symptoms, as well as apathy, were evaluated by the Hamilton Depression Rating Scale, the Beck Depression Inventory, Hamilton Anxiety Rating Scale, and the Apathy Scale, respectively. Statistical analysis of baseline data included both correlation and linear univariate and multivariate regression analyses. The value of changes of selected variables over one-year follow-up period, was quantified using the Wilcoxon signed ranks test. The level of these differences was calculated as an effect size.
Results: The most common symptoms were apathy and depression, which were also found to be the independent determinants of increased NPI total score in the longitudinal study. Apathy deteriorated most profoundly over the follow-up period.
Conclusion: Our study implied that apathy was a predominant feature of the behavior profile of PSP. Finally, the NPI seemed to be a sensitive measure of behavioral changes in PSP and could be included among potential outcome measures in future clinical trials in PSP.
Disclosure: This work has been funded by the Ministry of Education, Science and Technological Development Republic of Serbia (project no. 175090).

EP2131

Levodopa/carbidopa intestinal gel can improve both motor and non-motor experiences of daily living in Parkinson's disease: An open-label study

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Background and aims: Levodopa/carbidopa intestinal gel therapy (LCIG) can efficiently improve several motor and non-motor symptoms of advanced Parkinson's disease (PD). The recently developed Movement Disorder Society-sponsored Unified Parkinson's Disease Rating Scale (MDS-UPDRS) improved the original UPDRS making it a more robust tool to evaluate therapeutic changes. However, previous studies have not used the MDS-UPDRS and the Unified Dyskinesia Rating Scale (UDysRS) to assess the efficacy of LCIG. Our aim was to determine if the MDS-UPDRS and UDysRS could detect improvement in the experiences of daily living following 1-year LCIG treatment.
Methods: In this prospective, multicenter, open-label study, 34 consecutive patients undergoing LCIG treatment were enrolled. Patients were examined twice: prior to LCIG initiation and 12 months later. Impact of PD-related symptoms and dyskinesia was assessed by the MDS-UPDRS and UDysRS.
Results: Non-motor Experiences of Daily Living part of MDS-UPDRS improved from 20 (median, interquartile-range, IQR:14-23) to 16 points (median, IQR:12-20, p=0.044) and the Motor Experiences of Daily Living ameliorated from 24 (median, IQR:20-29) to 18 points (median, IQR:13-25, p=0.025). Health-related quality of life, measured by PDQ-39, also improved from 35.4 (median, IQR:26.9-50.3) to 27.0 (median, IQR:21.3-31.4) points (p=0.003). The total score of UDysRS decreased from 47 (median, IQR:36-54) to 34 (median, IQR:21-45) points (p=0.003).
Conclusion: As far as the authors are aware of, our paper is the first to evaluate the impact of LCIG on dyskinesia by the means of UDysRS. Changes in MDS-UPDRS and UDysRS confirm that LCIG treatment can efficiently improve experiences of daily living in advanced PD.

EP2132

Quantitative assessment of gait parameters in Parkinsonian patients treated with bilateral subthalamic stimulation

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Background and aims: The effects of bilateral subthalamic stimulation (STN-DBS) on gait in Parkinson's disease varied in previous studies. Our aim was to analyse how bilateral STN-DBS influences the kinematic parameters of gait in Parkinson's disease during an instrumented timed up-and-go (ITUG) test.

Methods: Thirteen Parkinsonian patients treated with STN-DBS performed the ITUG-test in both OFF (NON), left ON (LON), right ON (RON) and both ON (BON) stimulation conditions in randomized order, in medication OFF stage. Six Opal monitors (APDM Inc.) consisting of a 3-axis accelerometer and gyroscope were placed on the two wrists and ankles, trunk and chest. Mobility Lab software (APDM Inc.) was used for data analysis. The Wilcoxon signed rank test was performed to compare gait parameters in the conditions.

Results: The total duration of the ITUG-test, stride length, and stride velocity improved in BON compared to NON state (Table1). The gait rhythmicity and the time proportion of double support were similar in the two conditions. Bilateral stimulation significantly improved the trunk velocities during gait, the turning duration, and the turn peak velocity. The RON – but not LON, condition improved the parameters of turning. Turn-to-sit time was shorter in BON than in NON state, but their difference was not significant.

	Total duration (sec)	Stride Length (% of Stature)	Stride Velocity (% of stature/sec)	Cadence (steps/min)	Double Support (% of gait cycle time)	Turning Duration (sec)	Turning Peak velocity (degree/sec)	Turn-to-sit Time (sec)
NON median(IQR)	30(6,3)	68(12,9)	61(11,7)	108(19)	23(3,7)	2,7(1,29)	129(39,6)	4,1 (1,74)
BON median(IQR)	20(4,4)	72(6,9)	65(12,7)	106(14)	21(5,1)	2,2(0,55)	158(32,5)	3,7(0,96)
level of sign.: p	0,02	0,009	0,007	NS	NS	0,023	0,013	0,055

Table 1. Gait parameters during ITUG test in BON (both ON) and NON (both OFF) states

Table 1.

Conclusion: Many gait and turning parameters improved with bilateral stimulation consistently with previous findings. Unilateral stimulation had lower effects on most parameters than bilateral stimulation, but right and left-sided stimulation still need to be further examined with a detailed analysis of the electrode positions.

EP2133

Paroxismal painful dystonia of leg muscles in vascular parkinsonism

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Background and aims: Vascular parkinsonism (VP) is a nosology the clinical picture of which is not clearly delineated. Objective of our investigation was to study all the clinical manifestations of the patients with VP.

Methods: 12 patients (5 women/7men, aged 65-80 years) were investigated using UPDRS, Tinnetti scale and MoCA. Diagnosis of VP was based on the presence of multiple lacunes on brain MRI along with lower-body parkinsonism. All the patients were receiving L-Dopa (500-1000 mg/day).

Results: In all patients most prominent symptom was gait disturbance- start hesitation, freezing and festination. There was prominent hypokinesia and rigidity in legs as opposed to hands. 7 patients had rigidity of axial muscles. 5 patients had mild postural tremor in hands. There was no gaze palsy detected. 10 patient have mild cognitive impairment. Response to L-Dopa was poor in all the cases. All women patients experienced attacks of severe and very painful dystonic spasm of leg muscles with enormous hypertonia of leg extensors, so that it was impossible to perform passive flexion. Spasm lasted from 10 min up to 1 hour and repeated several times a day and at night. No such phenomena was observed in male patients. In all 5 patients gabapentin 900-1600 mg/day effectively reduced attacks of painful dystonia.

Conclusion: Painful leg dystonia can be regarded as a characteristic symptom of vascular parkinsonism. Dystonic attacks are not related to L-Dopa wearing-off and can be effectively controlled with gabapentine.

Disclosure: Nothing to disclose

Movement disorders 4

EP2134

A novel SCN4A N440K transgenic zebrafish model of human nondystrophic myotonia

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Background and aims: The present study aimed to gain insight into the pathophysiological basis of nondystrophic myotonia and the phenotypic heterogeneity of the human SCN4A(hSCN4A) N440K mutation.

Methods: A novel transgenic zebrafish model of human nondystrophic myotonia was generated and validated using electromyography (EMG) and behavioral tests.

Results: The hSCN4AN440K mutant zebrafish exhibited both exercise- and cold-induced myotonia, as determined by thetypical EMG finding of myotonic discharges with dive-bomber sound and a typical "dive-bombing behavior", respectively. The mutant fish achieved lower values in the parameters tested (mean velocity and distance moved, and time spent and number of visits in zones)than control fish. No consistent pattern indicative of the warm-up phenomenon or paramyotonia was observed.

Conclusion: We report herein the first zebrafish model of exercise- and cold-induced human nondystrophicmyotonia. The phenotypic heterogeneity of hSCN4A N440K might not be attributed to the mutation alone. Our results provide insight into the pathophysiology of myotonia in sodium channelopathy and could be used for exploring a new therapeutic avenue.

Disclosure: This work was in part funded by a grant from the Korea Health 21 R&D Project, Ministry of Health, Welfare & Family Affairs, Republic of Korea (A100402).

EP2135

Cerebrospinal fluid biomarkers in a cohort of p.A53T SNCA mutation carriers: Correlation with clinical phenotype

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Background and aims: The p.A53T point mutation in the α-synuclein gene is a rare cause of autosomal-dominant Parkinson's disease (PD). The classical phenotypes include PD, PD with dementia (PDD), or dementia with Lewy bodies. However, data available on cerebrospinal fluid (CSF) biomarkers in p.A53T carriers are largely lacking. Our study aims to measure CSF levels of beta-amyloid1-42, total-tau, and phospho-tau181, in A53T PD and non-manifesting carriers.

Methods: A total of 9 CSF samples were analyzed: 7 A53T PD patients and 2 asymptomatic p.A53T carriers. All participants underwent a detailed diagnostic assessment, including clinical (MDS-UPDRS), neuropsychological investigations (MOCA, GDS), brain MRI scans and CSF biomarker analysis.

Results: The phenotype of symptomatic carriers was variable, with 3 patients manifestating typical motor parkinsonian symptoms without cognitive involvement, 2 PDD patients with initial motor symptoms and later onset cognitive decline, and 2 patients exhibiting an atypical frontotemporal dementia (FTD)like phenotype prior to parkinsonism onset. CSF Aβ42 levels were marginally decreased only in 2 PDD patients. CSF total-tau level was elevated in both FTD phenotype patients, but was normal in the remaining A53T carriers (5 symptomatic/2 asymptomatic), regardless of their cognitive profile. Phospho-tau181 were within normal limits. Brain MRI scans were normal in all subjects, with the exception of the 2 FTD phenotype patients who demonstrated fronto-temporo-parietal atrophy.

Conclusion: p.A53T carriers demonstrate an heterogeneous CSF biomarker profile which could correlate with their variable degree of motor and cognitive deterioration. Further investigations are required to test the predictive performance of CSF biomarkers in this rare genetic PD cohort.

Disclosure: Nothing to disclose

EP2136

Middle cerebellar peduncle lesions – various tremor characteristics

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Background and aims: Recent studies suggest that alterations of the cerebello-thalamo-cortical network are responsible for tremorogenesis in essential tremor. The middle cerebellar peduncle (MCP) represents a key connection in this network as it conveys afferent fibers from the cerebral cortex to the cerebellum. We report a case series of patients with lesions of the middle cerebellar peduncle (MCP) having different tremor characteristics.

Methods: We analyzed quantitatively the tremor of 116 patients with brainstem and/or cerebellar lesions and here we report the results of 5 patients with MCP lesion of different causes (1 patients with acute stroke, 1 with subacute stroke, 1 with multiple sclerosis, 1 with post-infectious ADEM, and 1 patient with fragileX tremor-ataxia syndrome (FXTAS). Tremor was measured by biaxial accelerometry. Center frequency, frequency dispersion and tremor intensity were calculated. In 4 patients, control measurements were performed to assess the evolution of tremor. Detailed analysis of the MRI-data were performed by a neuroradiologist.

Results: Pathologic tremor was detected in 3/5 patients (60%). Tremulous patients had acute stroke/MS-shub or FXTAS. Their tremor had low intensity, low center-frequency (2 Hz), whereas tremor of FXTAS-patient had higher intensity and a center-frequency of 5 Hz. Frequency dispersion was low in both categories. Acute patients presented a complete tremor recovery in cca. 4 weeks, whereas the FXTAS patient's tremor worsened.

Patients' MRI

Conclusion: Our results show that the location of the lesion does not explain the mechanism of tremorogenesis and tremor characteristics. The pathomechanism of the lesion might influence tremor frequency and evolution.

Disclosure: Nothing to disclose

Patients' data

EP2137

The mutual relationship of bilateral subthalamic stimulation impact on the non-motor and motor symptoms in Parkinson´s disease - an open prospective pilot study

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Background and aims: There are numerous studies which have documented significant improvement in motor symptoms and quality of life in patients with Parkinson´s disease after deep brain stimulation of the subthalamic nucleus (STN-DBS). However, relatively little is known about the effects STN-DBS on non-motor symptoms.

Methods: 24 patients with advanced PD who underwent STN-DBS were followed up in open prospective study. They were examined and assessed, using dedicated rating scales preoperatively and at 1 and 4 months following the implantation to determine changes in overall motor and non-motor symptoms.

Results: STN-DBS in patients with PD at Month 1 significantly reduced PDQ-39 score (p=0.018) and SCOPA-AUT score (p=0.002), but 4 months after implantation they were again increased. NMSS improved significantly at Month 1 (p=0.0001) and at Month 4 remained significantly lower than before stimulation (p=0.036). There was no significant difference in PDSS between baseline and Month 1 after DBS, but we can see a significant increase in PDSS at Month 4 (p=0.026). The UPDRS-MDS Part III scores show a significant improvement 1 month (p=0.0006) and also 4 months after DBS (p<0.0001). At Month 1 as well as at Month 4, DBS resulted in no significant changes in FSFI and IIEF. Impulse control disorder was present in only 4 patients, so we do not list the results as they cannot be considered relevant.

Conclusion: STN-DBS in patients with advanced Parkinson´s disease clearly improves not only motor symptoms, but also several domains of non-motor functions, namely sleep, autonomic functions and quality of life.

Disclosure: This work was supported by the grant IGA UPOL-LF-2016-033, grant AZV MZ CR Nr. 15-32715A.

EP2138

Cancelled

EP2139

Clinical manifestation of the Huntington's disease in Belarus

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Background and aims: Huntington's disease (HD) is an inherited, progressive disease, characterized by combination of motor, cognitive and psychiatric symptoms. It is caused by an expanded trinucleotide CAG repeats in the HTT gene.

Methods: We performed neurological examination of 65(100%) patients with HD. 45(69%) subjects were genetically tested for CAG repeats in the HTT gene.

Results: Age of the patients was 21 - 69 (47±9.3) years old; the age of the onset of HD was 18 - 65 (41.5±8.1). 56(85%) patients had positive family history and 9(15%) did't know all information about their relatives. Neurological examination revealed choreiform hyperkinesia and cognitive impairment in 65(100%) patients. Distonic hyperkinesis was observed in 41% cases; hypotonia in upper and lower extremities in 40%; coordination disturbances in 37%, piramidal signs in 29%, dysarthria in 17%. 2(3%) patients had predominance of marked cognitive impairment and 1(1.5%) akineticorigid syndrome in the onset of HD. Juvenile form was diagnosed in 1(1.5%) patient. The age of the onset was 18 years old; clinical signs included predominance of marked cognitive impairment and cerebellar ataxia, light choreiform hyperkinesia.

Genetic testing of 45 HD subjects revealed expansion of CAG repeats from 39 to 66 in the HTT gene.

Conclusion: The most of patients (95%) had tipical nevrological manifestation of HD. Only 4(6.1%) subjects presented atipical signs with dificulty of diagnostics. Significant reverse correlation between the age of the onset of HD and the number of trinucleotide CAG repeats in the HTT gene was determined (r=-0.846, p<0,01).

Disclosure: Nothing to disclose

EP2140

Globus pallidus internus deep brain stimulation in the treatment of generalized dystonia

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Background and aims: Deep brain stimulation (DBS) is well studied in the treatment of primary generalized dystonia and was approved by FDA in 2003 as a humanitarian device exemption. DBS has been also used in the experimental treatment of secondary dystonia.

Methods: We retrospectively reviewed all cases of generalized dystonia treated with pallidal DBS from December/2005 until January/2016. We collected and analysed clinical data.

Results: We selected 14 patients, 6 with primary and 8 with secondary dystonia. The median of improvement in Burke-Fahn-Marsden (BFM) score at 12 months was 59.9% (22.9%-90.0%) in primary and 43.6% (18.0%-54.0%) in secondary dystonia. The median of improvement in Dystonia Disability Scale (DDS) at 12 months was 48.1% (33.3%-85.2%) in primary and 20.3% (12.0%-50.0%) in secondary dystonia. 6 patients have long-term follow-up (>5 years). 3 of them have primary dystonia and sustained benefit in BFM (55%-90%) and DDS (50%-85%). The other 3 patients have secondary dystonia and heterogeneous results: 1 with PANK2 had sustained benefit at 5 years (BFM: 17%; DDS: 18%), 1 with perinatal anoxia improved after neurostimulation disconnection and 1 with iatrogenic dystonia from neuroleptics had improvement of 96% in BFM and 100% in DDS.

Conclusion: Our patients with generalized primary dystonia, similar to the existent literature results, had good response to DBS, sustained at long-term. Secondary dystonia group is heterogeneous, had lower median benefit and highly variable results at long-term. However, some of these patients had improvements in quality of life not always well translated by the existent formal scores.

Disclosure: Nothing to disclose

EP2141

Dopamine D2 receptor mediated neuroprotection in a LRRK2 genetic model of Parkinson's disease

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Background and aims: Parkinson's Disease (PD) is a neurodegenerative disease in which genetic and environmental factors are synergistically involved. Lrrk2 gene mutations are responsible for the majority of inherited cases of PD. We investigated the alterations of striatal medium spiny neurons (MSNs) activity and the neuronal vulnerability to mitochondrial dysfunction in a genetic mouse model carrying the G2019S knock-in (KI) mutation.

Methods: Excitatory postsynaptic currents (EPSCs) were recorded by patch-clamp experiments. Striatal dopamine (DA) release was measured by constant potential amperometry. Neuronal vulnerability to rotenone, a complex I inhibitor, was tested by measuring the progressive reduction of striatal field potential amplitude (FPA).

Results: In KI mice, we showed reduced striatal DA levels by 49% (p<.05). We found that the DA-D2 receptor agonist quinpirole markedly reduced spontaneous (31%,p<.05) and evoked EPSCs (38%,p<.05) in KI but not in control mice. The CB1-endocannabinoid receptor antagonist blocked this effect. The rotenone-induced loss of the FPA was markedly enhanced in KI compared to control mice (24%,p<.05). This detrimental effect was counteracted only in KI mice by the application of quinpirole, through the inhibition of the cAMP/PKA pathway.

Conclusion: The G2019S mutation is associated with an altered striatal DA and glutamate transmission. In KI mice, the DA-D2R activation was able to reduce striatal glutamate release through a CB1R-dependent mechanism and limited rotenone-induced neuronal dysfunction, via the inhibition of cAMP/PKA intracellular pathway. Neuroprotective strategies targeting DA-D2R could counteract the synergistic effect of genetic and environmental predisposing factors in patients carrying this mutation.

EP2142

Hereditary spastic paraplegia type 11 and 22q11 duplication syndrome in a single family

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Background and aims: Hereditary spastic paraplegia (HSP) type 11 is a rare autosomal recessive form of complex HSP with thin corpus callosum. The 22q11 duplication syndrome is an autosomal dominant disorder, characterized by developmental delay, intellectual disability, dysmorphias and wide intrafamilial phenotypic variability.

Methods: Case report.

Results: The index case is a 36-year-old man with a term birth and normal developmental milestones during childhood with early learning difficulties. At the age of 23, a rapid progressive spastic paraparesis appeared. Brain and cervical MRI were both normal. Neither of his nonconsanguineous parents showed similar symptoms. They had 10 children. One older female sibling (patient 2) also had paraparesis, more severe, with younger age of onset (4 years) and by the age of 15 she needed walking assistance. Brain MRI revealed white matter changes with thin corpus callosum. Another female sibling (patient 3) had intellectual disability with learning difficulties, but normal motor skills. On examination, the mother (patient 4) and three children had a dysmorphic appearance with hypertelorism and low implantation of ears. Genetic studies revealed a pathological variant in SPG11 gene in the index case and patient 2; and a pathological variant in chromosome 22 (22q11 duplication) in the index case, patients 2, 3 and 4.

Conclusion: The occurrence of two rare inherited conditions (one autosomal dominant and other autosomal recessive) in the same family is, beyond unlikely, responsible for phenotypic variability and also for diagnostic challenge.

Disclosure: Nothing to disclose

EP2143

New possibilities of the transcranial sonography in Parkinson's disease patients

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Background and aims: Transcranial sonography (TCS) is an inexpensive non-invasive safe method used for early diagnosis of Parkinson's disease (PD). We aimed to explore TCS to evaluate cerebral atrophy, accompanied by cognitive decline in PD patients.

Methods: 100 patients with PD underwent TCS and neuropsychological evaluation included Mini-Mental State Examination, Frontal Assessment Battery, Parkinson's Disease-Cognitive Rating Scale.

Results: According to neuropsychological testing PD patients were divided into three groups – cognitive-intact, with mild cognitive impairment (MCI), and with dementia. These groups differed on the following TCS parameter: substantia nigra (SN) hyperechogenicity (Kruskal-Wallis H=15,61;p<0.001), third ventricle width (H=23,92; p<0.001), and frontal horns of the lateral ventricle width (H=9,41;p=0.009). Pairwise comparisons revealed that cognitive-intact group differed (p<0.001) from the MCI group and from dementia group in an average size of SN hyperechogenicity and third ventricle width. In addition, a cognitive-intact group differed from dementia group in frontal horns of the lateral ventricle width (p=0.003). The MCI group differed from dementia group only in third ventricle width (p=0.016). Thus, we concluded that only the third ventricle width is a good marker of cognitive impairment in PD patients. We established that the optimum threshold separating III ventricle width allows detecting atrophic changes in the brain, accompanied by cognitive impairment calculated with ROC-analysis was ≥7.4 mm, AUC=0,78 (95% CI 0.68-0.89), p=0.001 testified that identified neuroimaging marker has a good informative value.

Conclusion: These findings suggest that TCS may be sensitive to cognitive changes in PD with optimal threshold division III ventricle width of 7,4 mm.

Disclosure: Nothing to disclose

EP2144

Acquired hepatocerebral degeneration - A metabolic acquired movement disorder

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Background and aims: Acquired hepatocerebral degeneration is a debilitating neurological disorder characterized by parkinsonism, ataxia and other movement disorders, which may accompany various forms of advanced liver disease.

Results: 58-year-old man with past medical history of nonalcoholic steatohepatitis with portal hypertension, progressively developed apathy, bradyphrenia, mild cognitive impairment and language disorder. Neurological examination revealed a palpable spleen, dysarthric speech, left resting tremor, asymmetric rigidity and a buco-lingual chorea. Blood test revealed an elevated AST, ALT, GGT and ammonia. Investigation also included a Brain CT and EEG that were normal. The MRI demonstrated increased T1 signal within the pallidal nuclei which may be associated with a toxic-metabolic disorder. The patient's diagnosis was an acquired hepatocerebral degenration and he refused liver transplantation.

Conclusion: Acquired hepatocerebral degeneration is an important differential diagnosis of movement disorders with MRI T1 hyperintensities in the basal ganglia. Portosystemic shunting leads to accumulation of toxins such as ammonia that are bypassing the first-pass elimination by the liver. Evidence suggests manganese plays a crucial role in the pathogenesis of this disease. They are no proven pharmacological therapies, although liver transplantation is helpful in some patient.

Disclosure: Nothing to disclose

EP2145

The identification of molecular-genetic background of familial atypical parkinsonism in "Hornacko", a specific region of south-eastern Moravia, Czech Republic

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Background and aims: Increased prevalence of parkinsonism was detected in a small region of the Czech Republic. Three large pedigrees with autosomal-dominant inheritance patterns of parkinsonism were identified. The aims of the study were to assess the genetic background of atypical familial neurodegenerative parkinsonism.

Methods: Molecular genetic examinations were performed in 12 clinically positive probands. Coding sequences, exon/intron regions and 5′/3′UTR sequences of ADH1C, ATP13A3, EIF4G1, FBXO7, GBA+GBAP1, GIGYF2, HTRA2, LRRK2, MAPT, PARK2, PARK7, PINK1, PLA2G6, SNCA, UCHL1, and VPS35genes were tested with a massive parallel sequencing method using Ion Torrent technology and confirmed by Sanger sequencing. In total, 93% of gene sequences were covered.

Results: 31 rare heterozygous variants have been identified. The most interesting variants (PhyloP score ≥ 2 and/or missense variants) included: one variant in coding sequence - c.143C>T in ADH1C gene, one variant in coding sequence - c.689A>G in MAPT gene, one variant in UTR-3 region sequence - c.*77G>T in SNCA gene, one variant in exon - c.1180C>T in PARK2 gene, one variant in coding sequence - c.344A>T in PINK1 gene, three exon variants - c.2167A>G, c.6241A>G, c.4541G>A in LRRK2 gene, one variant in coding sequence - c.3662C>T in GIGYF2 gene, one exon variant - c.1027C>T in PLA2G6 gene and one variant in coding sequence - c.3706C>G in EIF4G1 gene.

Conclusion: It seems that several molecular-genetic factors play role in the genetic background of this newly detected atypical familial neurodegenerative parkinsonism.

EP2146

Atypical phenotypes of CADASIL: Two cases

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Background and aims: Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is central nervous system inherited disease that is caused by NOTCH3 gene mutation. It is characterized by headaches, strokes, dementia. Specific magnetic resonance imaging (MRI) signs are lacunar infarctions, focal lesions of temporal poles, capsula externa, periventricular and subcortical areas and diffuse white matter changes. Rarely CADASIL begins with unusual symptoms. We hereby present two clinical cases of the disease manifested by movement disorders.

Methods: We examined two female patients (A, 79 y.o., B, 47 y.o.) using neurologic and neuropsychological testing, brain MRI, NOTCH3 gene sequencing.

Results: Both patients complained of tremor and gait instability. No factors for stroke were revealed. Family history: A-hereditary untainted; B - father died of repeat stroke. Neurologic examination: A-broken pursuit eye movements, vocal tremor, head and body titubation, proximal arm tremor, intension tremor and coordination disturbances in arms, ataxic gait; B-euphoria, judgement declined, mild rigidity in left hand, wrists postural tremor (S>D), intension tremor and coordination disturbances in arms, ataxic gait. Montreal Cognitive Assessment and Frontal Assessment Battery revealed cognitive decline and frontal dysfunction in both cases. Neurodegenerative process was considered in both cases, so the brain MRI were performed. In both cases classical CADASIL signs were found (fig.1, 2). NOTCH3 gene sequencing revealed mutations in the 4th exon of the gene: A - R207C (fig.3); B - C222Y.

Axial T2-FLAIR weighted image shows confluent lesions of deep white matter and periventicular area

Pathogenic R207C mutation in the NOTCH3 gene.

Conclusion: This report emphasizes that CADASIL is clinically heterogeneous and should be considered in the study of patients with atypical movement disorders.

Disclosure: Nothing to disclose
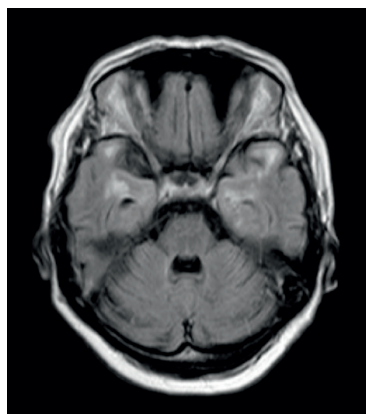
Axial T2-FLAIR weighted image shows temporal poles hyperintensity

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EP2147

The role of neutrophil-to-lymphocyte ratio in multiple sclerosis and optic neuritis

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Background and aims: This study evaluates the significance of the blood neutrophil-to-lymphocyte ratio (NLR) in the different courses of multiple sclerosis (MS); relapsing-remitting MS (RRMS), secondary progressive MS (SPMS), primary progressive MS (PPMS) and optic neuritis (ON). The NLR is measured in relation to relapse and remission and Expanded Disability Status Scale (EDSS).

Methods: 382 patients suffering from RRMS (n=138), SPMS (n=30), PPMS (n=55), CIS (n=19) or ON (n=140) and 813 healthy controls (HC) were included. Complete blood count, demographic, and clinical data from MS patients were evaluated retrospectively. The NLRs were calculated and compared for all participants by Student's t-test. Logistic regression models were constructed for EDSS ≥ 4,0 as outcome and age, gender, NLR, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), erythrocyte distribution width (ERYDRW) and disease duration as predictor variables.

Results: The NLR is significant higher (p<0.001) in MS and ON patients compared to HC. Patients in relapse had a significant higher NLR (p<0.005) than patients in remission, but no difference in the CRP, ESR, ERYDRW and EDSS. No variance in NLR was found between RRMS and progressive MS patients and neither between SPMS and PPMS patients. No significance was found between any of the predicting variables and an EDSS score ≥4.0.

Conclusion: MS and ON patients have a significantly higher NLR than HC, indicating the occurrence of chronic inflammation. NLR may be a marker of disease activity, because of the significantly higher NLR in patients with relapse compared to patients in remission. This needs confirmation in future trials.

Disclosure: Nothing to disclose

EP2148

Adherence comparison in multiple sclerosis in a real-world setting: New oral versus classic injectable disease modifying treatments

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Background and aims: New oral disease modifying therapies (oDMT) for relapsing remitting multiple sclerosis (RRMS) are available. The aim was to assess patient adherence to oDMT: dimethyl fumarate (DMF) and teriflunomide (TE) in comparison with classic injectable therapies (iDMT).

Methods: RRMS patients switched from iDMT (interferon-beta-1a/1b/glatiramer acetate) to new oDMT between June 2015 and March 2016 in Hospital Alvaro Cunqueiro were recruited. Adherence, measured by medication possession ratio (MPR) and expressed in%, was compared for oDMT versus iDMT. Adherent patient was considered if MPR≥90%.

Results: 38 patients were switched from iDMT to DMF (n=20) or TE (n=18). Women: 87.8%, mean age (±SD): 39.2±8.5years; mean disease duration: 6.0±5.0 years; median EDSS (range): 2[0-6.5]; annualized relapse rate (ARR): 0.7±0.8. 66.7% patients were switched from interferon-beta and 33.3% from GA. Prior mean treatment duration (SD): 423.4±167.2 days. The main reasons for change were inefficacy (59.4%) and intolerance (40.6%). 5 patients stopped oDMT (1 patient due to pregnancy, 3 patients due to GI intolerance and 1 due to lymphopenia). Mean oDMT duration: 166.5±59.3 days. MPR to iDMT=85.2% vs. MPR to oDMT=98.1% (p< 0.001). No MPR differences between oDMT were observed. iDMT adherence among patients who switched to TE was 83.4% and 85.7% in patients switched to DMF (p>0.05). Adherence >80% was observed in 70% of patients on iDMT and in 100% on oDMT.

Conclusion: Patients on oDMT present better adherence than those previously treated with iDMT. These changes may have an important impact on disease control. More real-world data are necessary to evaluate long-term adherence to oDMT.

Disclosure: Nothing to disclose

EP2149

Spinal cord lesions are frequently asymptomatic in relapsing remitting multiple sclerosis. A retrospective MRI survey

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Background and aims: Spinal cord (SC) lesion load is well known as a negative prognostic factor in multiple sclerosis (MS). Nevertheless, there is no consensus about MRI follow-up, mainly because new SC lesions (SCLs) are thought to be more likely symptomatic than brain ones. The aim of the present study was to investigate the impact of asymptomatic active SCLs, defined as new/enlarging T2 or gadolinium positive (Gd+), on SC MRI activity in a cohort of MS patients.

Methods: We retrospectively investigated all available SC MRI scans of clinically isolated syndrome and relapsing remitting (RR) MS patients referred to a single Italian MS centre, analysing those with active SCLs, both symptomatic and asymptomatic, collecting also clinical data since previous SC MRI or disease onset in case of first examination. Brain MRI data were also included.

Results: We analysed a total of 340 SC MRI scans from 230 patients. We found asymptomatic active SCLs in 31.2% of scans. At multivariate analysis, compared to symptomatic, asymptomatic active SCLs were associated with an older age at disease onset (34.0 ± 10.37 vs 31.0 ± 9.99 yrs, p=0.039), more frequent RR course (96.2 vs 92.7%, p=0.037) and sovratentorial location at onset (14.2 vs 6%, p=0.027), lower EDSS score (1.6 ± 0.88 vs 2.4 ± 1.29, p=0.001), less relapses since previous SC MRI or disease onset (1.1 ± 1.13 vs 2.1 ± 1.78, p=0.003) and less new/enlarging T2 SCLs (1.6 ± 1.07 vs 2.1 ± 1.54, p=0.043).

Conclusion: A consistent part of active SCLs seems to remain asymptomatic, suggesting the need of a regular SC MRI follow-up.

Disclosure: Nothing to disclose

EP2150

Low rate of conversion from relapsing-remitting MS to secondary progressive MS through 6 years among patients who received alemtuzumab in CARE-MS I and II

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Background and aims: Delaying conversion from relapsing-remitting MS (RRMS) to secondary progressive MS (SPMS) is an important MS treatment goal. In an MSBase patient cohort (17,356 MS patients; median baseline disease duration 3.8 years; median 5.8-year follow-up), 18% of all patients converted to SPMS using a recently developed SPMS definition based on EDSS scores and relapses. The aim of this analysis was to determine the rate of conversion to SPMS among well-defined cohorts of patients with active RRMS who were either treatment-naive (CARE-MS I [NCT00530348]) or had inadequate response (≥1 relapse) to prior therapy (CARE-MS II [NCT00548405]); extension study (CAMMS03409 [NCT00930553]).

Methods: Patients received 2 courses of alemtuzumab 12 mg (baseline: 5 consecutive days; 12 months later: 3 consecutive days) in CARE-MS I or CARE-MS II, and in the extension as-needed alemtuzumab for relapse/MRI activity, or another disease-modifying therapy per investigator discretion. We performed a pooled analysis to determine conversion from RRMS to SPMS in alemtuzumab-treated patients through 6 years. The definition of SPMS onset was as published by Lorscheider et al. (Brain 2016;139:2395-405).

Results: Of 811 CARE-MS I/II RRMS alemtuzumab-treated patients (median baseline disease duration 2.8 years), 669 (82.5%) remained on study through Year 6, and 20/811 (2.5%) met the definition of SPMS through 6 years using progression confirmation of ≥3 months (12/811 [1.5%] over ≥6 months). Additional sensitivity analyses, similar to those reported previously by Lorscheider et al, showed consistent results.

Conclusion: A low proportion of alemtuzumab-treated patients progressed to SPMS through 6 years.

Disclosure: Sanofi and Bayer HealthCare Pharmaceuticals

EP2151

Vitamin D status predicts brain MRI activity in patients with clinically isolated syndrome

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Background and aims: Lower Vitamin D levels have recently been associated with increased clinical activity among the patients with multiple sclerosis (MS) or clinically isolated syndrome(CIS).Aim of this study is to deteremine if vitamin D status is associated with developing new T2 lesions or contrast enhancing T1 lesions on brain magnetic resonance imaging (MRI) in the patients with CIS and could contribute to early conversion to MS.

Methods: A longtudinal prospective study was conducted on forty- three Egyptian patients diagnosed as CIS according to McDonald's criteria(2010).The patients underwent detailed clinical assessment, evaluation of MRI brain including the number of new hyperintense T2 lesions, new gadolinuim enhancing T1 lesions and 25- hydroxyvitamin D levels at baseline and after 1 year follow up.

Results: The CIS patients that converted to MS showed higher number of new T2 lesions than non convertors ($p<0.001$) after 1 year follow up. There was a significant negative correlation between 25 hydroxyvitamin D level and and MRI T2 lesions number (r=-0.38, p=0.01) and gadolinuim T1 lesions (r=0.37, p =0.02).It was shown that the CIS patients that had lower levels of 25-hydroxy vitamin D below 7.1 ng/ml were at higher risk for developing new T2 brain lesions at MRI brain with sensitvity (100%) and specificity (91.3%).

Conclusion: Vitamin D diffeciency could be associated with MRI brain activity and early predict conversion of CIS patients to MS.

Disclosure: Nothing to disclose

EP2152

Cancelled

EP2153

Hypothalamic damage in multiple sclerosis correlates with disease activity, disability, depression and fatigue

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Background and aims: Disturbances of the hypothalamo-pituitary (HPA) axis are supposed to modulate activity of multiple sclerosis (MS). We hypothesised that the extent of HYP damage may determine severity of MS and may be associated with the disease evolution. We suggested fatigue and depression may depend on the degree of damage of the area.

Methods: 33 MS patients with relapsing-remitting and secondary progressive disease, and 24 age and sex- related healthy individuals (CON) underwent 1H- MR spectroscopy (1H-MRS) of the hypothalamus. Concentrations of glutamate+glutamin (Glx), cholin (Cho), myoinositol (mIns), N-acetyl aspartate (NAA) expressed as ratio with creatine (Cr) and N-acetyl aspartate (NAA) were correlated with markers of disease activity (RIO score), Multiple Sclerosis Severity Scale (MSSS), Depressive-Severity Status Scale (SDSS) and Simple Numerical Fatigue Scale (SNFS).

Results: Cho/Cr and NAA/Cr ratios were decreased and Glx/NAA ratio was increased in MS patients vs CON. Glx/NAA, Glx/Cr, and mIns/NAA were significantly higher in active (RIO 1-2) vs non-active MS patients (RIO 0). Glx/NAA and Glx/Cr correlated with MSSS and fatigue score, and Glx/Cr with depressive score of MS patients. In CON relationships between Glx/Cr and age, and Glx/NAA and fatigue score were inverse.

Conclusion: Our study provides the first evidence about significant hypothalamic alterations correlating with clinical outcomes of MS, using 1H-MRS. The combination of increased Glu or mIns with reduced NAA in HYP reflects whole-brain activity of MS. In addition, excess of Glu is linked to severe disease course, depressive mood and fatigue in MS patients, suggesting superiority of Glu over other metabolites in determining MS burden.

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EP2154

ASCLEPIOS I and II: Adaptive design of two parallel phase 3 studies in relapsing multiple sclerosis

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Background and aims: In a phase 2b study, subcutaneously administered ofatumumab significantly reduced the cumulative number of new gadolinium-enhancing lesions during weeks 4–12 by ≥90% versus placebo in patients with relapsing multiple sclerosis (RMS). Here, we present the adaptive design features of the two ongoing, double-blind/double-dummy, identical design phase 3 studies of ofatumumab in RMS (ASCLEPIOS I [NCT02792218] and ASCLEPIOS II [NCT02792231]).

Methods: Patients (N=900, each trial) will be randomised to subcutaneous ofatumumab 20mg every 4 weeks or oral teriflunomide 14mg once daily. The primary endpoint is to demonstrate the superiority of ofatumumab over teriflunomide on annualised relapse rates. If both studies meet the primary endpoint, data will be combined to assess the key secondary disability-related endpoints.

Results: A pre-planned analysis of blinded data will be performed to: 1) re-assess sample size, increasing to a maximum of 1250 patients per study; 2) declare 'end of study' when each study is powered to 90% for primary and to ≥80% for the combined analysis of key secondary endpoints (≥90% for 3-month confirmed disability worsening endpoint). The study duration is flexible, but capped at a maximum of 30 months in individual patients. Statistical analysis methods adequate for a study with flexible duration will be applied (e.g. Cox regression and negative binomial models with offset). The sample size and study duration adapt according to the activity of the study population to provide sufficient power.

Conclusion: An adaptive design with flexible study duration ensures minimum patient exposure to the double-dummy treatment that is required to address the scientific objectives.

Disclosure: This study was funded by Novartis Pharma AG, Basel, Switzerland. Detailed disclosure of each author will be included in the poster.

EP2155

Cancelled

EP2156

The role of serum netrin-1 in early multiple sclerosis

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Background and aims: Netrin (NTN)-1, a secreted laminin-related protein, is known to affect axonal guidance and neuronal cell migration, but also blood-brain barrier integrity and inflammation. Two preliminary studies reported altered serum NTN-1 levels in multiple sclerosis (MS), however associations with longitudinal clinical and MRI data have not been investigated. We aimed to assess serum NTN-1 in MS and controls with respect to disease, disease activity, and temporal dynamics.

Methods: We included 79 MS patients (clinically isolated syndrome CIS n=32, relapsing-remitting MS RRMS n=47; age mean±SD 33.9±8.8 years) and 30 non-inflammatory neurological disease controls (age mean±SD 37.1±10.2 years). Serum samples were drawn in all subjects, in patients during two gadolinium (Gd)-enhanced 3T MRI examinations (initial contrast-enhancing Gd+ n=47, non-enhancing Gd- n=32; reference Gd- n=70; median time-lag 1.4 (IQR 1.0-2.3) years). Clinical data of patients were recorded. Serum NTN-1 was assessed by ELISA (Cusabio, China).

Results: Serum NTN-1 levels were similar in CIS, RRMS and controls, and Gd+ and Gd- patients. Among patients with MRI-based signs of disease activity, those who experienced an apparent clinical relapse within 30 days prior to sampling (n=8) showed decreased serum NTN-1 levels compared to clinically non-active Gd+ patients (n=39; p=0.041). Serum NTN-1 levels showed no temporal dynamics in the MS patients and were unrelated to clinical data.

Conclusion: Our study cannot confirm any MS specific changes of serum NTN-1 levels and they appear not sensitive to MS disease activity as evidenced by contrast enhancing lesions on MRI. NTN-1 changes during clinical relapses may deserve further examination.

Disclosure: This study represents a sub-study supported by the Austrian Federal Ministry of Science, Research and Economics (core-study named 'BIG-WIG MS' (Bildgebung, Immunpathogenese, Gesundungsfaktoren – Wien, Innsbruck, Graz – bei Multiple Sklerose'; 'Neuroimaging, immunopathogenesis and salutogenic factors in MS – a collaborative effort of the universities of Vienna, Innsbruck and Graz')).

EP2157

Frequency of restless leg syndrome and related sonographic parameters of brain parynchyma in relapsing remitting multiple sclerosis

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Background and aims: Restless leg syndrome (RLS) has been reported in MS patients. which may reflects deep grey matter pathology, A recent tool in monitoring aspects of neurodegeneration and deep grey matter pathology is transcranial sonography (TCS).
Aims: To estimate the frequency of RLS among relapsing remitting MS (RRMS) patients and to investigate related sonographic changes in the echogenicity of deep grey matter (DGM) and ventricular diameters.
Methods: A case-control study, conducted on 125 Egyptian subjects: 54 RRMS patients according to revised MacDonald's criteria, 2010, (16 males, 38 females), with a mean age of 29.24±8.23 and a mean EDSS of 2.34±1.11, and 71 age and sex matched healthy volunteers. All participants were subjected to clinical assessment and to the Cambridge-Hopkins RLS diagnostic questionnaire-short form-13. B-mode TCS of the brain parenchyma was done to evaluate ventricular diameter (marker of brain atrophy), and planimetric   measurement of the DGM echogenicity (marker of neurodegeneration).
Results: MS patients showed significantly higher frequency of RLS (29.6%)compared with controls (7.04%) (P=0.004). MS/RLS+ subjects displayed significantly larger frontal horn diameter and larger substantia nigra (SN) surface area than control/RLS+ [(0.45±0.11 versus 0.32±0.19cm; P=0.04)&(0.19±0.06 versus 0.13±0.05cm^2; P=0.03) respectively]. MS/RLS+ displayed significantly smaller surface area of the right red nucleus (RN) than MS/RLS- (P=0.04). None of the MS/RLS+ or control/RLS+ displayed the triad of RN hyperechogenicity, SN hypoechogenicity and interrupted raphe.
Conclusion: High frequency of RLS among RRMS patients may be related to a neurodegenerative process involving the SN.
Disclosure: Nothing to disclose

EP2158

The efficacy of patient education in preventing urinary tract infections in multiple sclerosis

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Background and aims: Urinary tract infections (UTI) are frequently observed in multiple sclerosis (MS) patients. Due to UTI, the treatment of MS becomes difficult and may be interrupted. Antibiotic use becomes necessary and a new MS attack may occur in this period. The aim of our study is to evaluate the efficacy of giving infection control training course to MS patients.
Methods: From January to November 2015, 72 registered MS patients of our clinic were recruited for this study. An infection control training course was conducted by the same specialized nurse of our hospital as a part of patient education programme for MS (23/05/2015). The pre-training period (Pre-TP) was between 01/January-22/May 2015 and the post-training period (Post-TP) was between 25 May and 01 November 2015. The demographic data, detailed medical history, neurological evaluation, symptoms for UTI and the haematologic and biochemical laboratory results were recorded from patient files. SPSS 18.0 was used for statistical analysis. p<0.05 was accepted as the level of significance.
Results: Out of 72 MS patients, 46 (63.8%) were male, 26 (36.1%) were female. Mean age of the patients were 39.8±10,0 (18-67). The number of MS patients who had UTI symptoms were 42/72 (58.3%) in the Pre-TP and 25/72 (34.7%) in the Post-TP (p=0.004).
Conclusion: Preventing infections will increase the quality of life of the patients and reduce the economic burden of the disease. Our study demonstrated that training MS patients to prevent infections effectively decreases the symptoms of UTI. A standardised and easily available infection control training programme should be developed for MS patients.
Disclosure: Nothing to disclose

EP2159

Effect of bilateral subthalamic deep brain stimulation on quality of life in Parkinson's disease

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Background and aims: Bilateral subthalamic deep brain stimulation (STN DBS) significantly improves motor symptoms in Parkinson's disease (PD). However, this motor improvement may not reflect the global therapeutic impact for the patient with regard to the social and emotional dimensions of the quality of life. The aim of this study was to assess the health related quality of life (HRQoL) in PD before and following STN DBS.

Methods: We evaluated 25 PD patients treated with STN DBS. HRQoL was assessed by both specific questionnaire of quality of life in PD -the Parkinson's Disease Questionnaire (PDQ39) and general quality of life-assessment questionnaires the Short Form 36 health survey questionnaire (SF36) and The Word Health Organization Quality of Life Test-Bref (WHOQOL-BREF) 2 weeks before and 3,6,12 months after surgery.

Results: Before STN DBS the lowest rating of HRQoL was related to daily activities at the mean level of 68.8 points, followed by mobility with the average of 65.3 and 61.3 points noted for stigma of the disease per 100-point scale PDQ-39. Three months after STN DBS HRQoL improved in all domains assessed in PDQ-39, with the exception of social support and communication. The same improvements were observed in 6 months and 1 year follow-up. Using the SF-36 and WHOQol-Bref questionnaires before STN DBS, we noted a lower HRQoL within the physical compared to the mental dimension score. After STN DBS, the improvement was more pronounced in the physical than the mental score.

Conclusion: STN DBS significantly improved HRQoL as measured by PDQ-39, SF-36, WHOQol-Bref.

Disclosure: Nothing to disclose

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EP2160

Disability progression in multiple sclerosis is biphasic with uniform trajectory after expanded disability status score of three

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Background and aims: Evidence suggests that multiple sclerosis (MS) has a two-stage progression rate before Expanded Disability Status Scale (EDSS) 6. In this study, we challenge the hypothesis that postulates a uniform progression rate of patients with MS between EDSS 3 and 6 despite disparate progression rates before EDSS 3.

Methods: We included patients with definite MS with a follow-up duration of at least one year. Demographic and clinical data including time to EDSS 3 and time to EDSS 6 were collected. We subgrouped the cohort according to their time to EDSS 3 and compared the rate of disability progression between EDSS 3 and 6 using Cox logistic regression.

Results: Of 876 (617 females, 259 males) patients, the ratios of MS subtypes were as follows: RRMS: 81.3%, SPMS: 9.8%, PPMS: 5.7%, and RPMS 3.2%. The most frequent symptoms at onset were sensory, optic neuritis, and sensory-motor in 19.3, 11.3, and 17.7% of patients respectively. After a mean follow-up duration of 8.8±7.1, 33.9% of patients reached EDSS 3 and 13.8% EDSS 6. Kaplan-Meier estimates of the mean time to EDSS 3 was 17.1±0.7 and the mean time to EDSS 6 was 28.8±1.8. We found nearly identical disability progression rates between EDSS 3 and 6 irrespective of time to EDSS 3 (Log rank test: p= 0.4) (Figure 1).

Figure 1: Kaplan-Meier estimate of the interval between EDSS 3 and 6 (p value was derived from log rank test).
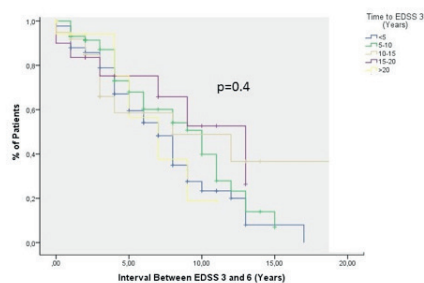
Figure 1

Conclusion: Our study confirms previous studies that suggest similar disability accumulation rates between EDSS 3 and 6 in patients with disparate progression rates between EDSS 0 and 3.

Disclosure: This study was sponsored by Neuroimmunological Society, Turkey.

EP2161

Cancelled

EP2162

Spanish registry of multiple sclerosis patients on glatiramer acetate 40 mg/ml treatment: Real-world results and baseline characteristics of initial patients

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Background and aims: To describe the profiles of patients undergoing treatment with glatiramer acetate (GA) 40mg/ml in Spanish real-world clinical practice.

Methods: This is a prospective, observational, multicentre patient registry from 41 Spanish multiple sclerosis (MS) hospital units. Relapsing MS patients on GA 40 mg/ml treatment were recruited and will be followed for a maximum of 5 years. All patients' visits were performed as per daily clinical practice.

Results: During the first six months of the registry 970 patients were recruited (664 females, median age 44 years). Mean age at diagnosis of the disease was 36 years (range 28 to 42) and time from diagnosis to registry recruitment was 8 years. The majority of patients (n=757, 78.4%) had previously been treated with other immunomodulatory/immunosuppressive drugs before entering the study. Prior therapies included GA 20 mg/ml (60.4%), interferons (31.3%) and other drugs (8.4%).

Main reasons for switching from other therapeutic options were mainly induced by adverse events (19.2%) or lack of response (16.5%). Additional baseline characteristics included a mean EDSS of 2.0 the year prior to participation in the registry, and an annualized relapse rate of 0.4. The vast majority of patients (n=684, 70.5%) showed no relapses during the 12 month period before entering the registry.

Conclusion: The baseline data from the 970 patients included in the Spanish GA 40 mg/ml registry indicate that the population is characterized by low disease activity (low relapse rate, lesion load, and mild disability scores).

Disclosure: This research has been supported by TEVA pharmaceuticals

EP2163

Cerebrospinal fluid and serum levels of interleukin-8 in patients with multiple sclerosis and its correlation with other markers

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Background and aims: The result of inflammatory and neurodegenerative processes in Multiple Sclerosis (MS) is axon and myelin breakdown. The paraclinical examination methods (MRI and an examination of cerebrospinal fluid (CSF)) are an important part of the diagnostic process. An increasing number of studies deal with CSF and serum levels of biomarkers and their role in MS. We hypothesized that the level of interleukin-8 (IL-8) could be different in MS patients than in controls. In the second step we hypothesized that the blood-brain barrier is damaged in the early stages of MS.

Methods: CSF and serum levels of IL-8 were assessed in 102 patients with newly diagnosed MS meeting McDonald's revised diagnostic criteria and in 102 subjects as a control group. We then correlated these results with Q-alb, oligoclonal bands and light chains.

Results: Levels of IL-8 in CSF were significantly higher in MS patients than in controls (Mann-Whitney U test, $p < 0.0001$). Spearman's correlation analysis proved a significant correlation between levels of IL-8 and Q-alb, IL-8 and oligoclonal bands, IL-8 and light chain lambda.

Conclusion: Based on our results, we hypothesized that IL-8 could partially come from the periphery, and that IL-8 could penetrate through the damaged BBB. This may be the reason that IL-8 is increased in CSF and decreased in serum in patients with MS. On the other hand, there were general opionions that the IL-8 is produced de novo in the CNS. The results also confirm the presence of inflammatory processes in the early stages of MS.

EP2164

Effectiveness of fingolimod in patients with relapsing-remitting multiple sclerosis in daily clinical practice in Spain: Results from a multivariate pool analysis called Fingoview

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Background and aims: Once-daily fingolimod (Gilenya®, Novartis Pharma AG) is a sphingosine 1-phosphate receptor modulator approved for relapsing MS treatment. Continuous collection and analysis of real world effectiveness and safety data is key to making accurate treatment decisions. The objective is to describe basal characteristics and effectiveness of fingolimod in patients with relapsing-remitting multiple sclerosis (RRMS) followed for ≥12 months in routine clinical practice in Spain.

Methods: Fingoview is a multivariate pool analysis of two observational, retrospective chart review, multicenter studies MS SECOND LINE GATE and MS NEXT, conducted in specialized MS centers in Spain, between November 2014 and December 2015. Pool analysis was prospectively planned. Both studies included patients of both sexes, ≥18 years, diagnosed with RRMS, treated with fingolimod according SmPC and followed up for ≥12 months after treatment initiation.

Results: Fingoview included 988 patients (70 naïve, 252 post-natalizumab, 666 post first-line injectable DMTs), 68.9% female, mean(SD) age: 40.44(9.1) years (Table 1). After 1, 2, 3 years of treatment mean annual relapse rate decreased by 76.5%(mean: 1.19 to 0.28), 82.4%(0.21) and 86.3%(0.16) compared to the year prior to fingolimod (all $p < 0.0001$) (Figure 1). At 12 months, 89.6% of patients had stable or improved EDSS which was maintained in 84.4% of patients at 24 months (Figure 2). New/enlarged T2 lesions, gadolinium-enhancing lesions on T1 or radiologically disease free will be discussed.

Annual relapse rate after 1, 2 and 3 years of treatment with fingolimod

		Post 1st-line injectable DMTs (N=666)	Post-NTZ (N=252)	Naïve (N=70)	Total (N=988)	p-value
Age, years	Mean (SD)	40.3 (8.9)	41.4 (8.8)	38.6 (9.5)	40.4 (9.1)	0.0449
	Range	(20 - 69)	(20 - 63)	(18 - 64)	(18-69)	
Sex, females	N (%)	474 (71.2%)	162 (64.3%)	45 (64.3%)	681 (68.9%)	0.0905
Time from MS diagnosis to start of fingolimod, in years	Mean (SD)	8.2 (5.8)	10.4 (5.5)	4.4 (6.4)	8.5 (5.9)	<0.0001
Time of treatment with fingolimod, in years	Mean (SD)	2.2 (0.8)	2.2 (0.9)	2.1 (0.9)	2.2 (0.8)	NA
ARR previous year	Mean (SD)	1.4 (0.9)	0.3 (0.8)	2.5 (1.8)	1.3 (1.1)	<0.0001
Number of relapses in the last 2 years	Mean (SD)	1.9 (1.2)	0.4 (0.9)	2.0 (1.03)	1.6 (1.3)	<0.0001
EDSS at study start	Mean (SD)	2.9 (1.5)	3.5 (1.8)	2.6 (1.8)	3.0 (1.6)	<0.0001
	Median (IQR)	2.5 (2.0 -4.0)	3.5 (2.0 -4.5)	2.5 (1.5 -3.5)	3.0 (2.0 -4.0)	
Number of T1 Gd+ enhancing lesions	N	405	57	40	502	<0.0001
	Mean (SD)	1.37 (2.8)	0.25 (1.2)	1.68 (2.6)	1.26 (2.7)	
Number of T2 lesions**						
< 9 lesions	No. patients (%)	25 (6.3%)	4 (7.4%)	7 (17.1%)	36 (7.3%)	0.0539
9 - 20 lesions	No. patients (%)	160 (40.2%)	28 (51.9%)	14 (34.1%)	202 (41.0%)	0.1711
> 20 lesions	No. patients (%)	213 (53.5%)	22 (40.7%)	20 (48.8%)	255 (51.7%)	0.1956

SD: Standard deviation. IQR: Interquartile range. NA = Not available
*Patients who had a baseline MRI during washout period were excluded (61 in the final sample)
**Calculations performed without Not Available category

Baseline characteristics

EDSS progression from baseline at Year 1 and Year 2, according to treatment group

Conclusion: After switching to fingolimod, RRMS had significantly suppressed clinical disease activity and most of the patients have a stable EDSS after one year of treatment.

Disclosure: Study Supported by: Novartis Farmacéutica S.A.

EP2165

Baseline cognitive impairment predicts one year disease progression in MS

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Background and aims: Cognitive impairment commonly affects Multiple Sclerosis (MS) patients and may have a dramatic impact on their quality of life, performance at work and social life. We aimed to assess the ability of specific computerized real-time cognitive tests to predict disability progression at 1 year after initiating immunomodulatory treatment for MS in comparison with the predictive value of the Expanded Disability Status Scale (EDSS).

Methods: Fifty three Relapsing-Remitting (RR) MS patients (F=42, mean age 36.02±9.25, mean EDSS 2.18±1.27) who started immunomodulatory treatment with glatiramer acetate or interferon beta preparations underwent cognitive evaluation using a computerized real-time battery of basic neuropsychological tests ("CogScan"; Anima Scan LTD), which includes: Finger Tapping Test (FTT), Simple Reaction Time (SRT), Choice Reaction Time (CRT), Immediate and Delayed Memory for Pictures, Words and Faces and Digit Running Test (DRT). EDSS scores were recorded every 3 months. Univariate logistic regression analysis was conducted for each predictor and the most robust predictor was analyzed by Receiver Operating Characteristic (ROC).

Results: At 1 year, 9 patients (17%) had 3-months sustained disability progression. Baseline EDSS could not predict disability progression, while assessment of simple cognitive functions yielded four statistically significant predictors: Standard deviation (SD) in both FTT and DRT, accuracy and latency in the DRT. The DRT-I SD showed the best predictive value for disability progression.

Conclusion: Baseline cognitive assessment, especially slow and highly variable performance on the DRT, but not baseline EDSS, can predict the progression of neurological disability after one year of immunomodulatory treatment in RRMS.

Disclosure: This study has been partially supported by research grants from Teva pharmaceuticals, Merck-Serono and Medison, Israel.

EP2166

Oxidative stress in multiple sclerosis: Effect of dietary supplementation with coenzyme Q10

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Background and aims: Oxidative stress plays an important role in multiple sclerosis (MS). We evaluated the effect of coenzyme Q10 (CoQ10), a compound with marked antioxidant effects, on MS-related laboratory and clinical outcomes.

Methods: We analysed serum and clinical data from 60 relapsing-remitting MS patients (age42.3 ∓ 8.9years;female 70%). Data were collected after 3 months of CoQ10 dietary supplementation (Skatto®, ChiesiFarmaceuticiSpA, 200mg/day) and during additional 3 months either before or after CoQ10 supplementation (no-CoQ10 status). Treatment with subcutaneous high-dose interferon beta-1a was maintained during the study period (Rebif®, Merck Serono SpA, 44microg/week). Laboratory outcomes included markers of free radical scavenging activity, oxidative damage and neuroinflammation. Patient-reported outcomes included questionnaires for cognition, fatigue, depression, pain and headache. Clinical outcomes included occurrence of relapses and EDSS variations.

Results: Regression models adjusted for age, gender, disease duration, duration of interferon beta-1a treatment and EDSS were used. Patients receiving CoQ10 supplements had a 0.6 mg increase in uric acid (Coeff=0.556;95%CI=0.179-0.933;p=0.004), compared with no-CoQ10 status. After receiving CoQ10 supplements, patients presented with improved cognitive scores on the MS neuropsychological questionnaire (Coeff=6.472;95%CI=1.197-11.748; p=0.016), and with reduced pain on the visual analogue scale (Coeff=-1.899;95%CI=-3.608--0.189; p=0.029).

Conclusion: Restoring an appropriate oxidative balance with CoQ10 dietary supplementation in combination with disease modifying treatment may be responsible for an improvement in patient-related outcomes such as cognition and pain. In the long-term, it is possible to hypothesize that a reduction in oxidative stress might exert positive effects on the disease course of MS. Future studies on larger populations and with longer follow-up are required to confirm present findings.

Disclosure: The present research received support by Merck Italy.

EP2167

A post-marketing observational monocentric study

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Background and aims: Registrative studies showed the effects of Dimethyl Fumarate (DMF), however real life studies are needed to confirm these results.

Methods: Currently, 444 RRMS patients are treated with DMF at San Raffaele Hospital. 255 pts received DMF for at least 12 months. 70.2% female, mean age 37.2; mean disease duration 10.2; mean EDSS 1.87. 16.9% of pts were naïve, 49.7% switched to DMF from injective disease modifying therapies (DMT) for intolerance, 24.7% for inefficacy, 7.4% for convenience (JC+ in Natalizumab or from Cyclophosphamide). All pts had a brain MRI at DMF initiation and a neurological examination every 3 months. The 74.9% had a MRI follow up at 6 months, the 53.6% at 12 months.

Results: At the last FU: 86.7% were relapse free. Compared to the year before treatment mean ARR was reduced from 0.35 to 0.1 (Wilcoxon; p<0.001); ARR reduction was significant (p<0.001) also in all subgroups: naïve, switchers for intolerance or inefficacy. The percentage of patients with active MRI was reduced from 34.5% to 14.8% (p<0.001). The analysis of ARR reduction in switchers from DMT for inefficacy could be biased by higher ARR before DMF; in fact, in these pts, ARR during DMF treatment was 0.175 whereas it was 0.04 in switchers for intolerance (Wilcoxon; p=0.012). DMF was well tolerated, 5% of patients discontinued for GI symptoms, 0.3% for flushing and 2.7% for lymphopenia.

Conclusion: Our data confirm the efficacy and safety of DMF as first line treatment for naïve pts or switchers from DMT for intolerance/mild inefficacy.

Disclosure: I received speaking and travel honoraria from: Biogen, TEVA, Merk, Genzyme

EP2168

Alemtuzumab post authorization safety study (PASS) study design: Evaluating the long-term safety profile of alemtuzumab in patients with RRMS

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Background and aims: Alemtuzumab is a humanised anti-CD52 monoclonal antibody approved for the treatment of relapsing-remitting MS (RRMS) in >60 countries. Alemtuzumab significantly improved clinical and MRI outcomes versus subcutaneous interferon beta-1a (CARE-MS I [NCT00530348]; CARE-MS II [NCT00548405]) over 2 years in patients with RRMS. Efficacy was durable through 6 years in the absence of continuous treatment (NCT00930553). Here we describe the design of the PASS study, which will further evaluate the necessary duration and appropriate safety monitoring conditions, including incidence of adverse events of special interest (AESI), after alemtuzumab treatment in RRMS patients under conditions of real use.

Methods: PASS is an international, prospective, multicentre, observational study. Duration per patient will be 10 years under the protocol amendment approved in US, currently under review by EMA. Inclusion criteria: patients with RRMS, having initiated alemtuzumab for the first time ≤8 weeks before enrolment. Target enrolment: 5000 worldwide (67% in Europe). Primary endpoint: incidence of AESI, defined as serious infection, pneumonitis, malignancy, and autoimmune-mediated conditions. Secondary endpoints: descriptive statistics on the natural history of incident AESI; relative risk of AESI in alemtuzumab-treated versus non-alemtuzumab-treated MS patients (external comparison cohort); potential associations between risk factors and incidence of AESI; incidence of AEs and SAEs; demographic and clinical characteristics of patients, and description of alemtuzumab utilization patterns.

Results: Enrolment is currently ongoing. Results will be reported following study completion.

Conclusion: The PASS study will evaluate the long-term safety profile of alemtuzumab treatment in patients with RRMS under real conditions of use.

Disclosure: Sanofi.

EP2169

Cancelled

EP2170

Smoking prior to multiple sclerosis diagnosis is associated with worse prognosis

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Background and aims: Smoking is a modifiable risk factor of multiple sclerosis (MS). There are controversial results about its influence on long-term disability progression. We investigate here the correlation between the number of smoking years and of packets-year accumulated at diagnosis with disability later on.

Methods: MS patients who accepted to complete a self-administered questionnaire (98%) about their exposure to tobacco were randomly selected. We also collected clinical and demographic variables from our database.

Results: 134 MS patients (69% women, 31% men). Mean age 40.32 (18-65) years. Mean duration of disease 10.45 (10-42) years. 35% smokers, 38% never smokers and 27% former smokers. A very significative positive correlation was found between the number of smoking years and packets-year accumulated at diagnosis and disability at the moment of the study ($p<0.01$) or disability during the first nine years after diagnosis (table 1). A statistically significant difference in time to reach EDSS 3.0 was found between smokers and non smokers before diagnosis of the disease ($p<0.05$). (Figure 1).

AT DIAGNOSIS		EDSS AT CURRENT MOMENT	EDSS YEARS AFTER DIAGNOSIS								
			1	2	3	4	5	6	7	8	9
	NUMBER OF SMOKING YEARS	R = 0,25**	R = 0,37**	R = 0,28**	R = 0,31**	R = 0,32**	R = 0,30**	R = 0,28*	R = 0,35**	R = 0,35*	R = 0,37*
	PACKETS-YEAR ACCUMULATED	R = 0,23**	R = 0,34**	R= 0,27**	R = 0,30**	R = 0,31**	R = 0,27*	R = 0,26*	R = 0,34*	R = 0,37*	R = 0,38*
* p< 0,05; ** p<0,01.											

Table 1. The table shows the correlation between the number of smoking years and packets-year accumulated at diagnosis and the disability as measured by EDSS in the first nine years after diagnosis and at the moment of the study. We found a significative positive correlation in each moment analyzed.
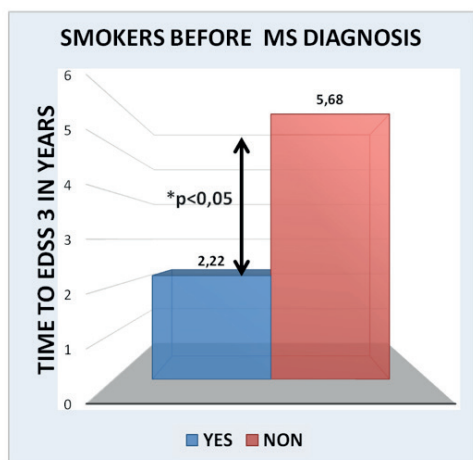
Figure 1. This figure shows that smoker patients before the MS diagnosis reach EDSS 3.0 before non smoker patients. We found a statistically significant difference (p<0,05) between groups.

Conclusion: MS patients who had smoked before the diagnosis of the disease had a more severe disease course and a faster disability progression rate (Figure 2).
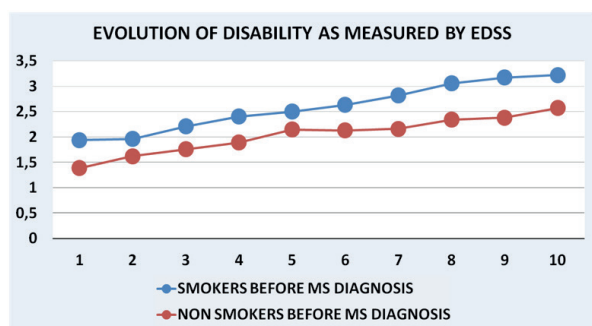
Figure 2. The figure shows the evolution of the disability as measured by EDSS in smoker and non smoker patients before MS diagnosis. A more severe disease course and a faster disability progression rate was found in patients who had been smokers before MS diagnosis. MS= multiple sclerosis.

Disclosure: Nothing to disclose

EP2171

Lymphocyte recovery in real life clinical practice after discontinuation of fingolimod in patients with multiple sclerosis

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Background and aims: Fingolimod induces a fast reduction of lymphocyte counts in the blood, however, less is known about the recovery of immune cells after treatment discontinuation in real life clinical practice.

Methods: We examined leukocyte, lymphocyte and neutrophil counts of 35 patients with multiple sclerosis, 90 (mean 80.6), 180 (mean 195.1) and 365 (mean 358.3) days after stopping fingolimod. Blood tests were available in 33 patients for the first and in 30 patients for the second and third time point. Leukopenia was defined as ≤3500, lymphopenia as ≤900, neutropenia as ≤1300 cells per microliter. We included age, fingolimod treatment duration, mean interruption before therapy switch, lymphocyte count at therapy switch and previous immunomodulatory regimens into our analysis to determine potential influencing factors of immune cell recovery.

Results: All patients showed a drop of lymphocyte count under fingolimod with no relevant leukopenia or neutropenia. Three months after treatment discontinuation 6 patients, while six and twelve months later still 5 patients showed decreased lymphocyte levels. Four out of these 5 patients received rituximab as a follow-up treatment. 44% (4 out of 9) patients that switched to rituximab showed a prolonged lymphocyte recovery. Lymphopenia at start with rituximab and pretreatment with mitoxantrone seemed to be contributing factors to a prolonged lymphopenia.

Conclusion: We observed lymphopenia in 16.7% of patients 1 year after discontinuation of fingolimod. Successive treatment with rituximab, low lymphocyte count at therapy switch, and pretreatment with mitoxantrone might contribute to a prolonged immune cell recovery. This should be considered when changing treatment regimens.

EP2172

Pregnancy outcomes following ocrelizumab treatment in patients with multiple sclerosis and other autoimmune diseases

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Background and aims: Ocrelizumab has been studied as a treatment in multiple sclerosis (MS), rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). This report reviews pregnancy outcomes in women treated with ocrelizumab.

Methods: This analysis included women who received ocrelizumab (20–2000 mg) in clinical trials of MS, RA or SLE. Two methods of contraception were required during the trials and for 1 year/48 weeks after the last ocrelizumab infusion or until B cells repleted, whichever was longer. An embryo/foetus was considered exposed to ocrelizumab if the last infusion occurred within 3 months of conception, during pregnancy or if the date was unknown.

Results: This analysis included 46 women (15 MS, 10 SLE, 21 RA) who reported 48 pregnancies (15 MS, 11 SLE, 22 RA) between 2008 and 14 September 2015. Among patients with MS, seven pregnancies with foetal ocrelizumab exposure ended in one healthy term baby and four elective terminations; two pregnancies were ongoing at the time of analysis. Seven pregnancies without foetal ocrelizumab exposure ended in two healthy term babies; one infant born at 34 weeks' gestation with nasopharyngeal neoplasm, jaundice, respiratory disease and low birth weight; two elective abortions; and two ongoing pregnancies. One pregnancy with unknown foetal ocrelizumab exposure ended in elective termination. Additional pregnancy outcomes in patients with SLE and RA will be reported.

Conclusion: Considering the prevalence of MS among women of reproductive age, pregnancy outcomes in treatment-exposed patients are important to understand. Pregnancy outcomes in ongoing ocrelizumab studies will continue to be assessed and reported.

Disclosure: Sponsored by F. Hoffmann-La Roche Ltd.

Muscle and neuromuscular junction disease 2

EP2173

Low serum vitamin D levels in patients with myasthenia gravis

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Background and aims: Myasthenia gravis (MG) is a chronic autoimmune neuromuscular disease. Vitamin D has important roles both in the autoimmune response and in skeletal muscles. We investigated the levels of 1, 25-dihydroxy vitamin D [1, 25(OH)2D] and 25-hydroxy vitamin D [25(OH)D] in patients with MG and healthy subjects.

Methods: Plasma levels of 1, 25(OH)2D and 25(OH)D were analyzed in 25 patients with MG and in 40 healthy age- and sex-matched healthy controls. MG patients were classified by disease stage (ocular or generalized) and treatment status whether or not to taking immunosuppressive agents. In addition, the MG composite (MGC) scale was assessed to evaluate the disease severity.

Results: MG patients without pre-existing vitamin D3 supplementation had lower plasma 25(OH)D levels (mean, 18.8 ± 8.4 ng/mL) than healthy controls (26.3 ± 6.1 ng/mL) ($p<0.05$). 1, 25(OH)2D levels showed slightly high in MG patients (46.4 ± 21.9 ng/mL) than healthy controls (42.1 ± 7.0 ng/mL), but had no significant difference between two groups. Vitamin D levels of 1,25(OH)2D and 25(OH)D did not significantly differ between ocular and generalized MG. In addition, levels of vitamin D did not significantly differ between MG patients under immunosuppressive therapy and taking anti-cholinesterase only. No correlation was observed between MGC scale score and 25(OH)D levels.

Conclusion: Plasma 25(OH)D levels significantly lower in patients with MG compared with healthy controls. We recommend monitoring of vitamin D status in patients with MG to avoid direct negative effects on the muscles or autoimmune response.

Disclosure: Nothing to disclose

EP2174

Cancelled

EP2175

Thymoma associated myasthenia gravis in Slovak Republic - a cohort of 129 patients (1978 - 2016)

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Background and aims: For immunopathogenesis of thymoma associated myasthenia gravis (TAMG) is typical combined presence of intrathymic (thymus, thymoma) and extrathymic autoimmune mechanisms.

Objective: We performed retrospective longitudinal study of 129 patients with TAMG registered at Slovak Centre for Neuromuscular Diseases in the years 1978-2016. The aim of the study was to analyze epidemiological and clinical data, laboratory findings and prognostic factors in TAMG.

Methods: We analyzed data and findings in medical records of TAMG patients including age at onset, sex, autoantibodies against acetylcholine receptors (AChRs), type of clinical symptomatology. We evaluated used therapies, clinical status at the last examination and prognosis of TAMG.

Results: Out of 2168 MG patients we found TAMG in 129 patients (6.0%), 49 men and 80 women. The mean age at disease onset was 51.7 years. We found positive titer of anti AChR antibodies in sera of all TAMG patients, except one. In 78 patients (63.4%) remission or significant improvement by immunotherapy and surgical treatment was achieved. MG was no primary cause of death for the last 20 years. 94 patients had benign and 35 malignant thymoma. Six patients with malignant thymoma died on thymoma dissemination, four out of them had MG in remission.

Conclusion: Both, MG severity and biological characteristics of thymoma, determine TAMG prognosis. Early diagnosis and optimal treatment of TAMG are crucial for favorable prognosis. Key words: myasthenia gravis, thymoma, epidemiology, diagnosis, treatment, prognosis

Disclosure: Nothing to disclose

EP2176

Electrophysiological investigation of autonomic involvement in patients with myasthenia gravis

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Background and aims: Myasthenia gravis (MG) is a autoimmune disorder of the neuromuscular transmission and has not a known association with autonomic dysfunction. There are however rare reports of MG coexisting with autonomic failure. We therefore conducted this study to evaluate autonomic functions electrophsiologically in patients with MG and find out subclinical autonomic disturbance.
Methods: This study comprised 29 autoimmune MG patients who were followed at Istanbul University Cerrahpasa Medical Faculty Neurology Department. Baseline characteristics for each patient were recorded. Sympathetic Skin Response (SSR) and R-R Interval Variability (RRIV) was carried out. The tests were performed two times for patients who were under acetylcholinesterase inhibitors:at the end of the longest period of time may be drug-free and an hour after taking the drug. The results of patients were compared with age and gender matched 30 normal subjects.
Results: There was no significant difference between the patient and the control groups' SSR results. The RRIV increased in both groups during hiperventilation as expected, but the rise was better in the control group ($p=0.006$). Valsalva ratio was lower in the patient group ($p=0.039$). The SSR results were compared prior to drug intake and afterwards; amplitudes of SSR were lower thereafter drug intake ($p=0.030$). There was no significant difference in SSR values according to the daily total dose of acetylcholinesterase inhibitors; but as much as time goes by after drug administration prolonged SSR latencies were obtained ($p=0.043$).
Conclusion: This study suggests that MG patients have a subclinical parasympathetic abnormality and piridostigmine has a peripheral sympathetic cholinergic noncumulative effect on these autonomic tests.
Disclosure: Our study was granted by Istanbul University | Scientific Research Projects Unit.

EP2177

Distinct clinical and genetic findings in Iranian patients with glycogen storage disease type 3

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Background and aims: glycogen storage disease type 3 (GSD-III) is a rare inherited metabolic disorder caused by glycogen debranching enzyme deficiency in liver, skeletal and cardiac muscles. Different pathogenic mutations of the AGL gene have been reported so far. Here, we report distinct clinical and genetic data of Iranian GSD-III patients.
Methods: clinical and laboratory data of 5 patients with GSD-III were recorded. Genetic analysis was performed to identify the causative mutations.
Results: Three of patients had typical liver involvement in childhood and one was diagnosed 2 years after liver transplantation for cirrhosis of unknown etiology. One of our patients presented with preferential involvement of skeletal muscles with an unusual pattern. All patients had homozygous mutation of AGL gene including 5 novel mutations: c.378T>A, c.1183C>T, c.3295T>C, c.3777G>A, c.2002-2A>G.
Conclusion: This is the first comprehensive report of patients with GSD-III in Iran. We have reported 2 uncommon clinical presentations and 5 novel mutations.
Disclosure: Nothing to disclose

EP2178

Detection of two novel DMD variants in a family with suspected hereditary muscular dystrophy

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Background and aims: A pair of twins (female and male) presented with muscle hypotonia of unknown genesis in the neonatal period. The father of the twins was diagnosed with Becker muscular dystrophy with first symptoms appearing at age 20. The purpose of the request was to perform molecular genetic analysis to test for hereditary muscular dystrophy.

Methods: To address this issue, Next Generation Sequencing (NGS)-gene panel analysis for muscular dystrophies was performed, followed by targeted carrier testing and segregation analysis.

Results: NGS-gene panel analysis of the twins DNA revealed a likely pathogenic variant and a variant of unknown significance (VUS) in the DMD gene. The detected variants had no known allele frequency and both variants have not yet been described in association with dystrophinopathies. The male twin was a hemizygote for the missense VUS c.5601A>C; p.Gln1867His, which results in the substitution of an amino acid at a highly conserved position in vertebrates. In the female twin the analysis revealed the variant identified in the brother, c.5601A>C; p.Gln1867His, and in addition the likely pathogenic frameshift variant c.79dupG; p.Ala27Glyfs*5, both in a heterozygous state. Subsequent testing of the parents showed that the symptomatic father was a hemizygote for the frameshift variant, the healthy mother was a heterozygous carrier of the missense VUS.

Conclusion: Based on the molecular genetic testing results of all family members we assume that both previously unreported DMD variants c.5601A>C; p.Gln1867His and c.79dupG; p.Ala27Glyfs*5 are most likely causative for the muscular dystrophy in the family.

Disclosure: Nothing to disclose

EP2179

Cancelled

EP2180

MicroRNAs and imaging phenotypes of trasportinopathy (limb-girdle muscular dystrophy type 1F)

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Background and aims: We report muscle histopathological, ultrastructural and radiological features of a large Italian-Spanish family with autosomal dominant LGMD, previously mapped to 7q32.2-32.2 (LGMD1F). Transportin-3 (TPNO3), which was found by NGS to be the causative gene in LGMD1F, is suggested to mediate the nuclear inport-export. The non-stop mutation identified in this family encodes for a longer protein which is expected to be unable to move to the nucleus. Clinical phenotype penetrance in this family correlates at 92% with mutation presence.

Methods: We collected serum microRNAs, clinical history, muscle biopsies histopathology of one LGMD1F kindship. Biopsy of two affected patients mother and daughter was studied (in the daughter two consecutive biopsies at 9 and 28 years and in the mother at 48 years). MicroRNA expecially miR-206 was several fold up-regulated in the doughter that hard relates at 92% with mutation presence.

Results: The daughter has a severe clinical course and the fiber atrophy was more prominent in the second biopsy at 28 years. The mother has a relatively compromised histopathology and many small muscle fibers, and autophagic changes by acid-phosphates stain. Immunofluorescence against desmin, myotilin, p62 and LC3 showed accumulation of myofibrils, ubiquitin binding proteins aggregates and autophagosomes. Ultrastructural analysis revealed myofibrillar disarray, vacuolar changes, granular material and dense subsarcolemmal bodies deriving from cytoskeleton-myofibrillar proteins. We hypotize that the pathogenetic mechanism in LGMD1F might lead to disarrangement of desmin-associated cytoskeletal network.

Conclusion: Both microRNAs and muscle imaging are powerful tools in follow up of LGMD-1F patients

Disclosure: Nothing to disclose

EP2181

A novel mutation in collagen XII causing Ullrich-like muscular dystrophy

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Background and aims: Mutations in three known collagen type VI genes (COL6A1, COL6A2, COL6A3) are responsible for a spectrum of myopathies, that range from the mild Bethlem myopathy to the more severe congenital Ullrich muscular dystrophy. Not all those patients have mutations in collagen VI. Recently, mutations in COL12A1 have been reported to cause myopathies similar to those caused by mutations in collagen VI. To date, nine patients with collagen XII mutations have been reported: six patients from 3 families with Bethlem-like myopathies and 3 patients with a more severe congenital form. We report a case of a patient with a novel mutation in collagen XII causing a phenotype resembling Ullrich muscular distrophy.

Methods: We decribe a one-year-old portuguese boy, who presented with profound axial hypotonia from the first month of life. The boy has a marked kyphoskoliosis, pectus excavatum, retrognathy, ogival palate and cryptorchidy. His mother had had a previous gestaton, with oligoamnios and spontaneous abortion at 20 weeks.

Results: We identified two rare variants in COL12A1 gene. One of them is a truncating mutation (W2332X) and the other one is a missense variant (C2739R) which is predicted as deleterious by CONDEL and GERP values.

Conclusion: We report a mutation in the collagen XII gene causing a Ullrich muscular dystrophy phenotype. This expands the spectrum of collagen XII mutations, that can lead to a wide spectrum of phenotypes ranging from severe Ullrich congenital muscular dystrophy-like forms to intermediate forms to milder Bethlem-like myopathies, similar to what happens with collagen VI mutations.

Disclosure: Nothing to disclose

EP2182

Serum vitamin D value is reduced in patients with myotonic dystrophy type 1

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Background and aims: Recently, vitamin D deficiency in patients myotonic dystrophy type 1 (DM1) was reported. Vitamin D deficiency is responsible of a secondary hyperparathyroidism or adverse effect of muscle strength in proximal muscles. The aim of this study was to investigate vitamin D deficiency state in DM1.

Methods: Forty-five genetically diagnosed DM1 patients with stable condition over three months (17 females and 28 males) were participated. The mean value of age was 47 years, and the number of CTG repeat (CTGn) was 1095. Serum level of 25-hydroxyvitamin D (OHD), 1,25dihydroxyvitamin D (OH2D), intact parathormone, Ca, and P were examined. Bone density was measured by dual-energy X-ray absorptiometry method. Body mass index (BMI) was calculated. Subjects were divided into two group according to motor disability, and data in each group were compared.

Results: OHD value was 10.8±5.7ng/ml (mean±SD). Markedly reduced OHD less than 10 ng/ml was observed 58% of patients. Whereas, OH2D was 46.6±17.2pg/ml and only 7% of patients showed low value. High value of parathormone was recognized in 9%. Hypocalcemia was in 4%. There was positive significant correlation between OHD and BMI, and negative correlation between OHD and parathormone or age. There was no significant correlation between OHD and CTGn. No evaluated items except for BMI indicated significant difference between the ambulatory group and the wheelchair or bedridden group.

Conclusion: Markedly reduced vitamin D level was common in patients DM1. However, it is still obscure what kind of symptoms vitamin D deficiency particularly affects in DM1.

Disclosure: Practical Research Project for Rare / Intractable Diseases from Japan Agency for Medical Research and Development(16ek0109172h003)

EP2183

Pseudo-dominant inheritance of a novel homozygous HACD1 mutation associated with congenital myopathy: The first Caucasian family

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Background and aims: Congenital myopathies are a clinical and genetic heterogeneous group of early onset muscle diseases. Mutations in HACD1 gene cause congenital centronuclear myopathy in dogs and have been recently described in one consanguineous Bedouin family with congenital myopathy that improved with age. We report herein the second family with congenital myopathy due to HACD1 mutations.

Methods: Clinical data were collected from the family members. Skeletal muscle biopsies were performed in two patients. The HACD1 mutation was identified by next-generation sequencing.

Results: The proband is a 28-year-old woman with facial and limb-girdle muscle weakness, that was born from consanguineous Caucasian parents. At birth, she presented with severe hypotonia that gradually improved. Muscle biopsy at 10 years of age revealed myopathic features with increased variation in myofiber size, type-1 fibers predominance, and slightly increased internal nuclei. The younger sister had similar clinical and histopathological findings. The mother and maternal grandmother had a slowly progressive proximal muscle weakness since childhood but, after neurological evaluation, surprisingly, also the father showed the same clinical picture. A novel homozygous variant in HACD1 gene (p.G213A) was detected in all the affected members.

Conclusion: To our knowledge, this is the second report on human mutations in HACD1. Our data highlight the implication of HACD1 in human pathology. Moreover, the long term follow-up of the affected individuals, revealed a mild and slowly progressive course, even at advanced age, which constitutes an important finding for patients' counseling.

Disclosure: Nothing to disclose

EP2184

Subclinical myocardial involvement in dysferlin deficient patients

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Background and aims: Different phenotypes have been recognized caused by mutations in dysferlin gene (DYSF): limb-girdle muscular dystrophy 2B, Miyoshi myopathy, and distal myopathy of anterior tibialis. Dysferlin is a large protein involved on plasma membrane repair. Recent evidence suggests that dysferlin deficiency could affect cardiac muscle, leading to cardiomyopathy.

We aim to identify a subclinical myocardial involvement in patients with molecular confirmation of dysferlin deficiency.

Methods: We conducted an observational prospective study of patients with molecular diagnosis of dysferlinopathy. Ten patients were enrolled and were subject to cardiac magnetic resonance (CMR) on a standard 1.5 Tesla clinical scanner with cine imaging for left ventricular volume (LVV) and ejection fraction (EF) calculation, and late post-gadolinium enhancement imaging (LGE) to assess for myocardial fibrosis.

Results: There was a slight predominance of male gender (60%). Mean actual age and age at diagnosis was 44.80 and 26.60 years, respectively. CMR revealed an average LVV of 147,5mL and average EF of 63%. One patient presented with severe dilated cardiomyopathy (LVV 329 mL and EF 29%). LGE imaging showed focal intramyocardial fibrosis in 3 patients (30%), two of these were asymptomatic. None of the clinical and laboratory parameters (functional status, CPK levels and molecular study) correlated with LGE.

Conclusion: Evidence of subclinical cardiac involvement in dysferlinopathies is increasing, although its real impact remains to be assessed. Phenotypic correlations were not able to yield any clinical predictor of LGE presence. Further studies are needed to evaluate the prognostic significance of subclinical findings detected by CMR.

Disclosure: Nothing to disclose

EP2185

The efficacy of non-invasive positive pressure ventilation for myotonic dystrophy type 1 in short and long-term

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Background and aims: Myotonic dystrophy is characterized by muscle and multiple organ dysfunctions. Respiratory failure related to life expectancy. However, there are few reports that examine the efficacy of non-invasive positive pressure ventilation (NIPPV) for myotonic dystrophy. We investigated the efficacy of this with blood gas analysis.

Methods: We recruited patients admitted to our hospital for myotonic dystrophy type 1 since 1993, using with NIPPV. We investigated the changes of blood gas analysis before and after that and longitude effects.

Results: There were 82 patients and 7 patients had been used NIPPV. The causes were one patient in CO_2 narcosis, one patient with pneumonia and 5 in the sensation of dyspnea. The mean of the partial pressure of arterial carbon dioxide ($PaCO_2$) before NIPPV is 59.0 Torr, the partial pressure of arterial oxide (PaO_2) is 66.8 Torr, the Base excess (BE) is 4.3, and pH is 7.35. After NIPPV, the mean of $PaCO_2$ is 54.9 Torr, PaO_2 is 75.0 Torr, BE is 4.1, and pH is 7.35. Four patients continued NIPPV after 1500 days. After 1500 days, the mean of $PaCO_2$ is 50.5 Torr, PaO_2 70.8 Torr, BE is 2.0 and pH is 7.36. There was no significant difference between before and after NIPPV including after 1500 days. All case improved the symptom of dyspnea.

Conclusion: This study showed no adverse effect of NIPPV in myotonic dystrophy type 1. The tendency of decreasing BE might show improving respiratory acidemia with NIPPV.

Disclosure: Nothing to disclose

Neuroepidemiology

EP2186

Successful neurology trainee research network collaborative audit

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Background and aims: Successful Trainee Clinical Research Networks have been established since 2007. Our network in the peninsula, the SOuthwest Neurology Audit and Research Group (SONAR) is the first such Neurology trainee network in the UK. To enable development of cohesive collaborative working of the network we designed an audit which would be deliverable across three neurology centres within the peninsula.

Methods: We audited management of suspected acute meningitis and meningococcal sepsis against national guidelines within a 4-week period in December. A standardised anonymsed data collation tool was used across the three centres and results were analysed at one centre.

Results: All 9 registrars on the rotation contributed to audit methodology design and data analysis; seven contributed cases (from all three centres). Ten cases were included in the audit, 6 (Exeter), 3 (Plymouth) & 1 (Truro). Our audit highlighted deficiencies in timely senior review, delivery of antibiotics and steroids, inappropriate administration of acyclovir and delay in lumbar puncture.
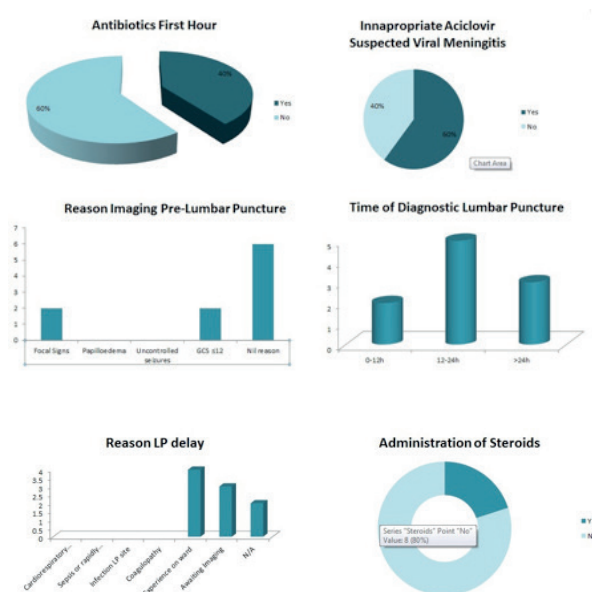
Conclusion: This was SONAR's first collaborative project and demonstrated that as a group of trainees we can successfully conduct a project across multiple hospital sites. We plan to extend the scope and ambition of our future undertakings.

Disclosure: Nothing to disclose
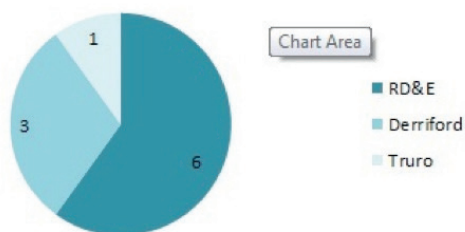
EP2187

Cancelled

EP2188

Six months as an emergency department neurologist in an University Emergency Hospital: A look back at referrals, diagnoses and admissions

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Background and aims: An Emergency Department (ED) neurologist has to deal with a plethora of diseases and symptoms, from the discomfort-causing benign ones to those posing a threat to the patient's life. We present a summary of the cases examined in our ED during 6 months in 2016.
Methods: We reviewed the logs from the Neurology ED from January 1st to June 30th 2016 and assessed the number of cases, the diagnoses and the percentage of patients admitted in the Department of Neurology for monitoring and treatment.
Results: A total of 7255 were examined by the ED neurologists, with an average of 39.86 patients per 24-hour shift. 1476 patients (20.34%) were admitted. Ischemic stroke (12.72% of total, 62.53% of admitted), transient ischemic attack (1.65% of total, 8.13% of admitted) and hemorrhagic stroke (1.16% of total, 5.69% of admitted) were the most common diagnoses. Out of the patients who weren't admitted, 1.020 (14.06%) had various types of headache, 954 (13.15%) vertigo and dizziness and 529 (7.29%) non-epileptic loss of consciousness; 1122 (15.47%) of the examined patients did not to have a neurologic cause for their presentation to the ED.
Conclusion: Poor referral and unnecessary presentation to the ED for diseases which can be managed in an outpatient setting significantly increase the workload for the ED neurologist and lead to inappropriate use of hospital resources. Better triage and systematic analysis of the ED logs can improve the quality of the medical care for real emergencies.
Disclosure: Nothing to disclose

EP2189

Clinical-epidemiologic aspects of myasthenia gravis (MG) in Georgia

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Background and aims: To investigate the data of MG distribution in Georgian territory – special with diversity of physical-geographic conditions.
Methods: Epidemiological aspects were studied in cities' and villages' population of East- and West-Georgia with various landscape areas. We used data of Georgian statistic department to calculate standard data. Investigation of epidemiologic aspects of MG conducted according to following data: sex, place of birth, place of living during disease manifestation, age of a patient during first signs of disease. We used for statistical evaluation SPSS 11.0.
Results: 365 MG patients were from 1931 to 2015: 55.8% - female, 44.2%-male, ratio 1.3/1. Age during the first signs of MG from 1 to 79, from that in 83.6% between 16-60 years, until 40 years in 61.1% of women, 43.5% - men. The highest index of disease manifestation was 16-30 years in women, and 36-50 in men. The prevalence of MG per 100 000 in whole Georgian territory was – 3.1; Eeast-Georgian – 3.4, West-Georgian - 1.9, in Tbilisi – 5.5, in city population – 4.0, village population – 1.5. According to physical-geographic areas MG is mainly distributed – in lowland and hilly regions, and practically not revealed in mountains' region. It should be noted, that lowland and hilly regions of Georgia are featured with dry climate and elevated mineralization of soil and underground waters.
Conclusion: The revealed higher prevalence of MG in cities' and some physical-geographic regions of Georgia confirm the opinion of several environmental factors has a high role in development of the disease.
Disclosure: Nothing to disclose

EP2190

Risk factors of cerebrovascular diseases and their impact on the development of acute vascular events: Epidemiological study in Belarus

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Background and aims: Significant differences in prevalence of cerebrovascular diseases (CVD) in the world are caused by variability of risk factors in different populations. The aim of study was to estimate the prevalence of risk factors of CVD and their influence on development of acute vascular events.

Methods: Screening of the open population of persons aged 40 to 59 years and dynamic monitoring after 1.5 and 3 years residing on the territory of one of districts of Minsk to identify risk factors of CVD. The following endpoints were evaluated: new cases of stroke, TIA or heart attack.

Results: 276 individuals were examined: 199 women (72%) and 77 men (28%). Mean age was 53±5.7 years. The most common risk factors in men were overweight, hypertension and smoking, in women - overweight, hypertension and hypodynamia. 1.5 years after screening dynamic observation of 270 patients was carried out, 71 patients - 3 years after. Six patients refused dynamic observation. During the observation, one case of stroke, one case of TIA and three cases of heart attack were recorded. Stroke and TIA was reported in women, and all cases of heart attack - in men. It was found out that all patients had a BMI ≥26, four of them suffered from not correctable hypertension, four - were burdened by family history of hypertension.

Conclusion: The findings indicate the need for in-depth study of CVD risk factors in specific populations and carrying out educational work among the population, which will contribute to the improvement of stroke prevention.

Disclosure: Nothing to disclose

EP2191

Characterisation of behavioural and psychological symptoms behind referrals to Dementia Units in patients with Alzheimer's disease

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Background and aims: Our goal is to evaluate whether the profile of behavioural and psychological symptoms (BPS) differs between Alzheimer Disease (AD) patients examined in Neurology Outpatient Clinics [NOC] and Dementia Units [DU].

Methods: This is an observational study that prospectively recorded data of 147 consecutive AD patients attended at NOC and 163 subjects with AD referred to DU in Spain (mean age at onset 75.3±6.7 years and mean duration of dementia 4.0±2.1 years, 67.8% women, Mini-Mental State Examination 15.8±6.4). The Neuropsychiatric Inventory (NPI) was used to assess BPS.

Results: At least one BPS occurred in 93.2% and 98,3% of AD participants evaluated in NOC and UD, the median NPI score was 48 and 36, with a median number of 4 and 6 symptoms per patient, respectively. The most frequent symptoms were depression (64.7%), anxiety (63.3%) and apathy (60.6%). In multivariate analysis, patients referred to DU had a higher risk of "clinically relevant" agitation [NPI ≥ 4] (OR:2.3, p=0.012), depression (OR:2.0, p=0.015), anxiety (OR:1.7, p=0.047), euphoria (OR:5.9, p=0.003), apathy (OR:2.9, p<0.001), disinhibition (OR:2.6, p=0.003), aberrant motor behaviour (OR:2.6, p= 0.001) and appetite/eating abnormalities (OR:1.8, p=0.024); and a lower risk of night-time behaviour disturbances (OR:0.29, p<0.001) than those attended at NOC.

Conclusion: In general, BPS are commoner in AD patients assessed in DU. That fact could be explained due to the diagnosis challenge that supposes the coexistence of affective symptoms in early stages and the management difficulties that involve hyperactive/frontal symptoms in all the stages of dementia.

Disclosure: Nothing to disclose

EP2192
Cancelled

EP2193
Cancelled

EP2194
Anxiety in patients with Parkinson's disease (PwPD)

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Background and aims: Anxiety is a common PD non-motor symptom. It's important that anxiety isn't simply reaction to the PD diagnosis instead a part of the disease itself, caused by changes in the brain chemistry. Estimates show that 25-45 percent of PwPD experience anxiety disorder [Joseph H. Friedman,2016]. Assessing PwPD anxiety profile is needed in Siberian region.

Methods: 798 PwPD are registered in movement disorders electronic database of the Siberian region. 269 PwPD were studied. Patients were clinically associated using neurologist-administered rating scales and self-administered questionnaires. Clinical assessments were conducted using the UPDRS, H&Y Scale, MoCA-test, Beck depression inventory II, Hospital anxiety and Depression Scale(HADS-A), Apathy Scale, PD Sleep Scale, Epworth Sleepiness Scale, Questionnaire for Impulsive-Compulsive Disorders in PD-Rating Scale(QUIP-RS), Bristol stool scale, Scale for Outcomes in PD for Autonomic Symptoms, Sniffing Stix Test, EuroQoL (EQ-5D), 39-item PD questionnaire (PDQ-39).

Results: Anxiety (65 men, 85 women) was diagnosed in 55.8%: 29.0% subclinical (78 PwPD: 40 women, 38 men), 26.8% clinically significant (72 PwPD: 45 women, 27 men). HADS-A score was negatively correlated with QoL scales and positively associated with apathy score (r=0.300, p<0.0001), depression severity (r=0.436, p<0.0001), QUIP-RS score (r=0.321; p=0.004), sleepiness (r=0.205; p=0.005), cognitive impartment (r=0.203; p=0.005). HADS-A scores weren't associated with onset age, illness duration, H&Y Stage, UPDRS scores. Generalized anxiety disorder, panic/phobic disorder, social phobia, agoraphobia, obsessive-compulsive and anxiety disorder not otherwise specified have been all identified in PwPD.

Conclusion: Anxiety can be even more disabling than the PD movement symptoms. It's important to recognize and treat it.

Disclosure: Nothing to disclose

Neuroimmunology 2

EP2195

Anti-MOG antibodies in a longitudinally extensive transverse myelitis after CMV virus infection

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Background and aims: Anti-myelin oligodendrocyte glycoprotein (anti-MOG) antibodies have been reported in different inflammatory disorders. The development of anti-MOG antibodies could be triggered by systemic infections but a clear association has not yet been established. We present a case with a longitudinally extensive transverse myelitis associated with anti-MOG antibodies, possibly triggered by Cytomegalovirus (CMV) infection.
Methods: A 41-year-old man had moderate fever during a primary CMV infection confirmed by significant increases in CMV IgM antibodies (8.04 Au/ml). Routine laboratory tests were within normal range. After a few days he developed symmetric progressive lower limb numbness and weakness with sphincter dysfunction. Neurological examination revealed a spastic paraparesis with lower trunk and limb hypoesthesia. MRI showed a spinal lesion involving C6-C7 and a longitudinally extensive lesion extended from T4 to the conus medullaris, with a slight enhancement at T4-T5 level after gadolinium administration. Cerebrospinal fluid (CSF) analysis, including CMV-PCR and serum anti-aquaporin 4 antibodies resulted negative.
Results: He fully recovered and had a five-year period of clinical stability. When the patient developed the onset of sexual disorders, anti-MOG antibody testing was performed and resulted positive (end point titre = 1:640). Considering the extent of the initial lesion, the new symptom and the antibody positivity, azathioprine was started.
Conclusion: This case highlights the possibility of an anti-MOG associated disease triggered by CMV infection. It is unknown whether this post-infectious entity is caused by mechanisms of molecular mimicry or failure of immunological tolerance towards anti-MOG antibodies.
Disclosure: Dr. De Rossi received speaker honoraria from Biogen and Teva and travel grants from Biogen, Teva and Merk Serono. Dr. Cordioli received consulting fees from Novartis and Merk Serono. Dr. Capra received consulting fees from Novartis, Biogen-Idec and lecture fees and/or travel grants from Novartis, Biogen-Idec, Genzyme and Sanofi-Aventis. Dr. Scarpazza, Dr. Mancinelli, Dr. Mariotto, Dr. Ferrari and Dr. Rasia have nothing to disclose.

EP2196

Acute necrotising encephalopathy syndrome: A rare cause of para-infectious encephalopathy in an adult

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Background and aims: We report a case of Acute Necrotising Encephalopathy Syndrome in an adult, and review the associated literature.
Methods: Case report.
Results: A 19-year-old man developed a febrile illness with cough, headache and progressive ataxia. On day 5 he collapsed without loss of consciousness, was incontinent of urine and subsequently unable to stand. Neurologically he was fully alert with signs of a spastic tetraparesis, however within one hour his GCS deteriorated to 8 and intubation was necessary. A Chest X-ray demonstrated consolidation throughout the left lung, and pneumococcal antigen was identified from urine. MRI brain demonstrated striking high-signal abnormalities involving the basal ganglia, midbrain and brainstem. CSF was unremarkable. The case met clinical and radiological criteria for Acute Necrotising Encephalopathy Syndrome (ANEC). The subsequent clinical course was in keeping with this diagnosis, with a prolonged period of spasticity and extrapyramidal signs associated with hyperpyrexia and deranged liver enzymes. There appeared to be a positive response to repeated plasma exchange and he fully recovered by 5 weeks.
Conclusion: ANEC is a rare para-infectious encephalopathy initially identified in East Asian children, but now recognised to occur throughout the world and occasionally in young adults. It can be distinguished clinically and radiologically from Acute Disseminated Encephalomyelitis (ADEM), its main differential diagnosis. The pathology also differs from ADEM, involving a 'cytokine storm' rather than inflammatory infiltration. We discuss the features of ANEC, its diagnostic criteria and proposed treatment. Although rare, this condition is almost certainly underdiagnosed, and earlier recognition may lead to more effective treatment.
Disclosure: Nothing to disclose

EP2197

Subacute brainstem syndrome compatible with CLIPPERS (Chronic Lymphocytic Inflammation with Pontine Perivascular Enhancement Responsive to Steroids)

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Background and aims: CLIPPERS was first described in 2010, comprising a subacute condition with brainstem clinical signs, punctate and curvilinear pontine enhancement on brain MRI and T lymphocytic infiltrate on histopathology. Clinical response to corticosteroids is observed, with frequent relapsing after treatment discontinuation. New clinical and imagiological presentations have been reported ever since, broadening the spectrum of CLIPPERS.

Methods: Case Report: A 47-year-old woman, with antecedents of in situ breast cancer in remission, presented with a 4-week history of progressing brainstem signs and symptoms. On neurological examination, hypoesthesia on the second territory of right trigeminal cranial nerve was first noticed. During the following month, the patient additionally developed ocular motility abnormalities and gait ataxia. Brain MRI disclosed multiple T2/FLAIR hyperintense lesions involving the pons, medulla and cerebellum. Subsequent MRI showed de novo bi-hemispheric hyperintensities involving the subcortical white matter. Cerebrospinal fluid analysis revealed CD19 lymphocitic pleocytosis, with no immunophenotypic atypia or evidence of B-cell monoclonality. Extensive differential diagnosis was excluded, making the diagnosis of CLIPPERS the most probable according to the established criteria. An optimal response to high-dose corticosteroids was observed, as expected in this entity. Three months after the first relapse, the patient remains assymptomatic and steroid free.
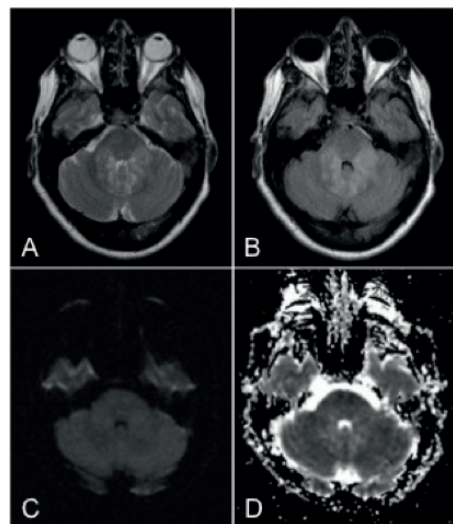
Brain MRI at clinical onset. (A) Axial T2-weighted (B) FLAIR (C) diffusion-weighted and (D) apparent diffusion coefficient map images obtained through. Diffuse patchy hyperintense lesions involving the pons, middle cerebellar peduncles, and bilateral medial cerebellum hemispheres and vermis, without areas of diffusion restriction.
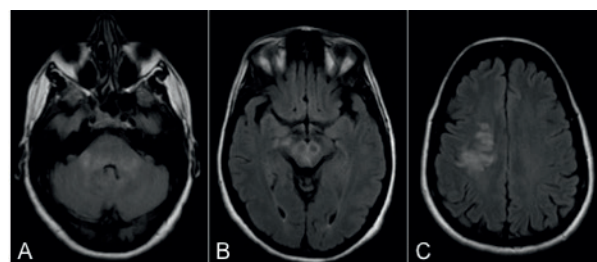
Fig. 2. Brain MRI 4 weeks after onset. (A) (B) and (C) Axial FLAIR images. Diffuse patchy hyperintensities at the pons and middle cerebellar peduncles. De novo lesions involving the mesencephalon and right centrum semiovale.
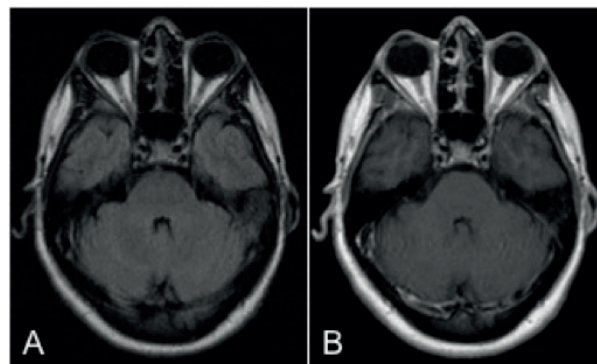
Fig. 3. Brain MRI after corticosteroid treatment and remission. (A) Axial FLAIR and (B) gadolinium T1-weighted images obtained through the level of the pons. Complete resolution of infratentorial lesions and no enhancement after gadolinium administration.

Results: NA

Conclusion: We report a case presenting with the clinical and neuroimaging features of CLIPPERS, according to recent literature. CLIPPERS is a diagnosis of exclusion, therefore a broad differential diagnosis must always be first considered. We underline the importance of a strict clinical and imagiological surveillance of these patients, in order to prevent incorrect diagnoses.

Disclosure: Nothing to disclose

EP2198
Cancelled

EP2199

MMP9 index as possible diagnostic marker of Neuro-Behçet's disease

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Background and aims: Neuro-Behçet's disease (NBD) is a neuroinflammatory disorder occurring in 5-30% of patients affected by systemic Behçet's disease (BD). NBD patients often show clinical and magnetic resonance (MRI) features "multiple sclerosis (MS) like" that make necessary a differential diagnosis from MS.

Methods: In this study we collected cerebrospinal fluid (CSF) and serum samples of 11 NBD and 21 relapsing remitting (RR) MS patients undergoing the diagnostic lumbar puncture. We measured the CSF and serum concentration of 18 soluble factors (MMP9, CXCL10, CXCL13, OPN, GM-CSF, TNF alpha, IFN gamma, IL-1 alpha, -1 beta, -2, -4, -6, -8, -10, -12p40, -12p70, -17, -23) by Milliplex.

Results: We found that NBD and RR-MS patients significantly differ about MMP9 content both in CSF and serum: NBD patients have a concentration of MMP9 lower in CSF (p=0,002) and higher in serum (p<0,0001) than RR-MS ones. By determining the ratio between CSF and serum MMP9 concentration and normalizing it versus CSF/serum albumin ratio, we defined the "MMP9 Index"; this parameter results significantly lower in NBD samples than RR-MS ones (p<0,0001). Furthermore, we detected a different CSF chemoattractant environment: higher IL8 amount in NBD and a higher CXCL13 amount in RRMS.

Conclusion: In conclusion, with this study we defined the "MMP9 index", that, if validated on an independent group of patients, could be proposed as a possible biomarker helpful to exclude the diagnosis of MS or to confirm the suspicion of NBD, especially in the cases of NBD positive for oligoclonal bands (OCB) (30% of NBD patients).

Disclosure: Nothing to disclose

EP2200

Safety of extended interval dosing of Natalizumab in clinical practice

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Background and aims: Natalizumab (NTZ) is a highly effective treatment for Relapsing-Remitting Multiple Sclerosis (RRMS), albeit associated with an increasing risk of progressive multifocal leukoencephalopathy (PML) in patients on treatment for over 24 months and who are seropositive for the JCV virus (PsJCV). NTZ is administered intravenously every 4 weeks, but clinicians have been extending infusion intervals in the attempt of reducing PML risk. This study aimed to evaluate the safety of extending interval dosing (EID) of NTZ from 4 to 5 weeks in our clinical practice.

Methods: We performed EID on clinically stable RRMS NTZ-treated patients with PsJCV (index ≥ 0'9) and >24 infusions. A retrospective review of all cases undergoing EID was conducted in 2016. Age, sex, disease duration, total NTZ-treatment time, clinical relapses, lesion load and EDSS progression were analyzed and compared with those occurring in the same group of patients in the year before EID.

Results: Seventeen patients were identified: 11 women (64.7%) with a mean age of 43.17 (±8.76), mean EDSS of 2.29 (±1.19), average disease duration of 10.76 years (±4.25), average NTZ-treatment time of 5 years (±2 years) and mean follow-up on EID of 8.4 months (±6.2). EID was not associated with clinical relapses, increasing lesion load or EDSS progression. No cases of PML were registered.

Number NTZ infusions/patient
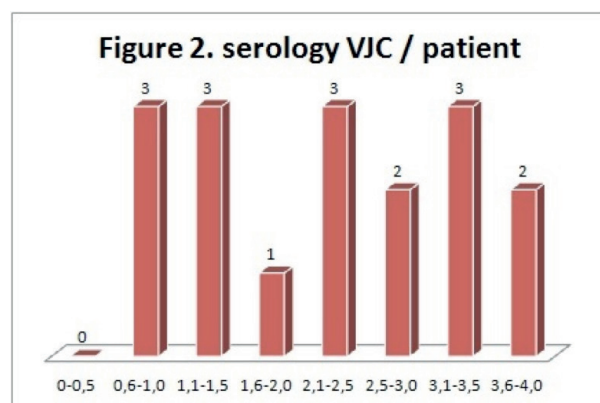
Serology vJC/patient

Conclusion: In our cohort EID did not compromise treatment outcomes. EID could be an option for maintenance therapy for patients on NTZ. Prospective studies are warranted to determine if the risk of PML is reduced in patients on EID.

Disclosure: Nothing to disclose

EP2201

Features of electroneuromyographic (EMG) diagnosis of paraneoplastic polyneuropathy (PPNP) in patients with small cell lung cancer (SCLC) who are seropositive for anti-CV2 antibodies

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Background and aims: PPNP one of the most common types of the course of paraneoplastic neurological syndrome. The most commonly it is encountered in SCLC. We study the features of EMG diagnostics of PPNP in patients with SCLC who are seropositive for anti-CV2 antibodies.

Methods: We examined 12 patients of the main group (MG) with SCLC morphologically confirmed (mean age 51.8 ± 12.8) and 20 patients of the control group (CG) (mean age 53.1 ± 6.8). Two groups of patients were examined neurologically, electroneuromyographically (nerves of the upper and lower extremities - motor and sensory fibers of the median, ulnar and peroneal nerves). Laboratory diagnostics by immunoblot (euroimmune) on paraneoplastic onconeural antibody revealed that all patients of MG were seropositive on anti-CV2(CRMP5) antibodies.

Results: When comparing the EMG amplitude performance and speed of median (SMN), ulnar (SUN) and peroneal nerves (SPN) through sensory fibers of patients of MG and CG statistically significant differences were revealed ($P=0,05$). The amplitude and speed of the SMN of MG - $4.4\pm2.7\mu V$ $44.5\pm7.2m/s$; CG - $7.3\pm0.4\mu V$, $57.4\pm4.2m/s$; amplitude and speed of SUN of MG $-7.1\pm1.9\mu V$ and - $41.5\pm7.1m/s$; CG - $15.4\pm6.8\mu V$ and 56.2 ± 6.4 m/s; amplitude and speed of SPN of MG $-4.4\pm2.7\mu V$, $40.5\pm7.2m/s$; CG - $7.4\pm0.4\mu V$, $57.4\pm4.2m/s$.

Conclusion: The patients with SCLC who are seropositive on anti-CV2 (CRMP5) antibodies develop sensory axonal-demyelinating paraneoplastic polyneuropathy.

Disclosure: Nothing to disclose

EP2202

Anti-aquaporin 4 IgG positive Neuromyelitis Optica with an atypical presentation

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Background and aims: Neuromyelitis Optica (NMO) is an astrocytopathy associated with anti-aquaporin 4 antibodies, classically characterized by severe relapses of optic neuritis (ON) and longitudinally extensive myelitis with poor recovery.

Methods: Case report

Results: Thirty seven-year-old black woman admitted in 2010 for paroxysmal dysesthesia involving progressively the right lower limb, torso and homolateral upper limb and lower left limb, in the previous three months. Neurological examination showed lower limbs hypopalesthesia. MRI disclosed heterogeneity of C1-C4 spinal cord signal, with T2 hyperintense areas, without T1 hypointensity, mild spinal expansion and mild enhancement after gadolinium, suggesting a demyelinating or tumoral lesion; brain MRI was normal. CSF cytochemical analysis, oligoclonal bands and screening for infectious/systemic autoimmune diseases were unremarkable. Symptomatic remission under pregabalin. In 2012, right ON, with compatible MRI, without new brain lesions and normal spinal exam (disappearance of the signal change previously described). In the following months, left ON and right ON, without recovery of right eye vision after methylprednisolone. Despite an initial negative investigation (anti-AQ4 and anti-MOG antibodies), anti-AQ4 IgG were detected at this stage. Clinical stability was achieved with AZA and PRD for three years. Recently, area postrema syndrome (poor therapeutic compliance), with total recovery with methylprednisolone, without new MRI lesions.
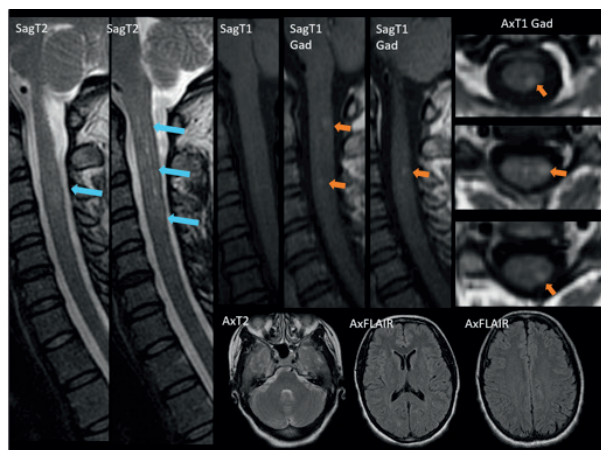
Spine MRI: heterogeneity of C1-C4 spinal cord signal, with T2 hyperintense areas, without T1 hypointensity, mild spinal expansion and mild enhancement after gadolinium. Brain MRI was normal.
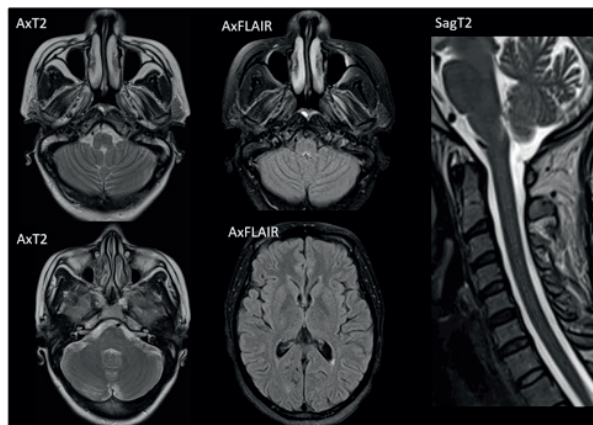
MRI performed 11 days after methylprednisolone for area postrema syndrome without new brain lesions and normal spinal exam.

Conclusion: We present a case of NMO spectrum disorder with anti-AQ4 IgG with a mild clinical presentation: paroxysmal symptoms associated with spinal cord lesion with atypical behavior - spontaneous resolution without subsequent atrophy. The expanding NMO phenotype includes mild ON and myelitis as manifestations, highlighting the importance of systematic screening for anti-AQP4 IgG.

Disclosure: Nothing to disclose

EP2203

Immunological reactivity in children with stroke

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Background and aims: Knowledge of the characteristics of stroke in children is necessary for the diagnosis, treatment and preventive care. Undoubtedly, in pathogenesis of stroke an important role plays immunological mechanisms.

Objectives: to study the immunological and autoimmune reactivity of children after stroke.

Methods: 74 children examined, 44 aged under 3 years in the acute and chronic phases of stroke and 30 healthy children at the same age. The levels of cytokines were detected by immunoenzyme method using commercial test kits "Vector-Best" (IL-1beta, IL-10). The sensitivity of the method was 2-30pg/mL. We analyzed the ANCA (Anti-neutrophil cytoplasmic antibodies) level to evaluate the general condition of the vascular system.

Results: The main pro-inflammatory cytokine IL-1beta levels in main group increased significantly (P<0.001) reaching an average level of 103.3±0.9 pg/mL, while in the control group, averaged 29.9±1.8 pg/mL. The level of IL-10 in the main group was slightly reduced (12.9±1.0), but the difference was not reliable (P>0.001) compared to the control group. ANCA level was 0.962±0.056 standard units, which is 3 times higher than in the control group and indicates the inflammatory process in the intima.

Conclusion: Immune reactions and related local inflammation involved in the pathogenesis of stroke and infarct changes in human brain tissue. Not only the excess releasing of proinflammatory cytokines like IL-1beta, but the deficit of anti-inflammatory cytokines like IL-10 plays important role in the development of inflammatory response. High levels of ANCA and IL-1beta has an unfavorable prognosis for a disease course.

Disclosure: Nothing to disclose

EP2204

Cancelled

EP2205

Bickerstaff brainstem encephalitis and Miller-Fisher syndrome - A recurrent case of ophthalmoplegia, ataxia and areflexia

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Background and aims: Guillain-Barré syndrome, Miller-Fisher syndrome (MFS) and Bickerstaff brainstem encephalitis (BBE) comprise a spectrum of the same immune-mediated disease, entitled anti-GQ1b antibody syndrome. While they are typically monophasic, a limited number of recurrent cases has been reported, usually similar to the inaugural episode.

Methods: Case report.

Results: A 63-year-old male presented with diplopia, unsteadiness, dysesthesia and dysphonia, following a respiratory tract infection. He had prominent truncal and appendicular cerebellar ataxia, generalized areflexia and nearly complete ophthalmoplegia. He also developed mild tetraparesis, distal proprioceptive deficits, nearly abolished vibration sense, left blepharoptosis, right relative afferent pupillary defect and bulbar palsy. A left Babinsky sign was noticed. Cerebrospinal fluid analysis and brain magnetic resonance imaging (MRI) were performed and were irrelevant. Electromyography exhibited low amplitude sensory nerve action potentials, F-waves' chrono-dispersion in the median nerve and abolished H reflexes. He was diagnosed with MFS and he underwent immunoglobulin therapy, with favorable outcome. Six years earlier, following mixed pollen extract immunotherapy, he developed ophthalmoplegia, ataxia, areflexia, with altered mental status and diminished vibration perception in the left side of his body. Anti-GQ1b antibody was noticeably elevated. Electromyogram revealed a sensory-motor polyneuropathy. Brain MRI was unspecific. MFS was assumed, and after treatment with intravenous immunoglobulin, plasmapheresis and steroids, complete recovery was attained.

Conclusion: It is our view that this patient suffered a first episode of BBE, and now presents to our care with MFS. Such cases of recurrent anti-GQ1b syndrome under different phenotypes are exceedingly rare, and whether genetic susceptibility mechanisms exist is still unclear.

Disclosure: Nothing to disclose

Neuro-ophthalmology/ neuro-otology

EP2206

Male idiopathic intracranial hypertension: A different entity? A 12-year tertiary centre experience

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Background and aims: Idiopathic intracranial hypertension is typically seen in females with high body mass index. The diagnosis of IIH in males must only be made after an extensive search for secondary causes of raised intracranial pressure. We have retrospectively reviewed the clinical characteristics and prognosis of male IIH at our centre.

Methods: We reviewed the notes of 14 men fulfilling the modified Dandy criteria for IIH, diagnosed under our services at University Hospitals of Leicester between 2004-2016.

Results: The case series included 14 male patients aged between 17 and 85 years old. BMI range was 23 to 43kg/m^2. 14% (n=2) of the patients presented with headache only, 43%(n=6) presented with vision changes only and 43% (n=6) presented with headache plus vision changes, 14%(n=2) patients reported tinnitus, 43 (n=6)patients required surgical intervention, of which 36% (n=5) had optic nerve fenestration, 7% (n=1) had ventriculoperitoneal (VP) and 14% (n=2) had lumbar theco-peritoneal (LP) shunt. Of the patients requiring surgical intervention, 50% (n=3) still had deterioration of their visual function. 60% (n=3) of patients having optic nerve fenestration also required a second surgical procedure (ventriculoperitoneal or lumbar theco-peritoneal shunt). On follow-up, 57% (n=4) of the patients originally presented with headache, reported resolution of this.

Conclusion: The commonest clinical presentation was visual impairment 86% (n=12), followed by headache 50% (n=7). There was a trend for our male cohort to be older, with disproportionately greater risk of severe visual loss and a higher proportion requiring surgical intervention. The findings suggest that males with IIH may require close monitoring and timely intervention in tertiary centres to avoid poor visual outcomes.

Disclosure: Nothing to disclose

EP2207

Risk factors and prognosis in isolated ischemic ocular motor cranial nerve palsy

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Background and aims: Ischemic isolated ocular motor cranial nerve palsies are frecuent in older and has been related with the presence of diabetes, hypertension and other risk factors. There are not previous studies to study the relationship between the presence of risk factors with the time to complete recovery.

Methods: Describe our serie of patients with isolated ocular cranial nerve ischemic palsy and investigate the vascular risk factors and the relationship with recovery time. Patients with third, fourth and sixth cranial nerve ischemic palsies treated at our Unit. Demographic data were collected, as well as cardiovascular risk factors (arterial hypertension, dyslipemia, smoking and ischemic heart disease) and time to recovery. Patients were divided into two groups depending the time to recovery (>3 or <3 months). we analyze the possible relationship between the recovery time and the presence of each risk factor.

Results: 48 patients with an average age 67.83 at diplopia onset. 11 (24.4%) developed a third nerve palsy (np), 2 (4.4%) a fourth np, and 35 (77.7%) a sixth np. Hypertension, diabetes mellitus and hyperlipidemia were significantly more prevalent than ischemic heart disease and smoking. In multivariant analysis we found a relationship between diabetes and time to recovery, longer in diabetics patients.

Conclusion: Ischemic ocular motor nerve palsy is the main cause of isolated cranial nerve palsy in adults. In our serie all patients were older than 50 and have at least one vascular risk factor. In our knowledge there are no previous data about the link between diabetes and time to recovery.

Disclosure: Nothing to disclose

EP2208
Cancelled

EP2209

From Miller-Fisher syndrome to functional convergence spasm

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Background and aims: Functional disorders may resemble many neurological disorders with a difficult diagnosis in some cases.
Methods: A 56-year-old male with no personal data of interest was admitted in May 2015 due to a slight instability. Brain CT was normal. The patient progressively developed an abduction disturbance in the left eye on looking to the left, an abduction disturbance in the right eye on looking to the right, and a limitation on vertical gaze with convergence spasm. He presented instability but preserved reflexes. A complete neurological and systemic study was done and was normal. The patient received intravenous immunoglobulins experiencing an aseptic meningitis as adverse event. The patient was discharged home with a diagnosis of probable Miller-Fisher syndrome. At follow-up, the patient was able to carry out all normal activities (including working, writing and driving) but neurological status still showed a convergence spasm. In addition to neurological disorder, systemic complains such as cardiological and digestive disorders were also studied and revealed normal results. A clinical improvement was seen under antidepressive treatment.
Results: Characterized by intermittent episodes of convergence that may mimic abducens paresis, converge spasm has not been well characterized, and may often be misdiagnosed by neurologists as brainstem pathology. In our patient a complete study was performed, and only a correct diagnosis was done at the follow up. Functional converge spasm often coexist with other psychogenic disorders.
Conclusion: The prompt awareness of detecting this syndrome may lead to an early correct clinical approach and avoid unnecessary diagnostic and invasive studies.
Disclosure: Nothing to disclose

EP2210

Positional nystagmus of central origin due to cerebellar PICA infarctions

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Background and aims: Brainstem and cerebellar infarctions may cause acute vertigo, often mimicking vestibular neuritis. In contrast, attacks of positional vertigo mostly reflect benign paroxysmal positional vertigo (BPPV), but may rarely be of central „pseudo-vestibular" origin, as the following cases show.
Methods: Case reports: Two females and one male patient were admitted because of acute attacks of severe positional vertigo, associated with nausea and omnidirectional ataxia of stance and gait.
Results: Case 1 (female, age 38) showed leftward saccadic smooth pursuit, but no pathological nystagmus. MR imaging revealed right cerebellar infarcts in the right PICA and SCA territories. Case 2 (female, age 71) presented with non-habituating ageotropic positional nystagmus with severe vertigo, further periodically alternating horizontal spontaneous nystagmus, obeying Alexander's law, due to acute left PICA infarction. Videonystagmography showed mildly reduced caloric excitability of the left labyrinth, the video head impulse test bilaterally reduced VOR gain. Case 3 male, age 68) developed persistent mild nausea and ageotropic positional nystagmus with vertigo. MR imaging showed right cerebellar PICA infarcts, due to V4 occlusion.
Conclusion: Our cases show that pseudo-vestibular infarctions in the PICA territory may be symptomatic by central positional vertigo with or without nystagmus. It often beats in ageotropic direction, similar to cupulolithiasis of the horizontal canal. Its central origin may be indicated by discrete clinical signs such as bilateral gaze-evoked nystagmus, saccadic smooth pursuit, missing habituation of positional nystagmus, which may also have a bad correlation with the intensity of vertigo. MR imaging should be initiated, even with pathological head impulse test.
Disclosure: Nothing to disclose

EP2211

Acute binocular double vision

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Background and aims: Acute binocular double vision is a diagnostic challenge in the emergency room and is most commonly due to extraocular nerve palsies. A precise clinical and etiological classification at first medical contact is of upmost importance for promptly taking the correct therapeutic decision.

Methods: We prospectively evaluated 54 patients (age 59.2±16.7 yrs) that presented to our emergency room with acute binocular double vision (no longer than ten days). Personal history was taken on the basis of a standardized questionnaire. Patients underwent a thorough neurological and neuro-orthoptical examination, including evaluation of ocular torsion using scanning laser ophthalmoscopy, subjective visual vertical (SVV) and harms targent screen test. Brain-MRI with was performed in all but five patients.

Results: Forty-six patients (85%) were diagnosed with an extraocular nerve palsy (26% NIII, 17% NIV and 43% NVI), two patients with an isolated extraocular muscle paresis, three with a vertical (skew) deviation, two with a internuclear ophthalmoplegia and one patient with a decompensated strabismus deorsoadductorius. The subjective visual vertical changed independently on both eyes according to the site of lesion (peripheral vs central). On the basis of the clinical findings and SVV changes in the paretic and normal eye, we developed a clinical diagnostic algorithm.

Conclusion: A systematical approach to acute, binocular double vision, especially when taking into account the subjective visual vertical on both eyes can help guide clinicians to differentiate peripheral from central lesions accurately.

Disclosure: Nothing to disclose

EP2212

Ophthalmic findings in CANVAS syndrome

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Background and aims: Cerebellar Ataxia, Neuronopathy, Vestibular Areflexia Syndrome (CANVAS) was recognised as a distinct clinical syndrome in 2011. Afferent visual system abnormalities are a common feature of other ataxias. We set out to characterise ophthalmic involvement in CANVAS

Methods: 16 patients with clinical diagnosis of CANVAS were compared with 15 healthy controls A Complete neuro-ophthalmic examination was performed including an optical coherence tomography (OCT) examination of peripapillary retinal nerve fibre layer (RNFL) and macula Patients'neurological impairmet was rated on the Scale for the assessment and rating of ataxia (SARA)

Results: There were no significant differences in demographics between cases and controls. (Figure 1) Visual acuity was worse iand cup-to-disc ratio was greater n cases compared with controls (Figure 1) While overall aberage Retinal Nerve Fibre Layer was the same in cases and controls the temoporal RNFL was thinner in patients than controls. (Figure 2) Total macular volume was increased and this was apparent all sectors but particularly in the outer macular regions, especially nasally. No association was seen between OCT findings and SARA ataxia scores.

Results

	CANVAS Patients (SD), N=16	Healthy Controls (SD), N=15	p Value
Age (years)	65.4 (8.6)	62.1 (6.9)	0.24
Female gender	11/16 (68.7%)	9/15 (60%)	0.26
Visual acuity (logMAR)	0.17 (0.15)	0.00 (0.04)	0.0002
Intraocular pressure	15.4 (3.2)	15.1 (2.0)	0.77
Cup to disc ratio	0.51 (0.16)	0.37 (0.11)	0.01
SARA score (/40)	12.8 (6.1)	-	
Symptom duration (years)	13.4 (8.5)	-	
Age at symptom onset (years)	51.9 (9.0)	-	

Figure 1. Demographics

Results

	CANVAS Patients (SD), N=9	Healthy Controls (SD), N=15	p Value
RNFL Thickness			
Average RNFL	92.8 (7.2)	96.6 (8.5)	0.27
Superior RNFL	111.9 (12.7)	117.1 (14.5)	0.38
Nasal RNFL	77.4 (12.3)	73.2 (12.5)	0.42
Inferior RNFL	123.3 (12.8)	124.0 (17.1)	0.91
Temporal RNFL	58.8 (6.1)	71.7 (11.6)	0.005

Figure 2. Optic Coherence Tomography measurements of the Retinal Nerve Fibre Layer

Conclusion: The observed decreased in Visual acuity is

likley to be due to nystagmus

The Temporal RNFL thinning in CANVAS may suggest mitochondrial dysfunction as mitochondrial diseases show a simliar pattern of change. The cause of the the thiskened macular is uncertain. This is a smaill preliminary study which is not surprising given that the condition is relatively rare. Further investigation into these OcT findings will be of interest

Disclosure: Nothing to disclose

EP2213

Examination of upright posture instability in senior patients by posturography with sensory tests

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Background and aims: Impairment of upright stance is very common in senior patients and strongly influences their quality of life. The causes of disequilibrium can be very different and often present a challenge in diagnostics... The aim of the presented work is to examine the contribution of static posturography in evaluation of instability in senior patients.

Methods: In the years 2013-2014 we examined 230 of the senior patients (over age of 65y). We performed posturography with sensory tests (galvanic vestibular stimulation, unilateral vibration of Achilles tendon). We evaluated the velocity and amplitude of body sways, total area, as well as frequency analysis was done

Results: Posturographic tests were able to quantify the extent of instability of patients and also to define the different characteristics of upright posture impairment. Patients with somatosensoric disorders (i.e. polyneuropathy) showed increased velocity and an increase of frequencies above sways points 1Hz in the anterior-posterior direction. Patients with diffuse cerebral white-matter lesions were characterized predominantly with increased body sways amplitude and with pronounced response to sensory stimulation. Patients with vestibular disorder were often unable to maintain a stance on soft (foam) platform. They showed asymmetrical responses to the galvanic vestibular stimulation and the improvement of stability in head-extension posture

Conclusion: Disorders of upright stance are very frequent in senior patient and usually several factors contribute to the impairments of stance... Static posturography is a useful method for detection of dominating cause of instability in senior patients.

Disclosure: Nothing to disclose

EP2214

Clinical characteristics of recurrent vestibulopathy: Clearly distinctive from vestibular migraine and Menière's disease?

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Background and aims: We aimed to systematically investigate the clinical characteristics of recurrent vestibulopathy (RV), Vestibular Migraine (VM) and Menière's Disease (MD). The second objective was to assess whether clinical symptoms existed that were unique to RV discriminating it from VM and MD.

Methods: Between January 2015 and November 2016, patients were prospectively recruited at a specialised dizziness unit. Patients were included if they met the diagnostic criteria for either RV, VM or MD. The clinical diagnosis was based on mutual consensus after consultation of an ENT-surgeon and a neurologist.

Results: A total of 122 patients were included , 65 (53%) were females in whom 29 (24%) were postmenopausal. The mean age was 55.5±13.7 years and the mean age of onset of vertigo attacks was 49.2±14.8 years (n=119). Forty-five (37%) patients had a clinical diagnosis of RV, 18 (15%) of pVM, 16 (13%) of dVM and 43 (35%) of MD. Clinical symptoms in these three vertigo disorders were comparable and no symptom could be identified which was specifically linked to RV. Patients with VM reported significantly more often a positive history of motion sickness. In addition, canal paresis was most profound in patients with MD.

Conclusion: We state that no clinical characteristics could be identified which were distinctive for RV. Nonetheless, we did find several distinctive clinical features for VM and MD which may assist the physician in his history taking. Prospective long-term might contribute to the discussion of whether or not RV can be identified as a separate clinical entity.

Disclosure: Nothing to disclose

Peripheral nerve disorders 2

EP2215

Effects of smart phone use on the median nerve

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Background and aims: We can understand the importance and the popularity of smart phones when we evaluate their sales. The median nerve is the main responsible nerve for the muscle movements while using smart phones (Fig 1). Various reasons; particularly frequent repetitive movements can lead to carpal tunnel syndrome (CTS) via median nerve damage. The aim of this study is to evaluate the effects of smart phone usage on the median nerve.

Methods: In this study, the sampling group was composed of 40 smart phone users and 22 classical mobile phone users (totally 62 individuals). The use of smart phone was assessed by using smart phone addiction scale (SAS). Participants were divided into three groups; high smartphone users (SAS >71), low smartphone users (SAS <71) and classical mobile phone users. In order to evaluate the upper extremity functions and symptoms, quick-disabilities of arm, shoulder, hand (qDASH) survey was applied to participants. Participants were also assessed by using visual analogue scale (VAS). Electrophysiological examination was performed by using Micromed SpA device.

Results: Totally 62 participants were included in the study. The 37 of the participants (57.9%) were female and 25 of them (40.3%) were male.

Table 1. Demographic and electrophysiological datas of participants

	Classical cell phone users (n=22)	Low smartphone users (n=19)	High smartphone users (n=22)	P
VAS pain (cm)	2,95 ± 2,01	2,15± 2,16	2,90 ±1,92	0,15
Q-dash score	16,63 ± 13,92	13,26± 10,74	19,80± 12,74	0,30
MN SCV	52,91 ± 4,69	60,62 ± 4,42	50,77± 9,24	0,00
MN SL	2,74 ± 0,37	2,28 ± 0,22	3,01± 0,62	0,00
MN MCV	54,38 ± 6,42	58,24± 3,53	51,93±6,32	0,03
MN ML	3,31±0,41	2,90± 0,34	3,55±0,55	0,00

Datas are mean±standard deviation. P-values are from analysis of Kruskal–Wallis tests. VAS, visual analog scale; Q-dash, Quick- Disabilities of Arm, Shoulder, Hand score; MN, median nerve; SCV, sensory conduction velocity; SL ,sensory latency; MCV, motor conduction velocity; ML, motor latency

Table 2. Comparison of dominant and non-dominant hand electrophysiological datas

	Dominant-side	Non-dominant side	P
Classical cell phone users (n=22)			
MN SCV	52,91±4,69	56,78±5,38	0,03
MN SL	2,74±0,37	2,43±0,25	0,02
MN MCV	54,38±6,42	58,00±4,59	0,01
MN ML	3,31±0,41	3,02±0,43	0,00
Low smartphone users (n=19)			
MN SCV	60,62±4,42	60,01±6,28	0,74
MN SL	2,28±,22	2,24±,22	0,22
MN MCV	58,24±3,53	58,61±5,40	0,77
MN ML	2,90±,34	3,06±,36	0,07
High smartphone users (n=22)			
MN SCV	50,77± 9,24	57,01± 6,37	0,00
MN SL	3,01±,62	2,43±,25	0,00
MN MCV	51,93±6,32	59,04±4,23	0,00
MN ML	3,55±,55	3,23±,47	0,06

Datas are mean±standard deviation. P-values are from analysis of Mann-Whitney U test. MN, median nerve; SCV, sensory conduction velocity; SL, sensory latency; MCV, motor conduction velocity; ML, motor latency

Conclusion: In our study, median nerve sensory, motor conduction velocity, and differences in latencies were examined. It was observed that smart phone usage rarely influenced median nerves according to the classical mobile phone usage. However, median nerves were adversely affected by the increasing use of smart phones.
Disclosure: Nothing to disclose

EP1213

A rare cause of facial asymmetry

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Background and aims: We report a patient presenting with facial asymmetry due to isolated unilateral trigeminal motor neuropathy.

Results: A 40-year-old woman presented with progressive facial asymmetry, left hemifacial numbness and pain for the last month. She denied past history of head or facial trauma, dental procedures, diabetes herpes-zoster or other infections, as well as systemic symptoms. On neurological examination it was disclosed left temporal and masseter muscle atrophy, left deviation of the mandible on opening of the mouth, and mild poorly-defined left hemifacial hypoesthesia. Electrophysiological study confirmed the diagnosis of pure motor trigeminal neuropathy, with chronic neurogenic potentials in the atrophic muscles. Trigeminal sensory fibers were normal on blink reflex and facial laser-evoked potential. Facial and cranial MRI revealed atrophy and fatty infiltration on left masticator muscles (figure 1) and regular thickening of the affected fifth cranial nerve at its origin in the anterolateral surface of the pons, extending to cisternal portion and Meckel´s cave (figure 2), which suggested an inflammatory lesion. Blood and cerebrospinal fluid studies were negative for autoimmune and infectious diseases. Clinical picture remained stable over 9 months of follow-up.

Facial MRI coronal. Fat infiltration on left masticatory muscles

Cranial MRI, T2 3D DRIVE HR, reformatted images along the trigeminal nerves. Thickening and hyperintense signal on apparent origin (white arrows), cisternal segment (black arrows) and Meckel's cavum (gray arrows) of the fifth cranial nerve.

Conclusion: Trigeminal neuropathy is usually characterized by motor and sensory involvement. Reviewing the literature we found that 16 similar cases have been reported. As described in some other patients, sensory symptoms were referred in spite of isolate motor involvement on neurophysiology investigation. There is a wide array of possible etiologies for this neuropathy, however in most of the cases, no apparent cause is found.

Disclosure: Nothing to disclose

EP1214

Bilateral carpal tunnel syndrome as an adverse effect of Pembrolizumab

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Background and aims: Pembrolizumab is a monoclonal antibody approved for treatment of metastatic melanoma and non-small cell lung cancer. We report a case of acute bilateral carpal tunnel syndrome as a possible adverse effect to Pembrolizumab.

Results: A 77-year-old man presented with progressive paresthesia and numbness in fingers and hands for the last month. Five months before he had started treatment with Pembrolizumab 2mg/kg IV every three weeks for metastatic melanoma. He denied similar symptoms on the past. He rejected recent repetitive manual activity, distal edema or arthritis symptoms. On neurological examination it was disclosed bilateral positive Phalen sign and hypoesthesia in median nerve territory. Nerve conduction studies confirmed severe bilateral carpal tunnel syndrome, without signs of peripheral neuropathy. Bilateral carpal infiltration with betamethasone dipropionate and levobupivacaine was performed, with major symptomatic and electrophysiological improvement over the following week. Pembrolizumab treatment was continued and three months later he remains clinically well, with continued neurophysiological recovery.

Conclusion: This is the first report of bilateral carpal tunnel as an adverse reaction to Pembrolizumab. One of the possible mechanisms could be a bilateral tenosynovitis of the wrist, as this condition has been reported as an uncommon adverse reaction to this drug. In our patient we found a segmental demyelization, in a local prone to nerve compression, as the most probable explanation.

Disclosure: Nothing to disclose

EP2216

Clinical and diagnostic aspects of sensory polyneuropathy in obese patients with impaired glucose

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Background and aims: Sensory neuropathy is a marker of preclinical lesions of the nerves in diabetes mellitus and prediabetes

Methods: We examined 46 patients aged from 28 to 65 years (50.32±4.4 years) with obesity, diabetes mellitus (DM) type 2 (disease duration of 5.33±3.16 years), impaired fasting glucose, impaired glucose tolerance. The obesity of the first degree was observed in 19 people (41.3%), second degree - in 22 (47.8%), third degree - in 5 (10.9%) patients rves in diabetes mellitus and prediabetes

Results: Sensory neuropathy diagnosed in 34 (74%) patients with obesity and glucose impairments. The main complaints of patients were pain, numbness and cramps in the legs, worse at night, that were observed in 68%, 15% and 17% cases respectively. The clinical symptoms in 82.4% of cases were confirmed by the results of the quantitative sensory testing. Clinical manifestations of sensory fibers lesions were more frequently detected in patients with prediabetes (80%). In patients with obesity without glucose disorders the prevalence of neuropathy was 68%, with severe polyneuropathy in 6 (46.1%) of them. In group with DM type 2 the diabetic polyneuropathy was detected in 75% of the patients, the most frequently (38.4%) it was mild polyneuropathy

Conclusion: Our data demonstrate the possibility of early development of sensory polyneuropathy in patients with obesity and prediabetes before the laboratory and clinical manifestation of DM type 2, and its progression with chronic hyperglycemia

Disclosure: Nothing to disclose

EP2217

Sural, ulnar sensory responses and sural/ulnar amplitude ratio (SUAR) in varying age group: Influence of age on nerve conduction

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Background and aims: In electrodiagnostic studies, age is probably the most significant variable, with sensory response amplitudes declining progressively with advancing age. Our purpose is to determine the lower limit of the normal value (LLN) for sural and ulnar SNAP amplitudes as well as for the SUAR at varying ages and confirm the hypothesis that the SUAR is independent of age.

Methods: The subject population was divided into four age groups: group 1: $\leq$39, group 2: 40-59, group 3: 60-69, and group 4: $\geq$70. All subjects were performed sensory nerve studies on ulnar (finger-to-wrist), sural nerves. The sural/ulnar SNAP amplitude ratio was calculated.

Results: We enrolled 49 men and 55 women, ranging in age from 20-80 years (mean, 52 years). The number of subjects in each group was 18 (group 1), 55 (group 2), 22 (group 3), 9 (group 4). In simple correlation analysis, sural and ulnar SNAPs were inversely correlated with age. However, SUARs were not correlated with age. The sural and ulnar SNAP mean amplitudes of each four groups were significantly different, respectively (sural amplitude: $p<0.001$, ulnar amplitude: $p<0.001$). However, mean SUARs of each groups were not significantly different ($p=0.296$).

Conclusion: Our results suggested that sural and ulnar SNAP amplitudes adjusted for age must be taken into account in the electrodiagnostic studies. Because SUAR is independent of age, that may be helpful in evaluation in polyneuropathy.

Disclosure: Nothing to disclose

EP2218

Peripheral stroke: Case report

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Background and aims: The vasculitis confined to the peripheral nervous system (PNS) rare. Classically this affection is revealed with a multifocal neuropathy, and a brutal onset is uncommon. We describe a case of PNS vasculitis with an acute <<vascular>> onset.

Methods: A 72 years old woman was admitted for weakness evaluation. Few hours before admission, she developed a symmetric numbness and tinglness of the limbs. The clinical examination showed a symmetric tetraparesis predominantly in the lower limbs and distally on the upper limbs, she had an absent tendon reflexes at the ankles, a gloves and socks type hypoesthesia, and troncular amyotrophy. The ENMG revealed a symmetric motor and sensitive polyneuropathy with denervation signs. The neuromuscular biopsy revealed a vasculitis of the nerve and muscle samples. All the other secondary causes of vasculitis (neoplastic, toxic, infectious, and systemic) were ruled out after several tests. The diagnosis of primitive vasculitis of the PNS was definite and the patient received steroids and immunosuppressants with a favorable evolution.

Results: We are before an acute <<vascular>> onset of the PNS vasculitis, with a bilateral, symmetric, and synchronized polyneuropathy. In our knowledge, no cases of brutal polyneuropathy revealing a PNS vasculitis were reported. In 30% of the cases, the affection had a distal onset, was both motor and sensitive, and non-symmetric with a tendency of becoming bilateral.

Conclusion: This case illustrates the importance of a meticulous examination and collection of the patient's history in finding the vascular onset of a peripheral neuropathy, and the importance of the biopsy in atypical cases.

Disclosure: Nothing to disclose

EP2219

Pseudotumour cerebri in the Guillain-Barré syndrome

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Background and aims: Pseudotumour cerebri is a rare complication of Guillain-Barre syndrome (GBS), occurring in about 4% of the cases.

Methods: A patient who had the GBS with associated increased intracranial pressure (ICP) and papilledema is described.

Results: A 22-year-old woman was admitted to our department with a two-week history of an upper respiratory tract infection, followed by tingling in the feet and weakness of the lower limbs. On examination, she had moderate proximal weakness of her legs. The limbs were areflexic with flexor plantar responses. Proprioceptive sensation was impaired. Nerve conduction studies showed slowing of velocities and a delay in F waves consistent with the GBS. Lumbar puncture (LP) yielded raised protein in the cerebrospinal fluid (CSF) (3,5 g/L), with a normal cell count. She had motor rehabilitation without recourse to plasma exchange since she was in the plateau phase. Seven weeks after presentation, the patient developed nausea, vomiting and headache. Fundoscopy revealed papilloedema. Brain MRA was normal. LP performed revealed clear CSF with an opening pressure of 36 cm H2O and no cells, a normal glucose level and a protein of 1.5 g/L. She was treated with a carbonic anhydrase inhibitor and repetitive LPs. Two months later, she was well with no headaches and the papilloedema had resolved.

Conclusion: Pathogenesis of raised ICP remains unclear. Both decreased absorption of CFS and cerebral edema have been suggested. The high concentration of CSF protein may lead to a decreased CSF absorption in arachnoid villi. Treatment remains poorly understood.

Disclosure: Nothing to disclose

EP2220

Questionnaires linked to the Charcot-Marie-Tooth Italian National Registry

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Background and aims: The Charcot-Marie-Tooth disease (CMT) Italian National Registry collects a series of genetic and clinical information.

Methods: Patients adhering to the Registry can also fill online self-reported questionnaires related to five issues: pregnancy; orthotics; skeletal deformity surgery; anesthesia; sleep disorders. By December 2016, 180 patients and 30 healthy controls filled the questionnaires. Data collection is ongoing.

Results: Pregnancy: 46/73 CMT women had at least one pregnancy; complications ranging from mild to severe occurred in 44/108 pregnancies (9/42 in controls). CMT worsened in 7 pregnancies (6 patients) with no recovery in 5 instances. Prenatal diagnosis was performed in 8/108 pregnancies. Satisfaction related to surgical procedures for foot deformities, assessed with VAS (score 0-10), was 6.4±3.5 (n=110). Repeat surgery was required in 9/72 instances. Sleep: the Epworth Sleepiness Scale questionnaire revealed abnormalities of sleep in 44/142 CMT patients (31%) and in 5/30 controls (17%). Pittsburgh Sleep Quality Index (range 0-21, 0 good sleep): most CMT subjects (123/138; mean 9.1±3.2), but also controls (27/30; 8.6±2.9) are not good sleepers. Fatigue: scores of Modified-Fatigue Impact Scale (range 0-82, 0 no fatigue) were higher for CMT (mean 33±18.2) than controls (mean 16.6±12.5). Hospital Scale for Anxiety and Depression: 63/138 CMT subjects had mild-to-severe anxiety and 35/138 mild-to-severe depression as compared to 7/29 and 4/29 controls, respectively. Data analysis on orthotics and anesthesia is ongoing.

Conclusion: The first data analyses confirm that there are problems related to all the five domains explored, that will need to be specifically addressed in patients' care.

Disclosure: Supported by Telethon-UILDM grant GUP13006. On behalf of the Italian CMT Network

EP2221

The importance of correlation between the conduction velocities values in different segments of median nerve and anti-insulin antibodies titer in the serum of patients with diabetes type1

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Background and aims: For early diagnosis of diabetic neuropathy (DN) different methods with various levels of sensitivity and specificity were used and they were often not satisfactory.

Methods: In 45 patients with diabetes type 1 (DM1) without clinical signs of neuropathy (experimental group-EG) and 45 healthy subjects (control group- CG), we registered motor (MCV) and sensory (SCV) conduction velocity (in m/s) in different segments of median nerve (MN) (on the hand, forearm and upper arm). In the serum of DM1 patients titer of anti-insulin antibodies was determined by Elisa method. Statistical analysis was done by using SPSS software (t-test, Pearson two-tail correlation study).

Results: In EG we registered significant lower MCV NM values in the hand - the middle third of forearm segment compared to CG (44.78±7.83 vs 64.65±6.93; p<0.05) and significant lower SCV NM values in the middle third of forearm - distal third upper arm segment in EG versus CG (45.92±9.74 vs 72.37±9.12; p<0.05). We registered significant correlation (p<0.05) between MCV NM in the hand - the middle third of forearm segment values and the titer of anti-insulin antibodies.

Conclusion: The determination of MCV NM values in the hand - the middle third of forearm segment at diabetics type1 without clinical signs of neuropathy is fast and simple method for early diagnosis of DN. Besides, titer of anti-insulin antibodies has some role in complex pathogenesis of DN at DM1 patients.

Disclosure: Nothing to disclose

EP2222
Cancelled

EP2223
Features of pain in chronic inflammatory demyelinating polyneuropathy (CIDP)

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Background and aims: Pain is the most common symptom of a variety of pathological conditions, including autoimmune diseases of the nervous system. It has a different character and intensity. CIDP is one of the most common forms of autoimmune disease.

Methods: Main group in our study consisted of 59 patients diagnosed with CIDP (mean age: 58.2±17.2 years) based on neurological examination and EMG that meets international criteria for diagnosis of CIDP (INCAT, 2001). Disease duration ranged from 6 months to 11 years. Pain was assessed quantitatively using of Visual Analog Scale (VAS) and qualitatively using of Leeds Assessment of Neuropathic Symptoms and Signs Pain Scale (LANSS).

Results: Pain as a the symptom of CIDP was found in 42 patients (71.2%) according to VAS. Neuropathic pain in these patients was found in 9 patients (15.3%) according LANSS. The median level of VAS was 6.16 [4.38; 7.35]. Correlations were found between the duration of disease and the degree of pain (R=-0.32, p=0.042), as well as between the degree of pain and the degree of paresis (R=-0.46, p=0.029).Thus, our results demonstrate that pain is less acute in cases with longer history of CIDP and in cases when paresis is more severe.

Conclusion: Neuropathic pain meets only in 21.43% of patients with pain symptom in CIDP.
The reduction of pain might be associated with degeneration of peripheral nerve during the progression of the disease, as suggested by the EMG results.

Disclosure: Nothing to disclose

EP2224
Microcirculatory and thermoregulatory dysfunctions in diabetic polyneuropathy

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Background: Diabetes mellitus (DM) is an increasing global epidemic, type 2 diabetes (T2DM) comprises the majority of diabetics, and associated diabetic polyneuropathy (DPN) is its most common and disabling complication. Microcirculatory dysfunctions in DM are of pivotal importance for the development of diabetic complications.
Aim: to evaluate microcirculatory and thermoregulatory disorders in patients with T2DM and DPN.
Methods: Fifty five T2DM subjects met the case definition for DPN and were included into research together with 46 sex and age matched healthy controls. The nutritious skin vessels were investigated by nailfold videocapillaroscopy and the big tiptoe skin blood flow was measured at baseline and during axon-mediated reactive hyperemia responses to cutaneous heating (44 degrees Celsius) followed by relative cooling to 32 degrees Celsius by laser Doppler flowmetry (LDF).
Results: Reduced capillary density and spastic capillaries were found in the prevailing part of the patients (89%) while the baseline LDF perfusions were higher in T2DM. The heat- and cold-induced perfusion responses were attenuated, the hyperemic peak was significantly reduced in the patients compared with the controls. The vasodilator heat-induced perfusion indices were lower and the vasoconstrictor perfusion indices during relative cooling were higher in DPN patients in relation to healthy subjects (p<0.0001).
Conclusion: The combination of T2DM and polyneuropathy is associated with a decreased number of nutritious skin vessels and capillary spasm, an increased thermoregulatory skin blood flow at rest and reduced axon-reflex mediated heat-induced cutaneous vasodilation in the feet.
Disclosure: Nothing to disclose

EP2225

Diagnostic validity of sympathetic skin response in small-fibre neuropathy

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Background and aims: Sympathetic skin response (SSR) is a simple and widely available test of sudomotor functions. The afferent part of this polysynaptic reflex is variable, while small unmyelinated C-fibres comprise the efferent part of its arch. The aim of the study was to evaluate the diagnostic validity of SSR in patients with sensory small-fibre neuropathy.

Methods: SSR was recorded from the palms and soles of 69 patients with painful sensory neuropathy (33 of them with pure SFN and 36 with mixed small and large nerve-fibre dysfunction) using electrical stimulation and inspiratory gasp stimuli. Small nerve-fibre affection had been confirmed by reduced intraepidermal nerve-fibre densities (IENFD) in skin biopsy samples in all cases. Further, 89 healthy controls were examined and age-stratified normal limits for amplitudes, latencies and reproducibility of response were established based on the results.

Results: The latencies of SSRs and their amplitudes were of very low diagnostic validity in sensory neuropathy patients. In fact, the absence of an SSR response proved the most reliable abnormality. However, using just this parameter, dysfunction of small autonomic nerve-fibres was disclosed in only in a small proportion of our sensory neuropathy patients: its sensitivity did not exceed 10% in pure SFN patients or 33% in those with mixed small and large nerve-fibre dysfunction (where more pronounced small sensory nerve-fibre affection had already been established in terms of IENFD values).

Conclusion: In view of its demonstrably low sensitivity, SSR should not be used as the only test when seeking to confirm sensory small-fibre neuropathy.

Disclosure: Nothing to disclose

EP2226

Crohn's disease and polyneuropathy

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Background and aims: Aim of the present study was to establish the clinical, electrophysiological and pathological features of neuropathy in patients with Crohn's disease (CD).

Methods: Biopsy specimens were obtained from over 700 sural nerves biopsies. The selection of patients was done according to the criteria for the diagnosis of CD. Complete laboratory, clinical electrophysiological and pathological studies were performed in all cases.

Results: We found nerve biopsies of 4 patients with neuropathy and CD. The pattern of neuropathy was distal symmetrical sensorimotor polyneuropathy, while the pathological findings showed demyelination with predominant axonal degeneration and a varying pattern of myelinated fiber loss with no vasculitic changes.

Conclusion: There is association of polyneuropathy and CD and it is important to recognize it in the early stage because remission depends on immunosuppressive therapy.

Disclosure: Nothing to disclose

EP2227

Thoracic outlet syndrome - amyotrophic form: Clinical and electrophysiological presentation of 9 cases

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Background and aims: Thoracic outlet syndrome (TOS) is a more unknown and rare entity, of polymorphous and misleading clinical presentation. A Meticulously electrophysiological study involving the study of the internal cutaneous brachial nerve (C8-D1) is essential.
We report the clinical and etiological aspects of the (TOS) in its amyotrophic form; underline the interest of the study of the internal brachial nerve brains (BCI).

Methods: Prospective analysis of the clinical, electrophysiological and etiological aspects of nine observations of (TOS) for 7 women and 2 men, aged from 18 to 61 with an average age of 41 years.

Results: The paresthesias of the hand and the forearm with heaviness and amyotrophy of the hand were noted in all our patients. At the Electromyogram (EMG) there was a decrease in the amplitudes of the motor potentials of the median and ulnar nerves. The sensory potentials of the median nerve were normal, those of the ulnar nerve decreased and there was an alteration of the sensory potential of the BCI. In 3 patients an apophysomegaly, 5 cervical ribs and 1 patient associating the two anomalies. At angioscanner an aberrant subclavian artery (1 case). There will be a discrete improvement post-surgery.

Conclusion: The syndrome of the DCTB is difficult to diagnose based on clinical arguments confronted by a meticulous ENMG study especially before the amyotrophic forms.

Disclosure: Nothing to disclose

EP2228

Clinical characteristics of patients with chronic axonal neuropathy with and without gluten sensitivity

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Background and aims: After cerebellar ataxia, peripheral neuropathy (PN) is the second commonest neurological manifestation of gluten sensitivity. We compared the clinical characteristics between PN patients with and without gluten sensitivity (GS).

Methods: Between January 2016 and December 2016 all consecutive patients attending a specialist clinic that focuses on gluten and idiopathic neuropathies, were invited to participate. All patients were examined clinically and neurophysiologically. Pain was assessed via the DN4 questionnaire and the visual analogue scale (VAS). Overall Neuropathy Limitations Scale (ONLS) was used to assess the severity of neuropathy.

Results: Of the 102 PN patients recruited, 76 (74.5%) had sensorimotor axonal neuropathy, 25 (24.5%) had sensory ganglionopathy and 1 (1.0%) had mononeuritis multiplex. Fifty-one patients (50%) had GS (positive serological markers for GS). Fifteen patients (14.7%) reported pain as the first symptom of their neuropathy. Prevalence of pain was 60.8%. The two groups did not differ significantly regarding age, gender, presence of pain, type and severity of neuropathy. Patients with GS reported less intense pain (VAS 6.8 ± 2.3 versus 8.3 ± 1.0, p<0.01). Total DN4 scores did not differ between the two groups. Patients with GS reported numbness whereas patients without GS reported tingling to be the commonest neuropathic feature accompanying their pain.

Conclusion: Although pain is similarly prevalent between patients with gluten neuropathy and those with idiopathic neuropathy, gluten neuropathy appears to be a less painful.

Disclosure: Nothing to disclose

Sleep disorders 2

EP2229

Evolution of sleep abnormalities in a patient with anti-Lgi1 antibody associated autoimmune encephalitis.

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Background: A 53-year-old man was referred to us for late-onset epilepsy with recurrent generalized tonic-clonic seizures. By the time of referral, he also complained of restless sleep with continuous irregular limb movements, vivid dreams, hypersomnolence, hyperhydrosis, mild progressive cognitive decline and increased emotionality. He experienced episodes with altered taste and smell and/or bilateral piloerection, and episodes with sudden motor unrest (often rising from prone/sitting position), staring, orofacial automatisms and/or confusion during 1-5 seconds. Symptoms first appeared 2 months prior to referral, shortly after resection of a melanoma (pT1a).

Methods: Neurological examination showed multifocal myoclonus, but was otherwise normal. Brain imaging was unremarkable. CSF analysis showed mildly elevated protein. Antibody testing in plasma and CSF was positive for anti- leucine-rich glioma-inactivated 1 (Lgi1) but not for anti- Caspr2 antibodies. Continuous EEG during episodes with smell/taste sensations did not show epileptiform abnormalities. EMG confirmed the presence of myoclonus, but showed no signs of neuromyotonia. Neuropsychological evaluation showed frontal involvement (attention deficits, slowed information processing speed). Polysomnography showed severe sleep fragmentation and absence of deep NREM and REM-sleep. Screening for malignancy was negative. Treatment with corticosteroids, plasmapheresis and azathioprine resulted in resolution of symptoms. On follow-up polysomnography, sleep fragmentation was resolved but sleep architecture remained disturbed with a sudden onset REM period and decreased amount of deep sleep.

Hypnogram at presentation:

Hypnogram 5 months after presentation:
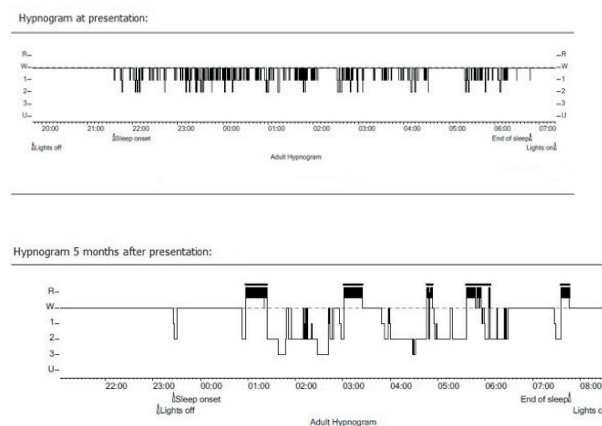
Conclusion: We describe a case of anti-Lgi1 antibody associated autoimmune encephalitis, with symptoms closely resembling Morvan's syndrome, but without myotonia. Treatment response in autoimmune encephalitis is variable, and signs and symptoms may persist or recur.
Disclosure: Nothing to disclose

EP2230
Cancelled

EP2231

Correlation between parameters of autonomic nervous system function and overnight polysomnography in patients with sleep disorders

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Background and aims: Previous studies suggest that patients with sleep disordes have higher risk of autonomic nervous system (ANS) dysfunction. The aim of this study was to correlate ANS parameters with overnight polysomnography (PSG) features.
Methods: In this cross- sectional study 47 consecutive patients (25 men, mean age 48.23±16.09 years) who underwent overnight polysomnography were recruited (19 patients with obstructive sleep apnea syndrome (OSAS), 28 non-OSAS subjects). They all underwent PSG and standardized batttery of ANS testing, including blood pressure and heart rate response to Valsalva maneuver, deep breathing test and head up tilt table test. Adrenergic and cardiovagal scores of the Composite Autonomic Scoring Scale (CASS) were determined.
Results: RESULTS: Out of 47 subjects, interpretation of both cardiovagal and adrenergic CASS score was available for 40 subjects, 42.5% had CASS cardiovagal score ≥ 1, 52.5% had CASS adrenergic score ≥ 1. Negative correlation was found between CASS cardiovagal score and total sleep time (rs= -0.368, p=0.020). Positive correlation was found between CASS cardiovagal score and sleep latency (rs= 0.445, p=0.004). Oxygen saturation was found to have a negative correlation with CASS cardiovagal score (rs=-0.379, p=0.027). Positive correlation was found between CASS cardiovagal score and desaturation index per hour (rs=0.393, p=0.022). CASS adrenergic score did not show significant correlation with any PSG parameters.
Conclusion: CONCLUSION: The results of this study are suggesting that parasympathetic nervous system dysfunction is associated with impaired sleep structure (sleep latency and total sleep time) and oxygen saturation.
Disclosure: Nothing to disclose

EP2232

Cancelled

EP2233

Catathrenia, a rare sleep disorder- Clinical experience, diagnosis and treatment at sleep unit

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Background and aims: Catathrenia is a rare sleep disorder that affects young adults characterised by expiratory groaning during sleep, preceded by a deep inspiration which occurs specially during REM phases. Since its original description, there have been few cases reported. Patients are normally unaware but typically bed partners are troubled, often deriving in social problems. Continuous positive airway pressure (CPAP) and surgery have been proposed as treatment. Mandibular advancement devices (MADs) have never been used before.

Methods: We studied the clinical course, polysomnogram (PSG), spirometric findings and outcomes after the treatment of eight patients with a diagnosis of catathrenia at our center.

Results: We included eight patients (5 men, 3 women) with a mean age at diagnosis of 28.6±4.9 years (range 22–38 years). The chief complaint was noises during sleep (62,5%), disturbances to bed partner (25%) and bad sleep quality (50%). All the patients referred that it was a nightly problem. The number of catathrenia events (single or cluster) during overnight PSG varied between 8 and 24 per patient (mean 14.8). Their exhalation and sound duration range was 23s - 423 s. CPAP treatment was proposed for two of the patients. One patient had Obstructive Sleep Apnea (OSA), showing an improvement in his sleep quality. The other patient had significantly fewer events of groaning with CPAP and improved her sleep quality. We proposed treatment with a MAD to one patient, without improvement.
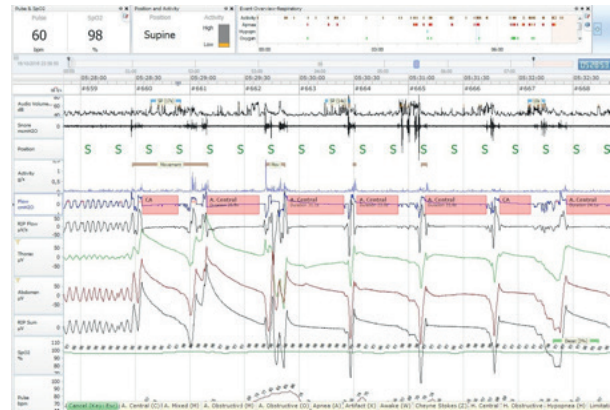
Catathrenia's cluster.

Conclusion: Catathrenia patients may benefit from CPAP, specially those with coexistence of OSA. In our experience, MAD was not an effective treatment.

Disclosure: Nothing to disclose
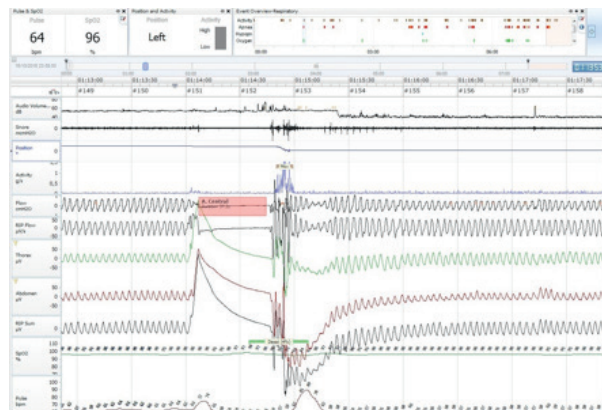
Catathrenia single

EP2234

Sleep disturbance and the risk for cognitive decline: Assessment of visual attention components in patients with insomnia

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Background and aims: Chronic primary insomnia (CPI) is a highly prevalent sleep disorder in subjects >50 years of age and related to psychological distress. As both sleep deprivation and increased stress susceptibility have been shown to represent risk factors for neurodegeneration, CPI patients may be subject to a higher probability for developing progressive cognitive impairment. In fact, in patients with CPI, lower sleep quality has been found to be associated with hippocampal atrophy and cognitive decline. Similar brain and cognitive changes prevail in patients with mild cognitive impairment (MCI), who bear an increased risk for developing dementia. Our own previous work in MCI patients, applying the conceptual framework of the 'theory of visual attention' (TVA), has identified an elevated perceptual threshold in comparison to age-matched healthy participants in a whole report task.

Methods: In the present study we assessed a sample of 16 CPI patients and and sex matched controls with TVA-based whole report to test the hypothesis that CPI patients also show a significant increase of the perceptual threshold.

Results: Compared to a healthy control group, we found no significant differences with respect to TVA-based parameters of processing capacity. However, within the patient group, the perceptual threshold values were significantly related to the subjective evaluation of insomnia severity (ISI questionnaire). Also, higher threshold values in CPI patients were significantly correlated to polysomnography indices, i.e. sleep efficiency index, and arousal index.

Conclusion: TVA-based assessment of visual processing capacity may be able to identify CPI patients with an increased risk for cognitive decline.

Disclosure: Nothing to disclose

EP2235

Narcolepsy with cataplexy in a patient with anti-Hu antibodies

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Background and aims: Type 1 narcolepsy (NT1) is a central hypersomnia due to the loss of hypocretin-producing neurons of a likely autoimmune etiology. 'Symptomatic' forms have been rarely described.

Methods: A 85-year-old male, heavy smoker and with many cardiovascular risks factors, was admitted because of a six-months history of subacute onset of behavioral change, excessive daytime sleepiness, generalized weakness, and episodes of loss of muscle tone in the limbs and slurred speech, triggered by emotions. Neurological examination revealed subcontinuous fluctuations in muscle tone with ptosis, facial grimaces, muscle sagging of upper limbs and generalized hypotonia. Polysomnography and multiple sleep latency test documented, respectively, disrupted nocturnal sleep with REM sleep behavior disorder and 5/5 sleep-onset REM sleep periods with pathologically sleep latency. Polygraphic recordings documented cataplectic status. HLA typing was negative for HLA-DR15-DQB1*0602 antigens. Paraneoplastic screening disclosed a serum positivity of anti-neuronal nuclear antibody, type 1 (anti Hu), while the analysis of the cerebrospinal fluid revealed decreased hypocretin-1 level (146,83 pg/mL). Total CT scans finally showed a hilar-perihilar lesion in the right lung that displayed hyperfixation at the whole-body fluorodeoxyglucose positron emission tomography (PET).
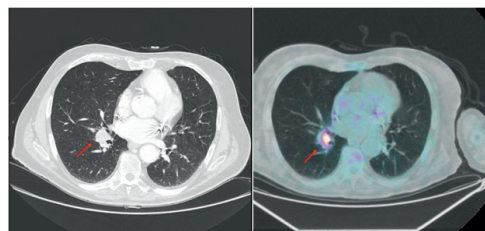
Chest CT scan with hilar-perihilar lesion in the right lung; 18F-FDG PET with hyperfixation of nodular formation

Results: A diagnosis of symptomatic narcolepsy with cataplexy in presence of anti-Hu antibodies and lung cancer was made. A symptomatic treatment with modafinil, sodium oxybate and venlafaxine was started, with only partial clinical benefit.

Conclusion: This is the first report of symptomatic narcolepsy with cataplexy in patient with positivity of anti-Hu antibodies. Atypical age, subacute onset and cataplexy severity point to a the secondary nature of the symptoms.

Disclosure: Nothing to disclose

EP2236
Cancelled

Monday, 26 June 2017

Cerebrovascular diseases 6

EP3001

The role of BNIP3 in acute cardiac injury following ischemic stroke

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Background and aims: Cardiac diseases are common post-stroke and are associated with increased morbidity and mortality. One possible mechanism of acute cardiac injury is the neurogenic myocardial damage, where the cerebral injury is disturbing the normal sympathetic and parasympathetic neuronal outflow to the heart leading to cardiac damage including myocardial infarctions. A consequence of an increased sympathetic activity is an exaggerated norepinephrine efflux from cardiac sympathetic nerve terminals into the myocardial interstitium with prolonged opening of the ß1-adrenergic receptor-controlled calcium channels. Abnormal intracellular Ca2±handling, leads to mitochondrial dysfunction, presumably mediated by the pro cell death protein BNIP3, and generation of reactive oxygen species (ROS). The exact mechanism is not completely understood and the major objective of this project is to characterize the molecular phenotype of the neurogenic myocardial damage post-stroke.

Methods: Our data demonstrate acute myocardial damage in wild-type mice after right-sided transient middle cerebral artery occlusion (tMCAO).

Results: Notably, the size of myocardial damage correlated with the brain infarct volume and triggered a ~4-fold elevation of troponin t levels that were detectable 20 h after stroke. Similar effects were found using the ß1-adrenergic receptor stimulator isoproterenol, an established model of heart failure. Following either cerebral stroke or isoproterenol treatment, higher levels of BNIP3, cardiac troponin t, ANP, BNP and norepinephrine were found in blood and heart samples at distinct time points.

Conclusion: We found expression of the pro cell death protein BNIP3 in the heart after cerebral ischemia and we will further investigate the role of BNIP3 in mediating neurogenic cardiac damage.

Disclosure: Nothing to disclose

EP3002

A study of clinical features, risk factors and short-term outcome of ischemic stroke in patients with and without atrial fibrillation in a North African population

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Background and aims: There is poor data concerning clinical profile and prognosis of ischemic stroke (IS) in patients with atrial fibrillation (AF) from North Africa. We attempted to estimate characteristics in demographic and clinical features, risk factors and short-term outcome of IS patients with and without AF from Tunisian population.

Methods: A prospective study was conducted from February to May 2015 at Habib Bourguiba Hospital (Sfax, Tunisia) including all first acute stroke patients (≥18 years). Patients with AF (group 1) and without AF (group 2) were analyzed for demographic characteristics, stroke risk factors, clinical characteristics, location of infarct and prognosis.

Results: Two hundred patients were enrolled. Out of 200, 152 had IS. Forty-nine (32.23%) patients had AF (non-valvular AF: 93.78%). There were significant differences seen in age (group1: 73.61±14.22 years versus group 2: 67.03±13.94 years; p=0.008) and gender (group 1: men 48.98%/ women 51.02% versus group 2 men 67%/women 33%; p=0.03). Risk factors such as diabetes (18.36% versus 42.71%, p=0.03) and active smoking (32.65% versus 49.51%, p=0.05) were less prevalent in patients with AF. The mean of initial NIHSS was significant (group 1:12.67 vs group 2: 8.60; p=0.003). Extensive middle cerebral artery infarction were more significant in group 1 (26.53% vs 10.37%). Patients with AF had poor outcome at one month (mean Functional Independence Measure score: 75.29 vs 92.13; p =0.029).

Conclusion: In our population, the frequency of non-valvular AF is quite high. These patients had less risk factors but poor outcome at one month.

Disclosure: Nothing to disclose

EP3003

Early and late epileptic seizures after stroke

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Background and aims: Epileptic seizures are common complication after stroke, devided into early seizures, which occur in the first fourteen days, and late ones which occur more than fourteen days after stroke. The aim of the research is to determine the relationship between the early and late seizures, and the influence of comorbidity on seizures.

Methods: The research is retrospective and includes patients with poststroke seizures who were hospitalized at the Clinic of Neurology in Novi Sad, in the period from 2013. to 2016. year.

Results: The research included 54 patients with poststroke seizures, half were male, half female, mean age $64,4\pm4,5$ years. 36 (67%) patients had ischemic, and 18 (33%) patients had hemorrhagic stroke. Generalized seizures had 36 (67%) patients, focal seizures had18 (33%) patients, while 2 patients had status epilepticus. In the group of patients with ischemic stroke late seizures were more common, while in the group of patients with intracranial hemorrhage early seizures were more often, which was statistically significant (p=0.04). Patients with cardioembolic stroke were more likely to have generalized seizures (p=0.048). Early attacks were more often registered in patients suffering from anemia and in group of smokers.

Conclusion: Age, gender, size and localization of morphological lesions do not significantly affect the type of seizures after stroke. Intracranial hemorrhage is often followed by early seizure, while ishemic stroke is accompanied by late seizures. Generalized seizures are more common in patients with cardioembolic stroke. Early attacks usually occur on first day after stroke.

Disclosure: Nothing to disclose

EP3004

Right hemisphere ischemic stroke in a 24-year-old patient with antithrombin III deficiency presenting as severe oral apraxia and anarthria

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Background and aims: Antithrombin III (ATIII) is a protease that inhibits coagulation by neutralizing thrombin activity. ATIII deficiency is a rare condition and an uncommon cause of stroke.

Methods: Case report

Results: A 24-year-old left-handed woman was admitted to the neurology department due to a sudden onset of speech impairment and mild weakness of her left arm. She had been on Acenocoumarol treatment for 6 years due to recurrent episodes of deep venous thrombosis. The anticoagulant medication was discontinued 10 days prior to the stroke. Her neurological examination revealed mild left central facial and left arm weakness and anarthria with normal comprehension and writing. Oral apraxia was present and the patient was unable to follow the instructions to protrude her tongue, whistle or puff out her cheeks. Spontaneous movements of the tongue, lips and jaw were intact. The patient was also unable to voluntarily swallow saliva. However, pharyngeal and esophageal phases of swallowing were preserved. Limb apraxia was absent. Magnetic resonance imaging of the brain showed a right insular cortex and frontal operculum infarction. The patient`s ATIII activity was decreased in two independent measurements (39.7% and 31%), while protein S (75.4%), protein C (113%), APC-R (2.31) and LAC (1.2) showed normal values. Limb weakness, speech, swallowing and oral praxia gradually recovered during the following weeks. The patient was treated with low molecular weight heparin, followed by Warfarin. Genetic testing is ongoing.

Conclusion: The incidence of thrombotic events, including stroke, is increased in ATIII deficient patients. This condition requires treatment with anticoagulant medication.

Disclosure: Nothing to disclose

EP3005

Cancelled

EP3006

The studying of shear stress in the development of endothelium dysfunction in patients with spondylogenic vertebrobasilar insufficiency

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Background and aims: A shear stress is known as a force applied to the upper layer of the laminar-flowing liquid that causes displacement of the underlying layers in relation to each other in direction of the applied force. The stream of blood deforms endothelial membrane, which leads to a wide range of regulatory influences.

The aim was to study the role of shear stress in the development of endothelium dysfunction (ED) in patients with spondylogenic vertebrobasilar insufficiency (SVBI).

Methods: For an assessment of nature of shear stress in vessels of vertebrobasilar system Stewart's index (ISD) was studied. Concentration of endothelin-1 (ET-1) in serum of blood by immunoenzymatic analysis was evaluated.

Results: In group of 98 patients with SVBI the rise of concentration of ET-1 in blood serum (2.84 ± 0.09 fentamol/ml against 1.25 ± 0.08 fentamol/ml) was found, against the S-NO level recession (0.18 ± 0.07 microns/l against 0.45 ± 0.02 microns/l)that demonstrated vasopressin tendency of the endothelial vasoregulation. The assessment of ISD revealed rising of it concerning left VA on $31.6 \pm 0.69\%$ from control, right VA of $20.7 \pm 0.64\%$, BA of $15.6 \pm 0.37\%$ ($p < 0.05$), indicating shear stress in the vertebrobasilar vessels in comparison with control.

Conclusion: The carried-out correlation analysis confirmed the interrelation of a condition of shear stress on the basis of the assessment of a ISD and ED of patients with SVBI, revealing positive correlation dependence between the ISD in BA and ET-1 level ($r = +0.41$); negative correlation dependence between S-NO and ISD in BA ($r = -0.22$) ($p < 0.05$).

Disclosure: Nothing to disclose

EP3007

Obstructive sleep apnea in stroke patients

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Background and aims: Ischemic stroke is one of the most sociologically important diseases and its linking with obstructive sleep apnea has been discussed throughout the recent years. Most of the data has come from many summary, cross, meta analyses which have shown a definite link between the two conditions. We present a localised study on acute stroke patients with obstructive sleep apnea (OSA), its treatment with CPAP or BPAP, and clinical outcome and follow up.

Methods: Detailed patient history, including socio-demographics; somatic and neurological status; asessment of concomitant diseases and treatment; stroke severity; OSA severity asessment; respiratory poligraphy and/or polisomnography; CPAP/BPAP treatment, patient follow up.

Results: 30 patients have been fully analysed including follow up. They were divided into several common groups - patients that started CPAP/BPAP treatment during hospital stay, patients starting treatment after hospital discharge, patients without therapy, patients with treatment only in the acute phase. All but one of the patients had newly diagnosed stroke and sleep apnea. 2 patients required BPAP therapy while all others had CPAP therapy initiated. We found a close relation to sleep apnea and stroke severity - those with a higher NIHSS score had severe OSA (marked by a high AHI) in most cases. Patients undergoing OSA treatment show a better clinical outcome on follow up but time of treatment initiation didn't show any influence on outcome.

Conclusion: Sleep apnea is a known risk factor for the development of stroke, but also a known consequence. Treatment of OSA following stroke shows a significant profit for clincal outcome.

Disclosure: Nothing to disclose

EP3008

Intravenous thrombolysis in minor ischaemic stroke – do the octogenarians worse?

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Background and aims: Minor ischaemic stroke (MIS) is not unanimously defined yet. Benefit of Intravenous thrombolysis (IVT) in MIS is not clear in general. Benefit of IVT in MIS in the elderly, is matter of discussion.

Aim of the study: Safety and benefit of IVT in patients over 80 years comparing to younger ones.

Methods: Prospectively and consecutively enrolled cohort in period 1/2014 to 9/2016. Inclusion criteria: MIS (defined as NIHSS 0-4), onset ≤ 4,5h or unknown, prestroke performance modified Rankin scale (mRS) 0-2. Exclusion criteria: haemorrhagic stroke. Cohort was split into two groups: „elderly" (means ≥ 80 years old) and „<80". Outcome: 3 month after stroke per mRS; symptomatic intracranial haemorrhage (sICH).

Results: Cohort comprised 177 patients. Group "elderly": 30 patients, 13 males (43.3%), mean age 84.0±3.15 years; OTT: 130.1±46.9, unknown onset: 3 (10.0%), DNT 36.9±21.0. Group "<80": 147 patients, 84 males (54.7%), mean age 65.9±9.8 years; OTT: 131.5±63.7, unknown onset: 19 (12.8%), DNT 40.2±20.1. Admission status and clinical outcome see tables 1-2. Excellent clinical outcome (mRS 0-1) in "elderly" and "<80"were 66.7% and 76.5% respectively, and sICH: 1 (3.3%) and 2 (1.3%) respectively.

NIHSS	Admission clinical finding			
	elderly		< 80	
0	1	3,3%	10	6,8%
1	2	6,7%	13	8,8%
2	9	30,0%	34	23,1%
3	9	30,0%	44	29,9%
4	9	30,0%	46	31,3%
total	30	100,0%	147	100,0%

Table 1: Admission NIHSS

mRS	3 month clinical outcome			
	elderly		< 80	
0	14	46,7%	96	65,3%
1	6	20,0%	18	12,2%
2	4	13,3%	16	10,9%
3-5	4	13,3%	13	8,8%
6	2	6,7%	4	2,7%
total	30	100,0%	147	100,0%

Table-2: 3month outcome (mRS)

Conclusion: IVT of MIS in the elderly is slightly worse than in the younger, but still highly beneficial and safe. Bleeding complications remain low.

Age should not be the exclusion for IVT neither in general nor in MIS.

Disclosure: Nothing to disclose

EP3009

Safety of acupuncture for patients taking warfarin or antiplatelet medications

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Background and aims: Anticoagulant and antiplatelet therapy are widely used as preventive measures and treatment for cardiovascular and cerebrovascular diseases. Bleeding is a significant complication of anticoagulant and antiplatelet medications. With the growing use of acupuncture and the potential concomitant use of such medications, studies on the safety of acupuncture are necessary. The objective of this study was to evaluate the safety of acupuncture for patients taking warfarin or antiplatelet medications by comparing the rate of side effects for patients who did not take either of these medications.

Methods: The medical records were searched to identify patients who had received acupuncture treatments at Stroke and Neurological Disorders Center, Kyung Hee University Hospital at Gangdong. Prescribed medications were identified from medical records and each patient was allocated to one of three groups based on the medication they were taking. Group A were taking warfarin, group B were taking antiplatelet medications but not warfarin, group C took neither warfarin nor antiplatelet medications and acted as a control group. Potential side effects that could be attributed to of acupuncture were identified.

Results: A total of 242 patients and 4891 acupuncture treatments were identified. No patients experienced serious adverse events such as extensive bleeding. The occurrence rate of microbleeding (bleeding which stopped within 30 s) was 4.8% for group A, 0.9% for group B and 3.0% for group C.

Conclusion: Acupuncture treatment appears safe even for patients taking warfarin or antiplatelet medications. Large-scale, well-designed studies are needed to confirm these results.

Disclosure: Nothing to disclose

EP3010

Bilateral carotid agenesis

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Background and aims: Agenesis of the internal carotid artery (ICA) (uni o bilateral) is a rare congenital anomaly, occurring in less than 0.01% of the population. The term absence has been chosen to encompass agenesis, aplasia and hypoplasia of the ICA. Agenesis is use when both, the artery and the carotid canal are absent. It may be asymptomatic or produce symptoms due to vascular insufficiency.

Methods: A 57-year-old female with a history of long-standing bilateral sensorineural hearing loss, hyper gonadotropic hypogonadism and hypothyroidism presented during the last month non-progressive blurry vision and headache. The neuro-ophthalmological examination was normal.

Results: MRI was performed, showing no brain, brainstem or cerebellar findings.

The MR angiogram revealed bilateral agenesis of the ICA with supply to the anterior circulation via carotid-vertebrobasilar anastomoses, accomplished through hypertrophy of the PCOM (posterior communication). The absence of both carotid canals on a skull base CT scan confirmed the bilateral carotid agenesis.
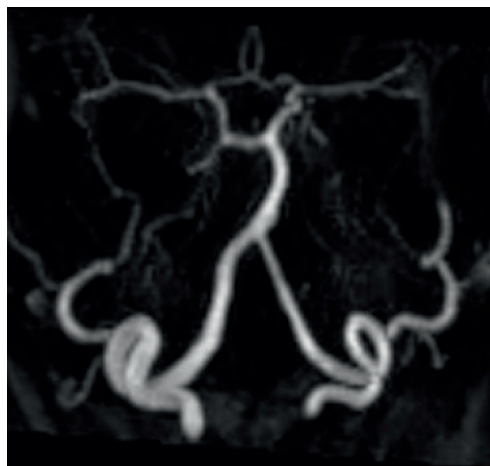
Fig. 1. Coronal time-of-flight MR angiography showing a posterior view of the circle of Willis. There is an enlarged basilar artery and posterior communicating arteries supplying both anterior and medial cerebral arteries. Neither internal carotid arteries are seen.
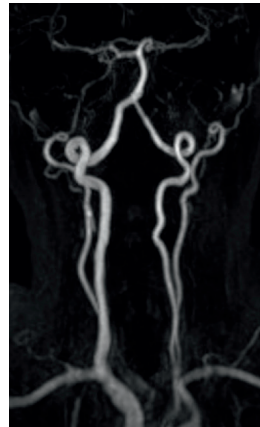
Fig. 2. Coronal time-of-flight MR angiography showing an anterior view of supraaortic vessels. There is an abscence of both internal carotid arteries, and an enlarged right vertebral artery.

Fig. 3. Axial bone window CT showing the abscense of both carotid canals.

Conclusion: The diagnosis of this anomaly has an important implication in thromboembolic disease, and in the surveillance and detection of associated cerebral aneurysms (approximately 35%).

Associations with congenital malformations in different organs have been described, like anomalies in the hypothalamic – pituitary axis and PHACE syndrome.

The cerebral angiography, MR angiogram and the CT scan and are powerful diagnostic tools in these patients, and also in their follow up.

Disclosure: Nothing to disclose

EP3011

Cancelled

EP3012

Cancelled

Cerebrovascular diseases 7

EP3013

An atypical clinical presentation of diffuse cerebral arteriovenous malformation: Diagnostic dilemma between diffuse AVM and cerebral proliferative angiopathy

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Background and aims: Here we present a 37-year-old male patient who was evaluated at our medical center with headache, right-sided weakness and aphasia that was progressively developed within one week. His past medical history was unremarkable and laboratory test results were found to be in normal limits. Cranial MRI (magnetic resonance imaging) revealed   diffuse arteriovenous malformation (AVM) that was confirmed with Cerebral DSA (digital subtraction angiography) showing diffuse AVM with nidus. Following Perfusion-weighted MRI revealed hyperperfusion in the entire left hemispheric area. Based on the short time of unresponsiveness symptom of the patient we aimed to evaluate long-term EEG monitoring that revealed electrographic seizure activity on the left centrotemporal region. We have initiated anti-epileptic treatment that led to improvement in his epileptic symptoms while his right-sided weakness and word finding difficulty symptoms remained stabile over three months.

Methods: This is an interesting case with subacutely developed clinical findings and prominent cerebral ischemic areas in MRI that are associated with variable cerebral perfussion abnormalities in MRI-Perfusion imaging which finally resembles also a possible cerebral proliferative angiopathy (CPA).

Results: The natural course of CPA has been reported to be less aggressive than the classical clinical progress of the brain AVMalformations. Furthermore, CPA differs from other arteriovenous malformations in their angiomorphology, histology, pathophysiology, epidemiology, natural history, and clinical presentation. However, despite these differences it can be in some atypical cases difficult to differentiate diffuse AVM from CPA.

Conclusion: Here, we present an atypical clinical presentation of radiologically confirmed AVM that is simulating the clinical symptoms of CPA.

Disclosure: Nothing to disclose

EP3014

Tenecteplase in wake-up ischaemic stroke trial

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Background and aims: Patients with wake-up stroke have traditionally been considered ineligible for intravenous thrombolytic treatment. Tenecteplase has pharmacological advantages over alteplase, and can be given as a bolus. We are doing a pragmatic, CT-based, randomised-controlled, open trial of tenecteplase for patients with wake-up stroke; the Tenecteplase in Wake-up Ischaemic Stroke Trial (TWIST).

Methods: Patients with wake-up stroke<4.5 hours and without evidence of large infarct or proximal artery occlusion will be randomised to tenecteplase 0.25 mg/kg plus standard care or standard care alone. Plain brain CT and CT angiography will be done before randomisation and repeated on day 2. CT perfusion will be done at selected centres. Follow-up will be done at discharge (or day 7) and by telephone at 3 months.

The primary effect variable is functional outcome at 3 months, measured by the modified Rankin Scale.

Results: The target is to include 500 patients from centres in Norway, Sweden, Denmark, Finland, Estonia, Lithuania, UK, Ireland and Switzerland. Start of patient inclusion: January 2017. Planned study period: two years. Study questions to be answered:

1. Can thrombolytic treatment with tenecteplase within 4.5 hours of wake-up improve functional outcome at 3 months?
2. Can findings on CT angiography or CT perfusion identify patients who benefit from such treatment, compared to patients without such findings?

Conclusion: TWIST will show whether patients with wake-

up stroke benefit from treatment with tenecteplase within 4.5 hours of awakening, and whether multi-modal CT can be used for selection of patients.

Disclosure: Nothing to disclose

EP3015

Hematoma evacuation or decompressive craniectomy: 11 years of experience in surgical treatment of patients with supratentorial intracerebral hemorrhage

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Background and aims: Management of patients with supratentorial intracerebral hemorrhage (SICH) remains controversial. Some studies showed that selected patients may benefit from large decompressive craniectomy (DC), instead of craniotomy with hematoma evacuation. Our aim is to describe our population and compare outcomes of both surgical techniques.

Methods: Retrospective analysis of clinical records from patients admitted at our center with SICH between January 2006 and October 2016 that underwent surgery. T-student and chi-square tests were used to compare continuous and categorical variables. Shift analysis was applied to compare outcomes of both surgical groups.

Results: 42 SICH patients (29 men, mean age 52) were operated, 10 of which underwent DC in addition to hematoma evacuation. There were no differences between groups regarding vascular risk factors, anticoagulation, baseline blood pressure or GCS score, hematoma location, intraventricular rupture or pre-op midline deviation, bleeding etiology, surgical reintervention or complications. The group requiring DC had lower alcohol abuse (0% vs. 32%, p=0.05), lower INR (1.1 vs. 2.2, p=0.041) and lower HASBLED score (0.6 vs. 1.6%, p=0.011). Shift analysis of mRS score and GOS score at 12 months revealed a worse outcome for DC patients (p=0.055 and p=0.061).

Conclusion: Our work shows that most SICH patients were not elected for DC and the small number of patients in this group is a limitation of the study. Since patients were not randomly assigned to the procedures, one must be cautious when interpreting the worse functional outcome of DC patients, since they might have a worse pre-op prognosis.

Disclosure: Nothing to disclose

EP3016

Bilateral vertebral artery occlusion resulting from giant cell arteritis: A case report

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Background and aims: Giant cell arteritis (GCA) is a systemic vasculitis which mostly affects large and medium-sized arteries. Bilateral vertebral artery occlusion (BVAO) is rare and it usually results from atherosclerotic disease; however it can also be influenced by the inflammatory process, related with higher mortality rates.

Methods: Diagnostic evaluation and short-term follow-up of a patient admitted in neurology department.

Results: An 86-year-old Portuguese man was admitted in neurology department with imbalance on walking, recurrent vomiting, progressive clinical deterioration, prostration and severe weight loss, beginning three months ago. Neurological exam revealed temporal and spatial disorientation without impairment of other higher functions, cranial nerves or muscle strength. Patient was unable to walk due to postural instability. Temporal artery pulses were present and symmetric, with no pain or induration on palpation. Many diagnostic examinations were performed: blood tests revealed normocytic normochromic anemia and high erythrocyte sedimentation rate (86 mm/h); CT scan showed subacute bilateral cerebellar infarction; cervical and transcranial doppler ultrasound showed BVAO with diffuse wall thickening suggestive of arteritis; Angio-MRI confirmed vertebral artery occlusion and peripheral concentric linear capture, supporting an inflammatory process in the artery wall. Temporal artery biopsy confirmed GCA. General condition and neurological deficits have gradually improved after early administration of corticotherapy.
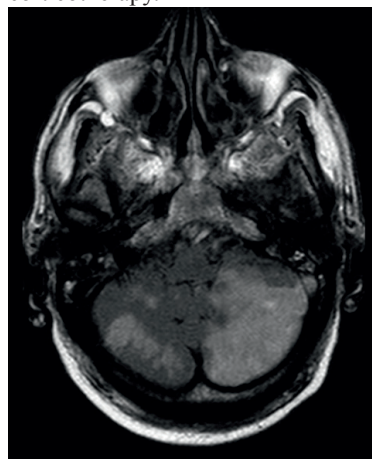
Bilateral cerebellar infarction (T2 FLAIR)
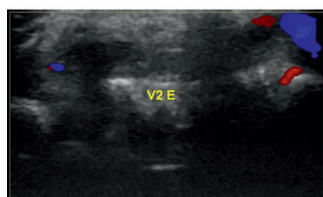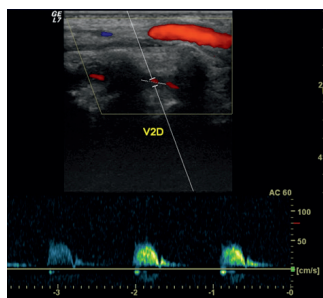
Bilateral vertebral artery occlusion (V2D and V2E)
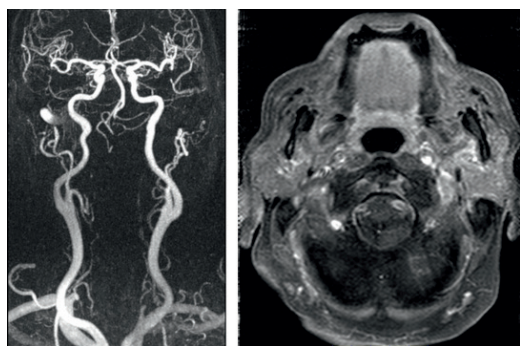
Left: non-filling of vertebral arteries; Right: peripheral concentric linear capture.

Conclusion: A few cases of BVAO in the context of GCA are described; however causality between these two entities cannot be demonstrated easily. In this case report, the findings suggestive of inflammation in the artery wall support that vasculitis is the main pathogenic mechanism of occlusion and consequent bilateral cerebellar infarction.

Disclosure: Nothing to disclose

EP3017

Cancelled

EP3018

Intracerebral haemorrhage and the role of the inflammatory response

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Background and aims: Spontaneous intracerebral hemorrhage (sICH) has been linked to a systemic inflammatory and stress response, translated by hyperglycaemia and increased neutrophil to lymphocyte ratio (NLR). We determined if these factors affect the prognosis.

Methods: From September to December 2014 we evaluated all the patients admitted to our centre with sICH. Clinical, laboratorial and radiological features were analysed to assess the influence in outcome, defined by mortality at 30 days and functional independence at 90 days (modified Rankin Scale (mRS) ≤2).

Results: We included 51 patients. The mortality rate was 40% and 74% had mRS>2 at 90 days. Higher mortality and long term dependence were associated with low Glasgow Coma Scale score at entrance (both $p<0.001$), higher systolic blood pressure (respectively $p=0.008$ and 0.005), glucose level (both $p=0.001$), NLR ($p=0.132$ and 0.008), larger haematoma ($p<0.001$ and 0.082) and intraventricular blood ($p=0.07$ and 0.021). In a multivariate logistic regression model, hyperglycaemia (beta=1.02, IC95% 1.01 – 1.05, $p=0.019$) and NLR (beta=1.49, IC95% 1.01 – 1.79, $p=0.046$) were predictors of poor outcome at 90 days, but not mortality ($p>0.05$).

Conclusion: The presence of high glucose level at admittance as well as increased NLR, a probable manifestation of stress response, were predictors of poor outcome in sICH. This could be new target for therapeutic intervention.

Disclosure: Nothing to disclose

EP3019

Antiplatelet usage alters clot density in acute ischemic stroke: A hyperdense middle cerebral artery study

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Background and aims: The hyperdense artery sign on computed tomography is a surrogate of intraluminal thrombus. Clot density can be quantified by means of Hounsfield Units (HU). Here, we explored whether clot density in middle cerebral artery (MCA) occlusion is related to blood constituents and prestroke medication.

Methods: We performed a retrospective review of patients with ischemic stroke admitted within 4.5 h of symptom onset. We assessed the site of MCA occlusion as well as density of the clot in 150 patients. The HU values for the clot were divided with contralateral MCA segment to yield relative HU ratio (rHU).

Results: We found an inverse correlation of rHU with erythrocyte count (p<0.001). Patients on antiplatelets had a significantly higher rHU compared to patients without (p=0.024). Higher rHU was more likely with the use of antiplatelets (OR 4.24, CI 1.10-16.31, p=0.036). Erythrocyte (OR 0.18, CI 0.05-0.55, p=0.003), and thrombocyte counts (OR 0.99, CI 0.98-0.99, p=0.029) were associated with odds for more hypodense clots.

Conclusion: Aspirin alters clot structure in vitro, resulting in the formation of clots with thicker fibbers and bigger pores, which subsequently allows better entanglement of erythrocytes and raises the efficacy of thrombolysis. Our study disclosed an effect of antiplatelet therapy on the composition of intracranial clots in the setting of acute ischemic stroke in the anterior circulation. This finding may in part explain the higher success of thrombolyis and better prognosis ischemic stroke in patients on aspirin.

Disclosure: Nothing to disclose

EP3020

Diagnosis challenges in Susac's syndrome: A case report

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Background and aims: Susac's syndrome is a rare neurologic disorder mainly affecting young women aged 20- to 40 years. It consists of a clinical triad including encephalopathy, branch retinal artery occlusions and sensorineural hearing loss.

Methods: We present a case of Susac's syndrome with an atypical delay in symptoms development.

Results: A 41-year-old woman was admitted to the ED due to her acute confusional state. She suffered from sudden bilateral hearing loss and general weakness two days before. Past medical history revealed recurrent retinal artery occlusions in both eyes from 2005 to 2007. Neurological examination revealed a relative afferent pupil defect in right eye and bilateral hearing impairment. She was treated with predinisone and vitamin E without significant improvement. After an extensive investigation including clinical, laboratory and MRI findings including "snowball lesions" in the corpus callosum and periventricular hyperintense lesions, the patient was found to suffer from Susac's syndrome. She was treated with i.v. methylprednisolone. Slow and light improvements were observed.

Conclusion: Patients suffering from SUSAC often present only part of the triad, and there is multisystemic involvement which imitates other more common neurologic disorders such as acute disseminated encephalomyelitis and multiple sclerosis. Our patient does not have at initial presentation all the classical features of the disease. About 10 years separate the first manifestations of the syndrome from the appearance of the other symptoms. MRI imaging characteristics specific to the disease allowed us to rule out of other clinical disorders and avoid delay in treatment.

Disclosure: Nothing to disclose

EP3021
Cancelled

EP3022
Cancelled

EP3023
Soluble urokinase plasminogen activator receptor levels are elevated in stroke and correlated with inflammatory and endothelial markers

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Background and aims: Soluble urokinase plasminogen activator receptor (SUPAR) has been recently described to be not only an important prothrombotic factor but also a sensitive marker of tissues' remodeling and an inflammatory marker, which can be used as an independent prognostic factor in prediction of various cardiovascular events (CVE). Therefore, the aim of our study was to evaluate the level of SUPAR in patients after ischemic stroke, in correlation with inflammatory markers (CRP, PCT, NT-proCNP) and markers of endothelial damage (endothelin 1-21, NT-proCNP).

Methods: The blood samples were collected from 50 patients (mean age 73.7 ± 11.9 years, 26F and 24M), which were admitted to the Department of Neurology due to first-time ischemic stroke episodes. We evaluated the serum level of SUPAR, CRP, PCT, endothelin and NT-proCNP during 1., 3. and 7. day from stroke onset.

Results: The mean level of SUPAR1/2/3 (1./3./7.-day measurement) was $3.43 \pm 2.2/3.58 \pm 3.0/4.22 \pm 3.9$ ng/ml. The serum level of SUPAR1/2/3 was strongly correlated with the serum level of PCT1/2/3 (R1=0.96/R2=0.96/R3=0.97,p<0.05) but not CRP (R1,2,3=ns,p>0.05). The serum level of SUPAR was also correlated with the serum level of NT-proCNP1/2/3 (R1=0.78/R2=0.77/R3=0.92,p<0.05). The serum level of NT-proCNP1/2/3 was correlated with the serum level of endothelin 1-21 (R1=0.44/R2=0.49/R3=ns,p<0.05).

Conclusion: The mean serum level of SUPAR in ischemic stroke patients is correlated with serum level of PCT (inflammatory marker) and NT-proCNP (inflammatory and endothelial marker) therefore it should be taken into consideration as a possible prognostic factor of inflammation and endothelial damage in this group of patients.

Disclosure: Nothing to disclose

EP3024
ApoE genotype and the outcome of thrombolysis in acute ischemic stroke

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Background and aims: The apolipoprotein E gene (apoE) influences susceptibility to atherosclerosis. ApoE ε4 is independently associated with lobar intracranial hemorrhage (ICH) and it enhances amyloid deposition in blood vessels, while the ε2 allele predisposes to vasculopathic changes leading to rupture of amyloid laden vessels. Thus, one might expect ε4 and ε2 carriers to have increased susceptibility to ICH, especially in a lobar location.

Aim: to study the impact of the different haplotypes in the outcome of thrombolysis, namely in the development of symptomatic ICH (sICH), recanalization, functional outcome and mortality.

Methods: We included 385 consecutive ischemic stroke patients submitted to recombinant tissue plasminogen activator treatment between January-2011 and March-2015. Admission CT-scans were reviewed to calculate ARWMC, Edema and ASPECTS scores. Patients were followed for up to at least 6 months post-stroke or until death. Outcome measures included evaluation of recanalization on the first 24hours (transcranial color coded Doppler or angio-CT), sICH and assessment of functional outcome at 3 months after stroke (using modified Rankin scale).

Results: Peripheral artery disease, higher uric acid and HDL levels were associated with the presence of at least one ε2 allele. In multivariate analysis, ε2 allele predicts mortality (HR: 1.907, [1.119,3.248],p=0.018). Considering radiologic measures, ε2 allele predicts ARWMC (OR: 2.093, [1.095,4.006],p=0.026).

Conclusion: The main findings of our study is the relationship of apoE ε2 with white matter changes and with a higher mortality rate. No association was found between with either allele and the predefined thrombolysis outcomes.

Disclosure: Nothing to disclose

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EP3025

Reorganization of cerebral hemodynamics in patients with arteriovenous malformations

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Background and aims: Although there are many works devoted to this problem, particularities of cerebral hemodynamic in patients with arteriovenous malformations (AVM) are poorly described.

Aims: Research the influence of arteriovenous shunting at the reorganization of cerebral hemodynamics in patients with AVM.

Methods: Between 2005 and 2016 years 357 consecutive patients with brain AVM were treated in Dnepropetrovsk regional hospital. We conducted a comprehensive clinical, neuropsychological and neuroimaging examination of this subjects.

Results: The relative increase of the linear velocity of blood flow (LBV) in the arteries feeding AVM was 143% (145.56±15.57 cm/s). Increasing of blood volume flowing through the AVM lead to significant increasing of total cerebral blood flow till 1679.05±448.03 ml\min (exceed normal range in 2 times). Lesion of autoregulation was found in 75% of patients with AVM during conducting of functional tests. During hyperventilation LBV decreased in average on 25±7.4% (significant lower (p 0.01) than normal). Response to hypercapnia was absent in 37.5%. Overshoot ratio in averaged 1.06±0.07. On computed tomography perfusion the cerebral blood flow (CBF) and cerebral blood volume (CBV) were markedly elevated within the AVM nidus. However, the perinidal areas demonstrated low CBF and CBV, suggestive of perinidal ischemia in follow areas: surrounding AVM-in 91.5%, remoted from AVM in the ipsilateral hemisphere-in 61% of cases; in the contralateral hemisphere - in 34.4%.

Conclusion: We have shown that features of cerebral gemodynamics depends on the structural and functional characteristics of AVM.

Disclosure: Nothing to disclose

EP3026

Low-dose versus standard-dose rtPA in acute ischemic stroke: An explorative single-centre study

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Background and aims: Low-dose rtPA is currently used in Japanese subjects (Yamaguchi, Stroke 2006) with acute ischemic stroke, while it was not shown to be non-inferior to standard dose in a recent trial involving predominantly Asian subjects (Anderson, NEJM 2016). We aimed to evaluate safety and efficacy of low-dose rtPA in a Caucasian cohort of acute stroke patients.

Methods: From our database, among 389 rtPA-treated patients we consecutively selected 19 subjects treated with low-dose rtPA ($\leq$0.75 mg/kg), matched by NIHSS score, age and onset-to-treatment time to 38 subjects treated with standard-dose rtPA (0.9 mg/kg). Primary efficacy outcome was defined by favourable 90-days functional outcome (mRS score$\leq$2). Secondary efficacy outcomes were NIHSS score and mRS at discharge. Safety outcome was the proportion of symptomatic ICH (according to SITS-MOST criteria) and death.

Results: Baseline clinical and demographic features were similar between groups. At discharge, low-dose rtPA patients had NIHSS and mRS scores comparable to control group (p=0.659; p=0.520). Good functional outcome occurred in 47.4% low-dose subjects vs. 52.6% in standard-dose group (p=0.925). In addition, the distribution of mRS scores at 90 days was not significantly different between the two treatment groups (p=0.987). The proportion of sICH and death similar as well (p=1.000).

Baseline clinical and demographic characteristics.

	rtPA dose		
	Standard (N = 38)	Low (N = 19)	p-value
Age (yr)	75.7 (12.12)	75.8 (9.85)	0.859
Gender: male	21/38 (55.3%)	7/19 (36.8%)	0.303
mRS score before stroke	0 (0)	0 (0)	0.939
NIHSS score at stroke onset	13.5 (11.5)	15 (11)	0.799
rtPA dose (mg/kg)	0.9 (0.01)	0.68 (0.12)	0.000
Estimated body weight (kg)	75 (10)	65 (18)	0.050
Time from onset to rtPA administration (min)	141 (57)	165 (46)	0.198
Additional endovascular treatment	4/38 (10.53%)	2/38 (10.5%)	1.000
Final diagnosis			0.243
Other cause of stroke	2/38 (5.3%)	2/19 (10.5%)	
Cardioembolism	17/38 (44.7%)	4/19 (21.1%)	
Dissection	0/38 (0.0%)	1/19 (5.3%)	
Large-artery occlusion	9/38 (23.7%)	3/19 (15.8%)	
Two or more causes	3/38 (7.9%)	1/19 (5.3%)	
Small-vessel disease	1/38 (2.6%)	1/19 (5.3%)	
Cryptogenic stroke	6/38 (15.8%)	7/19 (36.8%)	
Hypertension	26/38 (68.4%)	13/19 (68.4%)	1.000
Diabetes	4/38 (10.5%)	3/19 (15.8%)	0.887
Antiplatelet therapy at stroke onset	20/38 (52.6%)	7/19 (36.8%)	0.399
Dual antiplatelet therapy	1/38 (2.6%)	2/19 (10.5%)	0.529

mRS: modified Rankin Scale. *NIHSS*: National Institutes of Health Stroke Scale.
rtPA: recombinant tissue plasminogen activator.

For categorical variables, chi-squared test was performed. For numerical variables, Wilcoxon rank-sum test was performed; median and interquartile range are shown.

Table 1. Baseline clinical and demographic characteristics.

Outcomes of study groups.

	rtPA dose		
	Standard (N = 38)	Low (N = 19)	p-value
Primary outcome			
3-months mRS ≤ 2	20/38 (52.6%)	9/19 (47.4%)	0.925
Secondary outcomes			
3-months mRS score	2 (2.75)	3 (2)	0.938
NIHSS score at discharge	5 (12.5)	5 (8.5)	0.659
mRS score at discharge	3 (3.75)	3 (2.5)	0.520
Haemorrhagic transformation	5/38 (13.2%)	3/19 (15.8%)	1.000
Symptomatic intracerebral haemorrhage	2/38 (5.3%)	1/19 (5.3%)	1.000
Death	2/38 (5.3%)	3/19 (15.8%)	0.401

mRS: modified Rankin Scale. *NIHSS*: National Institutes of Health Stroke Scale.

Wilcoxon rank-sum test was performed; median and interquartile range are shown.

Table 2. Outcomes of study groups.
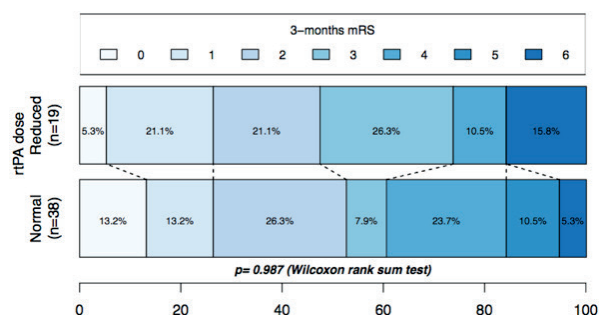
Figure 1. Distribution of 3-months mRS.

Conclusion: Efficacy and safety of low-dose rtPA were comparable to standard-dose rtPA. Due to the small number of patients, the results of this exploratory study cannot be generalized and need to be confirmed in a larger stroke population. However, it appears feasible to consider using low-dose rtPA in frail stroke subjects.

Disclosure: Nothing to disclose

EP3027

Genetic screening in cerebral cavernous malformations: A single center experience

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Background and aims: Cerebral cavernous malformations (CCM) are pathological vascular lesions formed by clusters of dilated capillaries in CNS. CCM may exist in a sporadic form or can be part of a familial autosomal dominant disorder with incomplete penetrance (FCCM). These abnormalities are caused by heterozygous mutations of three genes involved in angiogenesis and endothelial permeability: KRIT1, CCM2, or PDCD10. The main clinical manifestations are headache, seizures, focal neurological deficits and cerebral haemorrhage.

Methods: 21 patients from 13 families over a four years period underwent genetic screening at Policlinico Hospital in Milan. Multiple malformations (n ≥ 2) and/or a positive familial history of cerebral angiomatosis were mandatory to perform genetic analysis. We analyzed all exons and intronic boundaries of KRIT1, CCM2 and PDCD10 by Sanger sequencing. MLPA analysis with commercially available kits was used to detect large-scale rearrangements. RT-PCR analysis using cDNA retrotranscribed from blood leukocytes RNA evaluated the functional effects of the candidate variants.

Results: We established a molecular diagnosis in 10 independent probands (76.9%) of our cohort. We found nine independent mutations, four of which not previously described. In 4 familial and 3 sporadic cases we found causative mutations in KRIT1. CCM2 mutations were detected in 2 familial and 1 sporadic case. Segregation test was positive in familial cases. No mutation was found in PDCD10.

Conclusion: A firm diagnosis was established in 76.9% of our cohort using MRI followed by molecular analysis of KRIT1 and CCM2. These results give us the opportunity to undertake future therapies.

Disclosure: Nothing to disclose

EP3028
Cancelled

EP3029

The association between homocysteine and carotid restenosis after endarterectomy: A meta-analysis

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Background and aims: Carotid endarterectomy (CEA) is an effective treatment for symptomatic and asymptomatic patients with high-grade extra cranial carotid stenosis. However, its efficacy is dependent also by the maintaining of the arterial patency. Even if restenosis after CEA is uncommon, its occurrence could increase the risk of cerebrovascular accidents. The cause of this condition could be related with miointimal hyperplasia also sustained by atherosclerotic process. Homocysteine has been identified as a potential risk factor for atherosclerosis. For this reason, we conducted a meta-analysis to investigate the association between homocysteine levels and the risk of restenosis after CEA

Methods: We performed a literature search in the three main databases (PUBMED/MEDLINE, EMBASE, COCHRANE). We identified 4 main trials investigating the role of homocysteinemia as risk factor for carotid restenosis. We perfomed a meta-analysis using Hedges g statistic as a formulation for the standardized mean difference under the fixed effects model.

Results: A total of 562 patients were included in the analysis (116 with carotid restenosis – 19% of total). We did not observe a statistical association between homocysteine levels and the risk of carotid restenosis after CEA (SE for fixed effects: 0.112; p: 0.708). Test for heterogeneity showed a Q: 5.12 with I2of 61% (p: 0.07).

Conclusion: Hyperhomocysteinemia did not represent a risk factor for early restenosis after CEA. However, further studies with standardized methodology of laboratory tests and radiological evaluation of restenosis degree are required.

Disclosure: Nothing to disclose

EP3030

New approach to evaluation of stroke risk: Modification of social predictors

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Background and aims: The strategy of prevention of stroke is based on the detection and correction of stroke risk factors. However, descriptions of external (or social) risk factors of stroke are poorly presented in scientific researches and publications, although they play a significant role in the autoregulation of cerebral circulation.

Our objective is to study the spectrum of social risk factors and their impact on the incidence of different subtypes of cerebral ischemic stroke.

Methods: We have examined 140 patients with ischemic stroke (average age -65.2±8.7 years) using clinical and instrumental methods, laboratory examination and detailed clinical and anamnestic survey. 45 patients without stroke (average age -63.3±3.1 years) were included in control group. Among known social predictors of development of cerebral ischemia we discover 7 risk factors with higher incidence and use them to evaluate risk of cerebral stroke with help of specialized social risk of stroke scale (SSRS).

Occurrence of social predictors of ischemic stroke (%)

Social factors	Groups of patients	
	A1 (n = 140) %	A2 (n = 45) %
Sleep disturbance	100	24,4
Excessive stress	100	31,1
Abnormal night activity	100	11,1
Long-term work with monitors	87,9	35,5
Physical inactivity	85,8	11,1
Meal problems	75,0	24,4
Alcohol, smoking	70,0	6,6
Marriage	70,0	84,4
Physical hard work	62,1	46,6
Owerheat	57,1	40,0
Miss of antihypertensive drugs	57,8	40,0
Constant travels by plane	46,4	24,4
No sex	37,1	17,7
Depression	17,9	11,1

Occurrence of social predictors of stroke

Results: Adequate correction of predictors has resulted in 13.5% of decreasing of risk of stroke incidence (2 years of observation). The incidence of lacunar stroke was tied with excessive stress, high nocturnal activity, long-term work with monitors and irregular meals. Atherothrombotic stroke was connected with excessive stress, sleep disturbance, reduced physical activity, irregular meals and smoke and alcohol addiction. Cardioembolic stroke subtype was associated with excessive stress, smoking and irregular meals.

Social risk of stroke evaluation (n=140)

- High risk of stroke (17-21 points of SRSS)
- Moderate risk of stroke (10-16 points of SRSS)
- Low risk of stroke (5-9 points of SRSS)
- Minimal risk of stroke (0-4 points of SRSS)
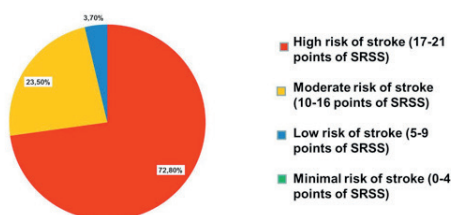
Evaluation of stroke risk

Association of social predictors with subtype of stroke (n=140)

- Lacunar (n=11)
- Atherothrombosis (n=105)
- Cardioembolic (n=24)
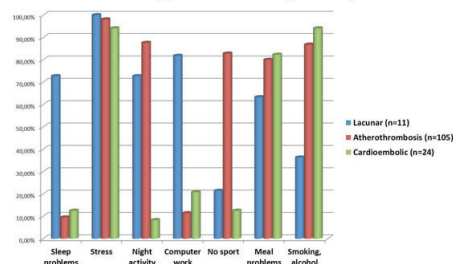
Association of predictors with stroke subtype

Conclusion: Discovered complex of social risk factors of stroke will allow clinicians to define patients with high risk of stroke and to develop an appropriate strategy of individual prevention.

Disclosure: Nothing to disclose

EP3031
Cancelled

EP3032

A case of direct caroticocavernous fistula after mechanical thrombectomy in acute stroke: Case report

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Background and aims: Mechanical thrombectomy is now the advance treatment in acute large vessel occlusion. The complications after thrombectomy are variety.

Methods: We purpose an interesting case of direct caroticocavernous fistula (CCF) after thrombectomy.

Results: Case: A 76 years old man presented with sudden left hemiparesis for 3 hours. He was administrated with intravenous thrombolysis but clinical not improved. The MRA brain showed right proximal M1 occlusion. Then, he was sent to mechanical thrombectomy using stent retriever for 3 times. Control angiogram showed complete recanalization of right M1 (TICI 3) and small tear vessel at right internal carotid artery (ICA) and right cavernous sinus with blood flow drained to right inferior petrosal vein, right sphenoparietal sinus but not seen drained in ophthalmic vein, so called direct CCF. We decided to observe this CCF and clinical of stroke. His clinical improved, power motor from grade 0 to grade 3. He stayed in hospital for 2 weeks with no clinical of direct CCF. Two months later, he developed the clinical of direct CCF with proptosis, chemosis, limit extraocular muscle movement and ophthalmic bruit at right eye. He was sent to transvenous embolization using fiber coils at right cavernous sinus. Twenty-four hours after procedure, his clinical of direct CCF significantly improved and turn to normal within 2 weeks.

Conclusion: Direct CCF is a rare complication from mechanical thrombectomy that endovascular devices injured the cavernous segment of ICA. It can be treated by transvenous coil embolization or transarterial detachable balloon embolization.

Disclosure: Nothing to disclose

EP3033

Case report of a patient with symptomatic, bilateral, gigantic extracranial carotid artery aneurysms and the accompanying multimodality imaging findings.

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Background and aims: We are reporting the case of a patient with stroke related to bilateral, gigantic extracranial carotid artery aneurysms (ECCAs), with significant mural thrombus affecting both carotid bifurcations. Aneurysms of the common carotid artery are a rather rare condition, and a bilateral presentation increases additionally the sparseness of such a finding.

Methods: A 59-year-old male developed an acute symptomatology corresponding to a left hemispheric stroke. The neurological examination revealed dysarthria, paresis of the lower part of the right facial nerve (VII cranial nerve), right hemihypesthesia, right hemiparesis (2/5 on upper and 1/5 of lower limp of the MRC Scale) and right Babinski sign. His medical history included smoking, mild consumption of alcohol and hypertension. Multimodality imaging (on contrast-enhanced ultrasound (CEUS), Multidetector Computed Tomography Angiography (MDCTA) and contrast-enhanced Magnetic Resonance Angiography (MRA) revealed the bilateral presence of ECCAs.

Results: Due to the presence of mural thrombus, the patient was initially treated with both anticoagulant and antithrombotic agents and, in second phase, with surgical reconstruction of the carotid axis (with aneurysmatectomy, graft interposition and ligation of the external carotid arteries), without any complications.

Conclusion: Bilateral aneurysms of the common carotid artery are an extremely rare condition, with an unclear etiology. Review of recent literature showed a possible shift in etiology of ECCAs. Previous studies reported domination of atherosclerotic aneurysms, while recent ones reveal an increase in the frequency of post-carotid endarterectomy (CEA) aneurysms, highlighting the importance of post-surgical monitoring, in order to prevent permanent neurological deficits.

Disclosure: Nothing to disclose

EP3034

Poor outcome after complete recanalization with mechanical thrombectomy in acute basilar artery occlusion: Two cases

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Background and aims: Basilar artery occlusion (BAO) is a rare but potentially fatal cause of stroke. BAO may lead to death or long-term disability if not promptly recanalized. After many positive results in thrombectomy trials of anterior circulation ischemic stroke, the question arises whether these positive results may also be applied to the patients with basilar artery occlusion.

Methods: We report two cases of 38-64-year-old male patients presented with acute BAO who underwent endovascular thrombectomy.

Results: Clinical presentation: Two consecutive patients admit emergency department with posterior circulation symptoms. Cranial CT was normal whereas DWI revealed acute ischemic infarct at basilar arter territory. NIHSS was 6 - 24 and GCS was 12-8, respectively. Their CTA showed middle-distal basilar artery occlusion. The patients were underwent mechanical thrombectomy by using stent retriever within 6 hour of symtoms onset. Despite complete recanalization according to TICI scale system, neurological signs progressed and patients transferred to neurointensive care unit. One patient was unconscious, tetraparetic and depended on mechanical ventilator who had hemorrhagic transformation on control CT at 24 hour. Brain death occured in the other patient at the 22nd day.

Conclusion: Mechanical thrombectomy with stent retrievers yielded high recanalization rates in BAO patients and good outcomes in approximately 1/3 of patients. As in our cases some patients have poor prognosis despite complete recanalization at eligible time window. Serebral microcirculation and collaterals, length of thrombi, initial infarction severity and technical devices may be important predictors and has to be kept in mind for good outcome beside early recanalization.

Disclosure: Nothing to disclose

EP3035

Prognostic factors of functional outcome after surgical treatment of putaminal hemorrhages

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Background and aims: The purpose of this study was to investigate the factors affecting the functional outcome in patients after surgically treated putaminal hemorrhages. Surgery for putaminal hemorrhages remains a controversial issue. Although numerous reports describe conflictive results regarding short-term outcome of surgically treated patients, very little is known about their long-term functional outcome.

Methods: We evaluated the data of 58 patients who underwent open surgical evacuation of putaminal hematomas admitted to a metropolitan hospital in southern Taiwan from January 2009 to December 2015. Patients were categorized into 2 groups based on their modified Rankin Scale (mRS) after 6 months from onset. Various presumptive prognostic factors were analyzed to investigate relationships between various clinical characteristics and outcomes.

Results: Of the enrolled patients, 11(19%) showed a mRS of 0-3, and were categorized as the good outcome group, while another 47(81%) patients showed a mRS of 4-6 and were categorized as the poor outcome group. (Table 1) By univariate analyses, poor outcome was associated with old age, poor initial GCS score, volume of parenchymal hematoma, presence of intraventricular hemorrhage (IVH), hydrocephalus and modified intracerebral hemorrhage (MICH) score. By multivariate analysis, among the factors above, old age and MICH score were independent prognostic factors for poor outcome

Table 1. Factors for functional outcome by univariate analysis

Variable	Good outcome mRS= 0-3 (N=11)	Poor outcome mRS= 4-6 (N=47)	p-value
Age, y(mean +- SD)	48.7 +- 9.3	59.0 +- 13.0	0.007
Gender [f(%):m(%)]	4(36):7(64)	16(34):31(66)	1.000
Hypertension, n (%)	6	34	0.290
DM, n (%)	1	7	1.000
Platelet inhibitor, n (%)	0	6	0.583
GCS (mean +- SD)	10.1+-2.1	7.5+-2.5	0.003
Pupil, loss of light reflex, n (%)	1	20	0.044
ICH volume, ml (mean +- SD)	36.97+-11.15	55.46+-28.51	0.021
Left side, n (%)	4	23	0.667
Midline shift, n (%)	7	38	0.244
Intraventricular blood, n(%)	3	32	0.018
Hydrocephalus, n(%)	2	32	0.005
Hematoma involved thalamus n(%)	0	10	0.182
Hematoma involved caudate, n(%)	0	7	0.327
MICH score			0.011
1	2	2	
2	6	11	
3	3	11	
4	0	21	
5	0	2	

Table 1

Conclusion: In patients who have large amounts of hematoma and require open surgical evacuation, the only significant risk factor for functional outcome are the preoperative GCS score and age. Most of patients with surgically treated putaminal hemorrhages remain dependent and significantly impaired activities of daily life status.

Disclosure: Nothing to disclose

EP3036

Relationship between bilateral occlusion ICA and neurological deficit level in correlation with re-established collateral flow.

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Background and aims: The purpose of this paper is to show relative relationship between bilateral occlusion ICA and neuralogical deficit level in correlation with re-established collateral flow.

Methods: Out of 2845 patients admited to the St Sava Hospital in 2016, examined by ultrasound diagnostic equipment, bilateral occlusion ICA was identified in 14 patients : M/F:12/2; average age 67. Clinical protocol included NIHSS examination, Colour Doppler flow imaging, TCD, MSCT or MR.Dominant risk factors were hypertension in 8; smoking in 10; hyperlipidemia in 4; and heart disease in 5/14 patients.

Results: Bilateral occlusion ICA was registered in 11 ; bilateral occlusion CCA in 3 patients. Collateral flow over Willis' circle from VB vessels to bilateral ICA vessels over PCoA was bilaterally registered in all 14 patients. Collateral flow over ECA-ICA ipsilateral anastomosis was bilaterally registered in 11 (with occlusion of both ICA). Flow was not registered through bilateral OA in 2 patients (with bilateral occlusion CCA).Neurological deficit unilaterally as hemiplegia was registered in 3 patients, medium to high level hemiparesis in 2, and low level hemiparesis in 9 (mobile) patients. Dominant finding on MSCT (MR) was bilateral lacunar ischemia (9/14 patients).

Conclusion: Bilateral occlusion ICA is found more often in male patients with hypertension and smoking as main risk factors. Activation of collateral cerebral circulation over ECA-ICA anastomosis, as well as over Willis' circle, makes distal cerebral perfusion sufficient. This has a minor neurological deficit as a consequence, with lacunar ischemic lesion as the dominant finding on MSCT (MR) of endocranium.

Disclosure: Nothing to disclose

Child neurology/developmental neurology

EP3037

Can serum levels of C-reactive protein (CRP), Interleukin-6 and copeptin discriminate between simple and complex febrile seizures?

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Background and aims: To evaluate serum levels of C-reactive protein (CRP), Interleukin-6 (IL-6) and copeptin in children with febrile seizure (FS) and their ability to discriminate between simple (SFS) and complex FS (XFS).

Methods: The study included 80 febrile children; 40 did not develop febrile seizure (FC), 29 developed SFS and 11 developed XFS. The study also included 10 healthy children as negative control (NC). Clinical evaluation included full history taking, general examination and neurological examination to evaluate patients' general conditions and to confirm inclusion criteria. On admission; body temperature was measured and a venous blood sample was obtained for determination of complete blood count (CBC.) and ELISA estimation of serum CRP, IL-6 and copeptin.

Results: Male-to-female ratio was 2.64:1 and frequency of family history of FS was 17.5%. At admission; body temperature was significantly higher in febrile patients with significantly higher temperature in FS patients than in FC patients. Serum CRP, IL-6 and copeptin levels and TLC were significantly higher in febrile patients compared to NC children and in FS patients compared to FC patients. Receiver operating characteristic (ROC) curve analysis defined high serum copeptin, IL-6, CRP, at admission body temperature, low Hb. Conc. and high total leucocytic count (TLC) as predictors for FS, in decreasing order of significance. Regression analysis defined high serum copeptin and IL-6 as the persistently significant predictors for FS among febrile patients and XFS among FS patients, respectively

Conclusion: Elevated serum levels of copeptin and IL-6 could discriminate febrile children susceptible to develop seizure. Elevated serum IL-6 could discriminate patients liable to develop XFS

Disclosure: Nothing to disclose

EP3038

Neurological and psychological characteristics of children with connective tissue dysplasia

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Background and aims: To study the clinical manifestations of cerebral venous insufficiency and psychological status in children with connective tissue dysplasia.

Methods: The main group consisted of 60 children with signs of connective tissue dysplasia in age from 10 to 16 years. The comparison group consisted of 40 healthy children. Psychological status was assessed by 20-MFI, CES-D, STAI, EPI.

Results: In the group of patients with connective tissue dysplasia were more common following symptoms: headache in the morning - 88% (group 2 - 29%), increased headaches during sleep with a low headboard - 55% (group 2 - 0%), sleep disturbances - 75% (group 2 - 44%), the noise in my head - 38% (group 2 - 0%), a feeling of nasal congestion - 50% (group 2 - 0%), injection sclera - 64% (group 2 - 12%), venous reticulum on the front surface of the chest - 100% (group 2 - 12%). In group 1 was detected higher levels of total (group 1: 45.9±2.89; group 2: 25.9±3.5) and physical fatigue (group 1: 43.4±3.76; group 2: 24.9±2.3). In group 1 had higher level of depression (group 1: 26.4±2.3; group 2: 12.3±4.5).

Conclusion: Children with severe manifestations of connective tissue dysplasia more often revealed signs of cerebral venous insufficiency than children without the disease. In children with connective tissue dysplasia more pronounced general and physical fatigue, as well as has a tendency to depressive disorders.

Disclosure: Nothing to disclose

EP3039

Expanding neuroradiological spectrum of Rubinstein Taybi syndrome: report of a case

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Background and aims: Rubinstein-Taybi syndrome (RTS) is a rare genetic disorder mainly caused by heterozygous mutations of the CREBBP (cAMP-response element binding protein) gene (16p 13.3). RTS is characterized by growth retardation, facial and limb dysmorphies and microcephaly with neurocognitive dysfunction. Epilepsy occurs in about 25% of cases. Brain MRI abnormalities are reported in a variable percentage of patients, involving corpus callosum, posterior periventricular white matter and posterior fossa; rarely, gyration abnormalities such as pachygyria and polymicrogyria have been reported. We report a case of a patient with an MRI pattern of bilateral superior temporal gyrus cortical dysplasia.

Methods: A 22-year-old was diagnosed with RTS at the age of 4 based on typical dysmorphies: broad thumbs and big toes, downward slanting palpebral fissures, microcephaly. Severe mental retardation, autism, hypoacusia and hypotonia were also noted on the neurological examination. Pharmacoresistant partial and generalized seizures started at 2 years.

Results: Sequencing of CREBBP gene revealed a de novo mutation in exon 27 (substitution c.4508A>T, p. Tyr1503Phe). Brain MRI with gadolinium performed at 6 years documented poor grey-white matter differentiation and abnormal gyral anatomy with hyperintensity of the sub-cortical white matter at the superior temporal gyri bilaterally (double ECHO). The corpus callosum was normal.

We were not able to find in literature the peculiar cerebral malformation we found in our patient.

Conclusion: The causal mutation impairs transcriptional regulation by damaging, in particular, neurogenesis and differentiation of the cortical neural progenitor cells. We think that cortical dysmorphologies in RTS are more frequent than expected based on literature reports.

Disclosure: Nothing to disclose

EP3040

Intranasal oxytocin administration reduces memory, anxiety and depression-related deficits in a valproic acid-induced perinatal model of autism

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Background and aims: Lately there is an increased interest for the beneficial effect of the intranasal oxytocin in the neuropsychiatric disorders, including autism. Also, one important animal model of autism in rodents is based on the perinatal administration of valproic acid. Thus, we studied the relevance of intranasal oxytocin administration in this valproic acid-induced rat model of autism, as tested on some behavioural tasks relevant for memory, anxiety or depression-like manifestations.

Methods: The model of autism was induced through the intraperitoneally administration of valproic acid (500mg/kg) in the 12.5 day of gestation. The offspring were weaned on postnatal day 21 and after that male animals (n=15) received intranasally administrated oxytocin (Sygma) for 10 consecutive days (20IU), while controls received intranasal saline (3 groups: control, valproic acid and valproic acid+intranasal oxytocin). Memory functions were tested through Y-maze, anxiety behaviour through elevated-plus-maze, while depression was analyzed through the forced-swim-task, during the last 3 days of treatment (days 8, 9 and 10).

Results: We showed an increased in the immediate working memory (e.g.spontaneous alternation behavior) in the valproic acid+intranasal oxytocin group, as compared to valproic acid alone in the Y-maze test. Moreover, the time spent in the open arms of the elevated-plus-maze and the mobility time in the forced-swim-test were increased in the valproic acid+intransal oxytocin group, as compared to valproic acid alone rats, suggesting facilitatory effects in anxiety and depression-related behaviours.

Conclusion: 10 days of intranasal oxytocin administration in a valproic acid-induced rat model of autism seems to reduce some associated memory, anxiety and depression-related deficits.

Disclosure: This work is supported by a PN-II-RU-TE-2014-4-1886 grant called "A complex study regarding the relevance of oxytocin administration in some animal models of neuropsychiatric disorders", number 120 from 01/10/2015.

EP3041

A rare case of H1N1 triggered recurrent acute necrotizing encephalopathy associated with RANBP2 mutation

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Background and aims: Acute necrotizing encephalopathy (ANE) is a rare disorder presenting with rapidly progressing encephalopathy, usually preceded by a virus-associated febrile illness. While most cases are sporadic and nonrecurrent, familial recurrent ANE due to mutations in the Ran Binding Protein 2 (RANBP2) gene have been recently reported.

Methods: We report the clinical course of a Portuguese child with recurrent ANE.

Results: A 4-year-old boy, with a previous history of encephalopathy due to ANE at the age of 5-months with residual language domain deficit and right motor hemiparesis, developed reduced consciousness and seizures following a febrile respiratory infection. Seizures were refractory to first and second antiepileptic drugs and he was sedated with midazolam. His EEG revealed mild background slowing and left temporal slow waves. Brain magnetic resonance imaging showed symmetric multifocal lesions involving bilateral thalami, brainstem, cerebellum and external capsules, consistent with ANE. Cerebrospinal fluid (CSF) examination revealed mildly elevated protein concentration and oligoclonal bands. Remaining investigation identified a positive polymerase chain reaction for human herpesvirus 7 (HHV-7) in CSF and influenza A H1N1 in bronchoalveolar lavage. He was treated with oseltamivir and high-dose steroid therapy followed by oral tapering. He recovered gradually with no de novo deficits. There was no family history of ANE. Genetic testing identified a missense mutation p.Thr585Met in the RANBP2 gene.

Conclusion: To our knowledge, this is the first reported case of recurrent ANE in Portugal. This report emphasizes the need for increased awareness and earlier recognition, since prophylaxis and symptomatic management of infections may be beneficial.

Disclosure: Nothing to disclose

EP3042

Features of the etiological structure of encephalitis in children in the Stavropol region

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Background and aims: Early diagnosis and timely adequate causal and pathogenetic treatment reduces the risk of severe consequences of infectious diseases of the brain. The study of etiological structure of encephalitis presented an interest.

Methods: We conducted dynamic observation of 66 patients (2 months-16 years) with encephalitis. Conducted direct microscopic, bacteriological, mycological study of CSF biological material.

Results: It is established that serious infectious diseases of brain tissue were caused both by bacterial and viral monoinfection and associated pathogens. Viral encephalitis was detected in 45 (68.2%) patients. Among patients with established etiology, predominance of monoinfection was observed (90%) over mixed infection. In mixed infection the pathological process was caused by a combination of herpes simplex virus enterovirus, cytomegalovirus. Monoinfection was caused by enterovirus (44.4%), herpes simplex virus (37%), the virus Varicella Zoster (14,8%), cytomegalovirus (3.7%). In 28.9% of cases occurring with involvement of the meninges (unknown etiology and enterovirus). Bacterial encephalitis (31.8%) in 100% of cases proceeded with meninges invovement. In 52.4% of cases monoinfection of H. infl., Str. pneum was observed, in 28.6%-mixed infection (bacterial-fungal, viral-bacterial, including-Mycobacterium tuberculosis), 19% - of unidentified etiology. Among patients with bacterial encephalitis rural areas prevailed. Patients with encephalitis of unknown etiology received at different times from the onset of the disease, which had an impact on the verification of the etiological diagnosis.

Conclusion: To improve the quality of etiologic diagnosis it is necessary to organize early hospitalization of patients with suspected neuroinfection in specialized hospitals of the Regional center.

Disclosure: Nothing to disclose

EP3043

From chronic recurrent headache to leukodystrophies

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Background and aims: Migraine is the most common recurrent headache in children and young adults. Little is known about the comorbidity of migraine and inherited white matter disorders. We investigated the accidental detection of leukodystrophies among patients with migraine.

Methods: The study comprised 400 patients referred to our Centres over the last six years because of the chronic recurrent headaches. The age of the patients ranged from 5-25 years. In all the patients the headache was the only presenting symptom at admission. Neurologic and neuro-ophthalmologic examination, psychological evaluation, evoked potentials, and radiological studies (CT, MRI, and MRA) were performed in all the subjects. Some underwent also further investigations: metabolic, cardiac, endocrine, and genetic analyses.

Results: In 270 out of the 400 studied patients the headache fulfilled the required diagnostic criteria for a migraine. Of note, among the 270 migraineurs the leukodystrophies were diagnosed in 5 patients (1. 85% of the examined migraineurs): Alexander Disease (a 15-year-old male), X-linked Adrenoleukodystrophy (a 24-year-old male), Vanishing White Matter Disease (two females: age 21 years, and 25 years), Pol III-related Leukodystrophy (a 9-year-old male). In the absence of neurologic abnormalities, the neuroimaging and genetic findings revealed the proper diagnosis. The observed interval between the onset of migraine and distinctive clinical features of the leukodystrophies was 1-4 years.

Conclusion: Migraine may precede the typical neurologic signs of leukodystrophies. In patients presenting solely with chronic recurrent headaches, MRI of the brain and genetic analyses can identify a leukodystrophy months/years before the onset of overt leukodystrophy-related symptoms.

Disclosure: Nothing to disclose

EP3044

Mesenchymal chondrosarcoma as a rare cause of lumbar pain in a pediatric patient: a case report.

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Background and aims: Prevalence of low back pain in pediatric patients ranges widely from 9% to 66% depending on the source population and definition of pain. It has been accepted that back pain in children is connected with highly possible organic etiology. Researches have shown, that MRI may reveal presence of significant pathology in around 25% of cases. In patients with prolonged history of back pain and those presenting significant neurological examination findings, neuroimaging needs to be used at all times to exclude severe and life-threatening conditions that need immediate intervention.

Methods: We present a case of 17-year-old female patient with a few weeks' history of back pain, headache and nonspecific bladder disturbances. No muscle weakness, deep tendon reflexes abnormalities or significant sensation disturbances were present.

Results: A CT scan revealed a tumour mass originating in S1 and S2. MRI confirmed presence of unevenly contrast - enhanced tumour, expanding into spinal canal and compressing dural sac. Patient was immediately admitted to an orthopedic department to perform laminectomy and tumour resection, followed by an adjuvant chemotherapy.

1. MRI scan (T1 sagitttal) - tumour mass in sacral area

2. MRI scan (T2 sagitttal) - tumour mass in sacral area

Conclusion: Primary CNS mesenchymal chondrosarcomas are rare, with several cases reported in intraspinal locations. Key elements in patient's health history that should raise index of suspicion for neoplasmatic diseases include presence of neurologic symptoms as well as systemic complaints - fever, weight loss or night pain. Only contrast enhanced MRI scans allow a precise assessment of neoplasmatic lesions in this area. Appropriate and prompt clinical workup leads to earlier diagnosis and management of tumours causing back pain.

Disclosure: Nothing to disclose

EP3045

Eyelid myoclonia with or without absences: an under diagnosed epileptic syndrome in the Arab Gulf region?

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Background and aims: The clinical manifestations of eyelid myoclonia can be observed in idiopathic, symptomatic or epileptic syndromes. Epilepsy with eyelid myoclonia (EMA) or Jeavons syndrome is considered a form of idiopathic generalized epilepsy. A series of patients showing homogeneous electroclinical features, including eyelid fluttering and typical EEG pattern. Many times, cases of EMA can be missed when video/EEG cannot be obtained and/or clinical ictal phenomena are minimal.

Methods: Children with electroclinical criteria of EMA were retrospectively identified and followed-up with sleep and awake EEGs between April 1995 to July 2016 who visited four hospitals/epilepsy centers in Saudi Arabia and United Arab Emirates.

Results: Ten patients who fulfilled the criteria for EMA were identified, 7 were females, and 3 were males. The age of onset was from 2 years and 4 months to 9 years. The manifestations of EMA included mild impairment of consciousness, rhythmic myoclonic jerks without evident tonic contraction of the upper extremities in 6 patients, and 2 cases presented with versive seizures with deviation of head and body to one side. A twin presented with continuous flutter of eyes and their EEGs showed consistently the phenomenon of fixation-off sensitivity (Figure 1). The ictal EEG consisted of rhythmic, bilateral, synchronous and symmetrical ,3 Hz spike and wave discharges in all patients.
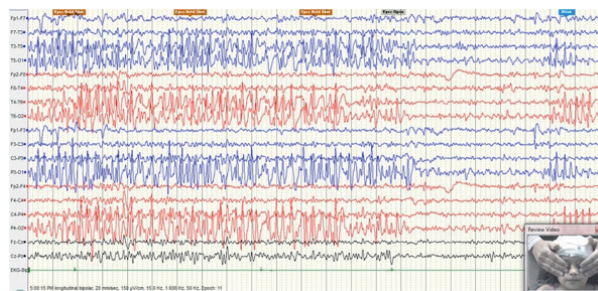
Figure 1. 6.5-year-old Emirati twin II with eye lid myoclonia. Fixation-off sensitivity suspected when high-voltage bilateral occipital epileptiform discharges appeared when her eyes were held closed and persisted as long as her eyes were closed. Low-cut filter, 1.6 Hz; high-cut filter, 70 Hz.

Conclusion: Video EEG is consequently of paramount importance in the diagnosis of EMA, as the opinion of the author that the condition is underrecognized, at least in the Arab Gulf region, as Video EEG is not routinely applied for pediatric population with epilepsy.

Disclosure: Nothing to disclose

EP3046
Cancelled

EP3047

Autonomic cardiac control system response to walking task and executive cognitive task in children with acquired brain injury and typically developed controls

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Background and aims: Children with acquired brain injury (ABI) present dysfunction in a range of physical executive cognitive as well as cardiac autonomic control system (CACS) dysfunctions.

Aim: To examine the CACS response to an executive task, to walking, and to a combined walking and executive task in children with ABI and typically developed (TD) controls.

Methods: 17 children (11-18 years) with ABI, in an active rehabilitation process and had independent walking capability. The control group consisted of 18 age and gender-matched TD children. A Polar RS800CX device was used for assessing heart-rate-variability (HRV), walking endurance assessed by the Six-Minute-Walk-test and executive cognitive function was assessed using the Behavior Rating Inventory of Executive Function questionnaire. The study includes four trials: A five-minute walk on a treadmill set at the average speed measured in the 6MW test, a cognitive manipulation using the Digit Span Backward test at rest, while walking on the treadmill, and during the recovery period post-walking on the treadmill.

Results: Children with ABI presented higher heart rate and lower HRV measures at rest (P-value<0.01). A significant interaction effect was found between the groups; walking on the treadmill has a significant smaller effects on HRV parameters in children with ABI as compared to controls ($F_{2,64}=7.9$, p<0.001). Interaction effect of cognitive and walking on treadmill task on HR and HRV was noted with no significant between groups effect.

Conclusion: ABI associated with reduce CACS activity at rest and during and after walking training. Performing cognitive task during walking training may modify these differences.

Disclosure: Nothing to disclose

Critical care

EP3048

Precocious Lance-Adams syndrome in comatose survivors after cardiac arrest: early pharmacological management and outcome

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Background and aims: Comatose Cardiac Arrest (CA) survivors frequently develop early myoclonus, viewed as a poor prognostic sign (status myoclonus); however, a small subset may present precocious Lance-Adams syndrome (LAS); they can markedly improve with treatment. Our aim was to review these patients, focusing on pharmacologic management in the Intensive Care Unit (ICU), time to awakening, and long-term prognosis.

Methods: From our prospective CA registry over 10 years (2006 to 2016), we retrospectively indentified adult patients with precocious LAS (defined as generalized myoclonus within 7 days with epileptiform EEG within 48 hours after CA). Functional outcome was assessed through Cerebral Performance Categories (CPC) at three months, CPC 1-2 defined good outcome.

Results: We identified 458 patients, 7 of them (1.5%) developed precocious LAS (4 women, median age 57 years). Within 72 hours after CA, normothermia and off sedation, all had preserved brainstem reflexes, localized pain, and showed epileptiform activity and preserved background reactivity on early EEG. All received valproate, levetiracetam and clonazepam as first line; additionally, topiramate was prescribed in 4, pregabaline in 2, piracetam and perampanel in one each. Valproate serum levels were subtherapeutic in 5/6 tested patients, despite maximal doses. Patients started to show awareness after 3-23 days (median 12); at the three months 3/7 had a good outcome.

Conclusion: Precocious LAS needs to be diagnosed and treated soon, because patients may reach a good functional outcome. A combination of highly dosed, mostly large spectrum antiepileptic agents is often necessary. Awakening may be delayed.

Disclosure: Nothing to disclose

EP3049

Evoked potentials as a potential predictive markers of the outcome in severe hemorrhagic stroke patients

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Background and aims: Our goal was to assess the usefulness of the evoked potentials in the prediction of the outcome in severe hemorrhagic stroke patients.

Methods: In 22 patients (13 men, mean age 61.95+/- 11.63) with hemorrhagic stroke (19 intracerebral and 3 subarachnoid hemorrhage) within the 48 hours after admission to neurointensive care unit (NICU), brainstem auditory evoked potentials (BAEP) and somatosensory evoked potentials (mSSEP) of median nerve were performed in every patient. Glasgow Coma Score (GCS), Full Outline of Unresponsiveness (FOUR) were assessed on the arrival and on the day of release. Modified Rankin scale (mRS) was assessed on the day of release.

Results: There was statistically significant negative correlation between GCS at the day of release and BAEP interlatency III-V for the left side (rs= -0.444, p=0.039). BAEP III amplitude for the left side positively correlated with GCS at release (rs=0.435, p=0.049). SSEP amplitude P14-N18 for the right side negatively correlated (rs=-0.453, p=0.034) with mRS at release. SSEP interlatency P14-N20 for the left side had a negative correlation with GCS at the day of recording (rs=-0.448,p=0.036), GCS at the release (rs=-0.542, p=0.009) and FOUR at release (rs=-0.505, p=0.017). SSEP amplitude P15-N20 positively correlated with GCS and FOUR at the day of recording (rs=0.506, p=0.027; rs=0.563,p=0.015, respectively), and GCS and FOUR at release (rs=0.468, p=0.043; rs=0.583, p=0.009, respectively), while negative correlation was found with mRS at release (rs=-0.457, p=0.049).

Conclusion: Results of our study indicate that BAEP and mSSEP have potential value in prediction of outcome in hemorrhagic stroke patients.

Disclosure: Nothing to disclose

EP3050

Decompressive craniectomy in acute large cerebral infarction: experience from Chang Gung Memorial Hospital, Kaohsiung, Taiwan

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Background and aims: Decompressive craniectomy (DC) is thought to be one of the measures alleviating the impact of large hemisphere infarction with partial evidence. Limited data regarding the frequency and results of DC were reported from Asia.

Methods: Patients underwent DC due to large infarction from 2001 to 2007 were reviewed National Institute of Health Stroke Scale (NIHSS) at admission and serial Glasgow Coma Scale (GCS) at admission, before DC, 48 hours after DC, and at discharge were assessed retrospectively by one independent neurologist.

Results: 58 patients (right: 36, left: 21 and bilateral 1) were included. There were 22 (37.9%) women with mean age 64.3. The observation period was 415.1±529.8 days. Mortality rate was 32.8% (19/58) at discharge, 31.0% 30 days after stroke and 48.3% during observation period. Among survivors, NIHSS score was 21.3±6.6 at baseline (58), 21.9±7.6 at discharge (39) and 18.9±9.3 (30) at last observation. Among survivors, GCS was 10.7±3.0 at admission, 10.9±3.4 at discharge and 12.1±2.9 at last observation. Among survivors, mRS was 4.8±0.5 at admission, 4.9±0.4 at discharge and 4.6±0.8 at last observation. Among survivors, BI was 6.9±14.6 at admission, 7.7±11.8 at discharge and 19.0±26.6 at last observation. Among survivors, there was 23.3% (7/30) with MRS ≤4.

Conclusion: DC might be used in restricted incidence. Further well designed prospective trials are needed to prove the indication of DC.

Disclosure: Nothing to disclose

EP3051

An overlooked cause of coma - refeeding syndrome

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Background and aims: The refeeding syndrome is characterized by complex metabolic abnormalities, among them hypophosphatemia being the dominant one. The syndrome usually follows a period of fasting, has a heterogenous clinical presentation with a potentially fatal outcome if not recognized and treated accordingly.

Methods: We present the case of a 60-year-old male, suffering from chronic alcoholism, who 1 week prior to presentation in our unit was admitted in a detox centre. During his stay there he developed dysphagia, dysarthria, gait difficulty and eventually respiratory failure. He was then transferred to our unit, where he was intubated and mechanically ventilated. Computed tomography scan of the brain was suggestive of central pontine myelinolysis, but a subsequent magnetic resonance imaging study refuted this diagnosis. During his stay the patient displayed fluctuating levels of consciousness, ranging from 15 point on the Glasgow Coma Scale to 3 points within the same day, with corresponding fluctuation of the respiratory function (requiring reintubation and mechanical ventilation).

Results: On reevaluation of the history, it was revealed that he had precarious nutrition in the past months, and during the stay at the detox centre he consumed large quantities of food, with a high carbohydrate content. This fact combined with the history of alcoholism and lab results led to the diagnosis of refeeding syndrome. Parenteral phosphate supplementation was initiated, with gradual improvement of the clinical picture. He was discharged 1 week later with no neurological deficits.

Conclusion: Although often overlooked, refeeding syndrome should be considered as a differential diagnosis in rapidly developing muscular weakness and coma.

Disclosure: Nothing to disclose

EP3052

Double filtration plasmapheresis and therapeutic plasma exchange in severe neuroimmune diseases, a case series

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Background and aims: Therapeutic Plasma Exchange (TPE) and Double Filtration plasmapheresis (DFPP) are used in severe neurological diseases with autoimmune etiology representing an alternative to treatment with IV Immunoglobulin. Neurological disorders that plasmapheresis is accepted as first-line treatment are: Guillain Barre Syndrome, Myasthenia Gravis in severe crisis, Chronic Inflammatory Demyelinating polyneuropathy and fulminant forms of Wilson disease. Plasmapheresis is accepted as second-line therapy in: Lambert-Eaton Myasthenic Syndrome, Multiple Sclerosis relapsing-remitting form, also indicated in Acute Disseminated Encephalomyelitis and Optic Neuromyelitis unresponsive to high-dose corticosteroids. The aim of this study is to analyze indications, side effects and results of TPE and DFPP in severe neuroimune diseases.

Methods: We present a retrospective study on 16 patients (6 Guillain-Barre Syndrome, 4 Myasthenia Gravis, 1 Chronic Inflammatory Demyelinating Polyneuropathy, 1 Multiple Sclerosis, 1 Necrotizing Myelitis, 1 Stiff-Man Syndrome, 1 West-Nile Encephalitis, 1 Optic Neuromyelitis), treated in our Intensive Care Unit with TPE and DFPP during 2013-2016.

Results: Thirteen patients had favorable evolution, only three died of sepsis developed during hospitalization. Side effects occuring during treatment were not severe (11 patients with hypocalcemia, 2 patients with hypotension, 3 patients with hypokaliemia, 4 patients with hyponatremia and 5 patients with sepsis) and did not require discontinuation of therapy.

Conclusion: This retrospective comparative study supports previous studies on the beneficial therapeutic effects and fast responsive of Plasmapheresis in neurological disabilities involving rapid progressive evolution.

Disclosure: Nothing to disclose

EP3053

Determining the factors affecting mortality of refractory status epilepticus in comparison with non-refractory status epilepticus - A retrospective study

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Background and aims: Afflicting up to 9-44% of all Status Epilepticus (SE) cases, Refractory Status Epilepticus (RSE) is an uncontrolled epileptic seizure activity unresponsive to first and second line SE therapy. Mortality of RSE is between 11-77%.

Aim: The aim of the study is to determine the factors affecting mortality of RSE in comparison with non-RSE.

Methods: 109 SE cases hospitalized in our neurological intensive care unit between 2011 and 2016 were included to this retrospective study. 52 were RSE and 57 were non-RSE. All clinical data about the clinical follow-up were emerged from the archive of the hospital. Factors which may cause mortality were categorized for statistical analysis.

Results: No significant relationship was found between mortality and refractoriness. Multivariate analysis revealed Intubation (OR=11.579,95% G.A: 1.773-75.622, p=0.011), Glaskow Coma Score (GCS) at presentation (OR=0.149,95% CI: 0.031-0.708, p=0.017) and hypotension (OR=11.579, 95% CI: 1.773-75.622, p=0.011) were the independent predictors of the mortality of all the SE population. GCS at presentation was the independent predictor of the mortality in RSE subgroup (OR=0.013,95% CI: 0.001-0.319, p=0.008). No independent predictor of mortality was detected in non-RSE subgroup.

Conclusion: RSE is a serious clinical condition. Beside SE itself, mortality of SE is related with the complications of the interventions and the terapies which are applied during the follow-up. RSE cases could be more vulnerable in this term. Determining clinical features of RSE and defining predictors of mortality could be helpful for improving the outcome of RSE.

Disclosure: Nothing to disclose

EP3054

A retrospective study of psychiatric inpatients requiring intensive care unit admission

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Background and aims: Patients with mental and behavioral disorders may develop or inflict clinical conditions that require critical care. Here, we studied initial diagnoses, conditions necessitating critical care and mortality among psychiatric inpatients admitted to a neurological intensive care unit (NICU).

Methods: We performed a retrospective chart review of all patients hospitalized at the Department of Psychiatry Salzburg from 2000 to 2016 requiring admission to the NICU. We identified cases from the hospital documentation system and reviewed the NICU database for details of NICU interventions, course and outcome.

Results: We identified a total of 142 psychiatric inpatients which accounted for 2.2% of patients admitted to the NICU over the study period. The most common main psychiatric diagnoses (ICD-10) and reasons for admission are summarized in figure 1 and clinical details of the cohort are presented in table 1. Mean duration of stay was 6.5 days (range 1-55) and metabolic and hypoxic encephalopathies (62%) prevailed among patients with a stay beyond 10 days. Among the nine fatal cases (6%), four had been admitted after suicidal action (44%). The causes of death included cerebral hypoxia (n=6), multiple organ failure following intoxication, consequences of traumatic brain injury and respiratory insufficiency (n=1 each).
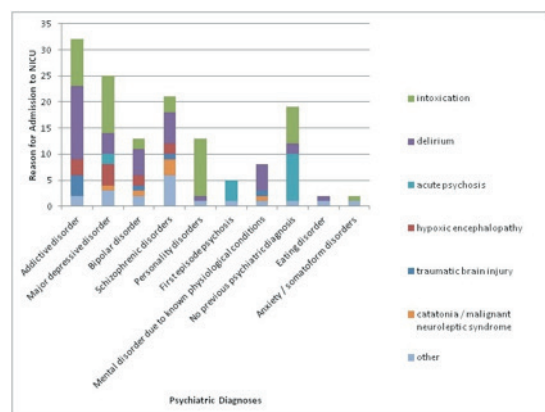
Reasons for ICU admission according to underlying psychiatric disorders

	Total n=142
Women, n (%)	72 (51)
Mean age, y (range)	46.7 (15-87)
Mean Glasgow Coma Scale on admission	9.6
Mean SAPS II score	25
Max. TISS 28 score	31
Mean Charlson Comorbidity Index	1.4
Mechanical ventilation, n (%)	38 (27)
Invasive hemodynamic monitoring, n (%)	129 (91)

Demographics and NICU parameters of psychiatric inpatients

Conclusion: Our study of psychiatric inpatients requiring critical care disclosed a broad range of reasons for NICU admission and underlying mental and behavioral disorders. The duration of ICU care was usually less than 10 days and need for mechanical ventilation was infrequent. Mortality was in part the consequence of suicidal action.

Disclosure: Nothing to disclose

Epilepsy 3

EP3055

Seizure semiology of temporal lobe epilepsy and outcome of anterior temporal lobectomy

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Background and aims: Seizure semiology is an indicator of the seizure onset zone, and can influence outcome of epilepsy surgery. We analysed the relationship between semiology of seizures during video-telemetry and outcomes following temporal lobectomy.

Methods: Adult patients undergoing anterior temporal lobectomy between 2008 and 2015 were included in the analysis. Demographic and clinical data were collected by review of patient records. Semiological features including presence and nature of aura, automatisms, and secondary generalised seizures were collected by review of video telemetry report. 12 month outcome was categorised based on Engel classification.

Results: 43 patients were included, with a median age of 41 years (21-63). 41 (95%) had MRI abnormalities, most commonly hippocampal sclerosis. Good (Engel class I) outcome was observed in 29 (69%) at 12 months. Seizure semiology was available for 42, of whom 32 (76%) reported an aura, most commonly epigastric (33%). Good outcome was seen in 23 (72%) of those who reported aura, and in 60% of those who did not (p=0.69) Automatisms were observed in 36 (87%) of patients, 25 (69%) of whom had good outcome, compared to 4 of 6 (67%) of those who did not have automatisms (p=0.61). Secondary generalised seizures occurred in 26 (62%), of whom 17 (65%) had a good outcome, compared to 12 of 16 (75%) who did not experience generalised seizures (p=0.73).

Conclusion: In this population of highly selected patients with lesional temporal lobe epilepsy, details of seizure semiology did not show significant association with outcomes from temporal lobectomy.

Disclosure: Nothing to disclose

EP3056

Idiopathic generalized epilepsy: valproic acid is still a main choice

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Background and aims: In the idiopathic generalized epilepsies (IGEs) there is no "underlying cause other than a possible hereditary predisposition". Their onset is usually age-related and they constitute one-third of all epilepsies. Although few, several treatment options are now available. Our objective was to study antiepileptic drug (AED) use in IGEs in a specialized epilepsy unit where the use of new AEDs is favored.

Methods: We performed an audit searching for adult IGE patients seen in our unit from January/2016 to June/2016. Seizure types, epilepsy syndromes and definition of drug-resistant epilepsy were based on ILAE.

Results: We identified 72 patients (37 men/35 women) aged 18-85 years (mean=40±15.7). Mean age at epilepsy onset was 16 years. Epilepsy syndromes were: epilepsy with generalized tonic-clonic seizures alone(39%), juvenile myoclonic epilepsy(33%), childhood absence epilepsy(14%), juvenile absence epilepsy(11.2%), Jeavons syndrome (1.4%), unclassified IGE (1.4%). Seventeen patients (23.6%) were drug-resistant. Most common AEDs used were: valproic acid (VPA;58%), levetiracetam (36%), and lamotrigine (21%). Forty-six patients (62%) were seizure free (> 1 year), most on monotherapy (23 VPA, 9 levetiracetam, 7 other AEDs). Among patients treated with VPA, 23 were men (65% >600 mg/day) and 19 women (58% >600 mg/day). Most patients on VPA had failed previous AEDs (61% seizure-free).

Conclusion: In this series of IGE patients, VPA was the most widely used AEDs and achieved better seizure control than other AEDs. Most seizure-free patients were on VPA. Despite the advent of new AEDs, VPA is still a major drug needed to achieve seizure freedom in the IGEs.

Disclosure: Nothing to disclose

EP3057

Diagnostic usefulness and outcome of 24-48 hours inpatient Diagnostic Video-EEG monitoring for cases with recent onset paroxysmal events.

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Background and aims: Inpatient long-term video-EEG Monitoring for Epilepsy(LTME) is widely used for patients with paroxysmal events(epileptic and non epileptic). The diagnostic usefulness varies considerably depending on patient selection and referral category-diagnosis, seizure classification and presurgical evaluation. The purpose of this study was to assess diagnostic usefulness and management decisions of LTME in patients with recent onset seizures (within the previous 12 months) and inconclusive standard investigations before LTME.

Methods: We retrospectively reviewed data from 336 consecutive LTME-investigations over a 3-year referral period (January 2014-December 2016). There were 96(57males and 39 females) patients having inconclusive previous routine EEG and MRI studies. Patient ages ranged from 2 months to 74 years (0-14 yr:48, 15-74yr: 48).

Results: Mean duration of LTME was 1,14 days. The events in question were recorded in 40/96 (41%). Interictal epileptiform abnormalities were detected in 52/96 (54%). In 24/96 (25%) studies there were no events and no interictal epileptiform abnormalities recorded. A diagnosis of epilepsy was established in 59(62%), of Non-epileptic Events in 31(32%), and was uncertain in 6(6%). Considering all information, treatment and management modifications were implemented in 60 patients (63%).

Conclusion: We conclude that the diagnostic yield of even short-lasting LTME studies is still considerable in the particularly challenging category of patients with new-onset suspected epilepsy and inconclusive standard diagnostic work-up. Information thus gained may suggest management and treatment changes in as many as 60% of investigated cases.

Disclosure: Nothing to disclose

EP3058

The significance of focal EEG abnormalities in typical absence seizures – long term observations

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Background and aims: In last years it becomes more and more evident that focal EEG changes can be detected in patients with idiopathic generalized epilepsies . The aim of the study was to estimate the frequency of focal interictal EEG abnormalities in pediatric patients with absence seizures (ASs) and to identify their clinical, EEG and semiological correlates

Methods: Patients with typical absence seizures who were hospitalized or consulted at Dept. of Developmental Neurology between 2000 and 2015 were included in the study and followed prospectively. All patients underwent video-EEG monitoring at regular intervals. 149 patients who fulfilled criteria for typical absence seizures were included in the study.

Results: In 15% of patients we found interictal epileptiform discharges, and in 31% intermittent fronto- temporal slow waves. We found significant correlation between presence of interictal focal epileptiform discharges and long term prognosis, but did not find the correlation between worse prognosis and presence of fronto- temporal interictal slow wave activity. Interestingly, we did not found correlation between presence of focal abnormalities and worse performance in cognitive tests. The presence of focal EEG-changes were associated more freqently with presence of automatisms.

Conclusion: The value of focal interictal EEG abnormalities should not be overestimated acoording to prognosis and cognitive performance in children with typical absence seizures. The cautious EEG interpretation of focal changes in absance seizures is needed in order to prevent wrong diagnosis of focal epilepsy

Disclosure: Nothing to disclose

EP3059

Status epilepticus: causes and short-term outcome

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Background and aims: Status epilepticus (SE) is a sever expression of an acute brain insult or systemic disturbance wich leads to excessive hyperexcitation of brain. This study aims to determine the most common causes and outcomes in patients hospitalized with SE in a regional academic hospital.

Methods: Over a 4-year period (Jan 1, 2012 to Dec 30, 2016) all patients older than 18 years with SE were included. The ethiology, and outcome under Glasgow Outcome Scale (GOS) in 156 patients with SE (convulsive or non-convulsive), have been reviewed.

Results: The most common cause of SE was nonadherence with antiepileptic drugs (nAED) and this accounted in 67.3% of the patients with previous seizures and in 32.7% of all the patients. The other causes in our series were alcohol-withdrawal, cerebrovascular disease, cerebral tumors or trauma, infection, metabolic disorders, anoxia. SE was never the initial manifestation of further epilepsy. 92.3% of patients developed generalized tonic-clonic SE and only 3 (1.92%) patients presented with nonconvulsive SE. A poor GOS outcome of SE was correlated with cerebral infarction and increased age, low mortality rates were noted in alcohol and nAED etiologies.

Conclusion: Cerebrovascular disease and nAED were the most prominent causes of SE in this study. Low incidence of non-convulsive SE requires a better clinical evaluation and continuous EEG monitoring in suspected cases. GOS scores and etiology SE showed a better outcome in patients with nAED and unfavorable outcomes in elderly patients and those with acute brain injury such as stroke or cerebral anoxia.

Disclosure: Nothing to disclose

EP3060

Deep brain stimulation in adult-onset Rasmussen with disabling dystonia.

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Background and aims: Rasmussen's syndrome (RS) is a progressive inflammatory disease that involves one cerebral hemisphere and causes neurological deterioration and seizures. Rare cases of adults with RS and movement disorders have been described. We report an unusual case of adult RS with disabling focal dystonia and excellent response to contralateral pallidal stimulation.

Methods: The patient is a 40-year-old female suffering from focal persylvian epilepsy since the age of 22. Seizures consisted of left hemiface paresthesias and tonic position of the left arm. Initially neurological examination and brain magnetic resonance imaging (MRI) were normal. At 38 she developed pain and abnormal dystonic posturing of the left leg two weeks after a motor vehicle accident. Lab tests for secondary dystonia were normal. MRI showed atrophy of the right cerebral hemisphere, predominantly in the insula and frontotemporal cortex, and decreased volume of right caudate nucleus. PET scan showed hypometabolism of right frontal and insular areas. Brain biopsy showed chronic encephalitis consistent with RS. Seizures remained under control with a combination of antiepileptic drugs but the dystonia increased in severity in spite of multiple immunomodulatory and antidystonic drugs. The patient was offered pallidal stimulation, which was performed eight years after onset of the dystonia.

Results: The abnormal movement has significantly improved and the patient is now able to stand and walk alone.

Conclusion: This case expands the clinical spectrum of movement disorders in adult RS. To our knowledge, this is the first case of disabling dystonia in adult RS treated with GPi-DBS, with good outcome.

Disclosure: Nothing to disclose

EP3061

Unusual ictal features in temporal lobe epilepsy

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Background and aims: Temporal Lobe Epilepsy (TLE) is the commonest form of location-related epilepsy. The ictal manifestations of TLE are typically quite stereotyped - it usually presents with recurrent complex focal seizures, often preceded by vegetative auras. However, unusual semiologic features have been described, rendering the localization of the epileptic discharge less straightforward.

Results: Case reports: Four drug-resistant epileptic patients (aged between 15 and 42 years) with uncommon seizure descriptions completed Video-Electroencephalography monitoring (VEEG) for diagnostic and pre-surgical evaluation purposes. All had seizures during the VEEG, and detailed video analysis was performed. Patient One had two seizures with hypermotor bilateral leg movements and left-hand dystonic posturing. Patient Two had two seizures with echolalia and echopraxia, and late right-hand dystonic posturing. Patient Three had four abrupt-onset hypermotor seizures and one complex focal seizure. Patient Four had eleven seizures with urinary urge and upper limbs choreiform movements. Ictal electroencephalogram was compatible with temporal lobe origin. All patients had lesions located in the temporal lobe; two of them underwent anterior temporal lobectomy, both with favorable outcomes. The remaining patients are currently undertaking further pre-surgical investigation.

Conclusion: Clinical semiology remains the starting point for the diagnosis and classification of epilepsy. It is equally invaluable for the determination of the seizure onset zone in surgical candidates. Nonetheless, although many semiologic features have high localizing value, each of them has also some potential to falsely localize. We present four patients whose ictal manifestations were unusual for TLE, reinforcing the importance of correlating clinical with EEG and imaging findings.

Disclosure: Nothing to disclose

EP3062

Experience with the use of Perampanel (PER) as first add-on in routine clinical practice. A multicenter study in Spain

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Background and aims: Some studies in clinical experience with Perampanel (PER) suggest that patients taking fewer prior AEDs had a more favourable clinical response, however there are no series focused exclusively early use. Based on these data, we aimed to evaluate the use of PER as first add-on treatment in patents with focal epilepsy and idiopathic generalized epilepsy (IGE).

Methods: We selected retrospectively with PER as first add-on from six Spanish centers. We collected demographics, type of epilepsy, concomitant treatment and we analysed the improvement of seizure frequency, the presence of adverse events (AEs) and the retention rate at 3 and 6 months.

Results: 49 patients were evaluated. Mean age: 44.8 (17-76) years old. 31(63.3%) were male. 18(36.7%) were diagnosed as symptomatic focal epilepsy, 17(34.7%) as cryptogenic focal epilepsy, 9(18.4%) as IGE and 5 (10.2%) as undefined epilepsy. At 3 months follow-up: 38 (77.8%) showed efficacy, including 15 (30.6%) seizure-free and 32 (65.3%) with a seizure reduction>50%. 17 (34.7%) had AEs (5 fatigue/somnolence, 4 irritability, 8 dizziness). The median dose was 4 mg. The retention rate was 77.6%. At 6 months (n=37), PER was effective in 33 (89.2%) remaining 14 (37.8% seizure-free and 29 (59.2%) and with a reduction>50%. 11(29.7%) had AEs (3 fatigue/somnolence, 2 irritability, 2 dizziness, 1 anosmia). Retention rate was 89.2%. The median dose was 6 mg.

Conclusion: In clinical practice, the adjunctive treatment with PER as first-add may lead to an improvement in seizures frequency. It seems a well tolerated a drug as add-on with a low rate of AEs.

Disclosure: Nothing to disclose

EP3063

Cluster seizures – what really counts?

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Background and aims: Cluster seizures (CS) are commonly observed among patients with drug resistant epilepsy or acute brain damage. However despite its occurrence, there was not indicated precisely prognostic factors or tools. The aim of this study was to determine a risk factors for poor outcome.

Methods: We retrospectively reviewed 200 patients with CS in a 5-year period and considered all potential predictors of poor outcome for patients with continuous seizures. Unfavorable outcome was defined as a modified Rankin Score ≥5. A univariate and multivariate analysis was used to determine the predictors.

Results: Mortality counted 20 cases (10%) of patients on analyzed cohort. The risk factors of death in univariate analysis included age ($p<0.001$), history of drug resistant epilepsy ($p=0.03$), acute ($p=0.005$) and idiopathic etiology ($p=0.017$), level of consciousness ($p<0.001$), seizure type (0.05) and seizure progressing to status epilepticus ($p<0.001$). Thereafter, independent predictors were definied as age (OR=0.1; years), acute etiology (OR=4.1), level of consciousness (OR=3.0) and seizure type (OR=3.2).

Conclusion: CS patients are frequently overlooked in literature, however represent important population due to its mortality rates. Therefore indicated predictive factors should be considered within diagnostic/treatment procedures.

Disclosure: Nothing to disclose

EP3064

Simple neurovascular reactivity in patients with idiopathic generalized epilepsy

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Background and aims: Simple neurovascular activation by transcranial Doppler (TCD) is not presented to date in drug responsive patients with idiopathic generalised epilepsy. The objective of this study is to assess the neurovascular activation to simple visual stimulation of patients with idiopathic generalised epilepsy during interictal period.

Methods: Thirty-four patients with idiopathic generalised epilepsy at least ten days later after last epileptic attack and 14 healthy subjects were screened for this study in our Neurosonology Laboratory. We performed trans-temporal TCD recordings from the P2-segments of both posterior cerebral arteries (PCA) simultaneously during simple visual stimulation. The individual reactivity was defined as a relative increase of the blood flow velocities as a percentage change of the baseline values.

Results: None of the patients has an epileptic focus on the brain documented by the MRI, nor EEG. The Doppler data of the patients and healthy subjects showed non-significant side difference, and therefore, were analysed 68 vessels in patients and 28 vessels in controls. The blood flow velocity during stimulation and simple visual reactivity were slightly lower in the patients (42.5 cm/s and 25.6%, respectively) from those of the controls (44.7 cm/s and 29.4%, respectively) ($p=0.3$ and $p=0.1$, respectively).

Conclusion: Our study showed the temporal and occipital region of brain perfused by PCA of the patients with idiopathic generalised epilepsy have normoactive neurones during the interictal period when comparing with the healthy subjects, or under appropriate antiepileptic treatment, neuronal hyperactivation could be successfully inhibited at least too weak stimulus likewise simple visual stimulation.

Disclosure: Nothing to disclose

EP3065

Long-term follow-up of five cases with late-onset Rasmussen encephalitis in University Hospital Bratislava, Slovakia.

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Background and aims: RE is a rare disease. Most cases start in children under 10 years, about 10% of cases in adolescence or early adulthood. These cases are typical with slowlier course of disease.

Methods: In University Hospital in Bratislava, Slovakia, we follow five patients with late onset of RE. 2/5 are women. Patients are 23 to 59 ys old, median 35ys.The patients suffered their first epileptic seizure between 6 and 30 ys of age, median 18. All 5 pts started with motor seizures. They suffered first epileptic state between 19-46ys, median 28y. Two of them presented with epilepsia partialis continua (EPC).Atrophy of the brain was verified in 4 of them. Two out of them presented with anti-GAD antibodies, three of them without detectable antibodies in the sera.

Results: All patients were treated with immunomodifying therapy - intravenous immunoglobulins, plasmaexchange, azathioprin, rituximab, kortikosteroids in individualized regimens. In 4/5 the neurological deficit is still mild, with mild cognitive decline, but the epilepsy is the main problem. The diagnosis of RE was delayed 1-16 years from the first epileptic seizures, median 4 years. The brain hemiatrophy was verified in patients 4-14 years after first epileptic seizure.

Conclusion: Late onset RE is extremelly rare. Due to its slowlier course, delay between first epileptic seizures and first epileptic state, it might be not recognized for many years. Immunotherapy of late onset RE is the treatment of the first choise. The hemispherectomy could be postponed.

Disclosure: Nothing to disclose

EP3066

Epilepsia Partialis Continua in Creutzfeldt Jacob Disease

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Background and aims: Creutzfeldt-Jacob Disease is a progressive, degenerative disease of the central nervous system. It occurs as a result of prion protein deposition. Progressive dementia, myoclonus, cerebellar, pyramidal and extrapyramidal symptoms are characteristic for this disease.

Methods: 57 years old male patient applied to emergency service with syptoidms of dementia, bizarre behaviours and continous unvoluntary contractions on the left arm. He was having calculation and memory problems for the last six months. And for the last four months he started to show psychiatric symtoms. At the same time unvoluntary movements on his left arm were seen. At another healt center, after a normal brain MRI scan he was putted on olanzapin and oxcarbamazepine. However his syptoms proceeded. He began to be very agitate and the unvoluntary contractions became worser. So his family brought him to emergency service. There he was diagnosed as encephalitis and interned to infection diseases department. However, his cerebrospinal fluid cultures did not show any evidence of infection. Later he was consultated to our neurolgy department because of these non-stop contractions on his left arm. His brain MRI scan showed bilateral basal ganglion intensity increase. There were PLEDS in his EEG. And 14.3.3 protein was positivi in his cerebrospinal fluid. With these finding he was diagnosed as Creutzfeldt-Jacob disease with epilepsia partialis continua.

Results: In the literature, there are very Creutzfeldt-Jacob disease cases that have epilepsia partialis continua.

Conclusion: We present this case to underlay that, at early stages of Creutzfeldt-Jacob disease focal motor seizures can be seen.

Disclosure: Nothing to disclose

EP3067

One-year experience with perampanel – focus on psychiatric adverse effects

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Background and aims: Perampanel (PER) is a new antiepileptic drug (AED) licensed as an adjunctive treatment of partial-onset seizures and primary generalized tonic-clonic seizures. In the Czech Republic, PER is available since June 2015. We performed a retrospective analysis of one-year experience with PER in 87 patients treated in tertiary epilepsy centre.

Methods: The demographic and clinical data of the patients were collected by review of medical records in the hospital database. Type of epilepsy, seizure type, used PER dosage, concomitant AEDs, adverse effects and reasons for withdrawal were analyzed.

Results: Out of 87 patients with drug-refractory epilepsy (49 females, median age 35, range 18-66), 78 had focal epilepsy, six generalized and four unclassified epilepsy. Apart from PER they were treated with median of three AEDs (range 1-5). At least transient positive effect was reported in 35 patients (40%). 35 patients (40%) were withdrawn from PER, 21 (60%) due to adverse effects, three because of no efficacy and 11 (31%) due to combination of both. Adverse effects at some point were reported by 47 patients (54%), most common were fatigue (30%), dizziness (14%) and instability (10%). Psychiatric adverse effects included change in behavior (11%), aggression (6%), lacrimosity (3%), one patient with depression and suicidal ideation and one case of psychosis. Psychiatric adverse effects led to withdrawal of PER in ten out of 11 patients.

Conclusion: PER showed at least transient positive clinical effect in 40% of patients. Psychiatric adverse effects were observed in 13% of patients and led to withdrawal of PER in most cases.

Disclosure: Nothing to disclose

EP3068

Cancelled

Headache and pain 3

EP3069

Measurement of the cerebrospinal fluid pressure in spontaneous intracranial hypotension syndrome

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Background and aims: The intracranial hypotension syndrome (IHS) is an entity whose main symptom is an intense headache that occurs or worsens with upright posture. The diagnosis is usually confirmed by demonstrating low cerebrospinal fluid (CSF) opening pressure, also supported by characteristic image findings in brain magnetic resonance (MR). To discuss whether lumbar puncture is indispensable or not, we describe a clinical case.
Methods: Woman of 27 years old with 20 days of spontaneous orthostatic headache, exacerbated by Valsalva maneuver, and relieved by recumbency, associating nausea and vomits. There were no relevant findings in physical and neurological exam, ophtalmoscopy or brain computed tomography (CT).
Results: Brain MR imaging detected descent of the hypothalamus, the optic chiasma and the cerebellar tonsil, important compression of the pons, and diffuse pachymeningeal enhancement. It also demonstrated a spinal meningeal diverticulum in D8-D9 that was the origin of the CSF leakage. After 33 days of postural treatment in Trendelemburg and caffeine, the patient presented spontaneous recovery. The diverticulum disappeared in the latest images.
Conclusion: Spontaneous IHS with no signs of complication usually respond to conservative treatment. The fact that the lumbar puncture it is not a harmless test, but it can make the headache worse, contribute to cerebral herniation or even create a new fistula, made us consider if it is essential to perform it when the whole symptomatology and the brain MR images are compatible with the diagnosis. It is a good argument to start with conservative measures, not making any more invasive tests if they are effective.
Disclosure: Nothing to disclose

EP3070

Early onset of efficacy with erenumab in a phase 2 clinical trial of subjects with chronic migraine

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Background and aims: Erenumab 70mg and 140mg reduced monthly migraine days at all time points assessed (weeks 4, 8, 12) in a phase 2 clinical trial of chronic migraine (NCT02066415). Here, we evaluated efficacy prior to week 4.
Methods: Post-hoc analyses evaluated achievement of ≥50% reduction in weekly migraine days (WMDs) and change from baseline in WMDs. P-values for these endpoints are based on odds ratios or mean differences from placebo, not adjusted for multiplicity. Also, to evaluate trends, a linear model was fitted to observed daily migraine days for days 1-7 (week 1), and pairwise comparisons of the slopes and moving averages were evaluated and overlaid with observed data.
Results: Both erenumab dose groups had a greater proportion of patients achieving ≥50% reduction in WMDs by week 1; 26% for both doses vs 16% placebo (p≤0.011), increasing to 31%, 41%, and 21% in the 70mg, 140mg, and placebo groups, respectively, at week 2 (p≤0.011). At weeks 1-4, reductions from baseline in WMDs were observed with both doses vs placebo (p=0.047 at week 1 for 70mg and p≤0.002 at weeks 2-4 for both doses). Moreover, 7-day moving averages of observed data showed that each treatment arm differed from placebo within the first several days. On pairwise comparisons, slopes for 140mg differed from placebo by day 4 (p=0.03). By day 6, both doses differed from placebo (p≤0.03), but differences between doses were not detected (p=0.86).
Conclusion: Erenumab showed early onset of efficacy, with separation from placebo within the first week.
Disclosure: Funding for this study was provided by Amgen Inc.

EP3071

Eagle Syndrome: An uncommon mimic of glosopharyngeal neuralgia (GN)

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Background and aims: Eagle syndrome (ES) is defined as a symptomatic elongation of the styloid process or mineralization of the stylohyoid ligament. Classic ES, is seen after tonsillectomy or minor trauma. Pain is often felt on the angle of the mandible and may radiate to the ipsilateral ear. Patients also complain of dysfphagia, tinnitus, sensation of foreign body in the throat and otalgia. Impingement of close cranial nerves is thought to cause the pain. Diagnosis is based on clinical signs, digital palpation of styloid process in the tonsillar fossa, radiological findings, and Lidocaine infiltration test. Three dimensional CT is considered the Gold standard for the diagnosis of ES. Differential diagnosis includes GN. The negativity of first examination and no reaction to infiltration of corticosteroid in the hyoid area, made the diagnosis delayed.

Methods: Clinical case report.

Results: We report a 55-year-old woman who presented with a constant pain in the right side of the face close to the angle of mandible and sensation of foreign body in the throat on swallowing.Physical examination revealed no exacerbation of the pain by palpation of the right tonsillar fossa. Carbamacepine and Eslicarbacepine were useless. Corticosteroid infiltration of the hyoid process was negative. Computed tomography (CT) of the neck with three-dimensional reconstruction showed elongation of the right styloid process. Surgery was proposed.

Conclusion: ES may be confused with GN, like in our case. It´s a rare condition but not uncommon. We should keep in mind   when managing refractory GN.

Disclosure: Nothing to disclose

EP3072

Brain white matter and infarct-like lesions in primary headache: an Italian single centre study

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Background and aims: White matter lesions (WMLs) and infarct-like lesions (ILLs) are frequently detected with brain imaging techniques in patients suffering from headache, especially among migraineurs. The aim of the study was to evaluate the prevalence of WMLs and ILLs in an Italian cohort of patients with primary headache.

Methods: This retrospective study collected data of patients admitted at the Headache Center of Perugia in 2012, undergoing MRI scan and diagnosed with a primary headache disorder. Patients were excluded in case of (i) secondary headache, (ii) major comorbidities and (iii) conditions associated with brain hyperintensities without migraine. Headache was classified following the 2nd ICHD revision. Brain MRI were performed on 1.5 T magnet device, with ILLs and WMLs being rated according to reported paradigms (Fig 1).

Figure 1 - ILLs: non-mass, high-signal intensity on T2-weighted MR images, hypointense in T1 (arrow-heads, top left: T2, centre: FLAIR, right: T1); WMLs: non-mass lesions, bright on T2-weighted, no correlates on T1-weighted images (bottom, arrows)
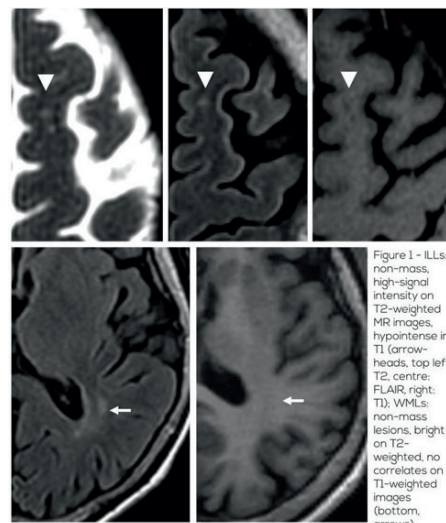
Figure 1. Infarct like lesions (ILLs) and white matter lesions (WMLs) appearance on brain MRI.

Results: Overall, 824 patients were enrolled: 721 (87.5%) had migraine without aura (M), 69 (8.3%) had migraine with aura (MA), 27 (3.2%) had medication overuse headache (MOH), 7 (0.8%) had cluster headache (CH). WMLs prevalence was higher in MOH compared to other groups, while ILLs were more frequent in CH (Table 1) (p<.05). M and MA had similar prevalence of WMLs and ILLs, though M was more associated with both.

	M	MA	CH	MOH
Number	721	69	7	27
Female	569	49	2	25
	79%	71%	29%	93%
Mean age	36.2	36.7	35.5	43.3
WMLs	77	6	1	7
	10.7%*	8.7%*	14.3%*	25.9%*
ILLs	82	6	3	4
	11.4%*	8.7%*	42.9%*	14.8%*

* p<.05

Abbreviations: CH=cluster headache; ILL=infarct-like lesions; M=migraine without aura; MA=migraine with aura; MOH=medication overuse headache; WMLS=white matter lesions.

Results and demographic data of the study cohort

Conclusion: Our data confirm the association between WMLs and ILLs with primary headache disorders. MOH was associated with the highest prevalence of WMLs, and had increased prevalence of ILLs compared to M and MA. Population-based assessment should continue in order to better define prevalence and implications of WMLs and ILLs in headache disorders in the Italian population.

Disclosure: Nothing to disclose

EP3073

Variation of the spontaneous blink rate (SBR) in light and dark: comparison between migraine patients and healthy subjects

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Background and aims: The spontaneous blink rate (SBR) is strongly modulated by dopamine (Karson et al., 1982) and by the occipital cortex (Karson et al., 1990) both of which also play a role in migraine pathophysiology (Charbit et al., 2010). Photophobia is a phenotypic hallmark of migraine both during and between attacks. We searched therefore whether the SBR could be increased in migraineurs because of their sensitivity to light.

Methods: We enrolled a total of 38 subjects: 7 healthy subjects (HS), 19 interictal episodic migraineurs (EM) and 10 ictal EM without prophylactic treatment. The SBR was measured in a lit room at a luminance intensity of 145 Lux or in almost total darkness, 12 Lux, using 2 electrodes placed on the orbicularis muscle of the right eye.

Results: We found no difference between groups during lightened sessions. By contrast, in the dark the SBR was reduced in HS and in ictal EM, but not in interictal EM (p=0.05). The percentage SBR change between light and dark was -36.71±22% in HS, -18.7±34.74% in ictal EM and 1.9±43.98% [SD] in interictal EM. This change was significant in HS (p=0.017).

Examples of SBR recordings in a healthy subject and an ictal migraine patient in lightened and dark room.
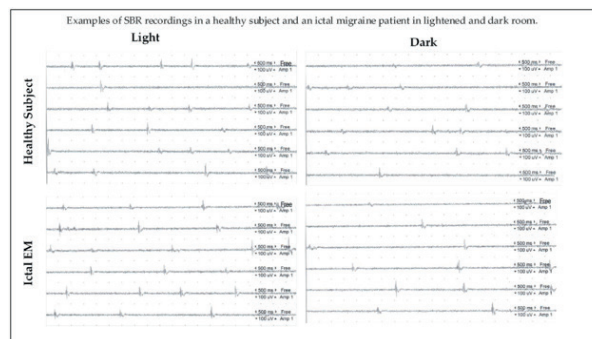
Conclusion: We show that in migraine patients between attacks the SBR is not decreased in the dark like in healthy subjects or migraineurs during an attack. This could be due to an abnormal interictal control by dopamine and/or the occipital cortex that normalizes during the attack.

EP3074

Differential sensitivity to blue or red flash light at 5 or 20 Hz in healthy subjects and migraine patients.

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Background and aims: Migraine patients are known to be sensitive to light during an attack, but also interictally. Our purpose was to determine whether flash light sensitivity differs between colours and stimulation frequencies in healthy subjects (HS) and episodic migraine patients (EM) during and between attacks.

Methods: We enrolled a total of 36 subjects: 7 HS, 10 interictal EM and 19 ictal EM. Stimulation intensity increased by steps of 50 Lux, beginning at 50 Lux. We tested in random chronological order 4 dynamic sequences: blue (~470 nm) at 5 Hz and 20 Hz, red (~720 nm) at 5 Hz and 20 Hz. The subjects were asked to request interruption of the stimulation as soon as they perceived it as uncomfortable.

Results: Compared to HS, interictal EM patients were more light-sensitive to the 5 Hz blue sequence (p=0.004) while ictal EM patients were more sensitive to the 5 Hz blue stimulation (p=0.00002), the 20 Hz blue (p=0.00005), the 5 Hz red (p=0.0007) and the 20 Hz red (p=0.00009).

EM patients reported a greater sensitivity during than outside of an attack for the 20 Hz blue sequence (p=0.002), 5 Hz blue (p=0.027) and 20 Hz red (p=0.00019).
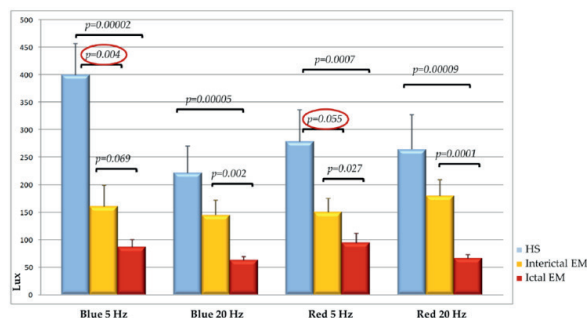
Conclusion: Compared to healthy subjects, migraineurs are more sensitive to blue light and low stimulation rates, suggesting that these parameters may not be suitable for therapeutic purposes and that the melanospin ipRGC pathway is involved. The study also confirms that patients are more sensitive to light during attacks whatever the light parameters are.

EP3075

Management and treatment challenges for patients with chronic migraine, application of OnabotulinumtoxinA: early results of 70 patients

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Background and aims: Chronic migraine is a distinct sub-type of Chronic Daily Headache. The impact of chronic migraine can be very disabling. Many of the therapies prescribed for chronic migraine are the same as those prescribed for episodic migraine. However, treatment still remains to be a challenge and application of OnabotulinumtoxinA might prove to be beneficial for this patient group. In this retrospective study, the effects of OnabotulinumtoxinA for the prophylactic treatment of headaches in chronic migraine patients were assessed.

Methods: Headache patients who were followed up between 2014 and 2016 at a headache unit were retrospectively assessed and patients with the diagnosis of chronic migraine who were refractory to medical treatments and were treated with OnabotulinumtoxinA were involved into the study. Patient records were reviewed and neurological exams, the frequency and severity of headache, the need for symptomatic treatment and effects on quality of life were all evaluated.

Results: 70 patients (52 females, 67.5%) were enrolled into the study. All patients had previous history of multiple drugs but remained symptomatic. Patients were also evaluated before OnabotulinumtoxinA as well as 1. and 3. month after application. OnabotulinumtoxinA was easily tolerated with no serious side effects.

Conclusion: Chronic migraine is a debilitating disease effecting the quality of life of sufferers. For prophylaxis against chronic migraine, literature suggests that the average benefit for OnabotulinumtoxinA seems to be statistically significant. OnabotulinumtoxinA seems to be a safe and tolerable treatment method for chronic migraine.

Disclosure: Nothing to disclose

EP3076
Cancelled

EP3077

Repetitive TMS over the primary motor cortex for prophylactic treatment of migraine

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Background and aims: Patients with chronic migraine (CM) have worse quality of life, increased headache - related burden and worse psychiatric and medical comorbidities in comparison with patients with episodic migraine. We investigated the safety and efficacy of high frequency (HF) repetitive transcranial magnetic stimulation (rTMS) in 40 patients with CM.

Methods: All the patients were diagnosed with chronic migraine according to the criteria of IHS classification ICHD - 3 beta. The stimulation protocol was HF rTMS (15 Hz, 70% of the motor threshold, 1200 pulses/session) over the primary motor cortex (M1) for 5 consecutive sessions. The patients kept a headache diary and were evaluated 30 days after the last session. We studied the change in the frequency of headache, symptomatic medication use, headache intensity measured with visual analogue scale and the result on Headache Impact Test - 6 (HIT - 6). For statistical analysis we used Wilcoxon Signed Rank Test.

Results: In 77% of the patients we observed reduction of $\geq$ 50% of the number of migraine days; 78% had reduction of $\geq$ 50 of the number of days with acute medication use; 82% had reduction of migraine headache intensity; 85% had reduction of the overall headache intensity per month and 79% had clinically significant improvement in the HIT - 6 score. There were no serious adverse events.

Conclusion: Repetitive HF rTMS over M1 is safe and shows effectiveness for CM treatment.

Disclosure: Nothing to disclose

EP3078

Primary headaches in Armenia: An underestimated medical problem

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Background and aims: According to data of WHO Primary Headaches (PH) have both substantial burden on patients and their family life and consist serious social-economic problem. Aim of our study was investigation of prevalence of different types of PH (tension type, migraine, cluster and other cephalalgias) in patients under neurological control.

Methods: 150 (113 women/ 37 men) patients with PH (migraine, tension type ad trigemino-autonomic cephalgia correspondingly) underwent special investigations including questionnaires, created correspondingly to diagnostic criteria and recommendations of International Headache Society, HIT-6, SF -36 questionnaires. Age of participants was 42±16 years.

Results: Data analysis revealed that 90 patients (60%) has migraine, 47 (31%) tension type, 7 (5%) cluster headache, 4 (3%) paroxysmal hemicrania, 1 (1%) hemicrania continua and 1 (1%) SUNCT –syndrom. Main part of patients - 91 patient (60%) was adressed to doctors (68 from which adressed to neurologists) previously and were misdiagnosed with other conditions. Therefore, previous treatment failed to heal the headaches.

Conclusion: Our data shows some different distribution of PH types than international, in our opinion those are patients from the selected treated group, but not from general population. We conclude that is serious misdiagnosing and low awareness of all types of PH by many doctors. We need improvement in both education of medical specialists and patients, to improve both awareness and management of PH in the country.

Disclosure: Nothing to disclose

EP3079

Burden of migraine in the 5EU from the patient perspective: A cross-sectional analysis of National Health and Wellness Survey (NHWS) data

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Background and aims: Migraine is one of the most disabling neurological conditions worldwide. The purpose of this study was to characterize the incremental burden of migraine on quality of life (QoL), productivity, and healthcare resource utilization (HRU) by the frequency of migraine in adults using European data from the National Health and Wellness Survey (NHWS), a self-administered, internet-based questionnaire.

Methods: A retrospective, cross-sectional analysis of responses from the 2016 NHWS was performed using data from the France, Germany, Italy, Spain, and UK (5EU). Adult NHWS respondents with a self-reported migraine diagnosis who completed the migraine module were matched by propensity scores to those without migraines (controls) using sociodemographic characteristics. Outcomes of interest analyzed were from EQ-5D, SF-36v2, HRU and the Work Productivity and Activity Impairment (WPAI-GH) questionnaires. Migraine respondents were stratified by frequency of migraines (headache days/month): 4-7 episodic migraine (EM), 8-14 EM, and chronic migraine (≥15; CM). Independent sample t-tests were used to determine significant differences between controls and the frequency of migraine groups.

Results: Results from the propensity score matched analysis demonstrated that migraineurs reported statistically significant lower QoL and higher HRU as compared to their matched controls. Impairment while at work and total activity impairment was statistically significant higher among all migraineurs compared to matched controls (Table 1).

	Non-migraine controls (a) (N=218)	Migraine (b) (N=218)	4-7 EM (c) (N=106)	8-14 EM (d) (N=49)	CM (e) (N=63)
SF6 Utility Score (mean, SD)	0.71 (0.14)ₐ	0.62 (0.12)ᵦ	0.64 (0.13)ᵨ	0.62 (0.12)𝒹	0.57 (0.11)ₑ
EQ-5D utility index (mean, SD)	0.81 (0.21)ₐ	0.68 (0.28)ᵦ	0.74 (0.25)ᵨ	0.70 (0.28)ₑ	0.56 (0.27)ₑ
SF-36v2 MCS (mean, SD)	44.82 (11.39)ₐ	37.69 (11.72)ᵦ	39.64 (11.27)ᵨ	36.34 (11.09)ᵨ,𝒹	35.47 (12.55)𝒹
SF-36v2 PCS (mean, SD)	50.51 (9.54)ₐ	46.00 (9.81)ᵦ	47.89 (9.89)ᵨ	47.28 (7.53)ᵨ	41.81 (10.09)𝒹
Health status (EQ-5D VAS, mean, SD)	70.99 (24.11)ₐ	60.06 (24.14)ᵦ	64.54 (22.63)ᵨ	62.98 (24.93)ₑ	50.24 (23.52)𝒹
*Absenteeism (% work time missed, mean, SD)	9.46 (24.61)ₐ	14.43 (27.17)ᵦ	7.98 (19.57)ᵨ	22.19 (34.00)ₑ	19.65 (30.36)ₑ
*Presenteeism (% impairment while at work, mean SD)	20.97 (25.77)ₐ	35.52 (29.22)ᵦ	29.38 (29.70)ᵨ	33.79 (27.44)ᵨ	49.38 (25.77)ₑ
*Overall work impairment (% overall impairment related to work, mean, SD)	23.27 (28.24)ₐ	38.70 (31.59)ᵦ	31.09 (30.82)ᵨ,𝒹	39.10 (32.26)ᵨ,𝒹	53.56 (27.81)𝒹
Total activity impairment (%, mean, SD)	27.75 (28.48)ₐ	44.17 (30.35)ᵦ	37.74 (31.12)ᵨ	42.86 (30.89)ₑ	56.03 (25.12)𝒹
Number of healthcare provider visits in the past 6 months (mean, SD)	5.13 (6.86)ₐ	8.48 (10.89)ᵦ	7.25 (7.29)ᵨ	7.06 (7.64)ᵨ,ₑ	11.65 (16.30)𝒹

Footnote: Statistical significant was indicated by the different subscripts (e.g. a and c). If subscripts were similar, it indicates there was no statistical significance.
*Includes only employed respondents.
SF-36v2 scores range from 0-100 where higher the score indicate better QoL. WPAI scores range from 0-100% where higher scores indicate greater impairment. EQ-5D and SF-6 score range from 0-1 where 0 indicates death and 1 indicates perfect health.
CM: Chronic Migraine; EM: Episodic migraine; EQ-5D: EuroQol - 5D;MCS: Mental component score ; PCS Physical component score; QOL: Quality of life; SD: Standard deviation; SF-6: Short Form – 6, SF-36: Short Form (36) Health Survey; VAS: Visual analogue scale

Table 1 Results on domains of health status, QOL and work productivity in migraine subgroups after propensity score matched analysis with non-migraine controls across 5EU

Conclusion: Migraine is a chronic disorder negatively affecting multiple domains of individuals' lives. This study demonstrated that there is a statistically significant incremental burden due to migraine on QoL, HRU and work productivity amongst the migraineurs in comparison to matched controls.

Disclosure: This study was sponsored by Novartis Pharma AG, Basel, Switzerland.

EP3080

A descriptive analysis of the burden of migraine based on self-reported migraine diary data using the Migraine Buddy application in Europe

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Background and aims: Migraine is a neurological disorder that can cause severe disabling pain. The purpose of the study was to describe the burden of migraine on health-related quality of life (HRQOL) as perceived by individuals suffering from migraine in the real world using a self-reported mobile application.

Methods: A retrospective, cross-sectional analysis was conducted using data captured through the Migraine-Buddy© smartphone application from adult, self-diagnosed migraineurs in several European countries including the UK, France, and Spain. Data was analyzed for the most recent 28-day period reported by migraineurs during the study period (June 2015-July 2016). Migraine respondents (n=3900) were randomly selected based on data completeness (fill rates >70%) and stratified by migraine headache days/month: 4-7 episodic migraine (EM) (n=1500), 8-14EM (n=1500), and chronic migraine (≥15; CM) (n=900). Descriptive analysis was performed.

Results: More than 95% of 3900 self-reported migraineurs reported that migraine negatively impacted their daily activities in at least one migraine attack. Attacks affected 50.5% (184.4 days/year), 26.9% (98 days/year) and 14.5% (53 days/year) of their calendar year among CM, 8-14EM, and 4-7EM groups, respectively. On average, 44.8% CM, 40.9% 8-14EM and 34.7% of 4-7EM sufferers respectively reported anxiety and/or depression symptoms during migraine attacks. Social or home activities, productivity, or sleep were highly impacted in migraineurs (Table 1). Triptans (68%), opioids (46%) and nonsteroidal anti-inflammatory drugs (45%) were self-reported as the most common medicines used by migraineurs.

Type of activity	CM (N=900)		8-14EM (N=1500)		4-7EM (N=1500)	
	n	%	n	%	n	%
Home activities	520	57.8%	985	65.7%	933	62.2%
Productivity	590	65.6%	993	66.2%	841	56.1%
Sleep	470	52.2%	827	55.1%	676	45.1%
Social activities	553	61.4%	882	58.8%	736	49.1%
Others	268	29.8%	298	19.9%	204	13.6%

Impact of migraine on daily activities (Number and proportion of patients by subgroup reporting impact from migraine on daily activities is shown)

Conclusion: This study highlights the high burden of migraine on HRQOL and overall well-being of individuals suffering from migraines.

Disclosure: This study was sponsored by Novartis Pharma AG, Basel, Switzerland.

EP3081

Understanding the impact of migraine on work productivity using self-reported migraine diary data using the Migraine Buddy application in Europe

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Background and aims: The purpose of the study was to evaluate the impact of migraine on work productivity as perceived by individuals suffering from migraine in the real world using a self-reported smartphone application called Migraine-Buddy©.

Methods: A retrospective, cross-sectional analysis was conducted using data captured through Migraine-Buddy© from adult, self-diagnosed migraineurs in 17 European countries. Data was analyzed for the most recent 28-day period reported by migraineurs during the study period June 2015-July 2016. Data from chronic migraine (CM: ≥15 headache days/month, N=900), 4-7 episodic migraine (EM) (n=1500) and 8-14 EM (n=1500) individuals were randomly selected based on data completeness (fill rates >70%). Descriptive analysis was performed.

Results: A total of 10,347, 11,301 and 6,504 migraine records were retrieved from CM, 8-14 EM and 4-7 EM individuals, respectively corresponding to a total of 16,815, 14,398, and 7,693 migraine days. Among employed migraineurs (n=2,722) who declared `work` either as their migraine location or in 'affected activities' at least once, an average of 61.7, 31.6 and 18.4 work days missed per year were reported by CM (n=679), 8-14 EM (n=1084) and 4-7 EM (n=959) sufferers, respectively. The most commonly reported triggers of absenteeism-related migraines were psychological (38%), sleep (34%), nutrition (25%) and/or menstruation (23%). Employed sufferers reporting absenteeism recorded symptoms relating to pain/body, mood/cognition disturbances, environmental handicap and depression among others (Table 1).

Symptoms	CM (N=679)		8-14EM (N=1084)		4-7EM (N=959)	
	n	%	n	%	n	%
Pain/Body	638	94%	1017	94%	863	90%
Mood and cognition	622	92%	994	92%	829	86%
Environmental handicap	600	88%	949	88%	793	83%
Depression symptoms	411	61%	539	50%	393	41%
Sleep alterations	282	42%	393	36%	221	23%
Others	250	37%	258	24%	188	20%
No symptoms	112	16%	224	21%	135	14%

Abbreviations: EM, episodic migraine; CM, chronic migraine

Table 1. Symptoms related to absenteeism due to migraine reported by employed migraineurs (N=2722)

Conclusion: Migraine is reported to have a considerable impact in the lives of affected individuals with symptoms impacting the work productivity of employed migraineurs.

Disclosure: This study was sponsored by Novartis Pharma AG, Basel, Switzerland

Movement disorders 5

EP3082

An observational study of rotigotine transdermal patch and other currently prescribed therapies in patients with Parkinson's disease

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Background and aims: To describe real-world management of Parkinson's disease (PD) with dopaminergic treatments and the influence of routinely used management strategies on clinical outcomes. The study was also part of a European Medicines Agency risk-management plan for the non-ergoline dopamine agonist (DA) rotigotine, focusing on cardiovalvular fibrosis.

Methods: SP0854 (NCT00599339) was a prospective, multicentre (10 countries), non-interventional post-authorisation safety study of rotigotine and other dopaminergics, conducted under standard medical practice. Patients requiring either monotherapy (rotigotine/other DAs/levodopa), or levodopa in combination with rotigotine/other DA, were included and followed for ≤33 months. Baseline intended patient-ratio: 5:2:2:5:2 for "rotigotine", "other DA", "levodopa", "levodopa+rotigotine", "levodopa+other DA". Treatment modifications were allowed according to patients' needs. Primary safety objective: evaluation of cardiovalvular fibrosis. Primary efficacy variable: change from baseline in UPDRS-III (motor), assessed by treatment received at a particular post-baseline visit.

Results: 1531/2195 (69.7%) patients completed the study. Discontinuation reasons: lost to follow-up (221;10.1%), consent withdrawn (137;6.2%), adverse events ([AEs] 79;3.6%), other (179;8.2%). Demographics/disease characteristics: Table 1. 5 (0.2%) patients experienced AEs of structural cardiovalvular pathology: Table 2. Overall AEs: Table 2. Mean UPDRS-III score numerically improved when assessed by treatment received at Month 15, and in most treatments received at Month 33 (Figure 1).

Table 1. Baseline demographics and disease characteristics (safety set)

	All patients N=2179
Age, mean ± SD, years	67.7 ± 9.4 (n=2145)
Gender, n (%)	
Male	1199 (55.0)
Female	946 (43.4)
Race, n (%)	
White	2078 (95.4)
Black	2 (0.1)
Asian	2 (0.1)
Other	63 (2.9)
Years since PD diagnosis, mean ± SD	2.59 ± 3.61 (n=2034)
Hoehn & Yahr stage, during "on", n (%)[a]	
0	8 (0.4)
1	501 (23.0)
2	1014 (46.5)
3	515 (23.6)
4	96 (4.4)
5	8 (0.4)
Dopaminergic PD therapy at study onset, n (%)	
Dopaminergic monotherapy (rotigotine, other DA, or levodopa)	1482 (68.0)
Levodopa in combination with rotigotine or other DAs	600 (27.5)
Other dopaminergic PD therapy[b]	63 (2.9)

Data from patients without valid data consent form (n=34 in safety set) were not used for analysis.
The denominator for all %s presented is the full safety set (i.e. 2179), therefore total %s do not add up to 100.
[a]Hoehn & Yahr stage data missing for 3 patients.
[b]Other dopaminergic PD therapy: defined as therapy with multiple DAs without levodopa, or not treated with dopaminergic therapy (i.e. delay in start of PD treatment).

Table 1

Table 2. Overview of adverse events (safety set)

MedDRA Preferred term	All patients N=2179 n (%) [AEs]
Overview of AEs of structural cardiovalvular pathology (AE of special interest)	
All	5 (0.2) [5]
Cardiac valve disease	2 (0.1) [2]
Cardiac valve sclerosis	2 (0.1) [2]
Aortic valve sclerosis	1 (<0.1) [1]
Serious AE	2 (0.1) [2]
Intensity of AE	
Mild	4 (0.2) [4]
Moderate	1 (<0.1) [1]
Final outcome of AE	
Recovering	2
Not recovered, ongoing	1
Lost to follow-up	2
Temporally associated with rotigotine;[a] N=1390	2 (0.1) [2]
Not temporally associated with rotigotine;[a] N=1328	3 (0.2) [3]
Causally related to rotigotine[b]	0
Causally related to other dopaminergic study medication[c]	2
Overview of all AEs	
All AEs	1501 (68.9) [8013]
Serious AE	504 (23.1) [909]
AE leading to discontinuation of at least one PD medication	188 (8.6) [252]
AEs with an incidence of at least 5%	
Nausea	183 (8.4) [223]
Parkinson's disease	164 (7.5) [202]
Application and instillation type reactions[d]	145 (6.7) [161]
Fatigue	141 (6.5) [159]
Depression	134 (6.1) [137]
Fall	129 (5.9) [156]
Back pain	125 (5.7) [147]

AE: adverse event; n = number of patients reporting at least 1 AE; (%) = percentage of patients among the total N; [AEs] = count of individual AEs occurring among the n patients.
[a]An AE was considered to be temporally associated with rotigotine if rotigotine was administered at least once within 30 days prior to the onset of the AE.
[b]The study physician considered a causal relationship of the AE to treatment with rotigotine.
[c]The study physician considered a causal relationship of the AE to treatment with study medication (other than rotigotine): 1 with cabergoline and 1 with bromocriptine.
[d]MedDRA High level term.

Table 2
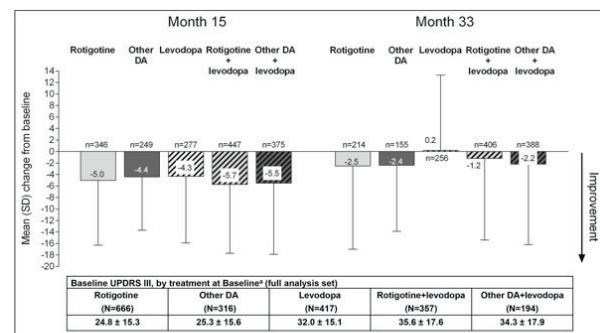
Figure 1. Change from Baseline in UPDRS III by treatment at visit: Month 15 and Month 33 (full analysis set).
Changes from baseline data are reported by the treatment a patient was receiving at the particular visit (at Month 15 and at Month 33); patients were not necessarily receiving that treatment at baseline.
UPDRS: Unified Parkinson's Disease Rating Scale.
[a]Only those treatments reported by ≥100 patients at baseline are reported; at baseline, 19 patients were receiving multiple DAs, 24 receiving multiple DAs+levodopa, and 33 were not treated (delay in start of treatment).

Figure 1

Conclusion: This study reports real-world data from >2000 PD patients receiving dopaminergic treatment for up to 3 years. Few patients (5) experienced AEs of structural cardiovalvular pathology; none were considered causally-related to rotigotine, and no new safety signal was observed. UPDRS results suggest adequate control of motor symptoms with dopaminergic treatment over time.

Funding: UCB Pharma.

Disclosure: Thomas Müller, Eduardo Tolosa, Letitia Badea and Lars Timmermann were study investigators on this UCB Pharma-funded study; Frank Grieger, Michael

Markowitz, Xavier Nondonfaz, and Lars Bauer are salaried employees of UCB Pharma, and receive stock options from their employment; Mahnaz Asgharnejad is a former salaried employee of UCB Pharma, and received stock options from her employment.

EP3083

Cardiac autonomic testing in Parkinson's disease and multiple system atrophy: A possible discriminating tool?

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Background and aims: The differential diagnosis of Parkinson's disease (PD) and multiple system atrophy (MSA) is difficult yet crucial. The aim of this study was to compare the neurophysiologic cardiac autonomic findings in these two degenerative diseases.
Methods: Retrospective study (from January 2015 to December 2016) including patients diagnosed with PD or MSA who had clinical cardiac autonomic function tests carried out according to Ewing's battery. We assessed cardiac parasympathetic (Heart rate variation to deep breathing(HR-DB), to Valsalva(HR-V), heart rate response to standing(HR-S)) and sympathetic (sympathetic skin response(SSR)) autonomic system. Patients were graded as per Ewing's criteria into normal, early or definite autonomic dysfunction.
Results: We collected 65 patients: 42PD and 23MSA (respectively: sex-ratio=2.8 and 0,8; dysautonomic complaints in 90.4%PD and 95.6%MSA). Neurophysiologic dysautomia was found respectively in 95.2% of PD and 100% of MSA. HR-DB was altered respectively in PD and MSA in 4.7% and 8.7% (mean variation=37 and 32.6), HR-V in 38% and 39% (mean variation=1.53 and 1.56) and HR-S in 78.5% and 82.6% (mean response=1.07 and 0.96). Parasympathetic dysautonomia was, respectively in PD and MSA, early in 66.6% and 47.8%, and definite in 26.2% and 43.5%. Sympathetic dysautonomia was associated in 16.6% in PD and 47.8% in MSA (p=0,009) and isolated in 2.4% of PD and 13% of MSA.
Conclusion: Our study showed that neurophysiologic autonomic dysfunction was constant in MSA. The association of sympathetic and parasympathetic dysautonomia was significantly more suggestive of MSA rather than PD. Further studies on larger cohorts are required to confirm these findings.
Disclosure: Nothing to disclose

EP3084
Cancelled

EP3085
Cancelled

EP3086

'Advanced' Parkinson's disease characteristics in clinical practice: Results from the OBSERVE-PD study, a cross-sectional observational study of 2615 patients

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Background and aims: 'Advanced' Parkinson's disease (PD) patients are often treated at specialized movement disorder centres. However, the defining features of 'advanced' PD patients are not well understood. This study characterized the clinical and non-clinical features and treatments (including device-aided options) in PD patients considered 'advanced' by movement disorder specialists.
Methods: A cross-sectional, observational study was conducted at 128 movement disorder centres in 18 countries. The primary outcome was the proportion of PD patients identified by their physician as 'advanced'. The clinical and non-clinical characteristics of 'advanced' and 'non-advanced' patients were compared using descriptive statistics. Physicians' assessment of 'advanced' PD was compared to a Delphi-criteria-based classification.
Results: According to the physicians' judgment, 51.3% (n=1342/2615) of PD patients were considered 'advanced', but this proportion varied regionally. A moderate correlation existed between the physician's judgment and the Delphi-consensus-based criteria for 'advanced' PD. 'Advanced' and 'non-advanced' patients were similar regarding age, gender, and living situation, but differed in terms of motor symptom severity (Unified Parkinson's Disease Rating Scale [UPDRS] Part III score), motor fluctuations (UPDRS Part IV Q32 and Q39), non-motor symptoms (NMS) (NMS Scale total score), quality of life (8-item Parkinson's Disease Questionnaire total score) and caregiver support status (Table). Of the 'advanced' patients 882/1342 (66%),

were eligible for device-aided treatment, and 548 (41%) had ongoing device-aided treatment or were about to start.

Table: Characteristics of Advanced and Non-advanced Parkinson Disease Patients

Characteristics	Advanced PD, N=1342		Non-advanced PD, N=1273	
	n/N (%)	Mean [SD]	n/N (%)	Mean [SD]
Age, years		67.6 [9.4]		66.4 [10.3]
Sex, male	817/1342 (61)		734/1273 (58)	
Living at home	1304/1342 (97)		1264/1273 (99)	
Caregiver support, yes	917/1327 (69)		328/1270 (26)	
Time since diagnosis, years		11.0 [5.8]		4.3 [3.7]
Motor fluctuations present, yes	1167/1342 (87)		295/1273 (23)	
Duration of motor fluctuations, years[a]		4.9 [3.9]		2.3 [2.1]
UPDRS II (ADL), score[b]		16.5 [8.3] ***		8.4 [5.4] ***
UPDRS III (motor), score[c]		30.2 [14.7] ***		21.1 [11.0]***
UPDRS IV Q32, dyskinesia, none	501/1338 (37)		1097/1268 (87)	
UPDRS IV Q39, off time, none	271/1336 (20)		931/1259 (74)	
UPDRS V: Modified Hoehn & Yahr, score[d]		2.9 [0.8]***		2.0 [0.6]***
NMSS, total score[e]		58.6 [43.0] ***		34.4 [30.9]***
PDQ-8, total score[f]		36.6 [19.3] ***		20.7 [16.4]***
Eligible for invasive treatment options, yes	882/1342 (66)		127/1272 (10)	
Status of invasive treatment for eligible patients				
Ongoing	384/882 (44)		15/127 (12)	
Decided at visit to start	164/882 (19)		17/127 (13)	
No	332/882 (38)		91/127 (72)	
Missing	2/882 (0.2)		4/127 (3.1)	

N for advanced PD, non-advanced PD: a. 1151, 272; b. 1341, 1270; c. 1341, 1272; d. 1342, 1272; e. 1070, 1018; f. 1326, 1262.
The UPDRS was measured in the "on" state. Statistical significance based on a t-test between the Advanced and non-advanced PD patients are indicated at the P<0.0001 (***). All proportions except for the invasive treatment status included patients with non-missing data. UPDRS = Unified Parkinson's Disease Rating Scale; NMSS = Non-motor Symptom Scale; PDQ-8 = 8-item Parkinson's Disease Questionnaire

Conclusion: This study demonstrated that physicians judged more than half of the PD patients in movement disorder centres across 18 countries as 'advanced', with distinct characteristics regarding motor fluctuations, non-motor symptoms and quality of life.

Disclosure: AbbVie funded the work and participated in the study design, research, data collection, analysis and interpretation of data, reviewing, and approving the publication; medical writing support was provided by Jane M. Rodgers and Amy M. Spiegel, of AbbVie Inc.

EP3087

A study assessing the effect of a structured medication review on quality of life in patients with Parkinson's disease: An interim analysis

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Background and aims: To investigate whether a structured medication review (SMR) executed by community pharmacists leads to better quality of life (QoL) in patients with Parkinson's disease (PD). The secondary objectives are measurements of activities of daily life, presence of non-motor symptoms, disease perception and quality of life of personal caregivers.

Background: Treatment of PD is symptomatic and frequently consists of complicated medication. This negatively influences therapy adherence, resulting in a substantial lower benefit of treatment and a decreased QoL. Little is known about the effects of a SMR on QoL and the feasibility of medication assessment within primary care.

Methods: In this multicenter randomized controlled study, 108 PD-patients with ≥ four different medications and ≥ four different medication intake moments daily were included. The intervention consisted of a SMR performed by community pharmacists. Primary outcome was PD-specific QoL (PDQ-39). Measurements were performed at baseline, 3 and 6 months of follow up. Analyses were performed using linear mixed model repeated measurements analyses.

Results: A total of 108 of the 200 patients were thus far included with a mean age of 74.2 years (SD±7.0), 8.2 (SD±2.8) different medications and 5.2 (SD±1.8) medication intake moments daily. After six months, there was no significant difference in overall score of the PDQ-39, although a clinically and statistically significant difference was found in the domain 'emotional well-being', in favour of the control group (Table 1).

PDQ-39	Intervention group (SMR[1])			Control group (usual care)			Treatment effect at 6 months	P-value[3]
	Baseline (n=44)	3 mo. (n=30)	6 mo. (n=31)	Baseline (n=64)	3 mo. (n=47)	6 mo. (n=41)	Δ I-C[2] (95% CI)	
Overall score	35.6 (2.4)	38.6 (2.8)	38.3 (2.9)	36.3 (2.0)	37.0 (2.3)	37.9 (2.4)	-1.2 (-5.5; 3.2)	0.69
Mobility	44.0 (3.9)	45.6 (4.2)	45.2 (4.3)	46.4 (3.2)	46.4 (3.4)	45.9 (3.6)	-1.7 (-8.3; 4.9)	0.85
Activities of daily living	42.5 (3.8)	44.8 (4.3)	46.9 (4.2)	41.9 (3.2)	43.5 (3.5)	44.7 (3.5)	-1.5 (-7.2; 4.1)	0.86
Emotional well-being	27.8 (2.8)	37.4 (4.9)	35.0 (3.3)	31.8 (2.4)	32.8 (4.0)	32.4 (2.8)	-6.6 (-12.7; -0.5)*	0.07
Stigma	19.5 (2.8)	21.7 (3.5)	21.1 (3.5)	21.6 (2.3)	23.2 (2.8)	22.7 (3.0)	-0.5 (-8.6; 7.5)	0.99
Social support	23.5 (3.9)	28.1 (4.2)	26.8 (4.4)	24.5 (3.2)	27.6 (3.4)	27.5 (3.7)	-0.2 (-8.9; 8.5)	0.94
Cognitions	35.1 (2.9)	39.4 (3.1)	39.7 (3.3)	33.6 (2.4)	36.4 (2.5)	37.7 (2.8)	-0.5 (-8.4; 7.5)	0.86
Communication	33.0 (3.1)	32.8 (3.4)	32.8 (3.8)	27.0 (2.6)	25.0 (2.8)	29.7 (3.2)	2.8 (-6.3; 12.0)	0.55
Pain	46.6 (3.0)	46.2 (3.8)	48.1 (3.4)	45.0 (2.5)	43.3 (3.1)	47.1 (2.9)	0.6 (-7.0; 8.1)	0.86

Table 1 Outcomes of the PDQ-39 questionnaire data (range 0 (best QoL) - 100 (worst QoL), analysed by 'Repeated measurement analysis', presented as mean (SE). * Exceeds the minimally important difference determined by Peto et al. [1]SMR: Structured medication review. [2]ΔI-C: Intervention group minus Control group; a positive change is in favour of the intervention group. [3]P-value based on 'group-by-time interaction'.

Conclusion: In this interim analysis, QoL in PD-patients did not improve six months after performing a SMR executed by community pharmacists.

Disclosure: Nothing to disclose

EP3088

A pilot study to examine the single dose pharmacokinetic properties of two formulations of Apomorphine Sublingual Film (APL-130277) 15 mg in health volunteers

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Background and aims: APL-130277 (apomorphine) is administered sublingually and being studied for OFF episodes. The primary objective of this study was to evaluate the pharmacokinetics (PK) parameters of a single 15 mg dose of APL-130277 in healthy volunteers and compare the bioavailability between the formulation used in study CTH-105 and the scaled-up formulation.

Methods: Twelve healthy male volunteers between 21 and 60 years inclusive were enrolled. All subjects received APL-130277 (CTH-105 formulation [drug-side facing up towards the tongue]), APL-130277 (scaled-up formulation [buffer-side facing up towards the tongue]), and APL-130277 (scaled-up formulation [drug-side facing up towards the tongue]) dosed on three separate days, crossed over with a 24-hour washout. PK assessments were evaluated from 0 to 12 hours post dosing. Subjects were pretreated with domperidone BID starting on Day -3. Study subjects and clinical staff members (except the staff member responsible for dosing) were blinded.

Results: The PK parameters were similar between the two formulations [i.e., CTH-105 formulation and the scaled-up formulation, irrespective of the orientation of the film under the tongue] (Table 1). The plasma apomorphine concentration was similar at all timepoints with the scaled-up formulation, irrespective of the orientation of the film under the tongue (Figure 1).
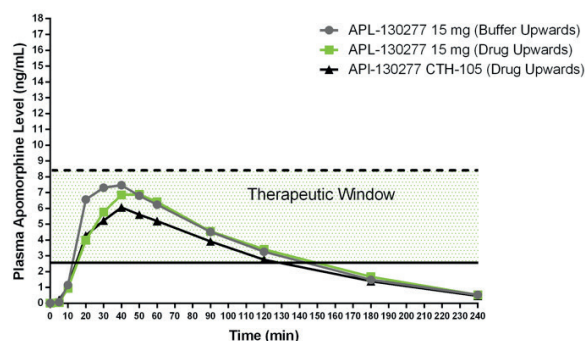
Figure 1: Plasma Apomorphine Level (ng/mL) Over Time: Scaled Up Formulation

Conclusion: These results indicated that the two formulations display very similar pharmacokinetic profiles with respect to Cmax and AUC values. The orientation of the film under the tongue for the scaled-up formulation did not have a meaningful impact on the bioavailability of the drug.

Disclosure: The study was funded by Sunovion CNS Development Canada ULC. Eric J. Pappert is employed by Sunovion Pharmaceuticals, Inc. Peter Gardzinski, Thierry Bilbault, and Albert Agro are employed by Sunovion CNS Development Canada ULC.

Table 1: Descriptive Statistics of the Pharmacokinetic Parameters for Plasma Apomorphine

Treatment 15 mg APL-130277	$t_{1/2}$ (hr) mean	C_{max} (ng/mL) mean	AUC_{last} (min*ng/mL) mean	$AUC_{infinity}$ (min*ng/mL) mean	MRT (min) mean
CTH-105 Formulation (drug side facing up towards to tongue)	50.6	6.41	650	685	100
Scaled-Up Formulation (buffer side facing up towards to tongue)	52.6	8.45	781	823	99.6
Scaled-Up Formulation (drug side facing up towards the tongue)	46.9	7.30	760	797	100

AUC=area under the plasma concentration vs. time curve (min*ng/mL); C_{max}=maximum plasma concentration; MRT=mean residence time; $T_{1/2}$=time from dosing to C_{max}

Table 1: Descriptive Statistics of the Pharmacokinetic Parameters for Plasma Apomorphine

EP3089

Cancelled

EP3090

Cancelled

EP3091

New application for the training in the use of ultrasound as a guidance in the Botulinum Toxin infiltrations for patients with cervical dystonia

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Background and aims: Botulinum toxin therapy (BTX) is the most effective treatment to ameliorate the symptoms in Cervical dystonia (CD) patients in accordance with the medical literature published to the present data. However, the efficacy and tolerance of BTX therapy is directly related to the accuracy of the muscles infiltrated.Some guidance tools for BTX infiltration such as ultrasound, axial tomography and MRI have been used successfully by different movement disorders groups around the world however most of them required a long and specialized training. We decided to create an App for facilitate the training and to give visual support to doctors involved in the BTX therapy in CD patients. We included 10 CD patients after a written consent. We made a video film of al least 18 muscles involved in the most common types of CD dystonia. the ultrasound images as well as the infiltration needle placement technique were recorded simultaneously for every recorded muscle.

Results: The function, the scout, the anatomical features as well as the ultrasound images and techniques of at least 18 muscles involved in cervical dystonia are described in this App

Conclusion: This multimedia App facilitates the trainning for doctors interested in the use of US as a guidance for BTX infiltration in CD patients

Disclosure: MERZ PHARMA lab has totally financed this study.

EP3092

Restless Legs Syndrome: The under-recognized non-motor burden assessed by a self reported tool

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Background and aims: Restless Legs Syndrome (RLS) is characterised by an urge to move the legs to provide relief. Non-motor symptoms (NMS) among RLS sufferers are often not recognized, although they may play a key role in driving patients' quality of life, similar to other neurological conditions such as Parkinson's disease (PD). Currently, no validated tools assess NMS in RLS. In this first ever UK-based study addressing NMS in RLS, we used the NMSQuestionnaire (NMSQuest) validated in PD to holistically assess NMS in RLS.

Methods: 55 patients with primary RLS according to the criteria of the International RLS Study Group (IRLSSG) were included. Patients underwent a physical examination, clinical interview and completed the NMSQuest and the IRLSSG Rating Scale.

Results: Of 55 patients (mean age 67.1 ± 13.5 years, mean age at RLS onset 37.2 ± 20.5 years, 65.5% female) 78.2% were on treatment for RLS and 49.1% reported augmentation at the time of interview. The majority of patients (67.3%) reported severe to very severe RLS on the Rating Scale. All patients reported at least one NMS. The most frequently reported NMS include difficulties falling/staying asleep (89.1%), nocturia (69.1%), feeling sad (63.6%) and memory problems (56.4%)(figure 1).
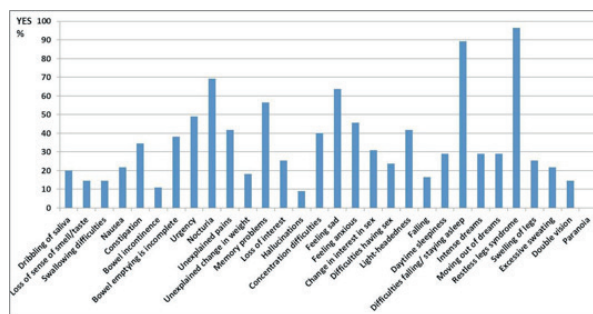
Prevalence of 30 different non-motor symptoms as assessed by NMSQuestionnaire

Conclusion: NMS are common amongst RLS sufferers, with the most commonly reported in our cohort being difficulties falling/staying asleep, feeling sad and memory problems. These are symptoms which might be related to RLS. It is important to increase awareness of NMS among patients and health professionals. We are now developing a RLS specific NMSQuest(R-NMSQuest).

Disclosure: This study was funded by RLS-UK.

Movement disorders 6

EP3093

Influence of food on Opicapone pharmacokinetics and pharmacodynamics

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Background and aims: To characterize the effect of food on the pharmacokinetics (PK) and pharmacodynamics (PD) of opicapone (OPC) after single and repeated doses.

Methods: Two open-label studies were conducted: Study-1 was a 50mg OPC single-dose, 2-period, 2-sequence, crossover fast versus fed (high-fat and high-caloric meal) study in 12 healthy subjects; Study-2 was a 12-day fasting once-daily 50mg OPC single-arm study in 28 healthy subjects, for which on day 10 OPC was administered in the evening with a moderate meal.

Results: In Study-1, following a 50mg OPC single-dose, the OPC rate and extent of absorption were significantly lower in the fed state compared to the fasted state (fed:fasted ratios of 31.73% for C_{max} and 47.11% for $AUCt$). The t_{max} was also significantly increased by the presence of food. In Study-2, following once-daily 50mg OPC, the OPC rate and extent of absorption were significantly lower in the fed state (day 10) compared to the fasted state (day 9, fed:fasted ratios of 38.21% for C_{max} and 68.70% for $AUCt$). The t_{max} was also significantly increased by the presence of food. However, despite AUEC being slightly higher (with upper limit of the 90%CI just outside the pre-specified acceptance interval of 80-125%), following a moderate meal (day 10), E_{max} and the threshold of efficacy, i.e., every 24 hour effect (E_{min}) of COMT were not affected in a relevant way.

Conclusion: Opicapone was safe and well tolerated and at steady-state, can be administered concomitantly with a moderate meal without affecting its COMT inhibition.

Disclosure: Nothing to disclose

EP3094

Opicapone's bedtime regimen and the decision-making process

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Background and aims: To clarify the decision-making process for opicapone's bedtime regimen.

Methods: Review of opicapone, levodopa, carbidopa and benserazide pharmacokinetic data. Five phase-1 studies were selected on the basis of concomitant, alone or 1-hour apart administration between oral single-doses of opicapone (25, 50 and 100mg) and immediate- (IR) or controlled-release (CR) levodopa/carbidopa (LC, 100/25) or levodopa/benserazide (LB, 100/25).

Results: In studies conducted with IR/CR-LB concomitant administration, an increase in rate (C_{max}) and extent (AUC) to levodopa and benserazide occurred at all doses of opicapone. The increase was statistically significant for IR formulation. Levodopa C_{max} decreased when doses of opicapone increased. In studies conducted with IR/CR-LC concomitant administration, a statistically significant increase in C_{max} and AUC to levodopa, but not to carbidopa, occurred at all doses of opicapone. Levodopa C_{max} decreased (more pronounced with CR formulation) when doses of opicapone increased. Similar levodopa and carbidopa C_{max} was observed when opicapone (50mg) was administered 1-hour apart from IR-LC. Opicapone's systemic exposure increased in a dose-proportional manner but an important variability was observed between different levodopa formulations and the use of carbidopa/benserazide.

Conclusion: The pharmacokinetic data suggest a certain degree of interaction at absorption phase that was minimized by separating both administrations for at least 1-hour. Opicapone was developed as an add-on to levodopa and, taking into consideration that Parkinson's disease patients may well necessitate several daily doses of levodopa, a bedtime regimen for opicapone was proposed to better allow the physician to individually tailor the levodopa daily regimen without any concern of a potential absorption interaction.

Disclosure: Nothing to disclose

EP3095

Visual hallucinations related to Parkinson's disease in Polish patients.

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Background and aims: Visual hallucinations (VH) are one of neuropsychiatric non-motor symptoms of Parkinson's Disease (PD). VH are mostly drug-induced but neurodegeneration, as primary reason, should also be considered. The aim of the study was to evaluate prevalence and clinical correlations of PD patients in Polish population.
Methods: 110 patients diagnosed with idiopathic PD according to UK Parkinson's Disease Society Brain Bank Criteria were enrolled into the study. All patients underwent Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) and Non-Motor Symptoms Questionnaire (NMS-Quest) evaluation and depression screening based on Hamilton Depression Rating Scale (HAM-D).
Results: Visual hallucinations occurred in 20.99% (n=23). The positive correlation was observed between hallucinations and patient's age as well as disease duration. Disease severity accessed in UPDRS part III was greater among patients with VS. Depression rate was higher in non-hallucination PD patients group.
Conclusion: Visual hallucinations are frequent among PD patients. Older patients with longer disease duration and greater disease severity are in a risk group of VH occurrence. Variability of VH is fascinating – from simple to complex and sophisticated.
Disclosure: Nothing to disclose

EP3096

Brain atrophy in Wilson's disease is related to neurological impairment and copper metabolism

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Background and aims: Brain atrophy is a prominent neuroimaging feature of Wilson's disease (WD). However, it is usually assessed qualitatively, and the relationship between quantitative measures of brain atrophy, neurological impairment, and copper metabolism in WD has not been investigated. Therefore, we aimed to address this issue.
Methods: We retrospectively analysed 47 newly diagnosed WD patients in whom brain MRI and copper metabolism studies were performed before treatment initiation. Neurological deficits were assessed on the Unified Wilson's Disease Rating Scale (UWDRS). Brain parenchymal fraction (BPF, i.e. brain volume normalized for intracranial volume) was calculated for each participant with Statistical Parametric Mapping software (v.12). Copper metabolism consisted of serum concentrations of ceruloplasmin, total copper, and non-ceruloplasmin bound copper (NCC). Statistical analysis included correlations between UWDRS, copper metabolism, and BPF.
Results: UWDRS scores correlated significantly with BPF (r=-0.631, p<0.001), and both UWDRS and BPF correlated with age at diagnosis (r=0.392, p=0.006 for UWDRS; r=-0.690, p<0.001 for BPF). The relationship between BPF and UWDRS remained significant after controlling for age and gender (r=-0.535; p<0.001). Moreover, after accounting for gender and age at diagnosis, both UWDRS and BPF correlated with the serum NCC concentration (r=0.285; p=0.037 for UWDRS; r=-0.295; p=0.032 for BPF). Ceruloplasmin and total serum copper were not significantly related to UWDRS scores nor to BPF.
Conclusion: Brain atrophy is related to neurological impairment in patients with WD and is associated with serum NCC concentration.
Disclosure: Nothing to disclose

EP3097

Differentiation between Lewy body diseases and atypical parkinsonian syndromes using combined brain SPECTs

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Background and aims: Neuroimaging facilitates the differential diagnosis of movement disorders. We aimed to assess whether an automated analysis of combined dopamine transporter (DA) and perfusion single photon emission computed tomography (SPECT) could discriminate patients with Lewy body diseases (LBD), including idiopathic Parkinson disease (PD) and diffuse Lewy body disease (DLB), and atypical parkinsonian syndromes (APS), including multiple system atrophy (MSA), progressive supranuclear palsy (PSP) and corticobasal syndrome (CBS).

Methods: We examined consecutive 32 patients with LBD and 21 patients with APS. The clinical diagnosis of each disease was made based on published criteria without imaging data. Anatomical MRI was segmented into cortical and subcortical regions using an automated process. Then, 123I-ioflupane (123I-FP-CIT)- and 123I-iodoamphetamine (IMP)-SPECT data were coregistered onto the anatomical MRI in each patient using mutual information algorithm. DAT activity and regional perfusion in each brain region were extracted in each patient and submitted to a logistic regression analysis as independent variables. A stepwise procedure was used to select predictive variables that should be included in the model to differentiate LBD and APS. Receiver operating characteristic (ROC) analysis was performed to measure diagnostic power.

Results: The stepwise logistic regression analysis yielded three predictive variables; striatal DAT activity, the regional perfusion in the lenticular nucleus and midline frontal lobe. ROC analysis revealed that the area under the curve was 0.876 (sensitivity 84.4%, specificity 90.5%).

Conclusion: An automated classification using combined dopamine transporter and perfusion SPECTs showed a high accuracy in distinguishing patients with LBD and APS without clinical information.

Disclosure: This study was supported by by Nihon Medi-Physics Co., Ltd. The sponsor had no role in the study design, data collection, data analysis, data interpretation, or writing of this report.

EP3098

Parkinsonism in Kennedy's disease (spinal and bulbar muscular atrophy, SBMA)

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Background and aims: Kennedy's disease (SBMA) is a rare, adult-onset, X-linked, recessive trinucleotide, neuromuscular disease, caused by expansion of a CAG-tandem-repeat in exon 1 of the androgen-receptor (AR) gene on chromosome Xq11-12.

Methods: Case report.

Results: We present the case of a 72-year-old male patient who developed the symptoms of parkinsonism in 2011 - bilateral rigidity, bradykinesia, frequent falls with early postural instability – and five years later he developed the symptoms of Kennedy's disease. In 2014 progressive dysphagia has been formed and from 2016 bulbar and spinal symptoms have appeared (perioral and lingual tremor, fibrillation, weakness and wasting of facial, bulbar, glossal and upper limb muscles, fasciculation, dysarthria, dysphagia, reduced deep tendon reflexes). At the last clinical admission beside the symptoms mentioned above we observed gynecomastia in July 2016. The fast progression of the parkinsonism has to be mentioned. Considering the clinical data and electrophysiological results we thought of the possibility of Kennedy's disease. The genetic testing gave the final diagnosis: SBMA (CAG-tandem-repeat number in exon 1 of the AR gene on chromosome Xq12: 44+/-1).

Conclusion: This is one of the first reported cases of Kennedy's disease with parkinsonism. Another lesson of the case is severe progressive dysphagia may be the manifestation of a rare genetic disorder.

Disclosure: Nothing to disclose

EP3099
Cancelled

EP3100
The INVEST study: A comparison of deep brain stimulation and continuous intrajejunal levodopa infusion in advanced Parkinson's disease

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Background and aims: Deep brain stimulation (DBS) and continuous intrajejunal levodopa infusion (CLI) are both efficacious treatments of motor symptoms in advanced Parkinson's disease (PD). They reduce medication induced motor fluctuations and dyskinesias. Moreover, they significantly improve quality of life. The costs of CLI seem higher. Yet, comparative knowledge with respect to effectiveness, complications and costs is lacking as a randomized controlled trial (RCT) comparing DBS and CLI has never been performed. As a result, there is unwanted variation in medical practice regarding treatment of advanced PD.

Methods: A prospective open label multicentre RCT is currently performed. A total of 66 PD patients with medication induced motor fluctuations will be randomised between DBS and CLI treatment. Patients not willing to be randomised are eligible for an observational patient-preference study. There are 6 assessment visits in the first year of treatment. The primary health economic outcomes are costs per unit on the quality of life scale PDQ-39 and costs per QALY (Quality Adjusted Life Years) at 12 months. Major secondary outcomes are quality of life, functional health and complications.

Results: The study started in December 2014, results are expected in 2019.

Conclusion: The INVEST study is the first randomised study to provide comparative knowledge on the therapies DBS and CLI in advanced PD.

Disclosure: Dr. Dijk, Dr. de Bie and Mr. van Poppelen are researchers of the INVEST study. This investigator initiated multicentre trial is funded by ZonMw Doelmatigheid, project number 837002509 and by an unconditional grant of Medtronic Netherlands.

EP3101
Gray matter atrophy in Parkinson's disease and freezing of gait reflected by software package Freesurfer

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Background and aims: Freezing of gait (FOG) is a troublesome symptom of Parkinson's disease (PD). The relationship between regional brain atropy and FOG has been poorly investigated. Using Freesurfer software we tested whethear gray matter (GM) atrophy contributes to FOG in PD.

Methods: We investigated 20 patients with PD, 10 with FOG and 10 without FOG, both groups of patients were assessed using FOG questionnaire, "Time up and go" test, Hoehn and Yahr staging. High resolution T1-weighted brain images were acquired for each subject using a 1.5T MRI scanner. Asurface-based method implemented in FreeSurfer was used to quantify GM atrophy. A vertex-wise and region of interest (ROI) two-sample t-test of normalized subject data was used to assess significant group differences. The analysis was controlled for age, gender and total intracranial volume.

Results: Gray matter was significantly reduced in the pre-supplementary motor area in freezers, compared to matched nonfreezers at $p < 0.001$, uncorrected. The ROI (region of interest) analysis controlled for age, gender and intracranial-volme yielded further differences in in gyrus cinguli (in the anterior part), in supplementary motor area (SMA) on the left side, in the area of frontal operculum on the right side. FOG- groups of our patients reported greated atrophy in the occipital cortex. Higher global level of cortical trophy were detected in freezers.

Conclusion: Our findings provide the additional evidence that the development of FOG in patients with PD is associated with local GM atrophy, which may play a role in the complex pathophysiology of this disabling symptom.

Disclosure: Nothing to disclose

EP3102

A clinical and genetic study of Huntington's disease, based on our Bulgarian team's 9 year experience

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Background and aims: Huntington's disease (HD) is a rare neurodegenerative disorder characterized by chorea, psychiatric disturbances and dementia. We aim to review the demographics, clinical and genetic features of HD in Bulgaria and create a local patient database.

Methods: The patients underwent clinical, neurophysiological examinations, brain magnetic resonance/ computed tomography imaging and molecular genetic studies.

Results: A total of 80 symptomatic individuals from 60 families, belonging to two large ethnic groups (Bulgarian and Turkish) were evaluated. There were no families from the Roma ethnic group. The affected originated from different regions in Bulgaria. HD was confirmed through genetic tests on 64 individuals, of whom 63 were symptomatic and 1 asymptomatic. The gene was inherited maternally in 28 and paternally in 18. In 4 participants there was no known family history, and in 14 the information was missing. Motor onset was the most common, followed by mixed onset (motor and cognitive signs) and non-motor onset (psychiatric problems). The age at onset varied from 17 to 66 years. Most participants were undergoing treatment for hyperkinesis with Haloperidol. According to family history, 60 additional family members showed signs of HD.

Conclusion: The observed phenotypes and genotypes are similar to those reported in literature. Anticipation and genome imprinting were also detected. Creation of a local patient database will help us with regular monitoring and timely implementation of latest therapeutic strategies.

Disclosure: Nothing to disclose

EP3103

Cancelled

MS and related disorders 5

EP3104

Comparison of fingolimod and teriflunomide on the basis of early relapse risk following the switch from injectables in patients with stable multiple sclerosis

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Background and aims: Both fingolimod and teriflunomide are oral agent effectively used in multiple sclerosis (MS). The aim of this study was to determine early relapse possibilities in multiple sclerosis (MS) patients switching to oral therapy following a period of stable disease on IFNb or GA and to compare fingolimod and teriflunomide in this respect.
Methods: A total of 164 patients included in the study from our cohort. Of the total patients, 126 (82.3%) switched to fingolimod, and 29 (17.7%) to teriflunomide. 110 patients were switched from IFNb and 54 patients from GA. Switchers were compared with 124 patients remaining on platform injectables with satisfactory disease control.
Results: Within the switchers, the most frequent reason was lack of tolerance (73.8%). There was no difference in the proportion of patients having at least one relapse in the first 6 months between switchers and patients remaining on platform injectables. The mean annualized relapse rate was 0.03 for switchers, and 0.04 for stayers (p=0.098). There was not any difference in disability progression in terms of number of patients in 6 months. There was also no difference between patients switched to fingolimod or teriflunomide in terms of annualized relapse rate (p=0.12) and EDSS progression (p=0.096).
Conclusion: In conclusion, our results indicated that there was no evidence of disease reactivation within the first 6 months in patients switching to oral therapy when they were previously stable, and both fingolimod and teriflunomide had similar results in this respect.
Disclosure: Nothing to disclose

EP3105

First reported case of Aquired Hemophilia A (AHA) as secondary autoimmune disease following alemtuzumab treatment in multiple sclerosis

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Background and aims: A female patient, 34 y.o. affected by multiple sclerosis since October 2004 experienced a high relapse rate in the first two years and underwent an induction therapy. Therapeutic attempts with mitoxantrone and cyclophosphamide failed in achieving disease stability. From 2008 she underwent 57 cycles of Natalizumab with complete disease control. She decided for tree times to discontinue treatment due to PML fear and invariably experienced massive disease reactivation. After the last reactivation we administered two courses of alemtuzumab (January 2015-2016). Since then she had no evidence of clinical or MRI disease activity, and referred high quality of life.
Methods: Clinical case
Results: Since August 2016 she had abnormal bruising for minimal trauma and four haemorrhages: on the left palm after squats, over the dorsalis pedis after tying shoes, over the right hand after having kept her mobile tightly. She was finally admitted at our hospital for limitation in walking abilities due to popliteus muscle's haemorrage. At blood tests we found high PTT and absence of FVIII. The finding of anti-FVIII antibodies confirmed the diagnosis of AHA. She was treated with rFVII and then with cyclophosphamide 100mg daily for two months and prednisone 100mg daily for a month plus tapering with initial response to treatment. In January 2016, an increase of FVIII-inhibitor without clinical manifestation was found. Due to relapse of AHA we started rituximab 375mg/m^2 weekly for 4 times.
Conclusion: In MS clinical studies, alemtuzumab-treated patients experienced autoimmune disorders such as AHA (0.2%). PT and PTT should be routinely monitored after alemtuzumab.
Disclosure: Nothing to disclose

EP3106

Mitochondrial targeting therapy: Does it work in MS patients?

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Background and aims: Neurodegeneration has proved to be the major reason of disability in multiple sclerosis (MS). Mitochondrial dysfunction results in functional disturbance without structural damage, then leads to disturbance of respiratory chain function and liberates electrons, giving rise to reactive oxygen species (ROS) and to axonal degeneration, cell death, and tissue destruction. There are no drugs with proven efficacy, nor non-invasive evaluation methods of drug's impact on neurodegeneration in central nervous system.

The aims of our research were: 1. to investigate the ability to influence neurodegeneration in MS of Ethyl-methyl-hydroxypyridine succinate (EMHS) – drug with antioxidant and antihypoxant effect, approved in Russian Federation. 2. to educe the potential of Diffusion tensor MRI with tractography (DTI) as an objective evaluation method of treatments efficacy.

Methods: 51 RR and SP MS patients without signs of disease activity were treated with EMHS, and fractional anisotropy of corticospinal tracts (FA CST) was assessed before and after treatment course.

Results: Compared with 24 healthy volunteers, the patients had significantly lower FA CST. After the treatment, locomotive ability improved as well as FA CST increased, with lasting clinical effect.

Conclusion: The decrease of FA CST is reversible and measuring FA CST can be used as an objective method in evaluating the efficacy of therapy of neurodegeneration in MS patients. EMHS therapy can be considered as a potentially effective method to prevent progressing neurodegeneration in MS patients. However, further controlled clinical trials are necessary in order to prove this effect.

Disclosure: The work was performed as part of state order scientific research at IHB RAS 0133-2016-0005

EP3107

A retrospective comparison of Rituximab vs Cyclophosphamide in neuromyelitis optica spectrum disorders patients

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Background and aims: Neuromyelitis Optica Spectrum Disorders (NMOSD) is a severe demyelinating disease antibody-mediated with no approved treatment. Rituximab (RTX) has been proposed as a first-line therapy, but few comparative studies have been published so far. We retrospectively evaluated the effect of RTX treatment respect to cyclophosphamide (CFX) which is one of the main alternative therapy used in these patients.

Methods: Overall among the 70 NMOSD patients followed at our centre, 42 patients received at least one cycle of RTX and 25 patients received at least two cycles of CFX.

Results: No differences in disease severity and clinical characteristics between the two cohorts were observed (Table1). The median treatment duration was 33 and 11 months for the RTX and CFX group respectively. Overall the proportion of relapse free patients was significantly higher in the RTX group (57% vs 20% p<0.0001) (Fig1). The reduction of the mean ARR was significantly higher in the group of patients receiving RTX (81 vs 43% p< 0,05) (Fig2). In both groups the EDSS was stable or improved in the majority of patients (83% in the group treated with RTX and 72% in the group receiving CFX). Since fourteen patients were treated with RTX after the failure of CFX, subgroup analysis confirming the results were performed.

A. Relapse-free survival in overall cohorts

P <0.0001 by log-rank test

No. at Risk					
Rituximab group	42 (100%)	39 (90%)	34 (83%)	31 (79%)	24 (70%)
Cyclophosphamide group	25 (100%)	15 (60%)	10 (26%)	4 (21%)	2 (14%)
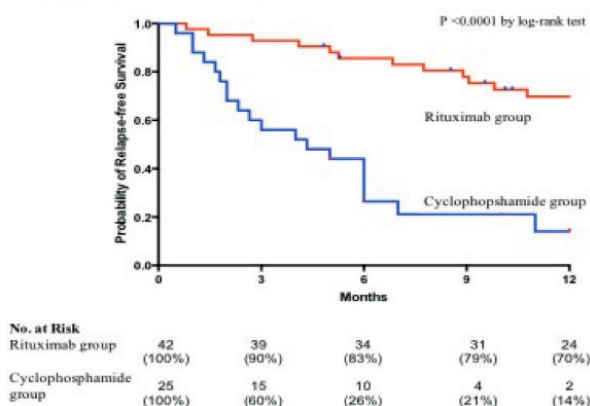
Figure1

Table 1: comparison of baseline characteristics between CFX population and RTX population.

	Study participants		
	Rituximab (n=42)	Cyclophosphamide (n=25)	P value
2006 diagnostic criteria	22/42 (52%)	12/ 25 (48%)	0.756
Age at disease onset (mean-SD)	39 (15)	39 (15)	0.921
Sex (F)	36/42 (86%)	20/25 (80%)	0.734
AQP4-IgG+	38/42 (90%)	20/25 (80%)	0.277
Disease duration pre RTX/CFX (median-range)	34m (0.5m-28y)	36m (1m-27y)	0.577
EDSS score before RTX/CFX (median-range)	4.00 (2-9)	5.00 (2-8)	0.138
ARR before RTX/CFX (mean-SD)	2.78 (2.7)	2.60 (2.4)	0.622
N° of relapses before RTX/CFX (median-range)	5.0 (1-18)	3.0 (1-17)	0.369
N° of relapses 2 years before RTX (median-range)	3.0 (1-7)	3.0 (1-5)	0.515
N° of therapies before RTX/CFX (mean-range)	1.2 (0-5)	0.6 (0-3)	**0.022**
Treatment naive patients	14/42 (33%)	16/25 (64%)	**0.022**

RTX, rituximab, CFX, Cyclophosphamide, AQP4, aquaporin 4; EDSS, Expanded Disability Status Scale; ARR, annualized relapsed rate; m, month; y, year; n°, number

Table1

A. ARR comparison pre- and post- RTX/CFX in whole cohort
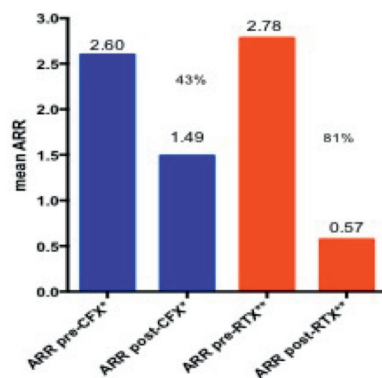
* measured on 21/25 patients
** measured on 38/42 patients

Figure2

Conclusion: Our study demonstrated a more efficacy of RTX in NMO patients respect to CFX. Even if our data have to be confirmed in larger study with a longer follow-up, our results justify an earlier use of RTX in clinical practice.
Disclosure: Nothing to disclose

EP3108

Early treatment is associated with a better long-term disability outcome in neuromyelitis optica spectrum disorders

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Background and aims: Neuromyelitis Optica (NMO) is a severe inflammatory disease of the CNS. We report the impact of an earlier treatment in clinical practice.
Methods: We included in our cohort only patients in which, at the end of a thorough investigation, other alternative diagnosis were excluded. Overall 70 patients reached a diagnosis of NMO. We evaluated how treatment approach changes overtime. We divided patients in "early treatment group" if the treatment was started after 1 or 2 relapses and "late-treatment group" if it started after more than 2 relapses.
Results: Overall the number of patients who received an "early treatment" was significantly higher for patients with a disease onset after 2007 (23% vs 50%, p<0.001). In order to test the beneficial effect of an earlier treatment, we excluded 20 patients because they reached a severe disability status within the second relapses. Overall 16 patients were treated "early" and 34 patients were treated "late". The proportion of patients who reached a severe disability was significantly higher in the "late treatment group" (59% vs 6%; p<0.05). The same results were observed evaluating the proportion of patients developing a permanent EDSS score of at least 6.0 (32% vs 0%; p<0.05) or a permanent severe ipovisus (32% vs 6%; p<0.05).
Conclusion: After the 2006 diagnostic criteria and the definition of NMO SD our treatment approach has significantly changed. An early treatment allowed a better outcome changing the natural history of the disease.
Disclosure: Nothing to disclose

EP3109

Link between overweight/obese in children and youngsters and the occurence of Multiple Sclerosis

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Background and aims: The prevalence of overweight/ obesity is a major problem in the world and the number of MS cases is increasing. This literature study examines the relationship between overweight/obesity in children and adolescents and occurrence of MS.

Methods: We performed a complete literature study resulting in 11 relevant original studies. The search database is primarily Pubmed using MeSH terms "Multiple Sclerosis", "Obesity" and "Overweight" and textwords not to restrict searches.

Results: All 11 relevant included studies show a link between overweight/obesity and the presence of MS among people below 20 years of age. The relation is especially true for young girls. There is a need for more and larger studies, and to investigate the molecular mechanisms that may link obesity and MS.

Conclusion: The literature study convincingly revealed a link between young overweight/obese and occurrence of MS, in particular for girls.

Disclosure: Nothing to disclose

EP3110

Extracellular vesicles in cerebrospinal fluid as possible biomarkers for multiple sclerosis

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Background and aims: Extracellular vesicles (EV) have been suggested as possible carriers of signals related to the pathogenic mechanisms in neurological diseases including multiple sclerosis (MS).

Methods: . We recruited individuals affected by MS at the Neurological Department of our University Hospital. CSF analysis was part of the diagnostic procedure for different neurological diseases. EV were isolated by differential ultracentrifugation of CSF samples, and characterized by flow cytometry. To identify EV origin a panel of fluorescent antibodies was used. CD19, CD200, CD4, CD193 and CD195, IB4. The same IgG labeled isotype of primary antibodies was used as negative control. Statistic analysis were carried out using t test or Mann–Whitney U test to compare subgroups of patients and Kolgomorov Smirnov test was used to compare three or more subgroups of patients.

Results: We analysed CSF by 60 individuals, 38 MS patients, and 22 with neurological disorders. We observed a higher EV concentration in PPMS and in CIS compared to the others. Among relapsing remitting patients EV were more represented during relapses ($p<0.05$). We detected more IB4 positive EV among PPMS and CIS compared to not inflammatory controls ($p< 0.05$). CD193/CD4+ EV were more expressed in RRMS compared to controls ($p<0.001$) while we did not detected CD19+ and CD200+ EV.

Conclusion: This study showed a higher EV concentration in MS patients particularly during relapses suggesting that EV concentration may be associated to disease activity. Our study support the hypothesis that EV analyses could represent promising ways to identify new markers underlying molecular mechanisms related to MS pathogenesis.

Disclosure: Dr Sabrina Realmuto received a post doctoral research fellowship, supported by Merck Serono.

EP3111

Impact of a patient support program (REBICARE) on interferon beta 1a adherence and clinical outcomes in relapse-remitting multiple sclerosis

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Background and aims: Poor treatment adherence is a challenge in multiple sclerosis (MS), affecting clinical outcomes and increasing disease burden. This study aimed to assess the impact of a nurse-led support program (REBICARE) on interferon beta 1a adherence among relapse-remitting MS (RRMS) patients in Portugal.

Methods: This was a multicentre, retrospective cohort study consisting of adult RRMS patients who used RebiSmart® for ≥24 months and started REBICARE between June 2010 and July 2013. The primary endpoint was the proportion of patients who adhered to interferon beta 1a at month 12 (adherence rate >75%). Adherence data was obtained from RebiSmart®. Clinical and safety outcomes were assessed through chart review.

Results: Overall, 103 patients were included (mean age 43 years; 69.9% female). Mean duration of MS was 6.6 years and median Expanded Disability Status Score (EDSS) at baseline was 1.75. At Month 12, 99.0% (95% Confidence Interval (CI): 97.1%-100.0%) of patients had an adherence rate >75%. At Month 24, the proportion of patients with adherence >75% was 98.1% (95% CI: 95.4%-100.0%). The proportion of relapse-free patients at Month 12 and 24 was 81.2% and 72.8%, respectively. The annualised relapse rate was 0.26 at Month 12 and 0.19 at Month 24. Four patients discontinued interferon beta 1a after 24 months. There were no serious adverse events.

Conclusion: This study showed the positive impact of REBICARE on adherence to interferon beta 1a in RRMS patients. This was associated with good clinical outcomes and no unexpected safety issues.

Disclosure: This study was funded by Merck SA.

EP3112

Adherence, cognition and behavioral outcomes in Multiple Sclerosis (MS) patients on dimethyl fumarate – 12-month results of a longitudinal registry study in German MS practices (TREAT)

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Background and aims: (1) to assess adherence, disability, cognition and patient-reported outcomes (PRO) in relapsing-remitting MS (RRMS) patients on dimethyl fumarate (DMF) (first-line treatment or switching from other disease-modifying therapies). (2) to identify relevant factors for non-adherence (discontinuation of study or DMF intake).

Methods: 12-month interim analysis (T12) of a 2-year prospective, multicenter, registry study with assessments at baseline/T0 and at T3, T6, T9, T12, T18 and T24 months. At T12, 721 RRMS patients on DMF (mean age 40.9 yr, 72.4% female, median EDSS 2.0) were analysed. Outcomes: Adherence (yes/no) and time to non-adherence, disability, cognition and PROs representing treatment/life satisfaction, depression, anxiety, fatigue, QoL, disease coping and personality. Descriptive analysis and regression models (logistic and Cox) were used to assess the factors associated with adherence.

Results: All clinical, behavioral and cognitive parameters remained stable during the first 12 months of DMF treatment. By T12, 26.8% (193/721) of patients were non-adherent. Women were more likely to be non-adherent (OR 1.9, HR1.8). The primary reason for non-adherence by T12 was physical complaints (13.0%; 94/721), mainly of gastrointestinal origin (7.9%; 57/721). Univariate (logistic/Cox) regression analyses (p<0.15) identified gender, premedication pause, pre-treatments (≥2), depression, QoL, life/treatment satisfaction, fatigue, anxiety and nonverbal memory as putative predictors of non-adherence.

Conclusion: (1) DMF prevents deterioration of clinical, cognitive and behavioral symptoms in RRMS.

(2) Behavioral factors, gender and pre-treatment issues may emerge as predictors of non-adherence.

(3) Multiple regression analyses considering collinearity after 2 years are warranted.

Disclosure: The study was funded by Biogen.

EP3113

MRI in transverse myelitis: Correlation with expanded disability status scale

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Background and aims: Magnetic resonance imaging is used as a diagnostic tool to detect spinal cord lesions.

The objective of this paper is to examine cross-sectional correlations of MR images with EDSS. Limited number of studies examined EDSS and MRI correlations in patients with Transverse Myelitis. MRI images can help predict recovery progress based on lesion characteristics.

Methods: We conducted a retrospective review of the last 42 monophasic TM admissions to the Johns Hopkins Hospital. Inclusion criteria included a single inflammatory attack localizing to the spinal cord presenting with a change in neurological examination and a new MRI lesion. Subjects were excluded if their TM was part of a recurring disease or if they tested positive for the NMO-IgG blood test. Extended Disability Status Scale (EDSS) score was calculated at baseline, at presentation, at discharge, and on follow-up. MR images were examined and broken down by Number of Vertebral Bodies Lesion Location Length of the lesion Results of the MRI were compared to the EDSS scores to evaluate outcome based on lesions characteristics.

Results: Of the 42 subjects enrolled, 37% with Long Lesion (more than 4 vertebral bodies) showed improvement by at least 1 point at one year follow up on EDSS exam. Whereas 19% with Short Lesion (3 or less vertebral bodies) show improvement from admission to one year follow up.

Conclusion: Longer lesion on MR images from admission to follow up resulted in better long term recovery outcome.

Disclosure: Nothing to disclose

EP3114

To and from multiple sclerosis: The diagnostic revision dilemma

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Background and aims: The diagnostic criteria for inflammatory demyelinating diseases (IDDs) of the central nervous system (CNS) evolved over the last years. The close follow-up and accurate multiple sclerosis (MS) diagnosis are key to optimal treatment.

Methods: The medical records of patients referred to our MS Clinic (n=635), between 2009 and 2016, were retrospectively reviewed to select those who had a diagnostic revision. Sixty-two patients were identified, 44 were misdiagnosed with MS; 18 had another diagnosis, later redefined as MS. Forty-four controls (with MS diagnosis), were matched to the 44 misdiagnosed cases and a statistical analysis was performed to determine predictors of misdiagnosis.

Results: The mean age of our population (n=44) was 51 ± 11; 77% were women. The mean duration of misdiagnosis was 13 years. Optic neuritis was the most frequent presenting symptom (25%), followed by spinal cord syndrome and nonspecific neurologic symptoms (20% each). The mean EDSS and MSSS was 1.3 (sd=1.9) and 1.8 (sd=2.9) respectively in the misdiagnosed group and 3.7 (sd=2.5) and 3.7 (sd=3) respectively in the control group. From all the variables analysed, the absence of CSF oligoclonal bands (OCB) and MRI findings (dissemination in time) were predictors of misdiagnosis (p<0.05). Conversely, an abnormal autoimmune study and the presenting symptom didn´t alter the possibility of a diagnostic error.

Conclusion: Our series underlines the need to continuously rethink an MS diagnosis and to thoughtfully use paraclinical tests (OCB and MRI) avoiding an unfounded diagnosis. The first event may not be atypical, as reported in other series.

Disclosure: Nothing to disclose

EP3115

Transcranial sonography and cognitive performance among patients with relapsing remitting multiple sclerosis

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Background and aims: Brain atrophy occurs early in multiple sclerosis. It is associated with cognitive impairment. Transcranial sonography of the brain parenchyma (TCS) can assess ventricular diameter non-invasively, as marker of brain atrphy.
We aimed to correlate cognitive performance among patients with relapsing-remitting multiple sclerosis (RRMS) to ventricular diameters, as a marker of brain atrophy using TCS of brain parenchyma.
Methods: Case-control study, conducted on 125 Egyptian subjects, including 54 multiple sclerosis patients with RRMS, 16 males (29.6%) & 38 females (70.4%), with mean age of 29.22 ± 8.15 SD, mean EDSS of 2.34 ± 1.12 SD & at least 9 years of education. Control group included 71 age, sex and education matched healthy volunteers. All participants were subjected to clinical assessment, cognitive evaluation using California verbal leaning & memory test-2nd edition CVLT-II), Symbol digit modality test (SDMT) & Controlled oral ward association test (COWAT). B-mode TCS of the brain parenchyma was used to evaluate ventricular diameters as parameters of brain atrophy.
Results: In comparison to the healthy control, patients with RRMS showed significantly wider ventricular diameters (p<0.001) denoting brain atrophy. Physical disability & cognitive performance correlated significantly with parameters of brain atrophy. Impairment in executive function is an early marker of CI in patients with RRMS, which was correlated with brain atrophy.
Conclusion: TCS for brain parenchyma is a valuable & easily applicable method in detecting brain atrophy which is correlated with their physical disability & cognitive performance.
Disclosure: Nothing to disclose

EP3116

Clinical features of pseudotumoral Multiple Sclerosis in a Tunisian cohort

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Background and aims: Multiple sclerosis (MS) presenting with pseudotumoral lesion (PTL) on MRI is a rare condition. We investigated the clinical presentations, radiological features and disability progression of PTMS in a North African population
Methods: Among the patients seen at our department (Razi hospital, Tunis) between 2005 and 2016, we identified cases of definite MS (McDonald 2010 criteria) showing a well-circumscribed T2 lesion with a diameter of>2 cm. A total of 231 MS records were analysed using the local prospective MS database. We classified the lesions according to the recently proposed morphologic classification and the contrast enhancement pattern.
Results: Twenty-two patients (9.5%) (18 females, 4 males), mean age of 35.6 years [14-59], showed PTL. PTL at the onset of the disease were observed in 54.5%. All patients had a relapsing-remitting form. Ten patients (47.6%) had a polysymptomatic presentation at the disease onset. All PTL were supratentorial. Median largest lesion size was 32.4 mm [21-68]. The morphology of the largest PTL was categorized as being either Balo-like (n=2), megacystic (n=1), infiltrative (n=11) or ring-like (n=8). The contrast enhancement pattern was nodular (n=2), complete ring (n=1), incomplete ring (n=6) and diffuse (n=2). MR spectroscopy performed in four patients, showed an inflammatory profile. Annualized relapse rate was 0.7 and the mean final EDSS was 2.64. The mean progression index and MSSS were respectively 0.37 and 3.64.
Conclusion: Our findings showed a high frequency and a rather mild disease progression of PT forms of MS in our North African population.
Disclosure: Nothing to disclose

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EP3117
Cancelled

EP3118
Correlation between optical coherence tomography measures and visual evoked potentials in familial and sporadic MS patients

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Background and aims: The aim of this study was to find a correlation between the retinal nerve fiber layer (RNFL) thickness and macular volume (MV) measured by spectral-domain OCT (SD-OCT) with visual evoked potentials (VEP) in familial (fMS) and sporadic (sMS) multiple sclerosis patients.

Methods: 30 RR MS patients (17 fMS and 13 sMS) were recruited in the study. Both MS groups were matched according to disability measured by EDSS, annual relapse rate and disease duration. All patients had SD- OCT examination (Spectralis, Heildelberg Engineering) and VEP. Total RNFL thickness, MV, latency and amplitude of VEP were assessed in right and left eyes and were expressed as a mean value for both eyes for each patients

Results: Mean RNFL thickness in fMS were lower but not significantly than in sMS (91.5 ± 10.4 vs 93.03 ± 14.8 p=0.1). Mean MV in fMS did not differ from sMS (8.5 ± 0.5 vs 8.62 ± 0.4 p=0.3). Mean VEP latency was slightly longer, but not significantly, in fMS compared to sMS (120.40 ± 18.9 vs 116.7 ± 10.6 p=0.1). We observed a trend of lower mean VEP amplitude in sMS compared to fMS (8.64 ± 4.15 vs 11.84 ± 5.09 p=0.06). In fMS, but not in sMS, we found a modest correlation between mean RNFL and VEP latency (r=-0.5, p=0.02). In fMS we have also found modest a correlation between mean MV and VEP latency (r=-0.4, p=0.04).

Conclusion: Our results suggest that in fMS there is stronger correlation between structural retinal changes measured by OCT and visual system function measured by VEPs than in sMS patients.

Disclosure: Nothing to disclose

EP3119
Russian cohort of patients with NMO spectrum disorders: 58 cases

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Background and aims: Antibodies to aquaporin-4 (AQP4-Ab) is a sensitive and highly specific serum marker of neuromyelitis optica (NMO) and NMO-spectrum disorders (NMOSD). The aim of our research was to analyze the characteristics of patients with NMOSD according to demographics, clinical symptoms and MRI findings and estimate frequency of AQP4-Ab in Russian group patients with NMOSD.

Methods: Serum samples from 58 patients with NMOSD were analyzed. We used cell-based assay for the detection of AQP4-Ab (Euroimmun).

Results: 58 patients (81% female) aged 16-65 years (mean age 40.2 years) were included in the study. AQP4-Ab were detectable in 86.7% patients with NMOSD. The mean age of onset of symptoms was 38.4 years. The mean time to diagnosis was 16.9 months (range: 1 month-5 years). In most patients, the onset symptoms were longitudinally extensive transverse myelitis (LETM) and optic neuritis (ON) (62% and 34%, respectively). In three cases, the disease manifested with area postrema syndrome. In total, during disease course 6 patients developed area postrema syndrome, 2 − acute brainstem syndrome, and 2− symptomatic cerebral syndrome. According to MRI, 83% of the 58 patients had LETM lesions and 14% had short transverse myelitis lesions extending fewer than three vertebral segments. Spinal cord lesions spanned 1-13 vertebral segments (mean 5.5). The cervical cord was involved in 30% of cases, thoracic cord – in 30%, both cervical and thoracic cord – in 40%. 19% of patients had brain lesions.

Conclusion: Our results confirm high clinical heterogeneity of NMOSD and specificity of AQP4-Ab as a marker of NMOSD.

Disclosure: Nothing to disclose

EP3120

Absolute lymphocyte counts in patients with relapsing multiple sclerosis (RMS) treated with cladribine tablets 3.5 mg/kg in the CLARITY and CLARITY Extension studies

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Background and aims: In CLARITY, the most commonly reported adverse event was lymphopenia, consistent with the mechanism of action for cladribine tablets (CT). We investigate the absolute lymphocyte count (ALC) in patients with RMS receiving 2 year's treatment with CT 3.5mg/kg (CT3.5).

Methods: Data from patients randomised to CT3.5 for 2 years in CLARITY/CLARITY Extension including time spent in the PREMIERE registry (N=685) were pooled to provide long-term follow-up data. Data from patients randomised to placebo in CLARITY and followed up in CLARITY Extension and PREMIERE are also reported (PBO;N=435).

Results: At baseline (start of CLARITY or CLARITY Extension), median ALC was 1.86×10^9/L for CT3.5 and 1.91×10^9/L for PBO (Table). During Year 1, ALC in CT3.5 reached a nadir at 9 weeks post-treatment (1.00×10^9/L;Figure). At the end of Year 1 (48 weeks), median ALC had increased to 1.21×10^9/L. During Year 2, ALC in CT3.5 reached a nadir 7 weeks after re-treatment (0.81×10^9/L), increasing to 1.03×10^9/L at the end of Year 2 (96 weeks). At the end of Years 3 and 4 (144 and 192 weeks), ALC in the CT3.5 group (with no further treatment) increased to 1.36×10^9/L and 1.40×10^9/L, respectively, reaching a final median ALC of 1.76×10^9/L after 6.5 years (312 weeks). In PBO patients, median ALC values were between 1.69×10^9/L and 1.95×10^9/L (Figure).

Figure 1

Conclusion: Rapid reductions in ALC after CT3.5 treatment in Years 1 and 2 were followed by gradual returns toward baseline. Median lymphocyte counts were within normal range beyond Year 2 (96 weeks) in all patients for whom follow-up data are available.

Table: Median absolute lymphocyte counts in patients treated with cladribine tablets 3.5 mg/kg for 2 years or placebo: pooled data from CLARITY, CLARITY Extension and PREMIERE

Time point	Placebo (N=435*)	Cladribine tablets 3.5 mg/kg (N=685*)
Baseline	1.91×10^9/L (1.54–2.32)	1.86×10^9/L (1.50–2.29)
Year 1 (48 weeks)	1.84×10^9/L (1.52–2.26)	1.21×10^9/L (0.95–1.50)
Year 2 (96 weeks)	1.90×10^9/L (1.50–2.27)	1.03×10^9/L (0.80–1.30)
Year 3 (144 weeks)	1.79×10^9/L (1.50–2.56)	1.36×10^9/L (1.02–1.65)
Year 4 (192 weeks)	1.83×10^9/L (1.28–2.01)	1.40×10^9/L (1.10–1.81)
Year 5 (240 weeks)	1.89×10^9/L (1.18–2.74)	1.50×10^9/L (1.10–1.81)
Year 6.5 (312 weeks)	1.70×10^9/L (1.30–2.00)	1.76×10^9/L (1.17–2.65)

Data are median (Q1–Q3).
*Patient numbers decreased over time and are reported in Figure.

Table 1

EP3121

3T FLAIR* MRI evaluation of three lesions for central vessel sign demonstrates specificity for multiple sclerosis

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Background and aims: Multiple sclerosis (MS) diagnosis remains challenging due to reliance on radiographic assessments of imperfect specificity. FLAIR* MRI studies have demonstrated that detection of a "central vessel sign" (CVS) in MS lesions differentiates MS from other disorders. These studies have primarily evaluated identification of central veins in all MRI lesions, a method impractical for clinical application. This study evaluated the specificity and sensitivity of a limited assessment of CVS in only three lesions for MS diagnosis.

Methods: 40 participants were studied: 10 with MS without additional comorbidities for white matter abnormalities; 10 with MS with additional comorbidities for white matter abnormalities; 10 with migraine, MRI white matter abnormalities, and no additional comorbidities for white matter abnormalities; and 10 erroneously diagnosed with MS. 3T MRIs, performed with gadopentetate dimeglumine, were de-identified and randomly ordered and then provided to three MS physicians at three different institutions blinded to diagnosis. Three ovoid lesions 3mm³ in at least one plane and restricted to the subcortical or deep white matter were first selected in each patient on FLAIR and subsequently evaluated for CVS using FLAIR*.

Results: Two MS participants were excluded from analysis due to inadequate candidate lesions. Using a threshold of 3/3 lesions with CVS as diagnostic of MS resulted in mean specificity and sensitivity across readers of 0.98 and 0.52 respectively. With a threshold of 2/3 lesions, the corresponding values were 0.95 and 0.81.

Conclusion: Evaluation of only three lesions for CVS, using FLAIR* MRI, demonstrated high specificity and good sensitivity for MS.

Disclosure: Supported by the University of Vermont Department of Neurological Sciences, University of Vermont Department of Radiology, and the University of Vermont MRI Center for Biomedical Imaging, and partially supported by the Intramural Research Program of National Institute of Neurological Disorders and Stroke.

EP3122

Selective and discontinuous reduction of B and T lymphocytes by cladribine tablets in patients with early and relapsing multiple sclerosis (ORACLE-MS, CLARITY and CLARITY Extension)

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Background and aims: Efficacy of cladribine tablets (CT) 3.5mg/kg has been demonstrated in patients with early MS (ORACLE-MS) and in patients with relapsing multiple sclerosis (RMS) in CLARITY/CLARITY Extension studies.

Methods: Longitudinal (48 weeks) evaluation of peripheral blood lymphocyte subtypes from patients treated with CT 3.5mg/kg (N=274) or placebo (N=140) was conducted. CLARITY Extension patients received placebo in CLARITY and switched to CT 3.5mg/kg in the Extension phase. Lymphocytes were measured at baseline, and Weeks 5, 13, 24 and 48. Changes in absolute counts and changes in relative proportion of the lymphocyte subtypes were evaluated.

Results: The baseline distributions of absolute lymphocyte counts (ALC) were similar across studies. Profiles of CD19+ B lymphocytes and CD4+ and CD8+ T lymphocytes were generally consistent across studies. The most rapid reduction in cell numbers occurred in the CD19+ B cell compartment (approximately 75% at Week 5 in each study). Nadir was reached at Week 13 with >80% reduction, and reconstitution towards baseline occurred from Week 24 to 48. CD4+ and CD8+ T cells were also markedly reduced in numbers, but to a lesser degree than CD19+ B cells (at most 55%; ORACLE-MS). Cladribine had a stronger suppressive effect on CD4+ than CD8+ T cells. There was only incomplete reconstitution of T cells at Week 48. Changes in relative proportion confirmed the effect on CD19+ B cells at ALC nadir.

Table Lymphocyte profiles up to Week 48 in CLARITY, CLARITY Extension and ORACLE			
Median percent change from baseline in absolute counts	CD19+ B cells Week 5/13/24/48	CD4+ T cells Week 5/13/24/48	CD8+ T cells Week 5/13/24/48
Placebo CLARITY (N=93)	1/2/3/4	-4/-1/0/-3	2/1/2/5
3.5 mg/kg CLARITY (N=97)	-75/-81/-64/-34	-23/-48/-46/-43	-21/-35/-29/-30
3.5 mg/kg CLARITY EXT (PPLI) ([N=136)	-74/-84/-67/-32	-24/-50/-49/-43	-20/-29/-36/-33
Placebo ORACLE (N=47)	5/0/17/19	5/5/10/15	14/6/6/-3
3.5 mg/kg ORACLE (N=41)	-75/-82/-61/-34	-23/-55/-53/-51	-17/-44/-47/-48

Table 1

Figure. Percentage change from baseline in lymphocyte subtypes at nadir and at Week 48 in 1) the CLARITY/CLARITY Extension studies and 2) the ORACLE study
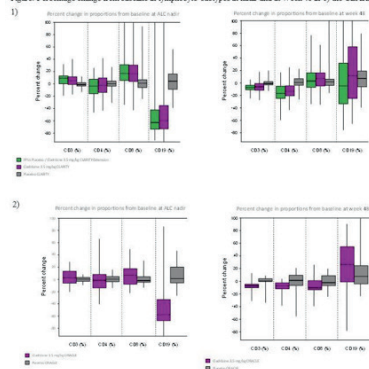
Figure 1

Conclusion: CT3.5 mg/kg achieved an early and discontinuous reduction of peripheral blood B cells with a rapid reconstitution to baseline, and a moderate reduction in T cell counts.

Disclosure: This study was funded by Merck KGaA, Darmstadt, Germany. Medical writing assistance was provided by inScience Communications, Springer Healthcare, Chester, UK, and was funded by Merck KGaA, Darmstadt, Germany.

EP3123

Levels of serum anti-Müllerian hormone in women with early stage of relapsing-remitting multiple sclerosis

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Background and aims: Multiple sclerosis (MS) is a neurological disease mostly affecting women of childbearing age. Recent studies suggest that MS may have a negative impact on fertility. Decreased ovarian reserve is supposed to be one of the most important factors for fertility impairment. It is not known if ovarian decline contributes to accumulation of disability in women with MS when evaluated using EDSS. Anti-Mullerian hormone (AMH) represents a measure of ovarian reserve unrelated to the menstrual cycle. The purpose of this study was to determine AMH levels in females with relapsing-remitting MS (RRMS) in comparison with healthy volunteers.

Methods: A total of 104 reproductive-age females (mean age 34.1±6.1, median EDSS 2.5) with RRMS and 77 age matched healthy controls (mean age 32.1±5.7) were included. An enzymatically amplified two-site immunoassay was used to measure serum AMH level.

Results: Mean AMH levels were similar in females with RRMS (2.78 ng/ml) and healthy controls (3.11 ng/ml) (p=0.31). However, on individual level, 9 MS patients (8.6%) showed very low AMH values (<0.4 ng/ml) compared 2 healthy controls (3%) (p<0.01). AMH levels were not associated with EDSS values (Pearson coefficient 0.23, p=0.05).

Conclusion: On the group level, no reduction of follicular reserve was found in women with MS. On individual level, however, higher proportion of women with very low AMH values was found in MS group comparing to healthy controls. These results suggest possible negative impact of MS disease on fertility of some of the patients.

Disclosure: Nothing to disclose

EP3124

Free radical pathology in early progression of multiple sclerosis

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Background and aims: Several factors can compromise the endogens protective system of organism and accelerate the induction of free radicals that may influence the course of MS.

Study aimed to investigate the role of several possible risk factors in secondary progression of MS.

Methods: We investigated smoking, dietary patterns, alcohol intake, severe and chronic stress in 60 secondary progressive MS (SPMS) patients, 33 (first group) from refuges, 27 from general population (second group). Age at disease onset, disease duration, number of relapses, length of period until the secondary progression of disease and the Kurtzke Expanded Disability Status Scale (EDSS) scores were collected. Control comprised 15 healthy volunteers. Brain was visualized by Magnetic Resonance Tomography (MRT-1.5-Tesla). Mood examined by Beck Depression Inventory (BDI-II). Blood free radicals detected by Electron Paramagnetic Resonance Method (EPR). Statistics was performed by SPSS-11.0

Results: First group developed SPMS in a shorter period compared to second group (7.2± 2.1 versus 16.4±3.8, p<0.05). Multiple logistic regression found the significance of smoking and depression for development of SPMS (p<0.05). Depression was found in 85% of first - and in 23% of second group (BDI> 9/10). Lypoperoxyradical (LOO-) and superoxide anion (O2-) were increased in first group as compared to second group and control. Positive correlation was established between BDI index and LOO- and O2- data (r=+0.33 and r=+0.19, p<0.05)

Conclusion: Smoking and depression due to chronic social stress may contribute to the promotion of free radical pathology in MS and thus, can stimulate the neurodegeneration.

Disclosure: Nothing to disclose

EP3125

The NLRP1 and NLRP3 inflammasomes are activated in multiple sclerosis and clinically isolated syndrome

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Background and aims: Inflammasome is a multiprotein oligomer expressed in myeloid cells and involved in inflammatory processes. In this study, we aimed to analyze the value of serum and cerebrospinal fluid (CSF) levels of NLRP1 and NLRP3 inflammasomes as predictors of conversion to multiple sclerosis (MS).

Methods: A total of 23 relapsing remitting MS (RRMS) patients, 18 clinically isolated syndrome (CIS) patients and 30 healthy controls were recruited for this study. Patients were in remission and were not under immunosuppressive treatment during serum and CSF sampling. Disease durations, EDSS scores, relapse numbers and oligoclonal band (OCB) status of all patients were recorded. Serum and CSF levels of NLRP1 and NLRP3 were measured using ELISA.

Results: While both RRMS and CIS patients had significantly higher serum and CSF levels of NLRP1 and NLRP3 than healthy controls, there were no significant differences between MS/CIS patients and healthy controls. Moreover, CSF but not serum levels of OCB positive patients were significantly higher than those of the OCB negative patients. There were no correlations between NLRP1/NLRP3 levels and clinical-demographic features of MS patients.

Conclusion: Inflammasome complex appears to be activated as early as during the first MS attack. However, levels of NLRP1 and NLRP3 are not altered in a time- or disability-dependent manner and thus cannot be used as indicators of MS conversion or as a prognostic biomarker. Increased CSF NLRP1/NLRP3 levels of OCB positive patients might indicate enhanced blood-brain barrier transport of myeloid cells in these patients.

Disclosure: Nothing to disclose

EP3126

Prognostic value of adipokines in multiple sclerosis

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Background and aims: Adipokines are known to be involved in numerous inflammatory diseases. This study aimed to analyze the value of serum adipokine levels as biomarkers in determining the clinical progression of multiple sclerosis (MS).

Methods: A total of 50 MS patients and 40 healthy individuals were recruited for this study. Clinical course of MS patients was classified as benign (>10 years of disease duration and £3 EDSS score) and classical (>10 years of disease duration and >3 EDSS score). Disease duration, annual relapse rate, EDSS and attack types of MS patients were recorded. Levels of serum adipokines and adipocyte-derived cytokines were measured using ELISA.

Results: Serum adiponectin, monocyte chemotactic protein 1 (MCP-1), TNF-a and IL-6 levels were significantly higher in classical MS patients than benign MS patients and healthy controls. There were no significant differences between levels of leptin, resistin, IL-1b and IL-8 among groups. Adiponectin, MCP-1 and TNF-a levels were directly correlated with EDSS scores. Notably, MS patients with an initial attack of optic neuritis displayed significantly lower EDSS scores, adiponectin, MCP-1 and TNF-a levels than other MS patients. There was no correlation between adipokine levels and other clinical-demographic features.

Conclusion: Adipokines appear to be involved in clinical progression of MS and thus adiponectin, MCP-1 and TNF-a might potentially serve as prognostic biomarkers in MS. Our results confirm previous studies which have claimed that MS initiating with optic neuritis has a relatively more benign course.

Disclosure: Nothing to disclose

EP3127

The effect of delayed-release dimethyl fumarate on lymphocyte subsets and immunoglobulins in patients with relapsing-remitting multiple sclerosis: Interim results of an open-label phase 3 study

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Background and aims: Delayed-release dimethyl fumarate (DMF, also known as gastro-resistant DMF) is a twice-daily (BID) oral medication approved for the treatment of relapsing-remitting multiple sclerosis (RRMS). In an integrated analysis of the DMF pivotal trials, the mean absolute lymphocyte count (ALC) decreased by ~30% in the first year of treatment and then stabilized, remaining above the lower limit of normal. This ongoing study (NCT02525874) evaluates the effect of DMF on lymphocyte subset counts and immunoglobulins during the first year of treatment in patients with RRMS.

Methods: This ongoing, open-label, multicenter, phase 3 study enrolled and treated (DMF, 240 mg BID) 218 patients diagnosed with RRMS aged 18-65 years. Blood samples were collected at screening, day 1, and at weeks 4, 8, 12, 24, 36, and 48. Changes in lymphocyte subsets were evaluated using a comprehensive panel of cell surface markers and intracellular cytokines by flow cytometry.

Results: Of the 218 enrolled patients, 163 patients had ≥6 months follow-up or had discontinued the study earlier and were included in this interim analysis. Detailed phenotypic characterizations of CD4+, CD8+, B, and natural killer cell subsets, changes in ALCs, and incidence of adverse events will be presented.

Conclusion: Interim data from this study will provide further understanding of how DMF influences immune cell subsets in the first 6 months of treatment and how those changes correlate with changes in ALCs.

Disclosure: CVH, DM, CP, LY, SL, and SIS are full-time employees of and hold stock/stock options in Biogen. SR performed the majority of the work while an employee of Biogen, Cambridge, MA.

EP3128

Durable clinical and MRI efficacy of Alemtuzumab over 6 years in CARE-MS I patients with active RRMS with relapse between courses 1 and 2

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Background and aims: Alemtuzumab 12 mg/day (baseline: 5 days; 12 months later: 3 days) improved 2-year outcomes versus SC IFNB-1a in treatment-naive patients with active relapsing-remitting MS (RRMS) (CARE-MS I; NCT00530348), with durable efficacy through 6 years (NCT00930553). 85% of alemtuzumab-treated patients were relapse-free between Courses 1–2. We evaluated 6-year efficacy in patients who relapsed in this interval.

Methods: Assessments: annualised relapse rate (ARR); freedom from 6-month confirmed disability worsening (CDW), MRI disease activity (gadolinium [Gd]-enhancing T1 and new/enlarging T2 lesions), or new T1 hypointense lesions; brain volume loss (BVL).

Results: 56/376 (15%) alemtuzumab-treated patients relapsed between Courses 1–2; 52/56 (93%) enrolled in extension; 45/52 (87%) remained through Year 6. In patients who relapsed, ARR in Year 1 (1.3) declined in the year after Course 2 (0.3); 27% relapsed in Year 2. ARR remained 0.3–0.5 over Years 3–6. 60% of patients remained 6-month CDW-free through Year 6. Most were free of Gd-enhancing T1 lesions (84%), new/enlarging T2 lesions (71%), MRI disease activity (69%), and new T1 hypointense lesions (90%) in Year 6. Median percent yearly BVL declined over time: Years 1–6: –0.67%, –0.17%, –0.20%, –0.11%, –0.21%, –0.24%. 46% of patients received ≥1 alemtuzumab retreatment.

Conclusion: Outcomes during Year 1 of alemtuzumab do not predict longer-term response. Patients who relapsed in Year 1 improved markedly in subsequent years. These data support administering alemtuzumab according to approved labeling (2 courses) for optimal and durable clinical/MRI benefits in the small population of patients experiencing relapse between Courses 1–2.

Disclosure: Sanofi and Bayer HealthCare Pharmaceuticals.

EP3129

Real world studies of glatiramer acetate: Differences of MS patient profiles between 2 non-interventional studies COPTIVITY and QualiCOP

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Background and aims: The MS treatment landscape has changed rapidly. With the approval of DMTs new first and second-line treatment options for RRMS became available. QualiCOP and COPTIVITY are two independent non-interventional studies (NIS) with glatiramer acetate (GA), representing an area before and after oral DMTs were approved. We aimed to determine if prior treatment with oral DMTs impact the treatment algorithm with GA and patients' treatment decision.

Methods: QualiCOP (n=754) was a prospective, observational, open-label NIS (recruitment Aug. 2007 - May 2009). COPTIVITY (n=969, interims analysis) is an ongoing two-year, multicentre, open-label NIS (recruitment Dec. 2014 - Mar. 2016).

Results: Baseline characteristics were comparable (mean age 39.4 vs. 38.6 years, 78.9% vs. 73.0% female, stable MS 39.5% vs. 34.0%). In COPTIVITY, patients were characterized by shorter disease duration (3.9 vs. 4.7 years), lower relapse rate (1.2 vs. 1.8 relapses), and a lower mean EDSS (2.0 vs. 2.3) compared to QualiCOP patients. In COPTIVITY, 15.1% of patients switched from a variety of DMTs (e.g. 7.5% fingolimod, 9% teriflunomide, 33.1% dimethylfumarate, and 66.9% IFN-beta drugs) compared to QualiCOP (31% IFN-beta drugs). Increasingly more patients using the new three-times-weekly 40 mg GA formulation.

Conclusion: Pre-treated patients in the recent COPTIVITY had undergone a greater variety of MS treatment before GA, reflecting the approval of new DMTs. Even though new oral DMTs are available these results emphasize the importance of GA as a platform therapy in RRMS.

Disclosure: This study is funded by TEVA GmbH Germany, Berlin.

Neurogenetics

EP3130

Digenic causes to Charcot-Marie-Tooth disease in two families

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Background and aims: Next-generation sequencing (NGS) or massively parallel sequencing detects the precise order of nucleotides within a DNA molecule. NGS is more effective than traditional sequencing methods, such as Sanger sequencing, when several genes are involved. Targeted NGS is starting to be used in diagnostics for disorders caused by several genes. About 100 genes may cause hereditary neuropathies. Charcot-Marie-Tooth disease (CMT) is the most frequent hereditary neuropathy with a prevalence of 40-80 per 100,000 in Norway. It is probable that some patients has mutations in more than one gene causing the phenotype.

Methods: CMT patients from two families were investigated for PMP22 duplications and point mutations in CMT genes with the methods Multiplex Ligation-dependent Probe Amplification (MLPA) and NGS.

Results: We identified a digenic cause to CMT in the two families, i.e. in the first family a duplication of PMP22 together with a compound heterozygous SH3TC2 mutation and in the other family point mutations in the genes PMP22 and NEFL.

Conclusion: If the phenotype is atypical or more severe than expected may be wortwhile to investigate selected CMT patients for more than one genetic cause to their phenotype. The pedigree may sometimes indicate a digenic cause to the overall phenotype of CMT patients. Digenic causes to CMT may be more frequent than previously anticipated – 1-2%.

Disclosure: Nothing to disclose

EP3131

The different faces of the p.A53T alpha-synuclein mutation: A screening of Greek patients with parkinsonism and/or dementia

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Background and aims: The p.A53T mutation in the alpha-synuclein (SNCA) gene is a rare cause of autosomal dominant Parkinson's disease (PD). Although generally rare, it is particularly common in the Greek population due to a founder effect. A53T-positive PD patients often develop dementia during disease course and may very rarely present with dementia.

Methods: We screened for the p. A53T SNCA mutation a total of 347 cases of Greek origin with parkinsonism and/or dementia, collected over 15 years at the Neurogenetics Unit, Eginition Hospital, University of Athens. Cases were classified into: "pure parkinsonism" (PD, atypical parkinsonism), "pure dementia" (frontotemporal dementia, Alzheimer disease, "other") and "parkinsonism plus dementia" (frontotemporal dementia with parkinsonism, PD dementia, Lewy Body disease, atypical parkinsonism).

Results: In total, 4 p.A53T SNCA mutation carriers were identified. All had autosomal dominant family history and early onset. Screening of the "pure parkinsonism" category (137 cases) revealed 2 cases with typical PD. The other two mutation carriers were identified in the "parkinsonism plus dementia" category (89 cases). One had a diagnosis of PD dementia and the other of behavioral variant frontotemporal dementia. Screening of patients with "pure dementia" (121 cases) failed to identify any further A53T-positive cases.

Conclusion: Our results confirm that the p.A53T SNCA mutation is relatively common in Greek patients with PD or PD plus dementia, particularly in cases with early onset and autosomal dominant family history. However, routine screening of patients with "pure dementia" is unlikely to be clinically useful even in the Greek population.

Disclosure: Nothing to disclose

EP3132

Gordon Holmes syndrome, one of the many faces of PNPLA6

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Background and aims: The association of cerebellar ataxia and hypogonadism was first described by Holmes in 1907. Recently, PNPLA6-spectrum of neurodegenerative disorders has been described, with a clinical phenotype ranging from pure cerebellar ataxia to Oliver-McFarlane syndrome. Although many cases are of familiar aggregation, often with consanguinity history, sporadic cases have been reported.

Methods: A clinical case and review of literature.

Results: A 66-year-old male presented to our clinic with progressive gait impairment, which started when he was 16. Due to his past heavy drinking, his symptoms were initially thought to be of toxic etiology. His past medical history also included delayed puberty due to hypogonadotropic hypogonadism and diabetes mellitus type 2. He had no history of consanguinity nor significant family history. On physical examination, he presented gynecoid appearance with gynecomastia and on neurological examination he had moderate dysarthria, multidirectional nystagmus, axial and peripheral ataxia and unstable gait. He had no retinopathy. His diagnostic work-up, which included nutritional, paraneoplastic and microbiologic studies, was normal and the brain MRI showed marked cerebellar atrophy. Due to the clinical suspected Gordon Holmes' syndrome a search for mutations in RNF216 gene was performed with negative results. Afterwards, biallelic mutations to the PNPLA6 gene were found, confirming the diagnosis.

Conclusion: Several confounders can delay the diagnosis of cerebellar ataxias presenting in adulthood, and a progressive ataxia after removal of aggressors should always lead to the search of another etiology. The coexistence of two of ataxia, hypogonadism, motor neuron disease or chorioretinal dystrophy should raise suspicion of a PNPLA6 spectrum disorder.

Disclosure: Nothing to disclose

EP3133

Primary appearing tremor-dystonia, due to homozygous mutation p.V2716A in ATM gene in Bulgarian muslims

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Background and aims: Ataxia-telangiectasia (A-T) is a rare autosomal recessive disorder due to mutations in the ATM-gene. The classical phenotype is characterized by progressive childhood-onset cerebellar ataxia, oculomotor apraxia, telangiectasias of the conjunctivae, hypersensitivity to ionizing radiation, and immunodeficiency. Recently some ATM mutations were found to manifest as generalized or focal dystonia without any of the classical signs of A-T.

The aim of the study is to evaluate the clinical features in a group of 14 Bulgarian patients, belonging to a religious minority, homozygous forV2716A in ATM-gene.

Methods: The study encompassed 14 patients, belonging to two big Bulgarian muslim pedigrees, with data of more than 25 affected from four consequent generations. All of them underwent neurological evaluation. Brain MRI was performed in 7, PET-CT- in 1, neuroophthalmological assessment- in 9. Exome sequencing was performed in 8- 5 affected and 3 healthy relatives.

Results: The age at onset in our group varies between 14 days and 20 years. The main symptoms are dystonic and choreic hyperkinesias, more prominent in the upper limbs and the neck, dystonic disarthria and dysphagia. The clinical course was very slowly progressive. Brain imaging was normal. In all the affected a homozygous mutation p.V2716A in ATM gene was found.

Conclusion: Clinical features, due to mutations in ATM gene can be very broad. The disease may appear as dystonia, especially of early onset, without frank cerebellar involvement and also normal cerebral imaging. A-T should be considered in all patients with unexplained, even mild movement disorders.

Disclosure: Nothing to disclose

EP3134

Cancelled

EP3135

Early onset autonomic dysfunction with both sympathetic and parasympathetic involvement in Charcot-Marie-Tooth Disease type 2J

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Background and aims: Charcot-Marie-Tooth type 2J (CMT2J) is an autosomal dominantly inherited axonal sensorimotor polyneuropathy caused by a few missense mutations in the MPZ gene. It is characterized by pupillary abnormalities, hearing loss, late onset sensorimotor polyneuropathy and parasympathetic autonomic dysfunction.
Methods: A Thr124Met MPZ mutation was found in a 52-year-old-male and his daughter. They presented at respectively 30 and 20 years of age with problems emptying the bladder and the daughter needed chronic intermittent catheterization at 24 years of age. The index patient underwent prostate resection and later developed erectile dysfunction. At 45 years of age he had onset of symptoms of sensory and motor symptoms in his feet. The patients underwent autonomic testing, nerve conduction studies (NCS), urodynamics in addition to neurological examination at 56 and 26 years of age, respectively.
Results: Clinical examination revealed tonic pupils in the daughter and clinical signs of CMT in the index patient. Autonomic testing of the daughter showed primarily sympathetic involvement, with an abnormal fall in pulse amplitude during Valsalva's maneuver and an abnormal heart rate increase during the head-up tilt, but minor abnormalities in the index patient. NCS showed an axonal sensorymotor polyneuropathy in the index patient and normal results in the daughter. Urodynamics showed hypotonic bladders and lack of sphincter relaxation.
Conclusion: We report clinical and paraclinical data on two patients with CMT2J. The data show a sympathetic dysfunction in CMT2J in addition to a parasympathetic involvement as previously reported. Autonomic symptoms precede classic polyneuropathy symptoms and can result in unnecessary surgery.
Disclosure: Nothing to disclose

EP3136

Neurological phenotype of Ataxia-Pancytopenia Syndrome caused by SAMD9L mutations in a Swedish family

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Background and aims: Missense mutations in SAMD9L have recently been identified as the cause of autosomal dominant Ataxia-pancytopenia syndrome, with neurological features, hematologic cytopenias and markedly increased leukaemia risk. We recently reported a Swedish family with this syndrome and a SAMD9L c.2956C>T (p.Arg986Cys) mutation (Tesi et al. Blood 2017).
Methods: We expanded the pedigree, examined additional family members, reviewed charts and radiological examinations, compiling data on a total of 21 members. Genetic analysis was performed on buccal swabs.
Results: Six members of the family had neurological signs or symptoms. Age at onset varied from 6 to 15 years. The initial symptom was gait imbalance in all affected individuals. Symptoms were slowly progressive but remained generally mild. Two individuals had dysmetria and only one dysarthria. Additional signs were horizontal and vertical nystagmus, hyperreflexia and foot clonus. One family member, who received matched unrelated HSC transplantation at age 4.5 years because of myelodysplastic syndrome, displayed marked neurological deficit after cytostatic treatment. Neuroimaging revealed cerebellar atrophy and supratentorial white matter changes in all patients examined. Seven of 13 family members tested carried the SAMD9L c.2956C>T mutation. Three mutation carriers have not been examined yet. For five mutation carriers a history of cytopenia was confirmed, but it may have been intermittent and mild.
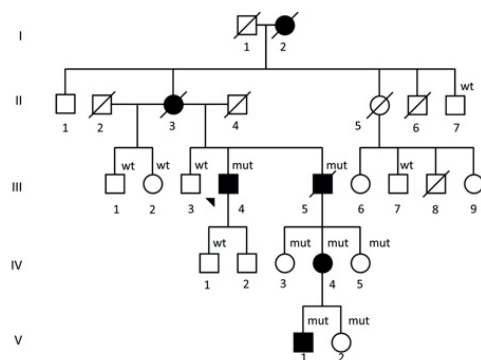
Family tree

Neurologic evaluation of patients with germline SAMD9L c.2956C>T mutations

Conclusion: The neurological phenotype of patients with SAMD9L mutation includes slowly progressive gait imbalance and nystagmus which often remain disproportionally mild compared to marked cerebellar atrophy on imaging. Testing for SAMD9L mutations should be performed on non-hematopoietic tissue due to mosaicism in blood.

Disclosure: Institutional support for this research has been granted by ALF, MultiPark, Lund University and Skåne University Hospital, Sweden.

EP3137
Cancelled

EP3138
Cancelled

EP3139

The AARS-related neuropathy in four Czech patients – clinical and electrophysiological study

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Background and aims: Mutations in genes encoding aminoacyl-tRNA synthetases(ARS) cause several forms of CMT2 with different clinical and electrophysiological features. In four CMT2 patients (3M + 1F) from one large family we found causative mutation c.986G>A (p. Arg329His) in heterozygous state in the AARS gene (alanyl t-RNA synthetase) (AARS).

Methods: The onset of disease ranged between age 10-18y, first symptoms were symmetrical weakness and atrophies of peroneal and calf muscles. Neurological exams were performed at different ages of patients (35F, 40M, 52M, 59M). We found mild pes cavus, severe peroneal and calf muscle atrophies drop and steppage gait. The sensory symptoms included deficit of vibration and touch at LL, except of a 35y old female.

Results: EDX studies confirmed intermediate conduction abnormalities on motor fibers at UL and no responses at LL. Sensory fibers of median nerve were excitable with low amplitude of SNAP, conduction slowing at wrist and no responses of sural nerve in all patiens. The conduction studies confirmed mixed demyelinating and axonal lesion in all patients.

Conclusion: The phenotype of our patients was similar. The clinical neuropathic symptoms at the onset were mostly motor and less sensory in symmetric distribution at LL and mimic distal motor neuropathy. The paraparesis of LL started during second decade and has a relatively slow progression, two patients were able to walk without support at age over fifty. Electrophysiological studies confirmed a mixed demyelinating and axonal lesion of motor and sensory nerve fibers at the onset of the disease and distinguish CMT2N from distal motor neuropathy.

Disclosure: Nothing to disclose

EP3140

APOE haplotypes modify the associations of the ACE insertion/deletion polymorphism with neuropsychiatric symptoms in dementia due to Alzheimer's disease

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Background and aims: Associations of the insertion allele of an Alu repeat insertion/deletion (I/D) polymorphism in intron 16 of ACE with dementia due to Alzheimer's disease (AD) are not consistent in all studies. We sought to examine associations of APOE haplotypes and the ACE I/D polymorphism with neuropsychiatric symptoms according to each stage of AD.

Methods: In this cross-sectional study, participants with AD according to National Institute on Aging – Alzheimer's Association criteria were screened with the Clinical Dementia Rating and the 10-item Neuropsychiatric Inventory. Genotyping was undertaken with TaqMan® Real-Time Polymerase Chain Reactions for rs7412 and rs429358 (APOE haplotypes), and with Polymerase Chain Reactions for the ACE I/D polymorphism. After stratification by APOE-ε4 carrier status, the ACE I/D polymorphism was correlated with neuropsychiatric symptom scores in each dementia stage by way of a linear regression model with and without adjustment for therapy with psychotropic drugs and angiotensin-converting enzyme inhibitors, significance at $\rho<0.05$.

Results: Among 207 consecutive outpatients, 108 (52.2%) were APOE-ε4 carriers and 99 (47.8%) were APOE-ε4 non-carriers; mean age at dementia onset was 73.27±6.7 years-old for 140 females (67.6%) and 67 males (32.4%). The ACE I/D polymorphism was in Hardy-Weinberg equilibrium ($\rho=0.37$). Considering mildly impaired patients, the insertion allele of ACE was cumulatively associated with agitation only for APOE-ε4 carriers in the unadjusted model ($\beta=1.710;\rho=0.042$), and with apathy only for APOE-ε4 non-carriers both in the unadjusted ($\beta=1.682;\rho=0.036$) and the adjusted ($\beta=1.759;\rho=0.035$) models.

Conclusion: Associations of the insertion allele of ACE with neuropsychiatric symptoms of mildly impaired patients with AD depend upon APOE haplotypes.

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EP3141

Clinical exome sequencing in muscular disorders

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Background and aims: Muscular disorders are characterized by clinical and genetic heterogeneity. There is no widespread consensus for clinical indications for next generations sequencing (NGS) nor standardized NGS methodological approaches. Our aim is to present the experience of systematic use of NGS in clinical diagnostics of muscular disorders.

Methods: Clinical indication for NGS testing in the period from 2014-2016 was a high risk for inherited muscular disorder, based on the history of disease, symptoms and signs as well as positive and negative characteristics of clinical diagnostic workup. NGS was performed using TruSight One (4813 genes) or whole exomes sequencing approaches followed by sequencing on HiSeq 2500 or MySeq platforms (Illumina). Interpretation of variants was done using in-house developed bioinformatic protocol.

Results: 50 patients with muscular disorders were offered NGS including 12 (24%) pediatric cases. 20% of patients had family history of disease. The largest group (52%) were patients with unspecific diagnosis of muscular disease, followed by congenital myopathies (26%), limb girdle muscular dystrophies and (12%), congenital myotonias (6%) and dystrophies (4%). Diagnostic yield was 62%; a high diagnostic rate of 69% was present in patients with unspecific diagnosis and 84% among pediatric patients. Average time to diagnosis was 17.7 years. We found pathologic gene variants in 21 genes and one pathologic CNV.

Conclusion: NGS proved to be a highly efficient diagnostic tool, especially in pediatric period and in patients with unspecific diagnosis of a muscular disorder.

Disclosure: Nothing to disclose

EP3142

A family with autosomal dominant late onset-Alexander disease, due to c.209G>A p.R70Q mutation in GFAP

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Background and aims: Alexander disease (AD) is a rare neurodegenerative disorder caused by mutations in the gene encoding glial fibrillary acidic protein (GFAP). AD is classified into three main forms: Infantile, juvenile and adult. Adult onset (AOAD) commonly presents with bulbar and pseudobulbar symptoms. Spastic paraparesis, urinary disturbances, ataxia, palatal myoclonus and dysautonomia have also been reported. We describe a family with four affected from three generations.

Methods: Whole exome sequencing (WES) was conducted on 10 family members. They underwent physical, neurological, neuropsychological examinations, cerebral magnetic resonance imaging (MRI), electromyography (EMG) and evoked potential (EP) testing.

Results: WES detected a missense heterozygous mutation (c.209G>A p.R70Q) in exon 1 of the GFAP gene in 5 individuals, four of whom were symptomatic and one still asymptomatic at age 28. The clinical onset varied from 15-25 years, presenting with ataxia, dysphagia, dysarthria, dysphonia, orofacial dystonia, lower spastic paraparesis, disturbed proprioception and paresthesia in the lower limbs, urinary incontinency and mild to severe cognitive decline. Two affected from the first and second generations died at ages 50 and 46 respectively. Brain and spinal cord MRI revealed confluent, symmetric white matter abnormalities in all cerebral lobes and atrophy of the cerebellum, medulla and upper cervical spinal cord. EMG was consistent with axonal polyneuropathy in the lower limbs; also EPs were abnormal.

Conclusion: We observe a wide interfamilial phenotypical variability in relation to disease onset and clinical severity, with no correlation between the two. The extensively distributed leucoencephalopathy and axonal polyneuropathy observed in our family are atypical to AOAD.

Disclosure: Nothing to disclose

EP3143

Association of BDNF Val66Met polymorphic variant with cognitive impairment in Parkinson's disease

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Background and aims: An association between Val66Met brain-derived neurotrophic factor (BDNF) polymorphism and Parkinson's disease (PD) has been disproved in the large meta-analysis of 15 studies. However, Val66Met BDNF polymorphism, resulting in abnormal intracellular distribution and low activity-dependent secretion of BDNF, has been associated with cognitive dysfunctions in PD patients in several studies. Our aim is to evaluate the impact of Val66Met BDNF polymorphic variant on cognitive functions in PD patients.

Methods: 200 patients and 150 ethnically, age and sex-matched controls without neurological disorders were included in the study. Genotyping was carried out by tetra-primer amplified refractory mutation system (ARMS)-PCR. We performed the cognitive examination in 105 patients with PD (62 PD patients with cognitive impairment and 43 without cognitive impairment). Cognitive functions were tested using mini-mental state examination (MMSE), Montreal Cognitive Assessment (MoCA), verbal fluency test, and clock-drawing test.

Table 1. Neuropsychological assessment of PD patients.

Test	66Met *BDNF* carriers*	Val/Val *BDNF* carriers*
MMSE	27 (15-30)	28 (24-30)
MoCA	24 (13-28)	25,5 (17-29)
Verbal fluency test	9 (2-10)	9 (5-10)
Clock drawing test	12 (5-18)	11 (5-21)

*Median (min-max)

Table1.

Results: Here we examined whether polymorphic variant Val66Met are relevant to idiopathic PD in Russia. There were no differences in genotypes distribution and alleles frequencies between PD patients and controls. Furthermore, there was no difference between Met66 allele frequency in PD patients with and without cognitive impairment. Cognitive functions in BDNF 66Met allele carriers were compared to carriers of Val/Val genotype. MMSE score in Met66 carriers has no difference compare to Val/Val carriers, p=0,241. The same results were obtained using MoCa, verbal fluency test, and clock-drawing test. (Table1)

Conclusion: Our data suggest that Val66Met BDNF polymorphism is not a risk factor for PD development and does not lead to cognitive impairment in PD.

Disclosure: The study was supported by RFBR, research project №16-54-76009 (EraNetRusPlus grant ID230)

EP3144

Targeted next-generation sequencing (NGS) as a diagnostic tool in syndromic autism spectrum disorder (ASD)

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Background and aims: Autism spectrum disorder (ASD) is a neurodevelopmental disorder, which etiological background is highly heterogeneous. Two major groups can be distinguished, syndromic and non-syndromic forms.
Aim: to analyse the diagnostic effectiveness of targeted NGS in 120 ASD patients and to estimate the frequency of monogenic forms.
Methods: Alltogether 120 patient were recruited by clinicians who met the DSM-5 criteria for ASD. After Fragile-X syndrome screening we performed next generation sequencing on MiSeq platform targeted on 103 known and candidate genes related to ASD (Illumina Trusight Autism Kit).
Results: After bioinformatic analysis we found in 102 patients rare variants in 66 genes. We identified in 11 monogenic ASD forms. We diagnosed patients with Fragile-X-, CHARGE-, Dravet-, ATRX-, Familial temporal lobe epilepsy syndrome and Duchenne muscular dystrophy concomitant with ASD phenotype. In further ASD cases mutations in CNTNAP2, CREBBP, SLC9A9, NLGN3, NSD1, and CHD8 supposed to be the best candidate to explain the neurodevelopmental phenotypes. In these cases segregation analysis is running now. Phenotypically 68 patients were considered as idiopathic ASD patient, and 52 had an additional feature beside autism, noted as syndromic ASD patients. In 13% of the cases no rare variant compatible to our variant inclusion criteria was found.
Conclusion: Targeted NGS sequencing is a useful tool to diagnose monogenic ASD forms. This method is highly recommended especially in ASD patients who have additional features beside ASD as well.
Disclosure: The Project is supported by the Hungarian Government and financed by the Research and Technology Innovation Fund. KTIA-AIK-12-1-2013-0017

EP3179

Brain MRI characteristics and scoring in adult onset Krabbe disease

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Background and aims: Krabbe disease is a recessively inherited lysosomal storage disease due to decreased galactocerebrosidase activity. Adult onset is rare, however probably underdiagnosed. Brain MRI showing a leukodystrophy is of great value to achieve diagnosis. We aimed at performing for the first time a systematic analysis of brain MRI features in adult onset Krabbe disease (> 10 years old).
Methods: Authors of articles describing adult onset Krabbe disease patients were asked to share the first available brain MRI of their patient. A score was established to describe the brain MRIs, with quantification according to severity (from 0 to 4 for non fascicular structures, from 0 to 2 for fascicular structures). Two neuro-radiologists first scored separately the MRIs, then reached a consensus for final scoring.
Results: 13 patients were included in the study. Pyramidal tract was the most frequent structure showing abnormal T2 hypersignal (100% of patients), however with some distinctions along the tractus : medial pre central gyrus (mean score 2.8/4), lateral pre central gyrus (1.77/4) and corona radiata (1.7/2) were highly abnormal whereas internal capsule (0.96/2), mesencephalon (0.69/2), pons (0.42/2) and spinal bulb (0/2) were quite spared. 9/13 patients (69%) had corpus callosum hypersignal especially in isthmus (mean score 0.69/2). Finally medial lemniscus was the most frequent abnormal structure found in posterior fossa (9/13 patients -69%-, mean score 0.96/2).
Conclusion: Upper pyramidal tract, corpus callosum isthmus and median lemniscus were the most frequently found structures with abnormal T2 hypersignals. This study should improve awareness of Krabbe disease in adult patients with leukodystrophy.
Disclosure: Nothing to disclose.

Neuroimaging

EP3145

The role of habenula and amygdala in Parkinson's disease patients with punding

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Background and aims: Punding is a poorly investigated impulsive-compulsive behavior (ICB) in Parkinson's disease (PD), causing severe threat to physical and psychosocial well-being. This study assessed whether a functional dysregulation of the habenula and amygdala, as modulators of the reward brain circuit, contributes to PD-punding.

Methods: Structural and resting state functional MRI were obtained from 22 PD-punding patients, 30 PD patients without any ICB (PD no-ICB) matched for disease stage and duration, motor impairment, and cognitive status, and 30 healthy controls. Resting state functional connectivity of the habenula and amygdala bilaterally was assessed using a seed-based approach. Habenula and amygdala volumes and cortical thickness measures were obtained.

Results: Compared to both controls and PD no-ICB cases, PD-punding patients showed higher functional connectivity of habenula and amygdala with thalamus and striatum bilaterally, and lower connectivity between bilateral habenula and left frontal and precentral cortices. In PD-punding relative to PD no-ICB patients, a lower functional connectivity between right amygdala and hippocampus was observed. Habenula and amygdala volumes were not different among groups. PD-punding patients showed a cortical thinning of the left superior frontal and precentral gyri and right middle temporal gyrus and isthmus cingulate compared to controls, and of the right inferior frontal gyrus compared to both controls and PD no-ICB patients.

Conclusion: A breakdown of the connectivity among the crucial nodes of the reward circuit (i.e., habenula, amygdala, basal ganglia, frontal cortex) might be a contributory factor to punding in PD. This study provides potential instruments to detect and monitor punding in PD patients.

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EP3146

Conventional MRI measurements in the differential diagnosis of Parkinson's disease and Multiple System Atrophy subtypes

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Background and aims: Multiple System Atrophy (MSA) is characterized by dysautonomia, extrapyramidal, cerebellar and pyramidal signs and is subdivided in MSA-P and MSA-C, depending on the predominant clinical features. Its' main differential diagnosis is Parkinson's disease (PD). The aim of this study was to implement MRI distance and surface measurements of brainstem structures to differentiate MSA-C, MSA-P and PD patients.

Methods: A total of 25 patients (8 MSA-C, 6 MSA-P and 11 PD) and 12 healthy controls were included. MRI measurements included simple brainstem distances. MRI planometry included midbrain, pons, corpus callosum and 4th ventricle surfaces. Relevant ratios of distances and surfaces, as well as the Magnetic Resonance Parkinsonism Index (MRPI) were calculated. Analysis of variance, Kruskal-Wallis and ROC curve analysis were used as appropriate.

Results: All measured brainstem distances, with the exception of midbrain (A-P) distance, pons surface, all relevant ratios and the MRPI were significantly lower in MSA-C patients. No MRI measurement could differentiate MSA-P from PD patients. MCP width was most potent in discriminating MSA-C patients (AUC=1.00, $p<0.0001$, 100% sensitivity and specificity, for a cut-off point of ≤ 7.6mm). Pons distance and surface, midbrain to pons distance and surface ratios as well as MRPI also provided excellent discriminative diagnostic value for MSA-C.

Conclusion: MSA-C can be differentiated from MSA-P and PD by a multitude of simple MRI distance and surface measurements. MSA-P did not differ from PD patients in any of the applied MRI measurements.

Disclosure: Nothing to disclose

EP3147

Baseline 18F Flortaucipir SUVR, but not amyloid or cognition, predicts cognitive decline over 18 months in Phase 2 trial subjects

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Background and aims: This study evaluates the relationships between Flortaucipir uptake and changes in cognition or function over time.

Methods: Flortaucipir scans (acquired 80-100 min post 370 MBq injection) were obtained in amyloid-positive healthy (n=5), MCI (N=47) or AD (N=30) subjects. VOI SUVr values were obtained from 1) a VOI determined by discriminant analysis to distinguish diagnostic groups (MUBADA) and 2) VOIs defined at baseline by the correlation between tau and domain-specific cognitive tests. Assessment included MMSE, ADAS-Cog, and the Functional Activities Questionnaire (FAQ). Correlations were used to compare baseline Flortaucipir or Florbetapir SUVr or cognitive scores to changes in cognition after 18 months.

Results: Strong correlations at baseline were seen between both Flortaucipir and Florbetapir SUVr relative to MMSE, ADAS-Cog and FAQ. Baseline Flortaucipir MUBADA SUVr was also correlated with all 18 month cognitive and functional change measurements (ADAS-Cog p=0.047,MMSE p=0.0007,FAQ p=0.0006). Amyloid SUVr was not correlated with 18 months changes in cognition or function, nor were baseline cognitive or functional measures correlated with changes with their respective measure. Heat map analysis showed that for most cognitive domains, MUBADA SUVr was at least as effective as the cognitive-correlation-derived VOIs at predicting 18 months changes.

Conclusion: Baseline tau was strongly correlated with 18 month change in MMSE, ADAS-Cog and FAQ, while baseline amyloid, cognitive and functional score were not. These data suggest that tau is relevant to the evolution of cognitive and functional decline in ways not evident for either amyloid or cognitive/functional measures themselves in MCI and AD patients.

Disclosure: This study is fully granted by Avid Radiopharmaceuticals a wholly owned subsidary of Eli Lilly & Co.

EP3148

Changes in grey matter volume and functional connectivity in cluster headache versus migraine

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Background and aims: Recent MRI studies suggest in the brain of cluster headache (CH) and migraine (M) structural and functional abnormalities. However, no between-group comparison of MRI measures has been performed

Methods: Multimodal MRI was acquired on a 3T MR scanner in age-matched patients with CH (n=12), M without aura (n=13), both during attack-free period, and normal controls (NC, n=13). MRI processing was performed with FSL. Voxelwise analyses of variance were done with nonparametric permutation testing (p≤0.05, corrected)

Results: Compared with NC, higher grey matter volume (GMV) occurred in CH in the cerebellum and occipital fusiform gyrus and in M in the lateral occipital cortex (LOC). GMV was lower than in NC in the inferior frontal gyrus of CH and in the lingual gyrus of M. Compared with M, GMV of CH was higher in the cerebellum and lower in the frontal pole and LOC. Functional connectivity (FC) was, compared with NC, higher in CH in the default mode, working memory and executive networks (DMN, WMN, EN) and altered in DMN of M, with lateral increase and medial decrease. FC in WMN and EN of CH was also higher than M. FC between cerebellar and temporo-insular networks was higher in CH than M.

Conclusion: The brain of attack-free CH seems to be characterized, compared with M, by (i) GMV changes, with decrease in a classical pain processing region (frontal cortex) and increase in an atypical region (cerebellum) and (ii) increased FC in key cognitive networks, probably with a maladaptive role.

Disclosure: Nothing to disclose

EP3149

3T MRI neurography of nerve plexuses in transthyretin familial amyloid polyneuropathy: Initial experience

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Background and aims: Transthyretin (TTR) familial amyloid polyneuropathy (FAP) is a relentless length-dependent sensori-motor axonal polyneuropathy. Amyloid fibrils unevenly accumulate for years in the nerve roots, plexuses and trunks before the onset of neuropathic manifestations. Nerve plexuses, which were so far not accessible to imaging, can now be explored by MRI neurography.

Objectives: To evaluate high-resolution 3T MRI neurography of the lumbo-sacral plexuses in a cohort of consecutive TTR-FAP patients or asymptomatic carriers.

Methods: 13 individuals with pathogenic mutation of the TTR gene were included (10 symptomatic, 3 asymptomatic carriers). The median neuropathy impairment score (NIS) was 38.5/244 (range 4-102). MRI neurography of the lumbo-sacral nerve plexuses was performed at 3T, including high-resolution T2-weighted and diffusion-weighted MR sequences in the coronal and axial planes. The same MRI protocol was applied in 10 controls. Two blinded readers assessed nerve plexus calibre and signal. Nerve enlargement was defined as an increase in nerve caliber of at least 50%.

Results: Agreement between readers was excellent (kappa of 0.88). MRI neurography revealed abnormalities of nerve plexuses in both symptomatic patients and asymptomatic gene carriers. Proximal and focal enlargement of nerve plexus was visible in 5 of the 13 patients with FAP, punctiform T2-weighted hyperintensities in 10. Of the 3 asymptomatic gene carriers, all exhibited punctiform hyperintensities and one also showed focal enlargement of nerve plexus. None of these abnormalities were observed in controls.

Conclusion: MRI neurography can show abnormalities in both symptomatic patients and asymptomatic gene carriers, providing new insights regarding the diagnosis of TTR-FAP.

Disclosure: Nothing to disclose

EP3150

Assessing longitudinal iron deposition in deep grey matter nuclei with high-pass filtered phase MR Imaging in Parkinson's disease

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Background and aims: Iron accumulation plays an important role in neurodegeneration in Parkinson's disease. Susceptibility weighted imaging (SWI) is a high-resolution MR-based imaging technique for quantifying iron depositions in vivo. Phase images offer greater specificity in quantifying brain iron load. We hypothesised that high-pass filtered phase imaging may be a useful monitoring tool for longitudinal clinical characterization of PD, and we sought to investigate the clinical associations of iron depositions in deep grey matter nuclei.

Methods: We evaluated forty-two PD subjects and six age and gender matched healthy volunteers (HV) longitudinally with high-pass filtered phase imaging at baseline and after 18 months. Average phase shifts (radians) in the caudate nucleus, putamen, globus pallidus, substantia nigra (SN) and dentate nucleus (DN) were analysed using SPIN software. Longitudinal changes of bilateral radians (Δ radians) were calculated by subtracting baseline values from follow up values. Parametric correlations of regional Δ radians were conducted with Δ UPDRS part III, tremor and bradykinesia-rigidity sub-scores.

Results: PD patients showed significantly higher radians in the SN ($p<0.001$) after 18 months, without significant change in controls. Δ SN radians positively correlated with Δ UPDRS-III ($p<0.001$) and bradykinesia-rigidity subscores ($p=0.001$). In addition Δ DN correlated with tremor subscores ($p<0.01$).

Conclusion: Our results show that high-pass filtered phase imaging might offer an interesting monitoring tool to evaluate longitudinal progression of motor severity and clinical phenotypes in PD, and could be useful to assess the effect on these structures of iron chelation therapies.

EP3151

Resting state nigral functional connectivity in Parkinson's disease: A cross-sectional study

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Background and aims: The clinical manifestation of neurodegenerative diseases is thought to result from disrupted functional brain networks. Parkinson's disease (PD) is a neurodegenerative disorder characterised by progressive dopaminergic neuronal loss of SNc with further dysfunction of striatal-thalamic-cortical loops. To investigate the pattern of network dysfunction resulting from SN neurodegeneration we subsequently performed a resting state fMRI cross-sectional study of nigral functional connectivity.

Methods: Twenty-nine early stage PD subjects during medication off state and twenty-six age and sex matched healthy controls were studied with resting state fMRI. Spontaneous low-frequency (0.08-0.1 Hz) blood oxygenation level-dependent (BOLD) signal intensity fluctuations of SN were used to identify significant temporal correlations with a priori striatal and motor cortical regions. For each individual the mean SN time series were correlated with the time series of striatal nuclei and the regions of the Human Motor Area Template (HMAT). Nigral seeds were divided into more and less affected sides according to clinical motor severity as assessed with UPDRS III.

Results: Nigral seed regions showed positive functional connectivity with thalamus, globus pallidus and putamen and was anticorrelated with sensorimotor cortex in both PD and HC groups. In contrast, additional negative connectivity was shown in premotor cortex (SMA and premotor dorsal areas) in PD group. Further decline of functional connectivity in premotor cortex were found in most affected SN when compared to the less affected.

Conclusion: Our results demonstrate the in vivo disrupted nigral functional connectivity using RS fMRI with the striato-thalamo-cortical structures in early PD patients, in keeping with o dopaminergic neurodegeneration.

Disclosure: This work was supported by Parkinson's UK (Parkinson's magnetic imaging repository, PaMIR).

EP3152

Quantitative MRI texture analysis of enhancing and non-enhancing T1-hypointense lesions without application of contrast agent in multiple sclerosis

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Background and aims: Gadolinium-enhanced MRI is a sensitive method to assess active inflammation in MS lesions. The aim of this study was to evaluate texture analysis(TA) in pre-contrast injection MR images to improve accuracy and to identify subtle differences between enhancing lesions (ELs), non-enhancing lesions (NELs) and persistent black holes (PBHs)

Methods: The MR image database comprised 90 patients; 30 of which had only PBHs, 25 had only ELs and 35 neither EL or PBH. These were assessed by the proposed TA method. Up to 300 statistical texture features were extracted as descriptors for each region of interest/lesion. Differences between the lesion groups were analyzed and evaluations were made for area under the receiver operating characteristic curve (Az) for each significant texture feature. Linear discriminant analysis (LDA) was employed to analyze significant features and increase power of discrimination. Lesions were classified by the 1-NN classifier.
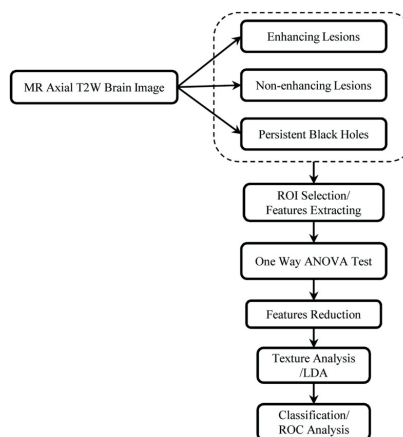
Overview of texture analysis process in the MR brain images

Results: At least 14 texture features showed significant difference between NELs and ELs, NELs and PBHs, and ELs and PBHs. By using all significant features, LDA indicated a promising level of performance for classification of NELs and PBHs with Az value of 0.975 that corresponds to sensitivity of 94.28, specificity of 96.30%, accuracy of 95.5%. In classification of ELs and NELs (or PBH), LDA demonstrated discrimination performance with sensitivity, specificity and accuracy of 100% and Az of 1.
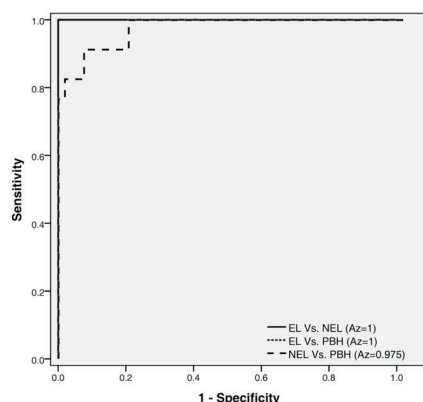
The diagrams of the ROC curve for texture analysis method with LDA in classification of NELs, ELs and PBHs

Conclusion: TA was a reliable method, with potential for characterization and the method can be applied by physicians to differentiate NELs, ELs and PBH in pre-contrast injection MR imaging.

Disclosure: Nothing to disclose

EP3153

Automated brain tissue and lesion segmentation in multiple sclerosis: A feasibility study in the state of Salzburg

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Background and aims: Brain atrophy and lesion load are related to clinical outcomes in multiple sclerosis (MS). Manual reading and semi-automated segmentation of magnetic resonance imaging (MRI) scans are used at institutions with scientific background. Fully-automated MRI segmentation methods could support individualized management and improve therapeutic success in clinical practice.

Aims: To assess feasibility and limitations of automated brain MRI analysis tools developed for patients with MS in a real-life setting.

Methods: We studied a cohort of 173 MS patients (64% women). Scans were acquired at ten radiology institutes in the state of Salzburg, Austria. MRI facilities were hospital based (n=5) or had private ownership (n=5). We uploaded scans for analysis of brain atrophy and total brain lesion volumes to online platforms of Icometrix/MSMetrix (Leuven, Belgium) and Jung Diagnostics (Hamburg, Germany). We further contacted the MRI providers for brain scan protocol details used for MS patients.

Results: We submitted 146 scans of 73 patients to Icometrix (25 patients with >2 scans) and 58 scans of 47 patients (7 patients with >2 scans) to Jung Diagnostics (Table 1).

Reasons for rejections were lack of minimal standard requirements. These included inappropriate slice thickness, low signal to noise ratio and incomplete field of view. Detailed field strength distribution and imaging properties, see Table 2.

Table 1

	Icometrix	Jung Diagnostics
No. of submitted scans	146	58
No. of feasible scans (%)	10 (7%)	49 (85%)
Overlapping No. of identical scans	12	

MRI Scan Databases

Table 2

Institution	Field Strength (Tesla)	Slice Thickness T1 (mm)	Slice Thickness FLAIR (mm)
A	1.5	n.a.	4
B	1.5	4	4
C*	3	4	4
D*	3	0.75	4
E	1	5	3.5
F	1.5	5	5
G	3	5	2
H*	1.5	n.a.	4
I*	3	1	4
J*	1.5	1	4
Minimal standards MAGNIMS group	3	<3	<3

Legend: Overall 10 institutions (A-J, *hospital based) provided MRI scans. Field strength of the MRI scanners used in the state of Salzburg was 3 Tesla (n=4), 1.5T (n=5) and 1T (n=1). Slice thickness for FLAIR sequences were 5mm (n=1), 4 mm (n=7), 3.5 mm (n=1) and 2mm (n=1).

MRI Properties

Conclusion: Technical limitations lead to high dropout rates for scans obtained in a real-world setting. MRI protocols for FLAIR images did not comply with minimal standards proposed by the MAGNIMS group. Moreover, minimal requirements among providers of automated segmentation are not uniform.

Disclosure: Nothing to disclose

EP3154

Stroke resulting aphasia and transcranial doppler findings

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Background and aims: Out of all possible causes of aphasia stroke is the leading one (18-35%).

We examined possibility of TCD in identifying most frequently affected vessels in post-stroke aphasic patients, type of aphasia and location of brain injury.

Methods: The study included 189 patients(pts) F/M=72/117, age 59±10 years with the first acute ischemic stroke and aphasia admitted to the St Sava Hospital from January 1 to October 31, 2016.with no brain MSCT/MR findings of an earlier stroke. In the first 48 hours Color Duplex Sonography (CDS) and Transcranial Color Duplex Sonography (TCD) examinations were done .The Western Aphasia Battery (WAB) was used to provide information of the type of aphasia and MSCT/MR on location of the lesion.

Results: RESULTS: The main aphasic syndrom was Broca's aphasia (61%). In 149 pts(79%) the lesions were located at classical language centers. According to TCD and CDS 62 pts (33%) had no changes in the intracranial hemodynamics; out of 127 pts (67%) with changes, 23 pts (17%) had terminal ICA stenosis/occlusions; 56 pts (45%) hypoperfusion of the L or R MCA; 48 pts (38%) had a significant stenosis/or occlusion of the extracranial ICA, with collateral circulation (through ACoA, PCoA or OA).

Conclusion: CONCLUSION: In our study, Broca's aphasia was the most frequent aphasic syndrome in the acute stage of ischemic stroke in the territory of the MCA. The damaged lesions were in classical language functional areas. TCD is a useful noninvasive method to monitor the hemodynamic state of the circle of Willis.

Disclosure: Nothing to disclose

Neurological manifestations of systemic diseases

EP3155

Neurological involvement in Gougerot Sjogren Syndrom from central to Peripheral nervous system: Diagnosis challenge

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Background and aims: Neurological manifestations in Gougerot-Sjogren syndrome (GSS) are valued differenly. This is essentially the achievement of the peripheral nervous system.

Methods: We report a series of 21 cases of neurological manifestation revealing a Sjogren Gougerot syndrome collected over a period of 12 years (2005 -2016).

Results: 95.2% of cases were female with a sex ratio of 0.05 with an average age of 42.3 years. Central involvement was noted in 9 cases with encephalic involvement in 6 cases, encephalic involvement associated with myelopathy in 2 cases. Cranial nerve involvement associated with encephalic involvement in one case. Peripheral nervous involvement was noted in 7 cases, with sensitivomotor polyneuropathy in 3 cases, the sensitive neuropathy in one case, isolated involvement of the cranial nerves in 2 cases and multiplex mononeuropathy in 1 case. Peripheral nervous involvement associated with central involvement in one case. An association with other neurological conditions in 4 cases

Conclusion: we found a concordance of the profile of the patients, with the literature, therefore the adult age and the female predominance. Central neurological involvement was predominant compared to peripheral nervous involvement, contrary to the literature. In terms of peripheral involvement, sensitivo-motor polyneuropathy was the most frequent in our series. Focal encephalic manifestations are the CNS manifestations most frequently observed in the literature, which is consistent with our study.

The neurological manifestations related to GSS are difficult to diagnose. Some neurological manifestations require systematically search for a GSS: myelopathy, neuropathy predominantly sensitive, cranial nerve damage or manifestation of MS after 50 years.

Disclosure: Nothing to disclose

EP3156

The physical anthropological factor in diagnosis of Wilson's disease

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Background and aims: Wilson's disease (WD) is a genetically based pathology and its neurological manifestations are often misdiagnosed. Thus, identification of additional diagnostic criteria is very important both for a primary and differential WD diagnosis.

Methods: An integrated anthropological examination (defining specific phenotypic variants (PhVs)) was performed in 50 patients with confirmed WD (E83.01) and 50 persons from a general population without WD and any other psychoneurological, metabolic or hepatic pathology (the control group).

Results: A positive association between presence of WD and a certain PhV was detected for Mediterranean PhV (54.00% of WD patients and 20.00% in the control; p<0.0005) and for Atlanto-Baltic PhV (20.00% of WD patients and 6.00% in the control; p<0.05). A negative association between presence of WD and a certain phenotypic variant (PhV) was detected for Alpine PhV (0.00% of WD patients and 32.00% in the control; p<0.00001), for Paleo-European PhV (4.00% of WD patients and 22.00% in the control; p<0.005), and for East-Baltic PhV (0.00% of WD patients and 8.00% in the control; p<0.05).

Conclusion: The range of a grade of association between the main phenotypic variants and risk of WD was formed: positively – Mediterranean PhV (a very high grade) and Atlanto-Baltic PhV (a high grade); neutral – Dinaric PhV; negatively – East-Baltic PhV, Paleo-European PhV (a high grade), and Alpine PhV (a very high grade). These data should be taken into account in examination of patients with WD and in a differential diagnosis of doubtful cases.

Disclosure: Nothing to disclose

EP3157

Diagnostic of systemic inflammatory disorders among patients admitted for acute aseptic meningitis: An observational study

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Background and aims: The aim of this study was to identify clinical indicators for systemic inflammatory disorders (SID) in patients admitted for acute aseptic meningitis.

Methods: All consecutive adults patients hospitalized over a 4-years period for acute aseptic meningitis were included retrospectively. Exclusion criteria included inability to confirm meningitis or a diagnosis of neoplastic meningitis after chart analysis. Extra-neurological signs were recorded using a systematic panel. SID diagnosis was made according to current international criteria. A multiple logistic regression analysis was carried out to identify factors independently associated with the etiology of meningitis.

Results: 88 patients were eligible. After exclusion, 43 (46[19-82] years, 60% females) patients hospitalized for an acute aseptic meningitis were analyzed. No patient was taking drugs known to induce aseptic meningitis. Among them, 23 (53.5%) had a SID that was revealed by the meningitis in 16 (69.5%) cases. Sarcoidosis and Behcet syndrome accounted for almost half of all SID. As compared to patients with idiopathic meningitis, patients with SID displayed a higher frequency of neurological (p=0.024), extra-neurological signs (p=0.007), and abnormal cerebral MRI findings (p=0.024) at diagnosis. Overall, the probability of SID in patients admitted with acute aseptic meningitis was of 93.7% in patients with neurological (such as focal neurological deficits, delirium or seizure) and extra-neurological signs (such as uveitis, arthralgia, aphthous ulcers and skin lesions) but fell to 14.9% in patients with neither neurological nor extra-neurological signs.

Conclusion: Structured clinical sorting according to both neurological and extra-neurological signs help to identify patients with acute aseptic meningitis caused by a systemic inflammatory disorder.

Disclosure: Nothing to disclose

EP3158

Nonsystemic and systemic vasculitic neuropathy: Experience of 25 years in terziary neurologic clinic

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Background and aims: Vasculitis of the peripheral nervous system (PNS) occurs rarely either in the context of systemic vasculitis or isolated (non-systemic vasculitic neuropathy-NSVN). This is the first large prospective study   which aims to investigated the clinical, and pathological features of both systemic and nonsystemic vasculitic neuropathy in order to establish the clinical manifestations and to promote the earlier diagnosis of the syndrome.

Methods: Biopsies were selected from over 855 sural nerve biopsies performed at the Section of Neuropathology, Neurological Clinic of Athens University Hospital between 1985 and 2005 and were followed up until 2014. The diagnosis of vasculitis was based on established clinicopathological criteria. Complete laboratory, clinical, electrophysiological, and pathological studies were performed in all cases.

Results: Nerve biopsies of 22 (2.5%) patients were diagnosed as NSVN . Systemic vasculitis (5.8%) included: 15 rheumatoid arthritis, 9 Churg-Strauss syndrome, 7 cryoglobulinemic vasculitis, 7 Systemic lupus erythematosus, 5 Sjogren disease, 3 polyarteritis nodosa, 2 Behcet's disease, 1 Crest Ankylosing spondylitis. The pathological features were vasculitis and predominant axonal degeneration with a varying pattern of myelinated fiber loss. The vasculitic changes were found mainly in small epineural blood vessels. Mononeuritis multiplex and distal symmetrical sensorimotor neuropathy were equally frequent.

Conclusion: Although less common than systemic vasculitis NSVN should be suspected in a case of unexplained polyneuropathy without evidence of systemic involvement. Clinical and neurophysiological studies are essential for the detection of nerve involvement, but the specific diagnosis of NSVN may be missed unless a biopsy is performed.

Disclosure: Nothing to disclose

EP3159

Neurological manifestations revealing Gougerot-Sjogren syndrome: 18 cases

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Background and aims: Gougerot-Sjogren Syndrome (GSS) is an autoimmune exocrinopathy caracterized by a xerophtalmia and a xerostomia. It can be primitive or secondary to another connective tissue disease. Neurological involements are observed in approximately in 20-25% of cases, inaugural in 25% of them. Our objective is to decribe the clinical, paraclinic and therapeutic aspects of 18 patients with neurological signs reavealing GSS.

Methods: We studied retrospectively over a period of eleven years from 2002 to 2013, 18 patients presenting a primitive GSS revealed par neurological symptoms. Diagnosis of primitive GSS is made according to the Criteria of American-European consensus 2002. All our patients has benefited of complete assement to confirm the diagnosis : Schirmer test, an accessory salivary glands biopsy and an immunological assessment.

Results: Eighteen patients were studied. The averge of age was 44 years and the sex ratio was 0.2. Peripheral nervous system involement was noted in 50% cases (9/18): 5 cases had sensitivo-motor polyneuropathy, 3 others had cranial nerves involvement and one case had anterior horn syndrome. Central nervous system involement was noted in 88.88% (16 cases). Multifocal signs affecting brain and spinal cord are described in 11 cases, chronic myelopathy and acute transverse myelitis in 3 cases. All patients received an oral corticosteroids, followed by a progressive regression.

Conclusion: Neurological involvements can be the first manifestation of GSS in 25% of the cases.Peripheral nervous system manifestations are well documented dominated par axonal polyneuropathy. Central nervous system involvements are under-diagnosticated.Treatment of GSS neurological manifestations is not codified.

Disclosure: Nothing to disclose

EP3160

Cerebrospinal fluid findings in NeuroBehçet disease

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Background and aims: Neurological manifestations during Behcet's disease are present in 20 to 30% of the cases. Given the difficulty of differential diagnosis, the CSF study is systematic.

Objective: To study the cyto-chemical and immunoelectrophoretic profile of the cerebrospinal fluid of a series of patients monitored for NB disease.

Methods: A retrospective study over a period of 15 years (2002-2016) of patient's files admitted for NB diseases (international criteria for NB disease). Cerebral imaging and CSF study were performed for all our patients

Results: 38 NB disease cases were recruited. The neurological form was inaugural in 68.4%. The appearance of CSF was clear in 34 patients, disturbed in 3 and hematic in only one case. There was hyperproteinorachy in 16 patients (42.1% average rate of 0.85 g/l). Glycorrachia was normal in all our patients (0.58g / l). Lymphocytic meningitis was found in 17 cases (44.7%). CSF isofocusation was performed in 16 patients (65.5%). The IgG index was increased in 4 patients (10.5%). In immunoelectrophoresis, oligo clonal bands were found in two patients (5.2%).

Conclusion: The presence of predominantly lymphocytic meningitis is classic in NB. Where as, an intrathecal synthesis of IgG and oligoclinic bands exclusively in CSF are less described. Our results indicate a B and T cell involvement in NB. Indeed, the activation of autoreactive T cells with involvement of cytokines and pro-inflammatory transcription factors would be proved.

Disclosure: Nothing to disclose

EP3161

Early diagnosis of diabetic neuropathy in young patients with type 1 DM – a 10-yr follow-up study

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Background and aims: The main objective of this work was to follow-up the development of peripheral neuropathy and its severity in patients with type 1 diabetes over 10 years. We observed potential risk factors and their impact on the development of neuropathy. The other objective was longitudinal study of electrophysiological parameters.

Methods: The prospective study included 62 patients with type 1 diabetes aged 13.9 ± 5.9 yr, with diabetes duration of 5.6 ± 5.1 yr, treated with an intensified insulin regimen. All patients underwent a neurological examination, nerve conduction study (NCS) and biothesiometry three times (baseline, after 5 yr, after 10 yr).

Results: During the follow-up there was an increase in DN prevalence from 24.2% to 62.9% (p<0.001). The proportion of patients with subclinical neuropathy increased from 17.7% to 46.8% (p<0.001), patients with clinical neuropathy from 6.5% to 16.1% (p<0.001). The main contribution factors for rapid growth of the DN prevalence were poor glycaemic control, diabetes duration and patient's age. Regarding the conduction parameters, the most significant changes were observed in sural SNAP amplitude (5.2 m/s, p<0.001) and sural NCV (8.2 uV, p<0.001).

Conclusion: The results of the study demonstrated a progressive increase in the DN prevalence over time, in particular its subclinical stages. The long-term poor glycaemic control was a determining factor in the rapid DN development. The sensory conduction parameters deteriorated faster than the motor parameters. The study is one of few of those in type 1 DM, which in relation to risk factors assess not only the presence of neuropathy, but also its severity.

Disclosure: Nothing to disclose

EP3162

Prolonged-release fampridine demonstrates rapid and sustained clinically meaningful improvements in walking ability over 24 weeks: MSWS-12 responders in the ENHANCE study

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Background and aims: The international Phase 3, double-blind, placebo-controlled ENHANCE study (NCT02219932) was the largest and longest randomised trial of prolonged-release (PR) fampridine. ENHANCE demonstrated that significantly more subjects had clinically meaningful improvements in walking ability, as assessed by the self-reported Multiple Sclerosis Walking Scale-12 (MSWS-12), with PR-fampridine versus placebo (43% vs. 34%; odds ratio=1.61; p=.006) over 24 weeks. This analysis evaluated the magnitude of mean change in MSWS-12 score over 24 weeks, based on clinically meaningful subject-level improvement.

Methods: An MSWS-12 responder was prospectively defined as an ≥ 8-point mean reduction (improvement) in MSWS-12 score over 24 weeks; least-square-mean (LSM) analyses used a mixed effects model for repeated measures, adjusted for screening EDSS, baseline MSWS-12, baseline TUG speed, age, and prior aminopyridine as covariates (missing data handled using multiple imputation).

Results: PR-fampridine–treated MSWS-12 responders demonstrated an LSM improvement of –20.58 points from baseline over 24 weeks; a small mean improvement was observed in the placebo group (–3.64 points), while MSWS-12 non-responders worsened slightly (+2.17 points; see figure). In PR-fampridine–treated MSWS-12 responders, improvements were detected as early as Week 2 and were sustained throughout the treatment period.
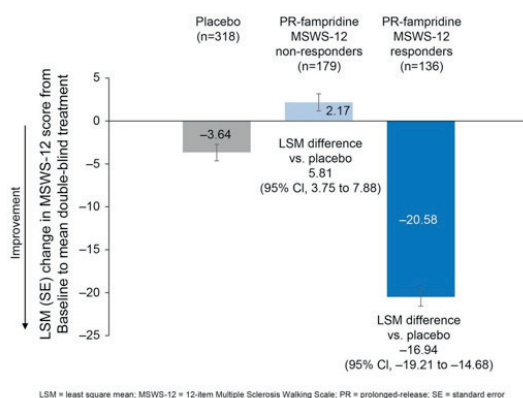
Least square mean change (LSM) in MSWS-12 score from baseline over 24 weeks in the placebo group and PR-fampridine–treated MSWS-12 responder and non-responder subjects. LSM, LSM difference, standard error (SE) calculated using mixed effects model for repeated measures.

Conclusion: Over 24 weeks, PR-fampridine–treated MSWS-12 responders experienced clinically meaningful improvement from baseline—a notable finding given the skewed nature of baseline scores across groups. Whilst the mode of action of PR-fampridine is understood, the pathophysiological explanation of MSWS-12 responders remains unclear. Therefore, MSWS-12 responders cannot be predicted a priori. Nevertheless, the fast-acting nature of PR-fampridine enables quick and efficient identification of MSWS-12 responders in clinical practice.

Disclosure: This study was funded by Biogen; medical writing support for the development of this abstract was provided by Excel Scientific Solutions and was funded by Biogen.

EP3163

Fabry disease: What should we know about neurologic involvement and MRI findings?

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Background and aims: Fabry disease (FD) is an X-linked inborn error of glycosphingolipid catabolism, caused by abnormalities in GLA gene leading to deficiency in α-galactosidase A and pathological accumulation of predominantly globotriaosylceramide into vascular endothelial, neural, renal cells, and cardiomyocytes. FD may lead to life-threatening complications such as kidney damage, heart attack and stroke. Imaging, clinical manifestations, lab data set and genetic testing play an important role in sustaining an early diagnosis of FD.

Methods: To present and illustrate the neurological manifestations and brain MRI findings of FD.

Material and Methods: 8 patients aged 20 to 59 years old, were tested for enzyme activity and gene mutations and were examined for cardiac, renal, dermatological and neurological involvement, including brain MRI and nerve conduction studies.

Results: All patients had chronic kidney disease, hypohidrosis and acroparesthesia; 4 patients had a previous ischemic stroke; 2 patients presented hearing loss; 6 patients presented angiokeratomas, and one patient presented cornea verticillata. Cardiac involvement was found in 5 patients. Brain MRI showed ischemic stroke or white matter hyperintensities by involvement of small-vessels. Nerve conduction studies showed no pathological changes. Six patients received enzyme replacement therapy.

Conclusion: Cerebral microangiopathy, ischemic stroke, autonomic dysfunction manifested as hypohidrosis and small fiber neuropathy were the neurological findings in our patients with Fabry's disease. MRI represents the most sensitive method to detect CNS involvement in Fabry disease and to monitor CNS lesions under enzyme replacement therapy. A multidisciplinary team is essential to establish an early diagnostic of FD.

Disclosure: Nothing to disclose

EP3164

Neurological and clinical findings in patients with tuberous sclerosis before and after treatment with Everolimus

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Background and aims: Tuberous sclerosis complex (TSC) is an autosomal-dominant, neurocutanous, multisystem disorder caused in 1/3 of cases by mutations in two tumor suppressor genes, TSC1 and TSC2. The classic clinical triad include in TSC facial angiofibromas, seizures, and mental retardation. Imaging plays an important role to assess TSC lesions and the evolution under treatment. Everolimus is an mTOR inhibitor used in a number of clinical indications including TSC.

Methods: To present and illustrate classical imaging findings of TSC. To investigate the efficiency and safety profile of Everolimus treatment in patients with TSC.

Methods: Eight patients aged 25 to 50 years old, half of them with epileptic seizures were diagnosed with TSC and treated with Everolimus for 7 to 15 months. Neurological examination, brain magnetic resonance imaging (MRI), electroencephalography (EEG), thoracic and abdominal computed tomography (CT), cardiologic, dermatological and ocular examination were performed before and after Everolimus treatment. Serum levels of Everolimus were also monitored.

Results: All patients presented typical brain MRI lesions (cortical and subcortical tubers, subependymal nodules and radial migration lines), renal angiomyolipomas and cutaneous angiofibromas.Pulmonary lesions were found in 3 cases. Everolimus treatment induced a decrease of brain tubers and epileptic seizures in 10 patients and a reduction of renal angiomyolipomas, cutaneous angiofibromas and pulmonary lesions in all patients. Stomatitis was the main adverse event that was reported.

Conclusion: Everolimus treatment reduced the brain, kidney, cutaneous and pulmonary lesions in TSC patients and was well tolerated. Epileptic seizures were diminished in the majority of patients.

Disclosure: Nothing to disclose

EP3165

Cognitive complaints in patients with active Systemic Lupus Erythematosus and past neuropsychiatric symptoms

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Background and aims: Cognitive complaints are common in patients with systemic lupus erythematosus (SLE). Their association with disease and non-disease related factors have been inconsistently reported. We studied their relation to disease related factors including disease activity, neuropsychiatric history and non-disease related factors such as anxiety or depression.

Methods: We used cognitive symptoms inventory (CSI) for measuring cognitive impairment at 3 time-points 12 months apart/2015-2016/ and Hospital Anxiety and Depression Scale (HADS)-HADS- A and D. Disease activity was measured by SLEDAI.

Results: 93 SLE patients were recruited at baseline (T0). Among them 59 had first re-evaluation (T1) and 34 had second re-evaluation (T2) at 12-month interval. Majority (72%, 24/34) of patients had stable CSI whereas 5.5% (2/34) of patients worsened CSI over 12 months. At T0, multivariate analysis revealed that higher CSI was associated with history of NPSLE (p=0.005) and psychiatric disease (p=0.04), higher HADS-A (p<0.001) and HADS-D (p<0.001) scores. CSI of active patients (SLEDAI>6) was not different from inactive patients. It did not change despite regression of disease activity in 12 months. There was no difference in CSI between T0 and T1 regardless of history of NPSLE, change in anxiety and depression at T1 (HADS-D>11 as cutoff).Multivariate linear regression analysis revealed change in HADS-A as the only significant predictive factor of change in CSI over time (β=0.774, 95% CI 0.43 – 1.12, p<0.001).

Conclusion: 11.5% of SLE patients reported persistent cognitive symptoms.CSI had worsened in patients with NPSLE and psychiatric illness, anxiety or depression.

Disclosure: Nothing to disclose

EP3166

Neuropathic pain in systemic disease: Clinical and electrophysiological features and therapeutic approach

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Background and aims: Pain is a common symptom in patients with systemic diseases. In addition to joint and muscle pain, neuropathic pain can worsen their quality of life.

We describe herein the clinical and electrophysiological feature of patients with systemic diseases and presenting for neuropathic pain and its effect on the quality of life.

Methods: Patients with various systemic diseases and referred to our department for neuropathic pain assessment from January 2016 to December 2016 were included. All patients had neurological examination, electromyography with nerve conduction study (NCS) and evaluation with the neuropathic pain questionnaire (NPQ) and quality of life assessment (McGILL QoL questionnaire). Response to medication was also related.

Results: Thirty-three patients were included (sex ratio= 0.36; mean age= 41.8 years). Underlying systemic disease was systemic lupus (16 patients, 48%) primary Sjögren syndrome (10 patients, 30%) scleroderma (4 patients, 12%) and sarcoidosis (3 patients, 9%). Mean NPQ score was 7.2 (5-10) and mean McGILL QoL questionnaire was 54 (33-76). NCS revealed axonal sensory or sensory motor neuropathy (30%), mononeuropathy multiplex (24%) and radiculopathy (9%). NCS did not show any abnormality in 12 patients (36%) suggesting small fiber neuropathy. Poorer quality of life was associated with mononeuropathy multiplex ($p<0.01$) and systemic lupus ($p<0.05$). Treatment options included tricyclic antidepressants, pregabalin and carbamazepin. Monotherapy was insufficient in 75% of patients and 36% of them were not satisfied despite the association of two or more molecules.

Conclusion: Neuropathic pain can represent an irritating thorn in the course of various systemic diseases. Adequate treatment can be challenging in order to improve patients' quality of life.

Disclosure: Nothing to disclose

EP3167

The assessment of brain metastases risk in cancer patients: The influence of primary tumor location, histological and immunohistochemical aspects (a retrospective observational descriptive study)

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Background and aims: The aim of this study was to identify cancer patients with high risk of brain metastases, in this way improving early detection of cases.

Methods: Retrospective observational descriptive study on 396 cancer patients admitted in hospital between 2013 and 2016, which received clinical neurological exam and brain CT/MRI in selected cases. Data regarding primary cancer location (breast, upper/lower digestive, small and non-small lung cancer-SCLC, NSCLC-,urogenital, skin, head and neck, others), histological and immunohistochemical characteristics were collected from the medical records. Statistical analysis was performed using SPSS Statistics v.23.0 (statistical significance assumed at $p<0.05$).

Results: Mean age (±SD) was 61.62±11.31 years. 94 patients had brain metastases (23.7%). Brain metastases were significantly correlated with younger age ($p=0.001$) and lung cancer ($p=0.002$). Upper and lower digestive cancers ($p=0.016$ and $p=0.034$) and head and neck cancers ($p<0.001$) correlated negatively with brain metastases. Patients with SCLC had more brain metastases than patients with NSCLC (46.6% versus 36.20%,without statistical significance, $p=0.555$). Negative hormone receptor status breast cancer patients had more frequently brain metastases than positive ones (40.90% versus 21.05%; $p=0.093$) and those with more than 70% of tumoral cells having hormone receptors seemed protected from brain metastases ($p=0.013$).

Conclusion: This work allowed identification of cancer patients with higher and lower risk for brain metastases. This is an important step in developing better future screening and early detection strategies thus facilitating early treatment and survival improvement

Disclosure: Nothing to disclose

Neuro-oncology

EP3168

Primary Leptomeningeal Lymphoma presenting as low back pain and dementia: A case report

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Background and aims: Primary leptomeningeal lymphoma (PLL), also called primary meningeal or dural lymphoma, is an extremely rare condition, with only a handful of cases reported in literature. Most often, these are misdiagnosed as other disease entities more commonly observed in practice. It is important to develop suspicion for leptomeningeal malignancy in atypical cases, especially those unresponsive to treatment, as the overall medial survival for PLL is only 24 months. Currently, there are no clinical algorithms that may guide clinicians to clinching a diagnosis of a primary leptomeningeal lymphoma.

Methods: This paper discusses a case of leptomeningeal lymphoma that initially presented as low back pain and dementia. He was initially treated for tuberculous meningitis. However, after numerous imaging studies which showed dural enhancement from the cervical to lumbosacral spine, most markedly in the cauda equina, a malignant process was suspected. A dural biopsy with immunohistochemistry confirmed the diagnosis of leptomeningeal lymphoma. A primary malignancy was ruled in after PET CT showed no other sites of high metabolic activity. His dementia is attributable to the communicating hydrocephalus appreciated in his cranial imaging studies.
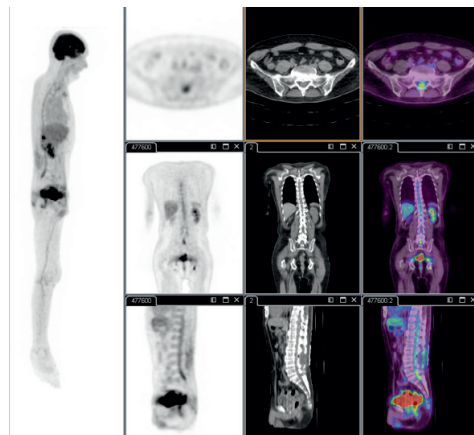
Results: A ventriculo-peritoneal shunt was inserted and he underwent six cycles of Methotrexate with Rituximab infusions. The patient is alive and well with almost a normal neurological status except for residual dementia symptoms
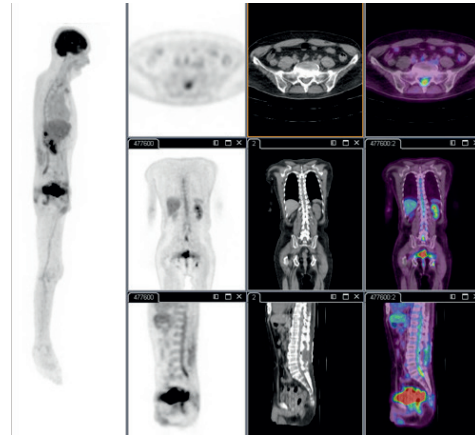
Conclusion: Primary Leptomeningeal Lymphoma is a rare disease that presents with a wide array of non-specific symptoms and is often misdiagnosed. A good index of suspicion is needed in patients who show atypical symptoms incompatible with other disease processes.

Disclosure: Nothing to disclose

EP3169

Cancelled

EP3170

Paraneoplastic neurological syndromes in Algeria: Clinical heterogeneity and atypical revelation patterns

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Background: Paraneoplastic neurological syndromes (PNSs) are rare autoimmune disorders that occur in association with cancer and are not explained by a metabolic, metatarsal, infectious or iatrogenic complication.
Aims: To study the clinical and paraclinical profiles of NPS in a hospital series.
Describe the peculiarities of these PNSs and compare them with the data of the literature.
Methods: A monocentric, retrospective study of PNSs supported in the Neurology department of Ait Idir Hospital in collaboration with the Immunology of the Pasteur Institute of Algeria.
Results: We included 12 patients, 10 men and 2 women, with SNPs with anti-neural antibodies positive. Antibodies found were anti-Yo (n=4), anti-Ma 2(N=2), anti-amphiphysin (n=1), anti-Zic (n=1) and anti-NMDAR (n=1). Two other patients had a POEMS. Most patients had a combination of at least two antibodies.
Conclusion: The SNPs described in our patients were characterized by high heterogeneity clinical and atypical modes of revelation. A postinfectious presentation subacute was particularly noted. PNSs can be revealed in atypical and deceptive presentations. Their recognition is, however, crucial for early care and better prognosis
Disclosure: Nothing to disclose

EP3171

Anti-Ri-antibody paraneoplastic syndrome with complete horizontal ophthalmoplegia

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Background and aims: Paraneoplastic neurological disorders associated with anti-Ri-antibodies mostly present with opsoclonus-myoclonus-ataxia. Anti-Ri-antibodies have been mainly reported in patients with breast cancer althought gynecological tumors and small-cell lung cancer (SCLC) are identified, too. Ophthalmoplegia without opsoclonus is very rare. We present a woman with SCLC who had atypical anti-Ri-antibody paraneoplastic syndrome presenting as complete horizontal ophthalmoplegia and truncal ataxia.
Methods: A 59-year-old woman with subacute onset of bilateral horizontal gaze palsy and gait disturbance. She has a history of hypertension, diabetes and smoking. Neurologic examination revealed complete horizontal gaze palsy without opsoclonus-myoclonus. Diplopia wasn´t reported. She presented a wide-based gait and couldn´t perform tandem-gait.
Results: Her CSF showed high cell count, normal protein values, and negative cytology and viral markers. Serum´s immunofluorescence analysis revealed anti-Ri-antibodies. Body-CT showed a solid lesion in left lower lung lobe with pathological lymph nodes and bilateral adrenal nodules. Fine-Needle-Aspiration through bronchoscope revealed a cytology compatible with SCLC. Brain-MRI revealed a high-signal-intensity lesion in the pontine tegmentum that wasn´t enhanced with gadolinium. She was diagnosed with anti-Ri positive paraneoplastic Rombencefalitis, secondary to SCLC. She was treated with high-dose intravenous methylprednisolone pulse therapy, 1gr for 5 days without response and started standar chemotherapy (Carboplatin plus etoposide). Neurological deficits persisted during the subsequent chemotherapy.
Conclusion: Anti-Ri-antibody-associated paraneoplastic syndrome has been linked to ataxia and opsoclonus-myoclonus. However, even in the absence of opsoclonus, oculomotor dysfunction is usually prominent and the brainstem is a major site of autoimmunity. This case, showing an Anti-Ri-antibody-associated syndrome with oftalmoplegia without opsoclonus, supports the clinical disparity of this entity.
Disclosure: Nothing to disclose

EP3172

Aggressive paraneoplastic encephalo-myelo-polyradiculoneuritis with anti-VGCC antibodies and anaplastic lymphoma in a 17-year-old patient: A case report

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Background and aims: Paraneoplastic neurological syndromes (PNS) in lymphomas have importnat diffrences compared with those in solid tumors. Classical PNS are rarer; onconeural antibodies are absent in most PNS; and at the time of diagnosis, lymphomas in people with PNS are already extended. This makes the diagnostic of PNS in lymphomas chalenging

Methods: We report the case of a 17-year-old girl with an aggresive form of encephalo-myelo-polyradiculoneuritis associated with anti-VGCC antibodies which led to the discovery of anaplastic lymphoma

Results: The patient presented with subacute headache, vomiting and drowsiness, cerebellar ataxia and axonal sensory-motor polyradiculoneuritis. These were followed by opsoclonus, urinary retention, severe limb weakness and dysarthria. The clinical peak was reached at 3 weeks from onset. Extensive workup ruled out infection. Brain MRI showed mild hiperintensity in the pons and cerebellar peduncles. Immunophenotyping from CSF was normal. Extensive screening of antineuronal antibodies was negative except for VGCC N and P/Q antibodies. The pathology from an axillary lymphadenopathy showed a CD30+, ALK-anaplastic lymphoma. Despite repeated courses of ivIg, plasma exchange, aggresive immunosuppresion and cytostatic chemotherapy she relentlessly worsened requiring nasogastric feeding and mechanical ventilation, and died at 2.5 months from onset.

Conclusion: Apart from cerebellar degeneration in Hodgkin's lymphoma and poly/deramtomyositis in both Hodgkin's and non-Hodgkin's lymphoma, other PNS are very rare in people with lymphoma. Of our knowledge, this is the firs reported case of encephalo-myelo-polyradiculoneuritis with anti-VGCC antibodies associated with anaplastic lymphoma. Screening for neoplasia in progressive subacute unexplained neurological syndromes is of utmost importance

Disclosure: Nothing to disclose

EP3173

Presenting features, referral pathways, and waiting times for patients with glioblastoma multiforme: A retrospective cross-sectional analysis

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Background and aims: Glioblastoma multiforme (GBM) is a highly malignant form of glioma with a universally poor prognosis, despite advances in treatment and the introduction of national UK cancer waiting time targets. We aimed to assess the common presenting features, and the effects of referral pathway on patient outcomes.

Methods: We collected data for all cases diagnosed locally between 2009 and 2016, including clinical features, referral route, and mortality. Patterns of presenting signs and symptoms were compared with previous studies, and current NICE guidelines for the referral of suspected brain cancer. Timelines for discussion, investigation and treatment were constructed for each patient, and compared for evidence of variation in care and clinical outcomes based on referral route.

Results: Of 58 cases, emergency admissions accounted for 69%, followed by non-urgent GP referrals (19%) and urgent referrals (9%). Presenting features were highly variable and included headache, weakness, seizures, and cognitive deficits. There was no difference in waiting time to first specialist discussion, biopsy, or treatment between emergency and urgent referral cases. Non-urgent referrals experienced longer waits for specialist discussion (p=0.037) and biopsy (p<0.001). However, this had no impact on time to initiation of treatment or on 1, 3, or 5-year survival.

Conclusion: Our study shows that the majority of patients with high-grade gliomas are not detected via the urgent referral system, and that referral route has a negligible impact on patient care. This highlights significant human and financial resources that could be more productively deployed elsewhere, and the need for more effective strategies of referral and investigation.

Disclosure: Nothing to disclose

EP3174

Oligodendroglioma with a microscopic pleomorphic xanthoastrocytoma-like perivascular lesion

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Background and aims: The coexistence of diffuse and localized glioma has rarely been reported. Herein, we present a histological and genetic case study of concurrent oligodendroglioma and pleomorphic xanthoastrocytoma (PXA).

Methods: A 48-year-old male presented with a generalized seizure. Magnetic resonance imaging (MRI) revealed a non-enhanced mass in the left frontal lobe, which was suggestive of low-grade glioma. The patient was monitored with serial MRI, which revealed slight enlargement of the tumor. The patient underwent a craniotomy and tumor resection about 18 months after the initial symptoms appeared.

Results: Examination of the surgical specimen showed an oligodendroglioma containing a localized astrocytoma element, which corresponded to PXA, measured only 0.9 mm in greatest diameter, and was almost completely limited to the Virchow-Robin space of the superficial cortex. No elevated mitotic activity, microvascular proliferation, or necrosis was found in either tumor. Immunohistochemistry confirmed that each tumor was mIDH1R132H-positive, p53-negative, and ATRX-positive. Genetic analysis demonstrated that each component harbored an IDH1 G395A mutation, 1p/19q co-deletion, and a TERT promoter C228T mutation, whereas no TP53 or BRAF mutations were detected. The diffuse glioma met the diagnostic criteria for oligodendroglioma, IDH-mutant and 1p/19q-codeleted, according to the 2016 World Health Organization classification of tumors of the central nervous system. Genetic testing of the microscopic PXA-like lesion was performed with laser microdissection.

Conclusion: Genetic analysis confirmed that this case involved an unusual type of combined glioma of the same genotype rather than a collision tumor. This case provides further insights into the pathogenesis of glioma.

Disclosure: Nothing to disclose

EP3175

Diagnostic markers of paraneoplastic peripheral neuropathy in patients with breast cancer

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Background and aims: Paraneopalstic peripheral neuropathy (PPN) occurs in 3-20% of patients with breast cancer (BC). Onkoneural antibodies appear in the blood of patients and lead to the appearance of neurological symptoms in 1-4 years before the diagnosis of cancer.

Objective: To detect the clinical, neurophysiological and neyroimmunological markers PPN in patients with BC.

Methods: 61 women with BC and complaints of weakness and sensory disorders in the limbs (mean age: 53.1±9.5 years; BC mean duration: 2.5±1.3 years; BC stages I–IV). Detection onkoneural of antibodies in the serum of patients were carried out using Neuronal Antigen Profile EUROLINE (IgG) in vitro by immunoblotting. Bioelectric potentials of peripheral nerves of the limbs were recorded using stimulation electroneuromyography.

Results: Clinical symptoms symmetric distal poly-neuropathy detected in 93% of patients. Movement disorders dominated -53%. Sensory motor polyneuropathy occurs in 47% of patients. Neurological symptoms PPN occurred an average for 2 years in 67% of women (24,0 (8,0-30,0) months) to the diagnosis of BC. Results of electromyography (low amplitude of motor response and speed of the nerves) are correlated with the clinical picture in 54% of patients. Onkoneural antibodies found in the sera of 71% of patients (anti-CV2-18%; anti-Hu-7%; anti-Ma2-58%; anti-Yo-17%).

Conclusion: Disorders of the peripheral nervous system in BC is associated at the first place with autoimmune response to antigens produced by tumor cells. Clinical manifestation of PPN ahead of clinical manifestation of cancer. Onkoneural antibodies in the serum of patients with neurological symptoms polyneuropathy can be used for BC in the early stages.

Disclosure: Nothing to disclose

EP3176

Paraneoplastic cerebral cytotoxic lymphocytic vasculitis associated with anaplastic ganglioglioma – a case report

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Background and aims: Gangliogliomas are rare (1.3% of all primary brain tumours) and consist of both neuronal and glial elements. Anaplastic gangliogliomas are even rarer, accounting for 1-5% of all gangliogliomas. Paraneoplastic T-cell vasculitis of the CNS is very rare.

Methods: We report the case of a 25-year-old man with a 6-month history of episodic anxiety, followed by left hemiparesis and partial complex seizures. A brain MRI revealed two large enhancing tumours (left temporal and right fronto-parietal) with necrotic areas and important oedema. The tumour in the temporal lobe was resected. The pathological examination showed a massive lymphocytic vascular and perivascular proliferation with activated CD8+CD4- T-cells and no lymphomatous cells. Infections that could mount the T-cell response (HIV, HTLV1 and Toxoplasma gondii) were ruled out. Hybridization in situ for EBV was negative. Further tissue immunocytochemistry showed anaplastic ganglioglioma (WHO 9505/3).

Coronal fluid attenuation inversion recovery brain MR image showing bilateral lesions suggestive of vasculitis
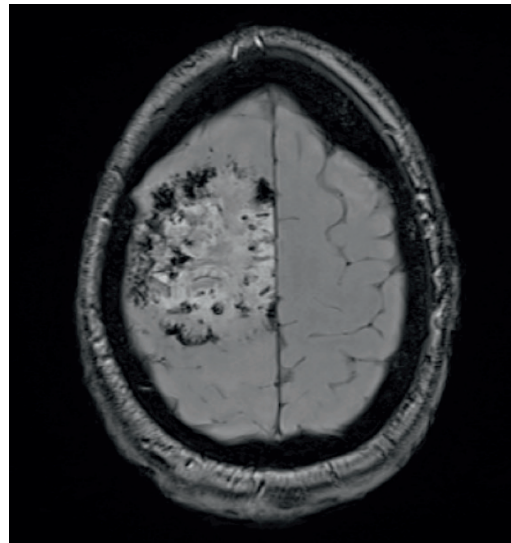
Susceptibility weighted MR image showing multiple bleedings in the periphery of the fronto-parietal lesion

Axial T2-weighted MR image showing the fronto-parietal lesion

Results: The massive vasogenic oedema secondary to the vasculitic cytotoxic T-cell response led to a relentless clinical worsening despite strong and early immunosuppression with high dose steroids, cyclophosphamide, methotrexate and ivIg, and a left decompressive hemicraniotomy. After four weeks the patient died.

Conclusion: The massive cytotoxic lymphocytic vasculitis in the presence of a aggressive type of brain tumour suggests a paraneoplastic mechanism. This is the first case reported of a secondary T cell response directed against brain vessels probably driven by anaplastic ganglioglioma.

Disclosure: Nothing to disclose

EP3177

Bilateral vestibulocochlear nerve enhancement as an isolated brain MRI sign of leptomeningeal carcinomatosis

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Background and aims: Leptomeningeal carcinomatosis occurs in approximately 5% of patients with cancer. Clinical manifestations can be highly variable and may affect both central and peripheral nervous system. Involvement of multiple cranial nerves is common, with III, IV, VI and VII nerves most often affected. Isolated vestibulocochlear nerve involvement is rare. This report describes a case of a patient with vertigo and a bilateral VIII nerves enhancement as clinical-imagological presentation of leptomingeal carcinomatosis.

Results: A 56-year-old woman presented, at our emergency room, with a one week history of vertigo and imbalance. She was a smoker and had a history of lung adenocarcinoma diagnosed one year before, treated with pulmonary lobectomy and chemotherapy. She denied other symptoms, namely headache. On examination, she had a right gaze-evoked nystagmus and a sensory ataxia with positive Romberg`s sign. She had no meningism and no obvious other neurological signs and the fundus oculi examination was normal. Head computed tomography (CT) showed no abnormalities. Brain MRI showed a contrast enhancement of both vestibulocochlear nerves. CSF analysis showed pleocytosis and the cytology revealed malignant cells, compatible with a diagnosis of metastatic adenocarcinoma.

Conclusion: Our data show that vestibulocochlear symptoms represent the only clinical manifestation in a small proportion of patients (about 10%) with leptomeningeal carcinomatosis. Isolated bilateral vestibulocochlear nerve enhancement is a rare imagological finding and should be considered in the differential diagnosis even in the absence of associated clinical symptoms and neuroimaging alterations more suggestive of meningeal carcinomatosis.

Disclosure: Nothing to disclose

EP3178

Glioblastoma as differential diagnosis of autoimmune encephalitis

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Background and aims: The diagnosis of autoimmune encephalitis (AE) relies on clinical, MRI and laboratory criteria. Since autoantibody (Ab) testing is not available in many centers, and its negativity does not always exclude the diagnosis, Ab-status was not included in the recent consensus criteria. By using these criteria, it is possible that other conditions (AE-mimics) could be diagnosed as AE. This study examined glioblastoma patients that present initially as AE.

Methods: Retrospective case series of patients referred for suspected AE (possible, probable or definite, using the 2016 criteria), that later received a final diagnosis of glioblastoma according to 2016 WHO criteria. An extensive literature search was also conducted for similar existing cases.

Results: 10 patients were included for analysis (4 from our series and 6 from the literature). 60% were male; median age was 63. Initially, a diagnosis of AE was clinically suspected based on: working memory deficits (80%), psychiatric symptoms (60%), seizures (50%) (including status epilepticus in 30%). Initial Brain MRI was not in favor of a typical glioblastoma pattern and showed unilateral (50%) or bilateral selective limbic involvement. Three patients exhibited initial slight contrast enhancement. When MR-spectroscopy was performed (3 cases), an increased Cho/NAA ratio was detected. A clear inflammatory CSF was present in 4 patients and 2 showed Ab-positivity (NMDAR, VGKC). Median delay between suspicion of AE to GBM diagnosis was 3 months.

Conclusion: An alternative diagnosis of glioblastoma should be considered in patients presenting initially as AE, especially if they are middle-aged/elderly, male, and with an atypical MR-spectroscopy.

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EP3179

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Ageing and dementia 1

PR1001

Structural and functional brain connectome architecture in Alzheimer's disease and amnesic mild cognitive impairment patients

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Background and aims: To investigate structural and functional brain network architecture in Alzheimer's disease (AD) and amnesic mild cognitive impairment (aMCI).
Methods: Ninety-seven AD, 51 aMCI (26 converters to AD [c-aMCI] within 2.5 years), and 51 controls underwent Diffusion Tensor (DT) and resting-state functional MRI. Graph analysis and connectomics assessed global and local topological network properties and regional structural and functional connectivity.
Results: Compared with controls and aMCI, AD patients showed altered global properties (lower mean structural local efficiency and functional nodal strength, longer mean functional path length). c-aMCI patients had altered structural and functional topological features of the frontal and temporal lobes relative to controls. At the regional level, compared to controls: AD and c-aMCI patients showed widespread structural connectivity alterations; AD had decreased functional connectivity involving medial/ lateral parietal, hippocampal, superior temporal and middle occipital nodes, bilaterally; c-aMCI patients showed decreased functional connectivity involving anterior cingulum bilaterally and left precuneus and hippocampus; nonconverters to AD (nc-aMCI) showed a few connections with altered structural connectivity and no functional abnormalities. Compared to nc-aMCI, AD and c-aMCI patients showed structural (but not functional) connectivity alterations involving hippocampi, parieto-occipital and fronto-temporal nodes. In patients, the loss of structural connectivity correlated with the decreased functional connectivity in the same regions.
Conclusion: Brain networks properties are severely altered in AD and, locally, in c-aMCI. DT MRI may help predicting the conversion into AD in aMCI. The larger pattern of structural than functional connectivity alterations in the AD spectrum suggests that a reduced structural integrity precedes functional connectivity changes.

PR1002

APOE genotype in cognitively intact nonagenarians

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Background and aims: The presence of ε4 alleles within the APOE genotype is associated with a higher risk of developing late-onset Alzheimer´s disease (AD). The prevalence of AD among individuals over 90 years of age is 30 to 40%. In this study we analyze APOE status in cognitively intact nonagenarians who seem resistant to cognitive impairment associated with aging.

Methods: DNA samples from 100 cognitively preserved nonagenarians were recruited in a hospital setting. Cognitive status was evaluated by interviews with subjects and relatives, preserved independence for ADL, and cognitive testing including MMSE >27/30 and Hopkins Verbal Learning Test with spared free-recall. ApoE genotype was compared with a series of late-onset AD cases and a control population using one sided tests for proportions.

Results: Age range was 90 to 101 years (mean 93); 65 subjects were women and 35 men. Ninety-four of the subjects carried an APOE ε3/ε3 genotype, 5 were ε3/ε4, and 1 case was ε4/ε4. There were no subjects with ε2 alleles. The overall frequency of ε4 alleles in this group (6%) was significantly lower than in controls (12%, p=0.032), and compared to sporadic (33%) or familial late-onset (66%) AD cases (p=0.001).

Conclusion: The absence of APOE ε4 alleles protects against cognitive decline in the very elderly, although rare cases may carry ε4 homozygousy without developing dementia.

Disclosure: Nothing to disclose

PR1003

Mental imagery of gait in normal pressure hydrocephalus

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Background and aims: Normal pressure hydrocephalus (NPH) represents the main cause of reversible dementia, but its diagnosis is complex, because its clinical and radiological presentations share similarities with its mimics (i.e. cerebrovascular dementia or parkinsonian syndromes). Gait improvement after CSF tapping is demonstrated in patients with NPH and helps to identify NPH from their mimics. However, changes in mental imagery of gait after CSF tapping have never been compared between NPH and their mimics. This study aims to compare the changes of the Timed up and go (TUG) and its imagined version (iTUG) after CSF tapping between NPH patients and mimics.

Methods: TUG and iTUG were performed before and 24 hours after CSF tapping in 117 patients (75.8±6.9 years; 35% female) with suspicion of NPH (68 NPH and 49 mimics) based on gait or cognitive abnormalities and ventriculomegaly. White matter abnormalities and ventriculomegaly were systematically assessed on brain imaging.

Results: NPH patients showed a decreased iTUG after CSF tapping, whereas mimics increased their performance (-17.29±37.56% versus +4.81±42.94%, p-value: 0.003). Multivariable logistic regressions showed that not only improved (i.e. decreased) TUG (O.R.: 0.98, 95%CI: [0.97;1.00], p-value: 0.013) but also mental imagery (iTUG) (O.R.: 0.98, 95%CI: [0.97;1.00], p-value: 0.004) after CSF tapping were both associated with NPH diagnosis, after adjusting for age, gender, white matter abnormalities and ventriculomegaly.

Conclusion: Mental imagery of gait is also modified after CSF tapping in NPH patients, and could be used to identify NPH patients from their mimics.

Disclosure: This study was supported by the Geneva University Hospitals (PRD 11-I-3 and PRD 12-2013-I); Gilles Allali was supported by the Baasch-Medicus Foundation.

PR1004

Phospholipase D3 (PLD3) mRNA expression is decreased in the hippocampus of Alzheimer's disease patients

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Background and aims: Whole-exome sequencing has recently revealed a rare missense variant in PDL3 gene (rs145999145) to be associated with late onset Alzheimer's disease (AD). Nevertheless, the association remains controversial and little is known about the role of PDL3 in AD. Interestingly, PLD3 encodes a phospholipase that may be involved in APP processing. Our objective was to assess PLD3 messenger RNA (mRNA) expression levels in the human hippocampus affected by AD and its relationship with beta-amyloid and phosphorylated-tau (p-tau) burden.

Methods: We measured PLD3 mRNA levels in the hippocampus by real time quantitative PCR within a cohort of neuropathologically confirmed controls (n=10) and AD (n=21) cases that passed our RNA quality control. We correlated PLD3 mRNA hippocampal levels with beta-amyloid and p-tau burden measured by an ImageJ-based semi-automated method. Statistical significance for intergroup differences was assessed by the Mann-Whitney U test. Spearman's rank correlation coefficient was used to determine correlation between AD-related pathology and PDL3 mRNA levels.

Results: A 1.7-fold decrease in PLD3 mRNA levels was observed in the hippocampus of AD cases compared to controls (p <0.05). Moreover, PLD3 mRNA levels in the hippocampus inversely correlated with the average area of beta-amyloid burden (rSpearman=-0.373, p<0.05) and p-tau deposition (rSpearman=-0.390, p<0.05).

Conclusion: PLD3 mRNA levels are decreased in the human hippocampus in AD cases compared to controls and inversely correlate with AD-related pathology in the human hippocampus. These data add evidence to support a link between PLD3 and AD.

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PR1005

Diagnostic utility of FDG-PET in detecting Alzheimer's disease in patients with persistent MCI of uncertain origin

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Background and aims: We performed a systematic review to assess the available evidence of FDG-PET utility in detecting probable Alzheimer's disease (AD) in MCI patients of uncertain origin.

Methods: The search was performed on Medline on December 20, 2015. Critical outcomes were sensitivity and specificity of FDG-PET in predicting AD in MCI, as compared to standard workup, and versus gold (pathology/biomarker) or reference standard (conversion). The minimum sample size was set a priori at n=15 patients with the target condition. Data were extracted and assessed as to publication bias, heterogeneity, imprecision, risk of bias, indirectness, and applicability.

Results: Out of the 35 papers obtained, only 16 reported the outcomes of interest. These included 1371 patients. Visual assessment led to higher sensitivity (91%, SD=6) but lower specificity (70%, SD 25) than semi-quantitative assessment (sensitivity: 63%, SD=21; specificity: 78.5%, SD=11) in predicting AD conversion in MCI patients (Table). The evidence assessment did not detect substantial risk of bias. Large inconsistency among semi-quantitative results is due to tools variability. Concerns regard applicability, as the more reliable semi-quantitative methods of image analysis are increasingly, but not routinely adopted in the clinical context. The typical hypometabolic pattern in MCI converting to AD includes posterior cingulate and tem:poparietal areas.

Table. FDG-PET in detecting AD in MCI patien

OUTCOME	ASSESSMENT	N° OF STUDIES	N° cMCI/nc-MCI	REFERENCE STANDARD	RISK OF STUDY BIAS	IMPRECISION	INDIRECTNESS	INCONSISTENCY	EFFECT (mean ±SD)	QUALITY OF EVIDENCE (GRADE)
SPECIFICITY	SEMI-QUANTITATIVE	14	369/453	CONVERSION AT FU	NOT SERIOUS	NOT SERIOUS	SERIOUS	SERIOUS	78.5% (SD 11.3)	MODERATE
	VISUAL	2	118/50	CONVERSION AT FU	NOT SERIOUS	NOT SERIOUS	SERIOUS	VERY SERIOUS	69.9% (SD 25.5)	HIGH
SENSITIVITY	SEMI-QUANTITATIVE	14	369/453	CONVERSION AT FU	NOT SERIOUS	NOT SERIOUS	SERIOUS	VERY SERIOUS	62.9% (SD 21.1)	MODERATE
	VISUAL	2	118/50	CONVERSION AT FU	NOT SERIOUS	NOT SERIOUS	SERIOUS	NOT SERIOUS	91.1% (SD 6.3)	HIGH
ACCURACY	SEMI-QUANTITATIVE	10	340/385	CONVERSION AT FU	NOT SERIOUS	NOT SERIOUS	SERIOUS	SERIOUS	75.4% (SD 13.0)	MODERATE
	VISUAL	2	118/50	CONVERSION AT FU	NOT SERIOUS	NOT SERIOUS	SERIOUS	SERIOUS	79.8% (SD 10.8)	HIGH
PPV	SEMI-QUANTITATIVE	6	194/203	CONVERSION AT FU	NOT SERIOUS	SERIOUS	SERIOUS	VERY SERIOUS	64.2 (SD 20.6)	MODERATE TO HIGH
	VISUAL	2	118/50	CONVERSION AT FU	NOT SERIOUS	NOT SERIOUS	SERIOUS	SERIOUS	73.3 (SD 12.6)	HIGH
NPV	SEMI-QUANTITATIVE	6	194/203	CONVERSION AT FU	NOT SERIOUS	SERIOUS	SERIOUS	NOT SERIOUS	84.5 (SD 8.1)	MODERATE TO HIGH
	VISUAL	2	118/50	CONVERSION AT FU	NOT SERIOUS	NOT SERIOUS	SERIOUS	NOT SERIOUS	92.0 (SD 3.0)	HIGH
AUC	SEMI-QUANTITATIVE	7	215/307	CONVERSION AT FU	NOT SERIOUS	NOT SERIOUS	SERIOUS	NOT SERIOUS	0.81 (SD 0.09)	MODERATE TO HIGH
ASSESSMENT OF THE EVIDENCE FOR DIAGNOSTIC UTILITY									**MODERATE**	
		STRENGTH OF RECOMMENDATION (N of studies/patients + GRADE score + critical outcomes effect size)							**STRONG RECOMMENDATION FOR DIAGNOSTIC UTILITY**	

Table. FDG-PET in detecting AD in MCI patients.

Conclusion: The available data provide moderate evidence for moderate diagnostic utility of FDG-PET in detecting AD in MCI. This pattern of evidence is consistent with a strong recommendation of the use of FDG-PET to ascertain the presence of probable Alzheimer's disease in patients with persistent MCI of uncertain origin.

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PR1006

Niemann Pick Type C heterozygosity may predispose to late-onset neurodegeneration

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Background and aims: Niemann-Pick type C (NPC) is an autosomal recessive lysosomal storage disorder with similarities to Gaucher disease due to beta-glucocerebrosidase (GBA) mutations. Given the increased risk of GBA mutation carriers of developing Parkinson's disease (PD), we hypothesize that heterozygous family members (hets) of NPC patients are also prone to late-onset neurodegeneration.

Methods: NPC hets and NPC patients were examined as follows: a neurological exam with video-recording, neuropsychological testing, smell testing, colour vision, optical coherence tomography, video-oculography to assess ocular motor function, "purdue pegboard test" to evaluate visuo-manual coordination, abdominal ultrasound and 18[FDG]-PET examination of brain metabolism. Tests are being performed at different study visits.

Results: So far 18 clinically subjectively-unaffected NPC hets (mean age 52 yrs) and 13 NPC patients (mean age 27.7 yrs) with single or compound NPC1 gene mutations participated. Clinical examination revealed neurological abnormalities in four male NPC hets (tremor, increased muscle tone, diminished reflexes, hearing impairment). Ultrasound showed organomegaly in 3 (out of 6 examined) NPC hets (hepatomegaly in 2, splenomegaly in 1). One male NPC het had slow vertical saccades. Half (n=3 of 6) of the NPC hets (all male, mean age 64.3 years) who underwent PET imaging demonstrated abnormal brain hypometabolism affecting the parietotemporal region (2 subjects) and left hemisphere.

Conclusion: NPC1 heterozygosity may be associated with clinical abnormalities affecting the nervous system and abdominal organs. Our findings suggest that male heterozygotes may be more prone. Neurodegeneration as underlying mechanism is supported by the preliminary PET data.

Disclosure: Nothing to disclose

PR1007

Assessing the independent associations of CSF biomarkers and white matter hyperintensities with grey matter atrophy in dementia

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Background and aims: Grey matter (GM) atrophy is considered a marker of disease progression in dementia.1 We assessed its relationship with the cerebrospinal fluid (CSF) biomarkers amyloid-1-42 (Aβ) and tau and white matter hyperintensities (WMHs) in demented patients and controls.

Methods: CSF Aβ and tau levels were obtained from 42 patients with Alzheimer's disease (AD), either symptomatic or prodromal (Aβ+) and 23 non-AD demented patients (Aβ-). All patients and 20 controls underwent brain MRI. GM atrophy was assessed using an optimized Voxel Based Morphometry protocol. We derived GM fraction (GMF) calculating the ratio of total GM volume to total intracranial volume. WMHs-lesion load was quantified with a semi-automated contouring software.

Results: Multiple regression analysis showed CSF tau levels to be a significant predictor of patients' GMF, with a percentage of variability of the regression model of 36%. CSF Aβ levels didn't correlate with GMF and no differences were observed between Aβ+ and Aβ-. WMHs-lesion load didn't correlate with total GMF. Total GMF resulted higher in patients compared to controls, but not between prodromal AD and AD. Local GMF in the right hippocampal and parahippocampal regions was significantly increased in AD compared to prodromal AD. Such differences weren't observed between prodromal AD and controls.

Conclusion: We found CSF tau levels to be a predictor of brain atrophy in dementia, suggesting a link between GM loss and neurofibrillary degeneration. Conversely, in line with previous studies,2,3 WMHs and Aβ levels are likely not correlated with GM atrophy, playing an independent role in dementia.

Disclosure: Nothing to disclose

PR1008

Use of amyloid PET imaging and cerebrospinal fluid biomarkers in clinical practice: Data from the Czech brain ageing study

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Background and aims: Current guidelines for Alzheimer's disease (AD) lay emphasis on earlier diagnosis and shift the focus from clinical findings to biomarkers. Most widely used metabolic biomarkers are cerebrospinal fluid (CSF) levels of amyloid-β1-42 (Aβ1-42), total-tau (t-tau), and phosphorylated tau (p-tau), as well as amyloid positron emission tomography (PET). However, the use and interpretation of biomarkers in clinical settings may be challenged by the cost, logistics, analytical procedures and cut-off values. We present clinical data from the Czech Brain Ageing Study. The aim was to compare concordance between amyloid PET and Aβ1-42, t-tau or p-tau CSF levels and to investigate the interrelation between the amyloid PET and ApoE status.

Methods: 32 patients with mild cognitive impairment or mild dementia classified as possible AD (National Institute on Aging–Alzheimer's Association criteria; McKhann 2011) underwent volumetric MRI, neuropsychological assessment, ApoE genotyping, flutemetamol PET and CSF sampling. PET results were evaluated visually and cutoffs of <550 pg/mL-and a more lenient cutoff of 650pg/mL (Aβ1-42), >358pg/mL (t-tau) and >48 (p-tau) were used to determine concordance between these two methods. Pearson Chi-square was used to determine PET and ApoE4 interrelation.

Results: Concordance between PET and Aβ1-42 was highest (88%) for both cutoffs, followed by p-tau (75%) and t-tau (63%). Concordance between all the CSF biomarkers combined and PET was only 47%. There were more ApoE4 carriers in the amyloid positive group (p=0,027; Cramérs V=0,411).

Conclusion: We found very high concordance between PET and CSF levels of Aβ1-42. ApoE4 status was associated with amyloid PET positivity in our cohort.

Disclosure: Nothing to disclose

Autonomic nervous system 1

PR1009

Cardiovascular autonomic function during tilt table testing in patients with syncopal migraine.

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Background: Tilt table testing (TTT) induces passive orthostatic stress that influences hemodynamics and determines cardiovascular system to react. When this process fails, the vasovagal syncope occurs. It could develop in three main patterns: classic, dysautonomic (hemodynamic parameters are falling from the beginning of TTT) and orthostatic intolerance (like dysautonomic but without abrupt drop in syncope).

Aim: to examine the hemodynamic parameters modification during TTT in patients with syncopal migraine.

Methods: Were studied 135 patients divided as: gr I (65 pts) – syncopal migraine, gr II (38 pts) - migraine and gr III (32 pts) - syncope. All patients underwent TTT (Westminster protocol). Hemodynamic parameters (heart rate, systolic and diastolic blood pressure) were recorded every minute. Values were analyzed from baseline (0*), at third (3*), sixth (6*) and ninth (9*) minutes, three minutes before syncope (-3), syncope (S) and three minutes after recovery (+3) as mean and variation from baseline. All data collected were analyzed using SPSS software.

Results: The heart rate and diastolic blood pressure mean values and variations from baseline presented a classical pattern with more pronounced modifications for syncopal migraine patients (fig. 1, 3). Systolic blood pressure in all groups demonstrated dysautonomic pattern (fig 2).
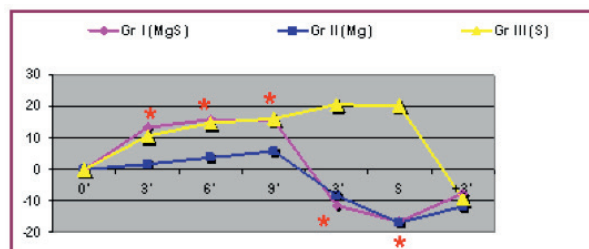
Fig. 1 Heart rate modification during tilt table testing
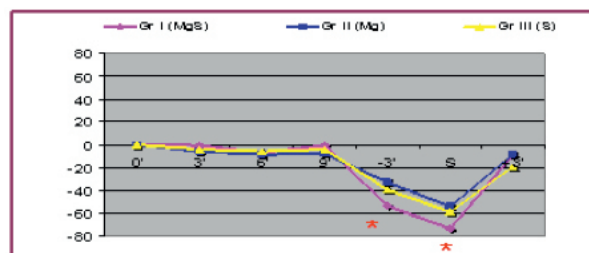
Fig. 2 Systolic blood pressure modification during tilt table testing
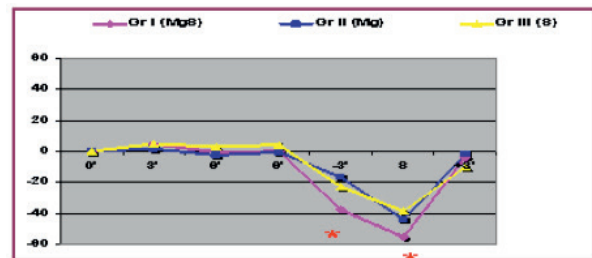
Fig.3 Diastolic blood pressure modification during tilt table testing

Conclusion: In syncopal migraine patients hemodynamic parameters react differently compared to migraine group and syncope group, presenting a classic pattern for heart rate and diastolic blood pressure modifications and a dysautonomic pattern for systolic blood pressure, suggesting an abnormal cardiovascular autonomic function during TTT in these patients.

Disclosure: Nothing to disclose

PR1010

Cardiovagal responses to autonomic challenges are reduced after six months of Fingolimod-therapy in patients with multiple sclerosis

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Background and aims: In patients with multiple sclerosis (MS), several months of Fingolimod-therapy might dampen cardiac autonomic modulation at rest (Hilz et al., Neurology, 2016: P5.119.). However, the effects of prolonged Fingolimod-therapy on cardiovascular responses to autonomic challenge remain unknown. Therefore, we aimed to assess cardiovascular responses to autonomic challenge manoeuvres in MS-patients after six months of Fingolimod-therapy.

Methods: In 15 MS-patients (10 women, age 32.9 ± 9.7 years, EDSS 2.27 ± 1.46), we monitored respiration, RR-intervals and blood pressure during metronomic deep breathing (MDB, 6 cycles/min for 180 seconds), Valsalva-Manoeuvre (40 mmHg expiratory strain for 15 seconds), and upon active standing-up. Measurements were performed before and six months after Fingolimod-therapy. We calculated expiratory-inspiratory-ratios (E/I-ratios) during MDB, Valsalva ratios (VRs), and 30/15-RRI-ratios upon standing-up. Values were compared before and six months after Fingolimod-therapy (paired t-test for normally distributed values; Wilcoxon-test for non-normally distributed values; significance: $p<0.05$).

Results: Values were significantly reduced six months after than before Fingolimod-initiation for E/I-ratios (1.57 ± 0.25 vs. 1.28 ± 0.12; $p<0.001$), 30/15-RRI-ratios (1.35 ± 0.26 vs. 1.20 ± 0.12; $p=0.001$) and VRs (1.78 ± 0.44 vs. 1.44 ± 0.26; $p=0.043$).

Conclusion: After six months of Fingolimod-therapy, decreased E/I ratios indicate reduced cardiovagal modulation, decreased 30/15-RRI-ratios suggest insufficient cardiovagal withdrawal in response to baroreflex-unloading, and decreased VRs indicate reduced cardiovagal activation upon baroreflex-loading. These results show that Fingolimod not only alters resting autonomic modulation (Hilz et al., Neurology, 2016: P5.119.) but impairs cardiovagal responses to challenge after six months of treatment.

Disclosure: This study was in part financially supported by Novartis Pharma, Germany.

PR1011

Absent cardiac and muscle sympathetic nerve activities involvement in Ross syndrome: A follow-up study

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Background and aims: Ross syndrome is a rare disorder characterized by selective involvement of post-ganglionic skin sympathetic nerve fibres with absent cholinergic sudomotor fibres as hallmark of the disease. It is still not well defined whether, through time, autonomic dysfunction remain localized to skin fibres or it spreads more widely affecting also cardiovascular autonomic system. To clarify this aspect we report a cardiovascular autonomic system follow-up study in 4 patients affected by Ross syndrome.

Methods: We studied 4 patients affected by Ross syndrome for follow-up mean period of 5 years (range 1-10 years). All patients complained of anhydrosis with heat intolerance and showed areflexia and mydriatic pupil not reacting to light (tonic pupil) on neurological examination and absent cholinergic sudomotor fibres on skin biopsy. All patients underwent cardiovascular reflexes (CVR) consisting in head up tilt test (10 min), Valsalva maneuver (40mmHg x 12 sec), deep breathing (6 breath/min x 2 min), isometric handgrip (1/3 of maximal effort for 3-5 min), cold face (i4°C° water in the front for 1 min) and microneurography recording of muscle sympathetic nerve activity (MSNA) from common peroneal nerve.

Results: CVR and MSNA resulted normal at baseline and unchanged over the follow-up in all patients although anhydrosis was usually widespread on patient's clinical re-evaluation.

Conclusion: Our study shows that cardiovascular autonomic system is not affected in Ross syndrome differently from skin autonomic activity dysfunction which tend to progress over time. However this study should be considered preliminary since a limited number of patients were studied. A study involving a large cohort of patients is needed before drawing any definite conclusion.

Disclosure: Nothing to disclose

PR1012

Moderate intensity exercise improves heart rate variability in obese adults with type 2 diabetes

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Background and aims: Exercise training may improve cardiac autonomic regulation in a variety of clinical populations including obese adults with type 2 diabetes. Thus, the main aim of this study was to determine the effect of thrice-a-week, six months, moderate aerobic exercise on cardiac autonomic function as measured by heart rate variability in obese adults with type 2 diabetes.

Methods: 41 obese adults with type 2 diabetes participated in this study. Anthropometric and metabolic parameters were measured, and resting electrocardiogram (ECG) for the HRV analysis at spontaneous respiration was recorded for 5 min in supine position before and after six months of supervised aerobic training given thrice-a-week.

Results: The mean age, body mass index (BMI), and duration of diabetes of the study population were 44.1±4.5 years, 30.94±1.36 kg/m2, and 16.3±2.7 years, respectively. In time domain variables, standard deviation of all RR intervals (SDNN), the square root of the mean of the sum of the squares of differences between adjacent RR intervals (RMSSD) and percentage of consecutive RR intervals that differ by more than 50 ms (pNN50) were significantly increased after exercise. In frequency domain variables, high frequency (HF) (ms2) and HF (nu) were significantly increased while low frequency (LF) (ms2) were significantly decreased after exercise. But LF (nu) and LF/HF (%) ratio were unaffected after exercise.

Conclusion: These data suggest that thrice-a-week moderate intensity aerobic exercise for six months improves cardiac rhythm regulation as measured by HRV in obese adults with type 2 diabetes.

Disclosure: Nothing to disclose

PR1013

Depression of daily autonomic rhythms as indicator of chronic stress

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Background and aims: Stress is associated with autonomic nervous system disbalance, so it may be assessed by study of heart rate variability (HRV).

The aim of the study was to identify the indicators of chronic stress by studying the periodic changes of heart rate variability during daylight hours

Methods: 98 students were examined with the use of psychological questionnaires and monitoring of HRV from 8 a.m to 8 p.m. A K-means cluster analysis was performed to identify groups of students with low (n=59), medium (n=22) and high (n=17) emotional stress based on the results of questionnaires measurements of the stress level.

Mean of the standard deviations of NN intervals in all 5-minute segments of each four-hour recording in the 8 a.m - 8 p.m period (4-hour SDNN index), low-frequency component (LF), high-frequency component (HF), total power (TP), the ratio of LF to HF power (LF/HF) were analyzed. The patterns of 4-hour HRV data in different thirds of the daytime were compared between low, medium and high stress groups with the use of repeated measures ANOVA.

Results: SDNN indexes, LF, HF and TP varied significantly in different thirds of the daytime in low stress subjects, which was not observed in the high stress students. The quantitative HRV criteria of chronic stress were formulated.

Conclusion: Monotony of daily heart autonomic regulation is associated with chronic emotional stress and can be regarded as its neurophysiological biomarker.

Disclosure: Nothing to disclose

PR1014

Structural and functional lesions in the brainstem and spinal cord protect against syncope

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Background and aims: The aim of this study was to investigate weather MS patients with functional and structural lesions of the brainstem and spinal cord can develop syncope.

Methods: Altogether 86 MS patients were enrolled (61 females, mean age 32.01±7.94, median EDSS 2.0, range 0-4). In all patients head-up tilt table test, ocular and cervical vestibular evoked myogenic potentials (VEMPs) and brain and cervical spinal cord MRIs were performed on a 1.5T scanner.

Results: Syncope developed in 18 (20.9%) patients. Twenty-three (26.7%) patients had lesions present in both the brainstem and cervical spinal cord. Only one of them developed syncope, while 94.4% of patients with syncope did not have lesion evident on both, the brainstem and cervical spinal cord (Chi square=5.217, p=0.022). Conduction block on VEMP was evident in 17 patients (19.8%). Only 2 out of 18 patients with syncope (11.1%) had conduction block on VEMP (Figure 1). Based on this results we introduced a model for predicting syncope in patients with MS. The model predicts that only patients who do not have conduction blocks on VEMP and do not have MR lesion both on brainstem and cervical spinal cord, could develop syncope. In our cohort, proposed model accurately detected 83.3% of patients with syncope (15 of 18); Chi-Square=4.980, p=0.026.

Conclusion: A finding that a MS patient with structural and functional damage of the brainstem cannot develop syncope points to the central role of the brainstem pathways in the pathophysiology of syncope.

Cerebrovascular diseases 1

PR1015

Rheological properties of blood in acute ischemic stroke and cerebral small vessel disease

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Background and aims: Microcirculation in tissues depends on the state of capillary vessels and one of the central part of the pathophysiology of acute stroke and cerebral small vessel disease is the deterioration of rheological properties of blood. Disturbances in hemorheological parameters provoke the development of zone of ischemia, local stasis, hypoxia. The aim of study is measuring rheological properties of blood in acute ischemic stroke (AIS) and cerebral small vessel disease (SVD).

Methods: The study included 47 patients with AIS, age 62 [53; 67] years, 48 patients with SVD, age 60 [53;65] years, and 20 control patients, age 55 [54;59] years. Hemorheological parameters assessed were: whole blood viscosity, plasma viscosity, hematocrit, erythrocyte aggregation (ErAg) and deformability (ErDef), plasma fibrinogen concentration.

Results: Patients with AIS had significant changes in hemorheological parameters: increased whole blood and plasma viscosity, increased plasma fibrinogen, decreased ErAg and increased ErDef. Patients with SVD had increased blood viscosity, reduced ErDef, increased ErAg and plasma fibrinogen. AIS patients had higher rates of blood viscosity, increasing of plasma viscosity, hematocrit, fibrinogen and ErAg in comparison with SVD patients (figure 1, 2). Patients with SVD had significantly reduced ErDef in shear rates 90-360 s-1, compared with patients with AIS and control group (figure 3).
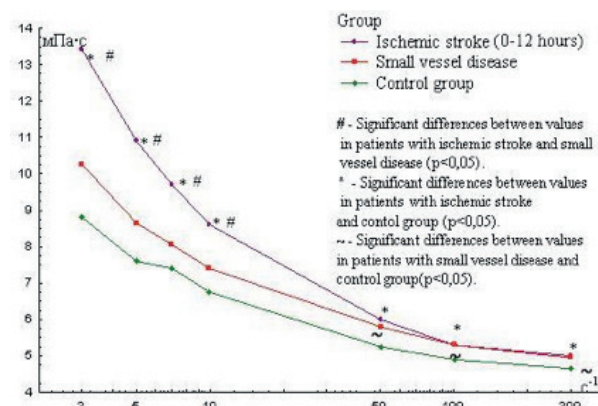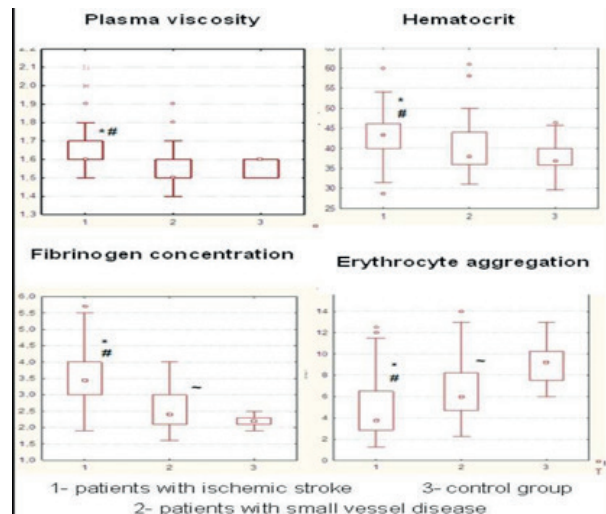
Figure 2. Plasma viscosity, hematocrit, erythrocyte aggregation and plasma fibrinogen concentration in patients with ischemic stroke, small vessel disease and control group
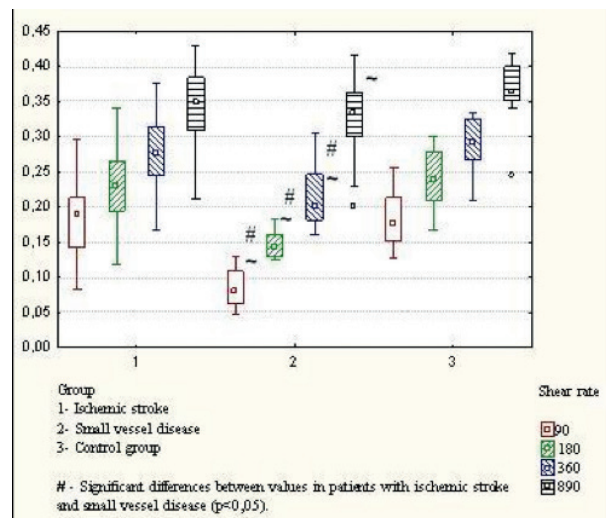
Figure 3. Erythrocyte deformability at different shear rates in patients with ischemic stroke, small vessel disease and control group

Conclusion: Increased blood viscosity, associated with disturbances of deformability in patients with cerebral small vessel disease could be one of the possible pathogenic mechanisms leading to the development of acute cerebral ischemia.

Persistent changes in hemorheological parameters lead to changes in microcirculation of patients with chronic and acute ischemic disorders.

Disclosure: Nothing to disclose

Figure 1. Blood viscosity at different shear rates in patients with ischemic stroke, small vessel disease and control group

PR1016

Cancelled

PR1017

Anticoagulation after acute ischemic stroke: What is happening to our patients?

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Background and aims: Optimal timing for initiation of oral anticoagulation (OAC) in acute ischemic stroke (AIS) of embolic source is undetermined. We aim to characterize AIS or hemorrhage after OAC for secondary stroke prevention.

Methods: Retrospective observational study of AIS outpatients, in two years. Stroke severity was defined as: 1) Minor: transient ischemic attack, lacunar or parcial stroke with National Institutes of Health Stroke Scale (NIHSS)<5; 2)Moderate: partial Middle Cerebral Artery (MCA), Anterior (ACA) or vertebrobasilar infarction, with NIHSS=6-16; 3) Major: NIHSS>16 and/or total ACA/MCA/vertebrobasilar infarction. Data on demographics, clinical characteristics and follow-up were collected. We present descriptive and inferential statistics.

Results: In 467 patients, 49 initiated OAC after AIS, (10.5%,95% confidence interval:7.7%-13.3%). 55.1% were men (median age:73 years), median admission NIHSS 7 (range:0-27), 49% underwent thrombolysis. OAC was initiated 9 days post AIS (median,range:0-94 days): Atrial fibrillation (59.2%), complex aortic atheromatosis (22.4%) and paradoxical embolism (22.4%) were the main reasons for OAC. In 704 days of median follow-up, eight patients (16.3%) had new events (median time to event: 274 days, range:10-899 days): TIA (n=2), AIS (n=4), hemorrhagic stroke (n=1) and fatal systemic hemorrhage (n=1). One AIS occurred before OAC start and two due to irregular OAC compliance. There was no association between initial stroke severity, starting time or type of OAC and new event.

Conclusion: OAC therapy initiation after AIS was safe regarding early bleeding complications. New AIS occurrence was similar to other studies, in some cases related to therapeutic failure. Best time to start OAC is a clinical challenge where prospective data is needed.

Disclosure: Nothing to disclose

PR1018

Progressive multifocal leukoencephalopathy mimicking ischemic stroke on imaging

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Background and aims: We report a case of progressive multifocal leukoencephalopathy (PML) presenting as ischemic stroke in an apparent immunocompetent patient.

Methods: Case report

Results: A 51-year-old woman with unremarkable history presented with a 7 week history of progressive occipital headache. During the last week it was accompanied by nausea, vomiting and an unsteady gait. On examination cerebellar signs with rotatory nystagmus on right-sided gaze were noted. CT (figure 1) showed a hypodensity in the right cerebellar hemisphere. MRI (figure 2) showed a T2 hyperintense lesion on FLAIR-imaging with slightly restricted diffusion (figure 3). These findings were suggestive for semi-recent ischemia, but the atypical presentation raised a broad differential diagnosis. Standardized work-up for stroke in the young revealed a positive HIV-serology with CD4+ cell count of 41 cells/μL. Lumbar puncture showed slight pleocytosis (8 cells/mm^3), with a positive PCR for polyomavirus. Upon review of the previous imaging the following factors were suggestive of PML: the lesion was confined to the white matter, it did not fit any typical vascular distribution, and it showed restricted diffusion in the margins of the lesion. Repeat brain MRI, 30 days later, showed a slight increase of the lesion, without gadolinium enhancement. Our patient progressively developed severe ataxia and a rubral tremor, until she died 46 days after the diagnosis.
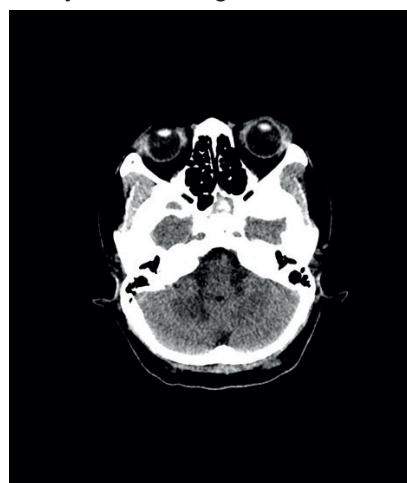
Figure 1: Brain CT upon presentation showing a hypodense zone in the right cerebellar hemisphere suggestive of semi-recent infarction.
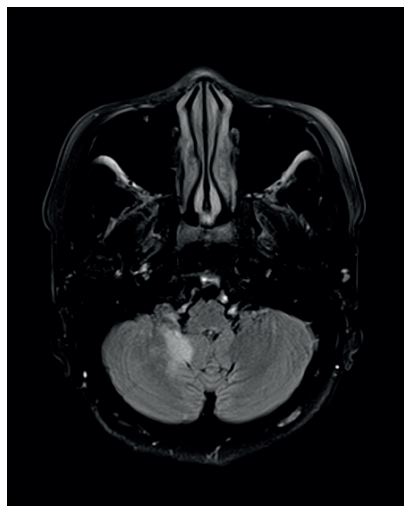
Figure 2: Brain MRI showing a T2-hyperintense lesion in the right cerebellar hemisphere on FLAIR-imaging, confined to the white matter. This zone is not typical of any vascular distribution, though the distributions are known to vary.
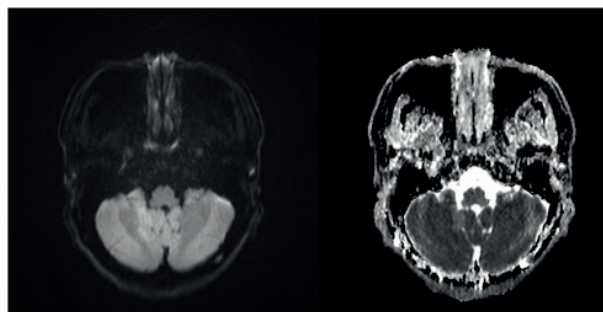
Figure 3: DWI (b1000) appears bright, while ADC appears slightly black, indicating restricted diffusion in the margins of the lesion. Considering the clinical information these findings are suggestive of PML.

Conclusion: This case illustrates PML mimicking ischemic stroke on imaging. The possibility of this rare pathology should be kept in mind in patients presenting with an atypical presentation of stroke, even in those previously thought to be immunocompetent.
Disclosure: Nothing to disclose

PR1019

The relationship between changes in risk factors over time and trends in incidence rates of intracerebral hemorrhage. The Tromsø study 1994-2013

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Background and aims: The aim of this study was to estimate the relationship between changes in risk factors and trends in incidence rates of ICH using individual data from the longitudinal cohort study, the Tromsø Study.
Methods: We included 28,167 individuals aged 30 to 97 years, who participated in at least one of three surveys conducted in 1994-2008. Individuals were followed up with registration of incident ICH until 31 December 2013. Incidence rates were analysed by Poisson regression and hazard ratios (HR) for ICH by Cox proportional hazards analysis. Risk factor levels over time were estimated by generalized estimating equations. Odds ratios for use of anticoagulants at time of ICH were calculated using logistic regression.
Results: A total of 220 ICHs were registered. Systolic blood pressure (HR 1.46, 95% confidence interval (CI) 1.29-1.66), age (HR 2.85, 95% CI 2.38-3.40) and male sex (HR 1.85, 95% CI 1.37-2.50) were independent risk factors for ICH. There was a significant decrease in incidence rates of ICH in women, while incidence rates in men remained stable. Blood pressure levels decreased over time with a steeper decrease in women compared with men, and women had lower blood-pressure levels during the whole period. There was a significant increase in the use of anticoagulants, but not in the proportion of ICHs associated with use of anticoagulants.
Conclusion: We observed a decrease in blood pressure levels which was associated with a reduction in the incidence of ICH in women, but not in men.
Disclosure: Nothing to disclose

PR1020

Carotid artery stenosis, an underestimated cause of recurrence in patients with ischaemic monocular visual loss

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Background and aims: We aimed to determine the prevalence and risk factors of significant carotid artery stenosis (CAS) ≥50% in patients with ischaemic transient or permanent monocular visual loss.

Methods: Setting: TIA clinic, regional referral centre for North-Central London and Moorfields Eye Hospital, London. Consecutive records for all patients with transient or permanent ischaemic monocular visual loss at presentation to the clinic were reviewed from 1st January 2014-30th September 2016. Stroke, TIA or ischaemic monocular visual loss recurrence within 90 days were recorded. CAS was assessed with duplex, CTA or MRA.

Results: 395 patients presented with visual loss, 214 were male(55.4%), mean age 64.5(SD15.0). Causality was symptomatic CAS≥70% according to the NASCET criteria in 8.0%, CAS≥50% in 13.7% and 5.4% had asymptomatic CAS≥50%. Patients with permanent visual loss (n=129) were more likely to have significant CAS compared to patients with transient visual loss (n=257), 20.2% versus 10.5%, p=0.012. 90-day recurrence rate of stroke/TIA/ monocular ischaemia was significantly greater in patients with symptomatic CAS≥50% compared to patients without symptomatic CAS≥50%,18.9% versus 8.7%,p=0.045. Recurrent stroke was 3.8% versus 0.6% p=0.093 in these groups respectively. Age, male sex and hypertension were associated with symptomatic CAS but hyper-cholesterolaemia, diabetes and smoking were not.

Conclusion: CAS≥50% in patients with ocular ischaemia is higher than previously described, approximately one fifth of those with persistent visual loss and 10% of those with transient visual loss. Those with CAS have a higher risk of recurrence and should be investigated and treated as aggressively as other forms of TIA.

Disclosure: Nothing to disclose

PR1021

ABCD2 score and predictors of stroke recurrence in patients with ischaemic monocular visual loss

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Background and aims: We aimed to describe risk factors, predictors and recurrences in patients with ischaemic transient or permanent monocular visual loss.

Methods: Setting: University College London Hospitals daily TIA clinic, main referral centre for North-Central London region and Moorfields Eye Hospital, London. We reviewed consecutive records for all patients with ocular ischaemia from 1st January 2014-30th September 2016. Recurrent ischaemic stroke/TIA/monocular ischaemia within 90days were recorded.

Results: 395 patients presented with visual loss, 220(55.7%) male, mean age 64.4(SD15.1). 292 had complete data to calculate the ABCD2 score at presentation, mainly due to incomplete recording of blood pressure at initial ophthalmology assessment. Median ABCD2 score in patients with ischaemic ocular events was 2. Transient visual loss was associated with lower median ABCD2 score than permanent visual loss of 2 versus 3,(p<0.0001). Hypertension, diabetes and history of smoking were more common in patients with permanent visual loss. Median vascular risk factors were greater in those with permanent events, 1 versus 2(p=0.005). Overall 39(9.9%) had recurrences (1.0% stroke, 7.9% TIA or transient monocular ischaemia, and 1.0% permanent monocular ischaemia). Median ABCD2 score and rate of ABCD2 score≥4 did not predict recurrence. 90-day recurrence rate of stroke/TIA/ monocular ischaemia were more common after transient rather than permanent ocular ischaemia 13.8% versus 2.2%,(p<0.001).

Conclusion: Approximately 10% of patients presenting with monocular ischaemia have further stroke, TIA or ocular ischaemia. High ABCD2 score was not predictive. Further studies are required to identify predictors of permanent visual loss and recurrent stroke in these patients.

Disclosure: Nothing to disclose

PR1022

Is reduced cardiac baroreceptor sensitivity in subacute stroke related to mental stress?

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Background and aims: Reduced cardiac baroreceptor sensitivity (BRS) after acute stroke is associated with worse outcome. The underlying mechanism of the reduced BRS is unclear.

Methods: We evaluated cross correlation BRS in 184 patients with suspected acute stroke within 72 h of symptom onset. Of these 22 patients had a transient ischemic attack and 27 patients had a stroke mimic. 64 age and sex-matched ambulant control subjects without stroke were included.

Results: Compared with controls, BRS was significantly lower in patients with ischemic stroke, TIA and stroke mimics (5.3, 5.7 and 4.3 versus 8.2, $p<0.01$). There was no difference in BRS between right and left hemispheric infarctions (4.6 versus 5.7, $p=0.144$), right and left insular infarctions (4.5 versus 5.9, p 0.286) and insular infarction versus non insular infarction (5.3 versus 5.3, $p=0.996$). Stroke patients with depression had lower BRS values than stroke patients with normal mental health (3.4 versus 5.6, $p<0.05$). Control patients with depression also had lower BRS compared to controls without depression (4 versus 9.3, $p=0.005$).

Conclusion: Our results suggest that decreased BRS in de subacute phase after stroke is not associated with infarct localization. Because depression significantly reduces BRS, the lower BRS values in the stroke group might be due to mental stress. This is supported by a similar reduction in BRS in the hospitalized TIA patients and stroke mimics.

Disclosure: Nothing to disclose

Cerebrovascular diseases 2

PR1023

Diagnostic and prognostic value of plasma light-chain neurofilaments in acute cerebrovascular events – a prospective cohort study

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Background and aims: Plasma Neurofilaments are markers of axonal injury. We addressed their diagnostic and prognostic role in acute ischemic stroke and TIA.

Methods: Nested within a prospective cohort study, we compared plasma neurofilament light chain levels (pNfL) drawn within 24 hours from symptom onset in patients with acute ischemic stroke or TIA and healthy controls. Associations with the presence and volume of acute infarcts on MR-diffusion weighted imaging were analyzed. The prognostic value of pNfL for unfavorable functional outcome three months after stroke was assessed.

Results: We analyzed 692 patients with acute ischemic stroke and 187 patients with TIA, along with 165 healthy controls. Higher levels of pNfL were found in patients with stroke, followed by TIA and controls (P <0.01). Among patients with stroke, the trend of increase in pNfL across patients with infarct volumes 1-10 cm3, 10-100 cm3, >100cm3 was not significant (P=0.10). A significant increase in pNfL over the first 24 hours of hospitalization was seen only among patients with a large infarct. Functional outcome three months after stroke was not associated with pNfL. Among patients with TIA, the presence of an acute ischemic injury was associated with pNfL, but the discriminatory accuracy for the presence of an acute infarct was moderate (Area Under the Curve 0.71, 95%-CI: 0.61-0.82).

Conclusion: pNfL-levels measured within 24h from onset of stroke or TIA cover no clinically relevant diagnostic or prognostic role beyond clinical severity and imaging. pNfL did not prove to be the "brain troponin" we were hoping for.

Disclosure: Nothing to disclose

PR1024

Derivation and validation of a novel, parsimonious, biomarker-based prognostic score in ischemic stroke: The CoRisk-Score

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Background and aims: Serum copeptin is, so far, the only biomarker fully validated to predict outcome three months after acute ischemic stroke (AIS). Here, we sought to derivate and externally validate a 3-item prognostic model (serum copeptin, age, NIHSS: the "CoRisk-Score") to predict disability and death within 3 months from AIS.

Methods: The derivation cohort consisted of 362 patients with AIS enrolled between 2006 and 2007 at the University Hospital of Basel, Switzerland (COSMOS-Study). The validation cohort consisted of 783 patients with AIS enrolled between 2009 and 2011 at the University Hospital of Bern, Switzerland, and Frankfurt, Germany (CoRisk-Study). All copeptin levels were measured on serum drawn within 24 hours from AIS-onset. Performance of the biomarker-based score was compared to the prognostic model with only age and NIHSS. The combined primary outcome of disability and death was defined as mRs 3-6.

Results: For 3-month combined prediction of disability and death, the CoRisk-score was well calibrated. The calibrated CoRisk-Score correctly classified 79% of patients. The net reclassification improvement between the calibrated CoRisk-Score with and without copeptin was 54%, indicating that copeptin improved prediction in more than half of patients when added to a score with age and NIHSS. For the prediction of 3-month mortality, the model was poorly calibrated, and could not be externally validated.

Conclusion: The parsimonious, biomarker-based CoRisk-Score for the combined prediction of disability and death was well calibrated, could be externally validated, and performed better than a risk-score with NIHSS and age alone, the main outcome predictors after AIS.

Disclosure: Nothing to disclose

PR1025

Fast-track versus open-end hospitalizations for patients with non-disabling, acute ischemic stroke requiring hospitalization

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Background and aims: Fast-track hospitalizations for patients with non-disabling, acute ischemic stroke (AIS) bear the potential to expedite return to daily life while optimizing the use of healthcare resources. This study aims at assessing the feasibility and safety of fast-track hospitalizations among patients with non-disabling AIS.
Methods: Retrospective cohort study on patients hospitalized in the Stroke Center of the University of Basel, Switzerland, between January 1st, 2014 and December 31st, 2015. Fast-track hospitalizations were defined as ≤72 hours. Patients with non-disabling AIS were those discharged directly home, i.e. not to a rehabilitation facility. The primary endpoint was the rate of unplanned rehospitalizations for any reason within 3 months from the index hospital discharge.
Results: During the study period, 2'220 patients were hospitalized for AIS. Of these, 558 patients (25%) had a non-disabling AIS, and their median length of hospitalization was 6 days (IQR: 4-9). Fast-track hospitalizations have been realized among 15% of the analyzed patients with non-disabling AIS (83/558). Patients discharged per fast-track had less severe AIS, were treated less frequently with thrombolysis, and had a lower comorbidity index. The rates of unplanned rehospitalization within 3 months from hospital discharge did not differ between fast-track (10%) and open-end hospitalizations (9%, P=0.83). After adjusting for stroke severity, thrombolysis rate, and comorbidity, the difference in the rehospitalization odds remained non-significant (ORfast-track 1.5 [95%-CI: 0.6-4.1], P=0.39).
Conclusion: Among patients with non-disabling AIS, fast-track hospitalizations are feasible and do not seem to be associated with a higher risk of unplanned rehospitalizations.
Disclosure: Nothing to disclose

PR1026

Predictive value of time in therapeutic range (TTR) over the risk of intracranial hemorrhage (ICH) in patients anticoagulated with vitamin K antagonists (VKA)

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Background and aims: To determine the quality of anticoagulation in the previous six months, in patients treated with vitamin K antagonists (VKA) that presented with an intracranial haemorrhage (ICH).
Methods: Prospective registry of patients treated with VKA admitted in our Stroke Unit due to ICH between 2013 and 2015. INRs were retrospectively collected during the six previous months in order to determine time in therapeutic range (TTR).
Results: 50 patients were included. Mean age was 79 years. 48% were women. 46 had non valvular atrial fibrillation and 4 mechanic prosthetic valves. ICH were deep in 44%, lobar in 26%, extensive parenchymal in 20% and in brainstem in 10%. Median NIHSS on admission was 10. Mean INR on admission was 2.8. 36% presented supratherapeutic INR on admission. TRT was 67%. Time over range and time below range were both 17%. 8/21 patients haematoma expansion was confirmed. Aggresive therapeutical interventions were discarded upon admission in 30%. In 60% anticoagulation was reversed. Three patients underwent surgery. After 3 months only 30% were independent (mRS: 0-2) and mortality was 57%.
Conclusion: Patients who presented with VKA-ICH were correctly anticoagulated during the six previous months.
Disclosure: Nothing to disclose

PR1027

Looking into the eyes: Oculomotor changes in patients with bilateral thalamic and midbrain infarcts after occlusion of artery of Percheron

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Background and aims: Artery of Percheron occlusion classically produces bilateral thalamic infarctions, frequently involving the midbrain. Gaze palsy is a frequent but poorly described finding. The aim of our study is to characterize the oculomotor disturbances in these patients and their outcome.

Methods: We prospectively collected all patients with brain imaging clearly demonstrating a pattern compatible with an artery of Percheron occlusion, with bilateral thalamic infarction and midbrain involvement, from 2013 to 2015. All patients had cerebral angiography (MRI or CT) to exclude occlusion or severe stenosis involving the basilar artery.

Results: Five patients were included, all of them with complex oculomotor findings: all had vertical gaze palsy with at least partial horizontal gaze disturbances, 3 had ptosis (in 2 cases it was bilateral) associated with pupillary changes. In addition to bilateral thalamic infarction, most patients (80%) also had unilateral deep midbrain lesions, with only 1 patient exhibiting rostral midbrain involvement. Only one patient had an almost complete recovery, presenting minor oculomotor changes at 1 month follow up. All the others, at 1 year follow up, still presented complex oculomotor findings and visual complaints severe enough to limit some daily activities.

Conclusion: To our knowledge, this is the first work specifically addressing oculomotor changes in patients with bilateral thalamic infarctions with additional midbrain involvement resulting from artery of Percheron occlusion. The prognosis seems to be not so good as some described, with 80% of patients still presenting significant visual symptoms and oculomotor findings 1 year after the acute stroke.

Disclosure: Nothing to disclose

PR1028

Analysis of lesion patterns in dysphagic patients with supratentorial recent small subcortical infarcts

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Background and aims: Dysphagia is a common symptom in stroke and associated with higher mortality. We recently reported that even in patients with recent small subcortical infarcts (RSSI) outside the brainstem, swallowing dysfunction occurs in a substantial number of cases. In this study, we investigated the impact of lesion topography for supratentorial RSSI on the occurrence of dysphagia.

Methods: We identified all inpatients with MRI-confirmed single supratentorial RSSI at our university hospital over a period of five years. Presence and severity of dysphagia was determined by speech-language therapists. Infarcts were marked on fluid-attenuated inversion recovery MRI scans. Those were compiled into a standard brain model, binarized to correct for sample size and compared using delta maps. Furthermore, the MRI scans were reviewed for the combination of acute and old vascular lesions along the corticospinal and corticobulbar tracts.

Results: We identified 243 patients with supratentorial RSSI (mean age 67.9±12.2 years, 64.2% male). Of those patients, 47 (19.3%) had dysphagia. Lesion probability maps showed no lesion location which clearly favored the occurrence of swallowing impairment. Patients with moderate-to-severe dysphagia had the corticospinal/corticobulbar tract significantly more often affected by the RSSI (100% vs. 86.2%, p<0.01) and more often had an old lacunar infarct (77.8% vs. 23.0%, p<0.001) or any major lesion (old infarct or confluent white matter hyperintensities, 100% vs. 57.7%, p<0.001) along the contralateral corticospinal/corticobulbar tract than patients without swallowing dysfunction.

Conclusion: Swallowing impairment appears to be associated with a bilateral disruption of subcortical networks by both acute (RSSI) and old (lacunes, confluent white matter hyperintensities) vascular lesions.

Disclosure: Nothing to disclose

PR1029

Serum neurofilament light chain protein: A promising biomarker for lacunar stroke and cerebral small vessel disease

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Background and aims: Neurofilament light chain (NfL) is a neurostructural protein that has been shown to correlate with axonal damage in multiple sclerosis, however scarce information is available for other disorders affecting the white matter such as cerebral small vessel disease (CSVD) and lacunar stroke. We hypothesized that serum NfL levels were increased in patients with a recent small subcortical infarct (RSSI) compared to age-matched healthy controls. Moreover, we aimed to assess longitudinal changes of NfL following RSSI and their association with progression of CSVD on MRI.

Methods: We analysed serum NfL using a single molecular array (Simoa) assay and rated the MRI scans of prospectively collected RSSI patients (n=79) at baseline and at three and 15 months post-stroke. Community-dwelling healthy age- and sex-matched individuals with balanced severities of MRI white matter hyperintensities (WMH) (n=53) served as controls.

Results: RSSI patients (mean age: 61±11 years, 67% male) had significantly higher NfL baseline levels compared to healthy controls (73.45 vs. 34.59 pg/ml, p<0.0001). NfL levels remained increased at the 3-months follow-up and returned to normal 15 months post-stroke. In patients, NfL was associated with RSSI size, WMH severity and the development of new CSVD-related lesions during the follow-up period.

Conclusion: Serum NfL is increased in patients with RSSI and associated with the progression of CSVD-related MRI markers. NfL is therefore a promising biomarker for lacunar stroke and CSVD.

Disclosure: Nothing to disclose

PR1030

Time-domain near-infrared spectroscopy oxygenation parameters in healthy volunteers and in acute ischemic stroke patients according to brain tissue and vascular status

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Background and aims: Time-Domain Near-Infrared Spectroscopy (TD-NIRS) is an optical technology able to non-invasively measure the absolute concentrations of deoxy-haemoglobin (HHB), oxy-haemoglobin (OHB) and to calculate tissue oxygen saturation [SO2=OHB/(OHB+HHB)] in the outer layers of brain tissue. Our aim was to compare SO2 values in control subjects with acute ischemic stroke patients according to brain tissue and middle-cerebral artery (MCA) recanalization status.

Methods: We enrolled 33 controls (mean age:71.6±8.4 y), and 15 ischemic stroke patients (mean age:76.4±12.1 y) (<48 h from onset). TD-NIRS measurements of at least 3 brain regions per hemisphere were performed using 3 wavelengths (690, 785, 830 nm). Data were fitted with the diffusion model for semi-infinite homogenous media. TD-NIRS optodes were placed on corresponding ischemic brain tissue according to fiducial markers in CT-/MRI-scans. Stroke patients were divided in 3 groups: MCA occlusion and early recanalization after rTPA and thrombectomy (n=3), spontaneous late recanalization (n=3), no evidence of recanalization (n=6), stroke in deep brain tissue without evidence of arterial occlusion (n=3).

Results: Mean (CI 95%) concentrations (mM) in controls were: HHB=23.5 (23.1-23.9), OHB=44.6 (43.6-45.6), SO2=65.1% (64.1-65.5). Early recanalization patients had significantly reduced mean SO2 in optodes above subcortical core compared to normal tissue of affected and unaffected hemisphere (respectively 54.7, 58.6, 59.3%; p<0.001) and compared to control subjects (p<0.001) and to patients with deep stroke, late recanalization or no recanalization (respectively 64.9, 61.6, 62.7%; p<0.001).

Conclusion: According to these data, SO2 is reduced in cortical brain regions rescued by recanalization in comparison to normal tissue of both hemispheres and respect to control subjects.

Disclosure: Nothing to disclose

PR1031

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Cognitive neurology/neuropsychology 1

PR1032

Relationship between lesion location and depression in patients with multiple sclerosis

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Background and aims: Our aim in this study is to examine the relationship between specific lesion areas in central nervous system (CNS) and the degree of depression in patients with multiple sclerosis (MS).

Methods: 65 MS patients were included in the study (35 Women, 31 Men, mean age 36.6±9 years). Expanded Disability Status Scale (EDSS) scores, Beck Depression Inventory (BDI) were calculated and brain and spinal magnetic resonance images (MRIs) were examined simultaneously for each patient. The CNS involvement of particular areas (temporal, frontal, spinal involvement etc.) compared with the BDI in MS patients. None of the patients had a relapse or a clinical exacerbation during BDI testing.

Results: BDI median score was 13.95±9.48. EDSS median score was 1.16±1.33. Regression analysis revealed that the involvement of the right internal capsule (R-CI) was the most effective factor when assessing the radiological involvement affecting the depression level of the patients (p<0.05). Patients were divided into two groups according to whether they had R-CI or not (R-CI) involvement, and the depression levels (t=5.345; p <0.001) was statistically significant. Depression scores were significantly higher in those with R-CI involvement (n=26) according to those who did not have R-CI involvement (n=26) (t=5.492, p <0.001).

Conclusion: The results show us the relationship between organic brain damage and depression. The corticospinal tractus forms a large part of the corona radiata. Clinically, lesions of this region usually cause hemiparesis to the contralateral side. Also these findings indicate a correlation between disability and depression.

Disclosure: Nothing to disclose

PR1033

Prevalence and temporal evolution of cognitive dysfunction in young stroke - first data from a prospective single-centre study

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Background and aims: The prevalence of young patients (55 years and younger) suffering from stroke globally increases. Studies assessing the prevalence of post-stroke cognitive deficits in young patients are rare. We therefore assessed the prevalence and course of cognitive dysfunction in a sample of young stroke patients at hospital admission (baseline, BL) and at three months follow-up (FU).

Methods: Both at BL and FU, patients underwent a comprehensive clinical and cognitive assessment, examining general cognitive function, processing speed, attention, executive function and word fluency.

Results: From February to November 2016, we consecutively examined 54 young patients (59% males; mean age: 44.7±8.2 years) with an ischaemic (90.7%) or haemorrhagic stroke (9.3%). Within this period, 27 patients attended the FU assessment. At BL, deficits (defined by 1.5 standard deviations below standardised mean) were highly prevalent in general cognitive function (56.6%), processing speed (61.5%), attention (42.3%), executive function (44.2%) and word fluency (33.3%). In most domains, cognitive performance remained stable over FU, except for improvements in general cognitive function, processing speed and attention. In about one third of patients, considerable cognitive deficits were still present three months after stroke (general cognitive function: 29.6%; executive function: 33.3%; word fluency: 30.2%).

Conclusion: The high prevalence and generally missing improvement of cognitive deficits over short-term FU in young stroke patients highlight the importance of post-stroke cognitive assessment. Potential implications of these deficits (e.g. reduced quality of life, difficulties to return to work), emphasize the need for further investigations including development of targeted cognitive rehabilitation strategies.

Disclosure: Nothing to disclose

PR1034

Neuropsychological assessment of patients with X-linked Charcot-Marie-Tooth disease

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Background and aims: X-linked Charcot-Marie-Tooth disease (CMTX) is a hereditary sensorimotor neuropathy caused by mutations in GJB1 coding for connexin-32 (Cx-32). Cx-32 is a gap-junction protein found in peripheral Schwann cells, but also expressed in oligodendrocytes within the central nervous system (CNS). Several reports have identified CMTX patients with CNS involvement that can range from asymptomatic white matter lesions on brain MRI to a transient encephalopathy. No systematic study of cognitive function in patients with CMTX has been reported to date.

Methods: In total, 24 patients with molecularly confirmed CMTX (13 males; mean age= 43.4±10.3, range 19-61 years; mean education= 14.0±3.3, range 6-18 years; 9 different GJB1 mutations) were assessed with a comprehensive neuropsychological battery consisting of language, executive and memory tests.

Results: A case by case investigation revealed selective deficits in individual patients with regard to language abilities, executive functions and memory. Most notably, a substantial subgroup of patients (29%) demonstrated prominent executive deficits and a different, non-overlapping subgroup (29%) demonstrated prominent reading (decoding) deficits. There was no evidence of generalized cognitive impairment in individual cases or in the group as a whole. No significant differences in cognitive performance were observed between males and females or between subjects with different GJB1 mutations.

Conclusion: Our study provides for the first time evidence of cognitive impairment in patients with CMTX. Results primarily suggest that two different types of core deficits can be demonstrated in these patients.

Disclosure: Nothing to disclose

PR1035

Memory, visuo-spatial functions and cortical atrophy in clinically isolated syndrome

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Background and aims: Memory and visuo-spatial functions may be impaired in multiple sclerosis, where pathology in the temporal and parietal regions plays a key role. It is poorly understood whether these cognitive deficits are present in clinically isolated syndrome (CIS) and what role plays here cortical pathology. The aim was to investigate performance in verbal, nonverbal memory and visuo-spatial functions and their associations with global and regional cortical atrophy in patients with CIS.

Methods: Patients with CIS on interferon-β (n=51) underwent MRI brain scan with voxel-based morphometry and neuropsychological testing including Rey Auditory Verbal Learning Test (RAVLT; verbal memory), Brief Visuospatial Memory Test Revised (BVMT-R; nonverbal memory) and Judgment of Line Orientation Test (JLO; visuo-spatial functions). Results were compared to age, gender and education matched healthy controls (n=44).

Results: The CIS and control groups did not differ in basic demographic characteristics. The CIS group had poorer performance in RAVLT learning trials 1-5 (p=0.031), RAVLT delayed recall (p=0.014), BVMT-R learning trials 1-3 (p=0.002), BVMT-R delayed recall (p=0.015) and JLO (p=0.040). The CIS group had reduced normalized brain parenchymal volume (p=0.006), normalized grey (p=0.027) and white matter (p=0.029) volumes and cortical volumes in temporal, parietal and frontal regions (p≤0.019). Among the CIS group, lower JLO score was associated with lower normalized white matter volume (ß=0.29; p=0.042).

Conclusion: Verbal and nonverbal memory together with visuo-spatial functions are impaired in patients with CIS. Despite widespread atrophy including temporal and parietal regions, only a single association between visuo-spatial functions and white matter volume was found in patients with CIS.

PR1036

IL1B rs16944 and depression symptoms in multiple sclerosis patients

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Background and aims: Depression is a frequent condition in autoimmune diseases (AID), such as Multiple Sclerosis (MS). Its prevalence is higher than in the general population. The etiology of depression is still unknown, but biochemical, genetic and social factors are acknowledged to contribute to its development. It has been reported that depressed individuals present higher levels of pro-inflammatory cytokines (e.g. IL1β).

Methods: To contribute to a better understanding of depression symptoms in patients with MS. With that purpose the role of a functional SNP in the promoter region of IL1B (rs16944) was studied in 158 patients with MS from the Hospital Santo António-Centro Hospitalar do Porto. The health survey Hospital Anxiety and Depression Scale (HADS) was applied for screening of depression. Fourteen MS patients had an elevated HADS' depression subscale score ($\geq$11). The rs16944 polymorphism was genotyped using a pre-designed TaqMan allelic discrimination assay.

Results: The rs16944TT frequency was significantly higher in MS patients with depression symptoms [28.6% depressed vs. 6.3% non-depressed, p=0.014, OR=6.40 (1.45-28.29)].

Conclusion: MS patients carrying the rs16944TT genotype may have higher predisposition to depression. This genotype is associated with higher IL-1β levels which can exacerbate inflammatory reactions causing central nervous system impairment. These observations are in line with previous studies on the role of inflammation in depression and may be especially relevant in AID.

Disclosure: Nothing to disclose

PR1037

The assessment of speech and language impairments in Primary Progressive Aphasia (PPA)

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Background and aims: Speech and language disorders can be the dominant feature in several neurodegenerative diseases, in particular they are the first symptoms in Primary Progressive Aphasia (PPA). Their correct and early identification may increase the diagnostic accuracy in the clinical setting, allowing better discrimination between the different neurodegenerative diseases and the different variants of PPA: i.e., non-fluent, semantic, logopenic variant. The aim of this work was to outline the utility of both speech and language assessment in PPA population. Thus, we review available speech and language tools for differentiating between the three variants of PPA.

Methods: This systematic review was conducted following PRISMA guidelines on papers published on speech/language tests aimed at assessing the presence and/or severity of progressive aphasia/apraxia of speech applied to patients meeting core criteria for PPA (Gorno-Tempini et al., 2011). The methodological quality of the studies was evaluated and the list of characteristics examined included the following risk of bias: blindness of personnel, consecutive inclusion of patients and representativeness of the sample size.

Results: Validation studies of nine tools were included in this review. These tools are able to highlight language disorders that are relevant for the characterization of the PPA profile, however they also present some psychometric and methodological limitations.

Conclusion: The literature is still limited. This brief review reveals the need of linguistically sophisticated tests to be used to systematically evaluate the linguistic abilities of individuals with PPA, in order to contribute to our understanding of the language impairments of different PPA variants.

Disclosure: Nothing to disclose

Epilepsy 1

PR1038

Risk factors for an atypical evolution of rolandic epilepsy

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Background and aims: The aim of the study was to analyse the clinical course and the treatment approaches in patients with rolandic epilepsy in order to look for risk factors for an atypical evolution.

Methods: We have retrospectively reviewed the medical data of 277 children with typical (TRE) and 66 children with atypical rolandic epilepsy (ARE) treated between 2006 and 2015 in the Clinic of Child Neurology in Sofia, Bulgaria.

Results: The analysis showed that patients under 5 years of age ($p=2.5 \times 10^{-5}$), those with diurnal seizures ($p=0.0129$), multiple seizures ($p=4.1 \times 10^{-17}$) and postictal paresis ($p=8.6 \times 10^{-7}$) had a greater risk for an atypical evolution. We compared the effects of the treatment in TRE and ARE, using the results before the atypical evolution. We did not achieve permanent seizure remission with valproate (VPA), levetiracetam (LEV), oxcarbazepine (OXC), lamotrigine (LTG) and clonazepam (CZP) in the patients that later showed an atypical evolution and we observed a statistically significant difference concerning the initial seizures' response between the two groups when using OXC ($t_{em}=2.4581>t$) and LTG ($t_{em}=2.3333>t$).

Conclusion: The earlier seizure onset (before 5 years), the appearance of multiple and diurnal seizures and of a postictal paresis are risk factors for an atypical evolution in rolandic epilepsy. The lack of initial seizure control with OXC, LTG and CBZ and the lack of permanent seizure remission with VPA, LEV, OXC, CZP and LTG can be used as factors for a selection of high risk patients for an atypical evolution.

Disclosure: Nothing to disclose

PR1039

Drug-resistant epileptic patients: Why patients are NOT operated

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Background and aims: Surgery is an effective option to treat drug-resistant epileptic patients, however, not everybody is a surgical candidate. In this study, we aim to determine the reasons why patients do not undergo curative or palliative surgical interventions or intracranial monitoring.

Methods: A total of 828 patients who underwent to preoperative evaluation between 1995-2016 were reviewed. The following classification of possible reasons of rejection was established: 1) multifocal and/or genetic, non-focal picture, 2) focus close to vital cortex, 3) unfavorable cost-weight benefit, 4) change of diagnosis due to phase I evaluation, 5) patient does not want to proceed, 6) psychiatric contraindication, 7) medical contraindication, 8) doctor is reluctant, 9) operation or phase II pending.

Results: 334 individuals (40%) were not operated. The seizure onset was 14±13.4 yrs (mean±sd), the duration of epilepsy was 15±11.7 yrs and the age at evaluation was 29±15.8 yrs, which is comparable to our surgical candidates. The most frequent reasons to decline surgical treatment were: multifocal/genetic (23%) and the rejection of the surgery by the patient or the child's parents (28%). Change in diagnosis (18%), i.e. absence of focal epilepsy, and the negative cost-weight benefit (14%) were also frequent reasons for non-operation.

Conclusion: An increased number of patients with difficult-to-treat epilepsy are evaluated, of which many are not unifocal epilepsies. The research should also focus on offering effective solutions for this population. Moreover, the number of patients that refuse surgery even if they are good candidates is worrisome suggesting the necessary of better support.

Disclosure: Nothing to disclose

PR1040

Effectiveness of sequential antiepileptic drug therapy in patients attending a regional epilepsy clinic

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Background and aims: To analyse the effect of sequential AED treatment in terms of seizure control and adverse events (AE) in patients attending a tertiary epilepsy clinic

Methods: New referrals to a specialist epilepsy clinic were included in the study. Demographic and clinical details, and response to treatment were documented by review of records. Seizure frequency changes were classed into 'non responder' 'seizure freedom' and 'transient response'. AE were recorded as 'none', 'mild AE' or 'intolerable AE', which led to discontinuation of AED

Results: A total of 127 treatment changes in 45 patients were examined. Overall seizure freedom rates were 28% for the first AED, 17% for the second, 10% for the third, 6% for the fourth, and 8% for the fifth. Subsequent AED regimen did not produce seizure freedom. Seizure freedom rate from the first 2 regimen was 27%, whereas that with subsequent treatment schedules was 5% (p= 0.003). Any beneficial effect (seizure freedom or 50% reduction in seizure frequency), occurred in 69% with the first 2 regimen, compared to 25% with subsequent regimen (p=0 .000001). Occurrence of any adverse effect (35% v 38%) and intolerable adverse effects (17% v 19%) were more common in the subsequent treatment groups compared to the first 2 treatment schedules, but the difference did not reach statistical significance.

Conclusion: Patients who have failed to achieve seizure control with the first 2 drugs should be counselled about the low likelihood of benefit from subsequent AED regimen when changes to AED therapy are made.

Disclosure: Nothing to disclose

PR1041

The association of the blood-brain barrier activation with disease activity in patients with chronic epilepsy

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Background and aims: The changes in blood-brain barrier (BBB) activity and its permeability are involved in the pathological processes during seizures inducement and propagation. Here we present the preliminary results of the study in which we measured levels of key molecules participating in BBB activation (MMP-9, S100B, CCL-2, ICAM-1) and TIMP-1 as a marker of BBB restoration.

Methods: Serum levels of MMP-9, S100B, CCL-2, ICAM-1, and TIMP-1 were examined in a group of 62 stable patients with epilepsy (16-one week of seizure free period, 15 - one month, 10 - six months, 21 – more than one year) with different etiology of the disease (17 - idiopathic, 32 -symptomatic, 13 - cryptogenic) and measured by ELISA.

Results: Serum levels of MMP-9, S100B and CCL-2 are higher in epilepsy patients independently of the length of seizure free period (for MMP-9: 1008.4ng/ml±80.7 vs. 681.1±42.0 ng/). The levels of TIMP-1 and ICAM-1 were similar in epilepsy patients (in all periods) and controls. The MMP-9/TIMP-1 ratio was higher in epilepsy patients (12.1±3.7 vs. 5.3±0.7 ng/ml) and increased with the length of seizure free period. MMP-9 level was higher in patients with idiopathic epilepsy while S100B, CCL-2 and MMP-9/TIMP-1 ratio were increased in patients with symptomatic epilepsy.

Conclusion: We have observed that epilepsy patients have increased markers of BBB activation in the seizure free period which indicates persistence of neuroinflammation. Increasing MMP-9/TIMP-1 ratio may suggest increasing prevalence of restoration processes with time.

Disclosure: Nothing to disclose

PR1042

A comparison of the Dutch assessment of Quality of Life-8D (AQoL-8D), the QOLIE-31p and the EQ-5D-5L in epilepsy

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Background and aims: Assessment of quality of life (QOL) is an essential element in epilepsy and economic evaluations in general. QOL of epilepsy patients can be measured using generic preference-based instruments (e.g. EQ-5D-5L and AQoL-8D) or condition-specific instruments (e.g. QOLIE-31p). Objective of this study was to determine the construct validity and responsiveness of the recently translated AQoL-8D compared to the EQ-5D-5L and QOLIE-31p in patients with epilepsy.

Methods: Data originated from a Dutch clinical trial among adults with epilepsy. Patients were measured at baseline and 12 months follow-up. Analysis of variances was used to determine whether instruments were able to discriminate between clinically different groups. Patients were categorized by number of seizures; seizure severity; number of AEDs; age; and Hospital Anxiety and Depression Scale dimension (HADS) cutoffs. In addition, effect sizes (Cohen's D; baseline – follow-up) of all instruments were calculated to compare the instruments' discriminative abilities.

Results: A total of 103 patients were included in the study. All instruments significantly discriminated between HADS cutoffs. In addition, the QOLIE-31p significantly discriminated between patients with different seizure frequencies. Instruments did not show significant differences between seizure frequency, age categories or number of AEDs. Effect sizes for EQ-5D-5L, QOLIE-31p and AQoL-8D were 0.08, 0.27, and 0.45 respectively. Ceiling effects were only found for EQ-5D-5L (26.2%). No floor effects were found.

Conclusion: QOLIE-31p was best able to discriminate between pre-specified groups. QOLIE-31p and AQoL-8D performed substantially better when looking at the effect size estimates. This may indicate that these instruments pose greater responsiveness in patients with epilepsy.

Disclosure: Nothing to disclose

PR1043

Differences of subcortical structures in patients with nocturnal, diurnal and mixed seizures.

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Background and aims: Sleep and daytime seizures are important pathophysiological models that can be adressed to improve our view on epileptogenic networks. Little is known about subcortical structures as parts of involved networks. We aimed to investigate MRI derived properties of subcortical structures involved.

Methods: 3D MPRAGE, 3T MRI were recorded from 13 patients (age: 25 ± 10.8 years, 9 male) with nocturnal, 12 patients (25 ± 10.1, 3 male) with diurnal and 12 patients (24 ± 5.4, 2 male) with mixed seizures and analysed with Freesurfer for subcortical volumes. Amygdala, hippocampus and thalamus volumes were included into a GLM-ANOVA with factors group and side and post hoc tests.

Results: We identified significant differences in volumes of amygdala and hippocampus between nocturnal and diurnal seizure groups. Amygdala analysis showed significant group difference ($F2, 34=3.772$, $p<0.05$) with post hoc test indicating ($p=0.01$) larger volumes in nocturnal (right/left $1729.1\pm185.0/1797.3\pm323.5$ mm3) vs diurnal ($1490.1\pm235.1/1500.5\pm246.2$ mm3) seizures. For hippocampus, the analysis showed similar group difference ($F2, 34=3.875$, $p<0.05$), with larger volumes in in patients with nocturnal ($4713.9\pm982.1/4421.9\pm621.0$ mm3) vs diurnal ($3945.7\pm618.0/3859.1\pm508.1$ mm3, $p=0.013$) seizures. Amygdala and hippocampus volumes did not differ in comparison to the studied patients with mixed seizures ($p>0.1$). There were no differences of thalamus volume between the groups. There were no differences between groups on epilepsy syndrome types (χ-tests, $p>0.1$).

Conclusion: Our results indicate significant differences in volumes of amygdala and hippocampus between nocturnal and diurnal seizure groups. These differences could endorse the pathophysiological alterations linked to epileptogenesis that provoke different types of sleep and daytime seizures.

Disclosure: Nothing to disclose

PR1044

Influence of the lunar cycle on the occurrence of epileptic seizures

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Background and aims: There are several risk factors and triggers for epileptic seizures reported in the literature. Among them, some suggest an influence of the lunar phase. A small number of studies on this topic offer possible explanations, including gravitational effects, electromagnetic changes, nocturnal luminance leading to sleep deprivation, along with behavioural factors and personal beliefs. Our aim was to investigate the relationship between seizures and lunar phase.

Methods: Retrospective single-center study which included adults (≥18 years) evaluated in a neurology emergency department due to seizures (either as a reason for admission or during stay) from January to December 2015. Treatment non-compliant patients and those with changes to therapeutic regimen in the previous three months were excluded.We compared variables between lunar phases using data from the Lisbon Astronomical Observatory.

Results: We identified 532 seizures, of which 377 episodes in 355 patients fit inclusion criteria. Mean number of seizures per day was 1.0±1.1. Ninety-four seizures (25%) were documented in the first quarter, 95 (25%) during the full moon, 97 (26%) in the last quarter and 91 (24%) during the new moon. There was no statistically significant difference in the number of seizures, nor in sex, age group and seizure type comparisons in each lunar phase.

Conclusion: We found no evidence of an association between lunar phase and epileptic seizures. This has been reported in some studies, while others have found an association. The influence of lunar phase on epileptic seizures, therefore, remains unclear, and further studies are needed to clarify this relationship and its pathophysiologic basis.

Disclosure: Nothing to disclose

Headache and pain 1

PR1045

A phase 3, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of erenumab in migraine prevention: Primary results of the ARISE trial

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Background and aims: Efficacy and safety of erenumab, a human anti-CGRP receptor monoclonal antibody, were evaluated in patients with episodic migraine (EM) in a phase 3 trial (NCT02483585).
Methods: 577 adults with EM were randomized 1:1 to subcutaneous, monthly placebo or erenumab (70mg). Primary endpoint was change in monthly migraine days (MMDs) from baseline to weeks 9-12 of a 12-week double-blind phase. Secondary endpoints were achievement of $\geq$50% reduction in MMDs, change in acute migraine-specific medication use, and $\geq$5-point reduction in Physical Impairment (PI) and Impact on Everyday Activities (EA) measured by the Migraine Physical Function Impact Diary. Statistical significance was determined after adjustment for multiple comparisons.
Results: Patients reported a mean 8.3 MMDs at baseline. Those receiving erenumab experienced a mean -2.9-day change (reduction) from baseline in MMDs, compared to a 1.8-day reduction for placebo (p<0.001). A $\geq$50% reduction in MMDs was achieved by 40% and 30% in erenumab and placebo groups (odds ratio: 1.6; p=0.010). Monthly acute migraine-specific medication use was reduced by mean -1.2 and -0.6 days (p=0.002). Respective $\geq$5-point reductions (improvement) in PI were achieved by 33% and 27% of patients (p=0.13) and in EA by 40% and 36% (p=0.26). The safety profile of erenumab was similar to placebo. Most frequently reported AEs across both groups were upper respiratory tract infection, injection site pain, and nasopharyngitis.
Conclusion: Erenumab statistically significantly reduced migraine frequency, acute migraine-specific medication use, and a greater proportion of patients achieved $\geq$50% reduction in MMDs compared to placebo in this phase 3 trial in EM.
Disclosure: Funded by Amgen Inc.

PR1046

Efficacy of erenumab (AMG 334) in chronic migraine patients with prior prophylactic treatment failure: Subgroup analysis of the phase 2, randomised, double-blind, placebo-controlled study

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Background and aims: Erenumab, a fully human monoclonal antibody, selectively targets the CGRP receptor. A phase 2, 12-week randomised, double-blind, placebo-controlled study demonstrated efficacy of erenumab (70mg and 140mg) in patients with chronic migraine (CM), with a safety profile comparable to placebo. We report a prespecified subgroup analysis on prior prophylactic treatment failure ($\geq$1, $\geq$2 and never failed) due to lack of efficacy and/or poor tolerability.
Methods: Patients (N=667; aged $\geq$18-65 years) with CM ($\geq$15 headache days/month; $\geq$8 migraine days) were randomised (2:2:3) to once-monthly subcutaneous erenumab 70mg, 140mg or placebo. Efficacy endpoints were change in monthly migraine days (MMD), achievement of $\geq$50% reduction in MMD, change in monthly acute migraine-specific medication treatment days, and change in cumulative monthly headache hours. Assessments compared weeks 9-12 to baseline. No correction for multiple comparisons was performed.
Results: With erenumab 70mg and 140mg, there were greater reductions at week 12 in MMD and more patients achieved $\geq$50% reduction in MMD versus placebo in all three subgroups. Moreover, greater reduction in monthly acute migraine-specific medication treatment days was observed with erenumab 70mg and 140mg in patients who previously failed prophylactic medications versus placebo. Cumulative monthly headache hours reduced with erenumab 140mg versus placebo in patients who failed prophylactic medications. Notably, placebo effect was greatest in patients who had never failed a prophylactic medication. Across endpoints, reductions were greater with erenumab 140mg than 70mg.

		Placebo	Erenumab 70mg	Erenumab 140mg
Change from baseline in MMD	Never failed prophylactic medication	17.46(4.77)[a] -5.67(-6.98,-4.36)[b]	17.08(4.17)[a] -7.86(-9.33,-6.39)[b]	17.05(4.80)[a] -6.14(-7.61,-4.66)[b]
	Failed ≥1 prophylactic medication	18.57(4.67)[a] -3.51(-4.33,-2.70)[b]	18.39(4.40)[a] -5.98(-6.99,-4.97)[b]	18.14(4.69)[a] -6.84(-7.84,-5.85)[b]
	Failed ≥2 prophylactic medications	18.34(4.45)[a] -2.68(-3.63,-1.72)[b]	18.21(4.37)[a] -5.38(-6.56,-4.20)[b]	18.75(4.37)[a] -6.96(-8.10,-5.82)[b]
≥50% reduction in MMD	Never failed prophylactic medication	38.1[c] -	50.0[c] 1.75(0.89,3.43)[d]	41.9[c] 1.33(0.67,2.66)[d]
	Failed ≥1 prophylactic medication	17.3[c] -	34.7[c] 2.64(1.56,4.48)[d]	40.8[c] 3.30(1.98,5.51)[d]
	Failed ≥2 prophylactic medications	14.2[c] -	35.6[c] 3.46(1.81,6.61)[d]	41.3[c] 4.18(2.21,7.91)[d]
Change in Monthly acute migraine-specific medication treatment days	Never failed prophylactic medication	6.12(6.50)[a] -1.78(-2.52,-1.05)[b]	6.92(6.97)[a] -2.48(-3.31,-1.64)[b]	6.19(6.63)[a] -2.48(-3.31,-1.64)[b]
	Failed ≥1 prophylactic medication	10.82(7.54)[a] -1.47(-2.07,-0.87)[b]	9.72(7.19)[a] -3.83(-4.58,-3.08)[b]	11.41(6.59)[a] -4.90(-5.64,-4.16)[b]
	Failed ≥2 prophylactic medications	11.45(7.40)[a] -1.26(-2.00,-0.53)[b]	10.52(7.25)[a] -4.05(-4.96,-3.15)[b]	12.41(8.23)[a] -5.39(-6.27,-4.51)[b]
Change in cumulative monthly headache hours	Never failed prophylactic medication	249.0(124.8)[a] -71.2(-92.4,-50.1)[b]	212.8(121.7)[a] -69.8(-93.7,-46.0)[b]	237.1(128.5)[a] -66.7(-90.5,-42.8)[b]
	Failed ≥1 prophylactic medication	229.4(126.5)[a] -46.2(-59.6,-32.9)[b]	229.2(129.2)[a] -58.2(-74.8,-41.6)[b]	204.1(120.0)[a] -77.9(-94.3,-61.5)[b]
	Failed ≥2 prophylactic medications	218.9(119.0)[a] -36.2(-51.9,-20.4)[b]	214.4(123.2)[a] -49.2(-68.6,-29.8)[b]	208.4(128.5)[a] -77.1(-95.9,-58.3)[b]

Number of subjects in the efficacy analysis set
Never failed prophylactic medication: Placebo (N=84); Erenumab 70mg (N=64); Erenumab 140mg (N=62)
Failed ≥1 prophylactic medication: Placebo (N=197); Erenumab 70mg (N=124); Erenumab 140mg (N=125)
Failed ≥2 prophylactic medications: Placebo (N=141); Erenumab 70mg (N=90); Erenumab 140mg (N=92)

Patients who failed ≤3 classes of prophylactic treatment due to lack of efficacy were included in the study

[a] Mean at baseline (SD)
[b] LSM estimate (95%CI of LSM) at week 12
[c] Responder rate (%) at week 12
[d] Adjusted OR (erenumab vs. placebo) (95%CI)

Note: pairwise comparisons compare each erenumab group versus placebo (reference group).

Abbreviations: CI, confidence interval; LSM, least squares mean; MMD, monthly migraine days; SD, standard deviation.

Table: Outcome measures by prior prophylactic treatment failure

Conclusion: Numerically, erenumab 140mg showed better efficacy in patients with CM who previously failed ≥1 or ≥2 current standard of care prophylactic medication(s).

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PR1047

Medication overuse headache: Investigation of integrity and volume of the grey and white matter

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Background and aims: Medication overuse headache (MOH) is one of the most common chronic headache disorders and a public health problem. The aims of this study were to evaluate the possible alterations or damage in the grey and white matter of brain due to medication overuse and to identify the integrity and volume of the grey and white matter with the advanced neuroradiological methods.

Methods: A prospective study of 27 patients with MOH and 27 age-, sex-, and education-matched healthy adults were evaluated. Cranial MRI and Diffusion Tensor Imaging (DTI) scans were obtained from control group and MOH patients before and 6 months after the treatment. Tract Based Spatial Statistics and Voxel Based Morphometry were used to analyze the changes in the grey and white matter.

Results: No correlation was found between age, gender, education and smoking in both groups. The most commonly used medication were simple analgesics, (96,3%) and combined analgesics (3.7%). The mean duration of the history of medication overuse and headaches was 56.7± 63.5 months. The volume, fractional anisotropy (FA), radial diffusivity (RD), and axial diffusivity (AD) analyses obtained from DTI showed no significant relationship in the patients before and after the treatment. There was also no significant difference in those analyses between the patients and the control group.

Conclusion: To our knowledge, this is the first study investigating the integrity and volume of the brain grey and white matter from the radioneurological aspect in the patients with MOH. Our data suggest that MOH is not associated with morphological alterations within brain networks.

Disclosure: Nothing to disclose

PR1048

Efficacy of erenumab for the treatment of patients with chronic migraine in presence of medication overuse

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Background and aims: Efficacy of erenumab, a human anti-CGRP receptor antibody, was evaluated in chronic migraine (CM) patients with medication overuse (MO) in prespecified subgroup analyses of a phase 2 study (NCT02066415).

Methods: CM patients ($\geq$15 headache [HA] days/month over 3 months with $\geq$8 migraine days) were randomized to erenumab (70 mg or 140 mg QM) or placebo for 12 weeks, stratified by region and MO. Data from patients with MO at baseline were used to assess changes in monthly migraine days (MMD), acute migraine-specific medication (AMSM) days, monthly HA hours, and proportion of patients achieving $\geq$50% reduction in MMD. P-values for pairwise comparisons were not adjusted for multiple comparisons.

Results: Of 667 patients randomized, 41% (n=274) met MO criteria. Mean (SD) baseline MMD in the MO subgroup were 19.6 (4.4), 18.8 (4.6), and 18.8 (4.5) in the placebo, 70-mg, and 140-mg groups. Compared with placebo, erenumab 70-mg or 140-mg groups had a greater reduction in change in MMD at week 12 (LS mean [SE]: -6.6 [0.7] and -6.6 [0.7] vs 3.5 [0.6]; p<0.001 for both) and a greater reduction in change in AMSM days (LS mean [SE]: -5.4 [0.6] and -4.9 [0.5] vs -2.1 [0.5]; p<0.001 for both). In the placebo, 70-mg, and 140-mg groups, $\geq$50% reductions in MMDs were achieved by 18%, 36% (OR: 2.67; p=0.004), and 35% (OR: 2.51; p=0.007). Respective changes in monthly HA hours were -73.2 [9.1] and 81.0 [9.1] vs -68.0 [7.4] (p>0.05).

Conclusion: Erenumab showed efficacy in CM patients with medication overuse in this study.

Disclosure: This study was funded by Amgen Inc.

PR1049

Spontaneous CFS leak complicated by brainstem infarction

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Background and aims: Spontaneous intracranial hypotension (SIH) typically results from spontaneous cerebrospinal fluid (CSF) leak. It has become a well-recognized cause of headaches. Strokes are rare complications of SIH. SIH can be cured by early epidural blood patch (EBP).

Methods: We report the case of a 62 years old man presented with a one-month history of severe persistent headache associated with confusion and vomiting. CT-scan revealed bilateral subdural hematoma and effacement of the cisterns. Two days later, he became progressively lethargic (GSC8) and facial paralysis was noted. He was intubated. Brain MRI showed brain sagging, bilateral subdural hematomas, pachymeningeal enhancement and a pontine arterial infartcs. Diagnosis of SIH was made. He underwent two lumbar EBP with transient improvement. Contrast myelography showed TWO irregular thoracic meningeal diverticula. A thoracic EBP under radiographic control were made. Patient made an uneventful recovery and remained well.

Results: Arterial cerebral infarcts are rare but potentially life-threatening complications of SIH. Strokes are due to downward displacement of brain and can be precipitated by craniotomy for evacuation of associated subdural hematomas. That's why it is important to recognized SIH as a cause of subdural hematoma. Even in severe cases of SIH, prompt treatment of the underlying CSF leak may prevent complications. If blinded EBP failed, the leak should be actively searched to realize targeted EBP.

Conclusion: Diagnosis of SIH might be challenging, a wide variety of complication have been reported including brainstem infarction, illustrating the spectrum of disease severity. After blinded EBPs failure, CSF leak should be sought by MRI or CT myelography.

Disclosure: Nothing to disclose

PR1050

Health-related quality of life in episodic migraine patients: Prophylaxis vs. abortive therapy

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Background and aims: Quality of life evaluations can enhance traditional measures of therapeutic efficacy. The aim of this study is to compare the health-related quality of life (HRQoL) between episodic migraine (EM) patients on prophylactic therapy (PT) and those exclusively on abortive treatments (AT).

Methods: The study sample consisted of 191 patients with EM (163 females and 28 males, mean age: 40 years). One hundred of them (52.4%) were using only abortive treatments, and the rest (47.6%) were taking prophylactic drugs in addition to their acute therapy. Patients' HRQoL was measured using the SF-36 survey. Data regarding frequency of migraine attacks were acquired from the patient's headache diary.

Results: Patients on AT reported a significantly higher level of HRQoL in physical functioning (p=0.02) and general health perception (GH) (p<0.001) domains. There wasn't any significant difference in mental health domains between AT and PT patient groups. We didn't find any statistical difference in the frequency of EM attacks between the observed treatment groups. In both groups there were negative correlations between the number of attacks reported during past 2 months and the following HRQoL domains: GH, vitality, social functioning, and most notably for the role limitation due to physical problems (rho -0.237, p=0.001).

Conclusion: Patients with migraine treated exclusively with the abortive therapy reported better HRQoL in domains of physical functioning and general health perception when compared to the patients on prophylactic therapy. Frequency of migraine attacks may have negative correlation to several domains of the HRQoL in migraine patients.

Disclosure: Nothing to disclose

Movement disorders 1

PR1051

Neuroprotective effects of exenatide in a rotenone-induced rat model of Parkinson's disease

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Background and aims: Several studies suggest an association between Parkinson's disease (PD) and type 2 diabetes mellitus; these two diseases are both known to affect the common molecular pathways. As a synthetic agonist for the glucagon-like peptide-1 receptor, exenatide has been evaluated as a neuroprotective agent in multiple animal models. Rotenone models of PD have great potential for the investigation of PD pathology and motor and non-motor symptoms, as well as the role of gene-environment interactions in PD causation and pathogenesis. Therefore, in this study, the neurochemical, behavioral, and histological effects of exenatide on a rotenone-induced rat model of PD were examined.

Methods: Eighteen adult male rats were randomly divided into 3 groups (n=6): one group received stereotaxical infusion of dimethyl sulfoxide (vehicle, Group 1) and the others received stereotaxical infusion of rotenone (groups 2, 3). Apomorphine-induced rotation test (AIRT) was applied to the rats after 10 days. Thereafter, isotonic saline was administered to Group 2, while Group 3 was administered exenatide for 28 days.

Results: Malondialdehyde and tumor necrosis factor-alpha (TNF-alpha) levels increased in the rats with PD induced by rotenone, whereas exenatide treatment resulted in markedly decreased malondialdehyde and TNF-alpha levels The AIRT scores of exenatide-treated rats were determined to be lower compared to the untreated group. Exenatide treatment resulted in improvement of striatal neurodegeneration and a significant increase in total number of neurons and immunohistochemical tyrosine hydroxylase-positive neurons.

Conclusion: These results have shown that exenatide has neuroprotective, anti-inflammatory, and antioxidant effects in a rotenone-induced rat model of Parkinson's disease.

Disclosure: Nothing to disclose

PR1052

NUBPL mutations cause combined dystonia with bilateral striatal necrosis and cerebellar atrophy

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Background and aims: With the advances of next generation sequencing technologies, we recognise an increasing number of genetically defined dystonia syndromes. Here we aimed to elucidate the genetic cause of a distinct combined dystonia syndrome, inherited in an autosomal recessive fashion in a small UK kindred (Figure 1A).
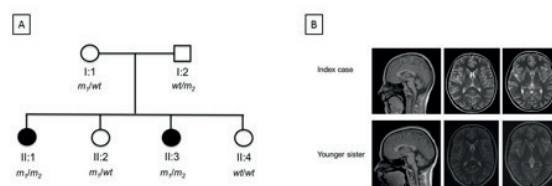
Figure 1 : A) Genetic pedigree of the family with mutational status. B) Brain MRI showing bilateral striatal necrosis and cerebellar atrophy in the index case and her sister.

Methods: Exome sequencing of both affected individuals and their mother was followed by variant filtration to look for rare or novel compound heterozygous or homozygous candidate mutations. Information from homozygosity mapping and linkage analysis was used in a supportive role. Known genetic causes of BSN were excluded by use of exome data or Sanger Sequencing.

Results: Using whole exome sequencing, linkage analysis and homozygosity mapping, we identified compound heterozygous mutations in the NUBPL gene as the cause of autosomal-recessive combined dystonia. The gene lay in a region of positive linkage and segregated with disease in the family. The phenotype is characterized by early-onset generalized dystonia, cerebellar ataxia and pyramidal signs, which gradually progressed and led to loss of independent ambulation in adolescence, whereas cognition remained preserved. The brain MRI featured bilateral striatal necrosis and cerebellar atrophy (Figure 1B).

Conclusion: We identified NUBPL mutations as the cause of autosomal-recessive dystonia combined with cerebellar ataxia and pyramidal involvement, with bilateral striatal necrosis and cerebellar atrophy on MRI. The here reported cases expand the clinical and radiological spectrum of NUBPL mutations. Bilateral striatal necrosis and cerebellar atrophy might be a useful handle in the differential diagnosis of the long list of early-onset combined dystonias.

Disclosure: Study funding: Supported by the Bachman-

PR1053

Thalamic proton MR spectroscopy distinguishes tremor-dominant PD from ET with resting tremor

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Aims: To investigate the presence of biochemical changes in the thalami of patients with tremor-dominant Parkinson's disease (tPD) and essential tremor with resting tremor (rET) using proton MR spectroscopy (1H-MRS).

Methods: Fourteen patients with tPD, 12 with rET and 10 controls participated in this study. All patients underwent DAT-SPECT with 123I-ioflupane, and a short-echo single-voxel 1H-MRS was performed on a 3T scanner. A voxel of $10 \times 15 \times 10$ mm involving the Vim nucleus was acquired in both thalami of all subjects. Peak areas of N-acetyl-aspartate (NAA), creatine (Cr), glycerophosphocholine (Cho), and glutamate (Glu) were calculated for each voxel using LCModel. Then, we calculated the following ratios: NAA/ Cr, a neural density marker; Cho/Cr, a membrane marker; and Glu/Cr, an intracellular neurotransmitter marker. We considered the values bilateral [(left+right)/2], ipsi- and contralateral to the more clinically affected side for tPD and rET groups, while only the bilateral values for control group.
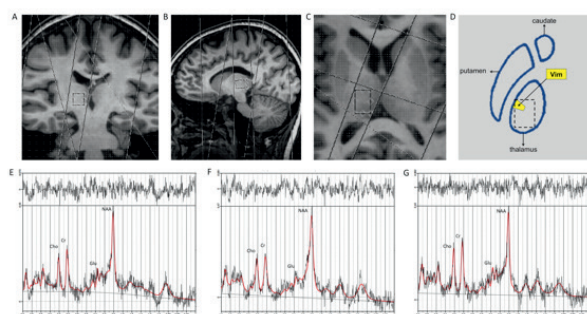
1H-MRS localization of the VOI involving the Vim nucleus in the right thalamus on coronal (A), sagittal (B), and axial (C) T1 images from a control. (D) Schematic drawing of the Vim nucleus location. (E-G) Spectra obtained from right thalami of a healthy control (E), a rET patient (F), and a tPD patient (G).

Results: DAT-SPECT was abnormal in tPD patients, while it was normal in rET patients. Patients with tPD showed a significant reduction of NAA/Cr and Cho/Cr in the thalami compared to rET and healthy controls. The combination of thalamic NAA/Cr and Cho/Cr ratios showed a 100% accuracy in distinguishing tPD patients from rET patients and controls.
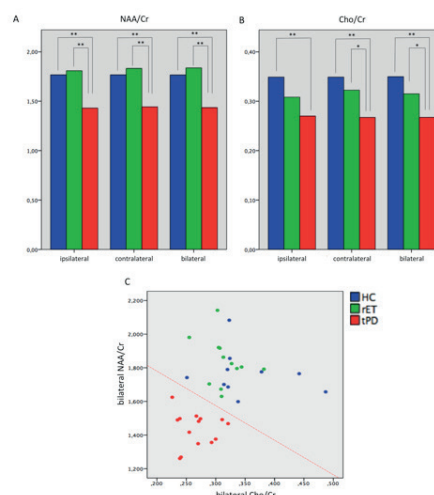
(A-B) NAA/Cr and Cho/Cr ratios from the thalami in all groups. (C) Scatter plot of bilateral NAA/Cr vs bilateral Cho/Cr ratios including tPD, rET, and control subjects. *=p-value<0.05; **=p-value<0.01.

Conclusion: This study demonstrates that 1H-MRS may help distinguish patients with tPD from those with rET, in the absence of evidence of damage to dopaminergic neurons. Our findings also confirm that these two disorders characterized by the presence of resting tremor are distinct clinical entities.

Disclosure: Nothing to disclose

PR1054

Effects of age and disease duration on quality of life in levodopa-carbidopa intestinal gel-treated advanced Parkinson's disease patients: A post-hoc analysis from the GLORIA registry

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Background and aims: Levodopa-carbidopa intestinal gel (LCIG) treatment improved quality of life (QoL) in this registry over 24 months (M). This analysis evaluates the influence of baseline characteristics on QoL and Activities of Daily Living (ADL) in LCIG-treated advanced Parkinson's disease (PD) patients.

Methods: Patients were allocated into subgroups based on baseline age (<65 [N=122], ≥65 [N=207] years), disease duration (<10 [N=111], ≥10 [N=217] years), OFF time (<3 [N=28], 3-6 [N=96], >6 [N=87] hours/day), and Levodopa Equivalent Dose (LED) (<800 [N=54], 800-1200 [N=101], >1200 [N=172] mg/day). The 8-item Parkinson's Disease Questionnaire (PDQ-8) QoL Summary Index and Unified Parkinson's Disease Rating Scale (UPDRS) part II scores were assessed.

Results: PDQ-8 total score improvements were observed at 24M across all ages and PD duration subgroups (Figure-1). Improvements in PDQ-8 scores were also observed in patients with ≥3 hours of baseline "Off" time (18M:3-6 hours=-10.95[22.8], P<0.001; 12M:>6 hours=-11.14[23.599], p<0.001) and baseline LED ≥800 mg/day (24M:800-1200 mg/day=-6.9[19.9], P=0.020; 24M:>1200 mg/day=-8.0[22.6], P<0.002). UPDRS II scores decreased across all subgroups; significant decreases occurred at 18M in patients <65 years old (-3.02[8.4], P=0.004) and those with 3-6 hours of "Off" time at baseline (-2.56[9.0], P=0.033) and at 24M in patients <10 years since PD diagnosis (-3.0[8.6], P=0.025) and with baseline LED >1200 mg/day (-3.1[9.1], P=0.002). Overall, 194/356 (54.5%) patients experienced ≥1 adverse drug reaction (ADR) and 109/356 (30.6%) had ≥1 serious ADR.

Figure-1. Mean Change from Baseline in PDQ-8 Total Score
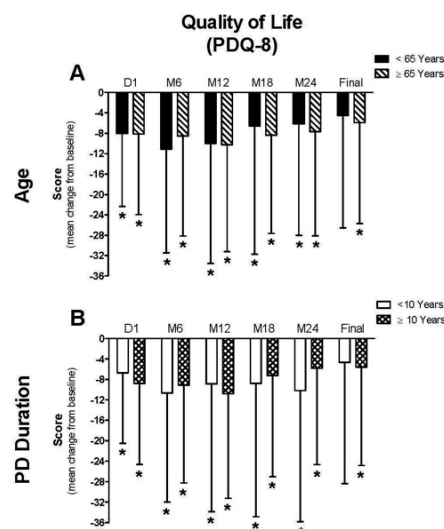
Asterisks indicate statistical significance compared to baseline in a paired t-test at the P<0.05 (*) level. PDQ-8 = Parkinson's Disease Questionnaire 8-item; D1 = first day of LCIG infusion via PEG-J after titration via nasojejunal tube; M = month; Final = last visit

Conclusion: LCIG led to improvements in QoL irrespective of patient age and disease duration. ADL improvements were greater in patients treated with LCIG earlier in life and after shorter disease duration.

Disclosure: AbbVie Inc. participated in the study design, research, data collection, analysis and interpretation of data, writing, reviewing, and approving the publication; medical writing support was provided by Amy M. Spiegel, of AbbVie.

PR1055

Adaptive DBS in Parkinson's disease patients with chronically implanted electrodes

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Background and aims: Continuous DBS (cDBS) is an established treatment for Parkinson's disease (PD). Preliminary evidence however suggests that intermittent, adaptive, DBS (aDBS) might be more efficacious, efficient and produce less side-effects. aDBS in PD can be delivered based on the presence of bursts of beta-oscillations in the subthalamic nucleus (STN) (Fig 1). Impulsivity is one of the side-effects of cDBS that could benefit from intelligent stimulation in the form of aDBS. A significant limitation in the aDBS studies to date is that they have been conducted in the immediate post-operative phase with concomitant lesional effects and sub-optimal cDBS settings. We compared aDBS in the chronically implanted phase against cDBS for both motor efficacy and decision making under conflict as an index of impulsivity.

Methods: In two PD patients (3 hemispheres) with cDBS for respectively 14 and 8 years aDBS was applied. We quantitatively assessed bradykinesia with a tablet task and assessed impulsivity using the Stroop task (one hemisphere). Each test was performed under three conditions: aDBS, no-stimulation and cDBS.
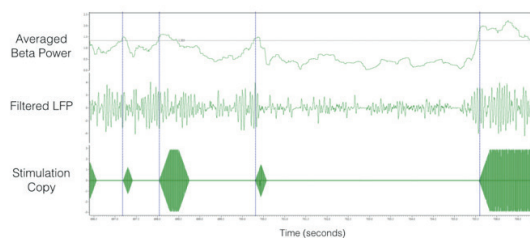
aDBS principle: The upper channel shows the averaged beta power over 400ms episodes. The black line demarcates the threshold for applying stimulation. The middle channel shows the LFP filtered around the dominant beta frequency (20±3 Hz). The bottom channel shows the stimulation copy that starts and ends with a 250 ms ramping period.

Results: The average bradykinesia dwell times for the no-stimulation, cDBS and aDBS conditions were 531±287, 449±127 and 405±49 ms, respectively and a significant main effect (p=0.04) was present (Fig 2a). Furthermore, aDBS showed a more optimal speed-accuracy trade-off in the Stroop task relative to no-stimulation and cDBS (Fig 2b).
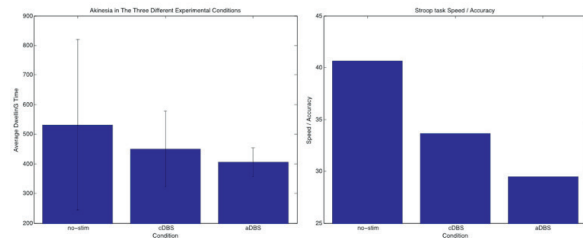
Tablet-based bradykinesia score (average dwelling time, left) and Stroop task speed/accuracy scores (a.u., right).

Conclusion: Our pilot data provide evidence that aDBS might be more effective for treating motor symptoms and less behavioural side-effects than conventional cDBS.

Disclosure: MB has been funded by the Dutch Brain Foundation and DPF has been funded by the Mexican CONACYT program.

PR1056
Cancelled

PR1057

Effects of non-invasive brain stimulation of the superior temporal gyrus on motor speech disorder in Parkinson's disease

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Background and aims: Hypokinetic dysarthria (HD) is a common symptom of Parkinson's disease (PD) which does not respond well to PD treatments. We investigated short-term effects of repetitive transcranial magnetic stimulation (rTMS) on HD in PD using acoustic analysis of speech. The main objective was to identify an optimal rTMS protocol and stimulation site to improve specific symptoms of HD in PD.

Methods: We used 10 Hz and 1 Hz stimulation protocols and applied rTMS over the right posterior superior temporal gyrus (STG), the left orofacial primary motor area (OFM1), and over the vertex (V, a control stimulation site) in 10 PD patients with mild to moderate HD and 4 age-matched healthy controls. Stimulation sites and protocols were randomised across subjects and sessions. A cross-over design was used. Acoustic analysis of a sentence reading task performed inside the MR scanner was used to evaluate rTMS-induced effects on motor speech. The study is ongoing and neural (fMRI) correlates of stimulation-induced changes will also be assessed.

Results: The preliminary results show particularly effects (p<0.05 in Wilcoxon test) of 1 Hz rTMS of the STG on total pause time, std of the 2nd formant, std of the fundamental voice frequency, and speech index of rhythmicity in PD, while some effects of 10 Hz rTMS of the OFM1 were also observed.

Conclusion: Preliminary results demonstrate for the first time that low-frequency stimulation of the right STG may improve articulation, rhythmicity, intonation and pausing of speech in PD with HD. The study is ongoing.

Disclosure: Acknowledgement This work was supported by the grant of the Ministry of Health of the Czech Republic 16-30805A and by the project "CEITEC - Central European Institute of Technology" (CZ.1.05/1.1.00/02.0068) from the European Regional Development Fund.

PR1058

Deep brain stimulation for dystonia – Cochrane review

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Background and aims: Dystonia is a disabling disorder. Deep brain stimulation (DBS) is an intervention typically reserved for refractory or severe cases, although uncertainty exists regarding its effectiveness. We performed a systematic review following Cochrane standards to estimate DBS effectiveness in people with dystonia.

Methods: The Cochrane Movement Disorders Trials Register, CENTRAL, MEDLINE, Embase, conference proceedings, grey literature, and trials registries were search up to October 2016. Double-blind, parallel, randomised, controlled trials (RCTs) comparing DBS versus sham-stimulation or best medical care in adults with dystonia were included. We performed meta-analyses using random-effects model. The primary efficacy outcome was improvement on any validated symptomatic rating scale, and the primary safety outcome was the proportion of participants with adverse events.

Results: We included two RCTs, with a total of 102 participants. Both evaluated Globus Pallidus interna (GPi) DBS versus sham-stimulation. One included participants with cervical dystonia, while the other included participants with generalised and segmental dystonia. Both RCTs were at high risk of bias. DBS improved Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) total score by 14.4 (95%CI:8-20.8) and 9.8 (95%CI:3.5-16.1) points in people with cervical and generalised/segmental dystonia, respectively. Overall risk of adverse events was not different between arms.

Conclusion: There is low-quality evidence that GPi-DBS is effective in the symptomatic improvement of cervical dystonia. It is unclear whether DBS may improve overall efficacy in generalised and segmental dystonia, as well as which subgroup of patients benefit the most. Treatment with DBS appears to be safe, but long-term controlled data is missing.

Disclosure: Nothing to disclose

PR1059

Validation and reliability study of Turkish version of the Non-Motor Symptoms Questionnaire (NMSQ-TR)

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Background and aims: Non-motor Symptoms of Parkinson's Disease are common and one of the most important determinant of quality of life of patients and carers. Many of these sypmtoms can began years before the motor signs. This study aimed to evaluate Turkish transcultural adaptation, reliability and validity of Non-motor Symptoms Questionnaire (NMSQ) which is a screening tool developed to asses non-motor symptoms of Parkinson's Disease.

Methods: 114 patients who were included in the study were diagnosed with Parkinson's Disease. They were presented to the outpatient clinic of the Marmara University Faculty of Medicine, Neurology department, between May 2016 and September 2016. The Turkish translated version of NMSQ (NMSQ-TR), UPDRS, Hoehn & Yahr(H&Y), Hospital anxiety and depression scale (HADs), Mini mental state examination(MMSE), Epworth Sleepiness Scale(ESS), Pittsburgh Sleep Quality index (PSQI) were used as the main outcome measures.

Results: There is a positive relationship between NMSQ-TR total scores and UPDRS total scores and they were found to be statistically significant at the 0.589 level (p<0.001). Although NMSQ-TR total scores and the H&Y stage was found to be statistically significant correlation (p<0.001), there was no statistically significant relationship between the duration of illness by the total scores(p>0.05). The correlation coeficients between NMSQ-TR subdomains and UPDRS, H&Y, MMSE scores , and between NMSQ-TR subdomains and other assessment tools is shown in table.

	r	p
NMSQ total		
MMSE	-0.237	0.011*
H&Y	0.419	<0.001**
UPDRS total	0.589	<0.001**
NMSQ sub-domains		
Sleep - PSQI	0.463	<0.001**
Depression/anxiety – HADS-D	0.531	<0.001**
Depression/anxiety – HADS-A	0.600	<0.001**
r:Spearman correlation coefficient	*p<0.05	**p<0.01

Table : The correlation coeficients between NMSQ-TR and subdomains and other assessment tools

Conclusion: The psychometric features of NMSQ-TR are satisfactory and our results are consistent with the previous literature findings. NMSQ-TR is a valid and reliable tool to screen NMS in Parkinson's disease.

Disclosure: Nothing to disclose

Movement disorders 2

PR1060

Borders of STN determined by MRI versus the electrophysiological STN.
A comparison using intraoperative CT

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Background and aims: Delineation of subthalamic nucleus (STN) dorsal and ventral borders is key in determining the location for lead placement in deep brain stimulation (DBS) for Parkinson's Disease (PD). Dorsal and ventral STN borders as seen on preoperative T2-weighted (T2) and Susceptibility Weighted Images (SWI) magnetic resonance images (MRI, MRI-STN) were compared with borders obtained during microelectrode recording (MER, MER-STN) using intraoperative-CT (iCT).

Methods: iCT was performed after each MER track. iCT images were merged with preoperative 3-Tesla (3T) MR images using planning software, allowing for projection of MER tracks on T2 and SWI sequences. Dorsal and ventral borders of each track were determined and compared to MRI-STN borders. Distances between T2 MRI-STN, SWI MRI-STN, and MER-STN borders were calculated.

Results: 125 MER tracks were evaluated in 45 patients. Dorsal MRI-STN borders showed MER-STN activity in 67% (T2) and 57% (SWI) of tracks. For Ventral MRI-STN borders this was 27% (T2) and 23% (SWI). Comparing MRI-STN to MER-STN, distances of 1.9±1.4 mm (T2) and 2.5±1.8 mm (SWI) were found between dorsal borders. Distances of 1.9±1.6 mm (T2) and 2.1±1.8 mm (SWI) were found between ventral borders. MER-STN started and ended more dorsally than respective dorsal and ventral MRI-STN borders on both sequences.

Conclusion: Border discrepancies between MRI-STN and MER-STN were found, most notably when comparing the ventral border, with T2 performing better than SWI. We suggest that a cautious approach should be taken when relying solely on MRI for delineation of both clinically relevant STN borders.

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PR1061

Altered topology of structural brain networks in patients with Gilles de la Tourette syndrome

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Background and aims: Gilles de la Tourette syndrome is a neurodevelopmental disorder characterized by tics which are hyperkinetic, repetitive movements misplaced in context and time. Abnormal neuronal circuits in a wide-spread structural and functional network involved in planning, execution and control of motor functions are thought to represent the underlying pathology. We therefore studied changes of structural brain networks in 13 adult GTS patients reconstructed by diffusion tensor imaging and probabilistic tractography.

Methods: Structural connectivity and network topology were characterized by graph theoretical measures of local and global network properties and compared to 13 age-matched controls.

Results: In GTS patients, significantly reduced connectivity was detected in right hemispheric networks. These were furthermore characterized by significantly reduced local graph parameters (local clustering, efficiency and strength) indicating decreased structural segregation of local subnetworks. Contrasting these results, whole brain and right hemispheric networks of GTS patients showed significantly increased normalized global efficiency indicating an overall increase of structural integration among distributed areas. Higher global efficiency was associated with tic severity (R=0.62, p=0.022) suggesting the clinical relevance of altered network topology.

Conclusion: Our findings reflect an imbalance between structural integration and segregation in right hemispheric structural connectome of patients with GTS. These changes might be related to an underlying pathology of impaired neuronal development, but could also indicate potential adaptive plasticity.

Disclosure: Nothing to disclose

PR1062

Extrapyramidal signs in neurosarcoidosis versus multiple sclerosis: Is TNF alpha the link?

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Background and aims: Specific inflammatory pathways and specifically Tumor necrosis alpha (TNFα) have been associated with the neurodegeneration in Parkinson's disease (PD). TNFα is also known to play an important role in the pathogenesis of sarcoidosis and TNF blockers can ameliorate the disease. In contrast, multiple sclerosis (MS) is clearly exacerbated by anti- TNFα medications. We have therefore hypothesized that Parkinson-like disease would be more common in neurosarcoidosis (NS) compared to MS. The aime of the study was to assess the frequency of extrapyramidal signs in patients with NS compared to patients with MS.

Methods: In this case-control study the medical records of patients with NS and of age and gender matched MS patients were reviewed and data regarding the clinical features associated with the disease, ancillary tests performed, treatment, and outcome were documented. Patients were then examined in a uniform manner for the presence of extrapyramidal signs.

Results: In the NS group 8 patients had minor signs, one had mild functional disability and 3 subjects had significant extrapyramidal signs compatible with the diagnosis of PD. All extrapyramidal signs found in 5 of the MS group were minor. The proportional severity of extrapyramidal signs was significantly higher (p=0.045, chi square test) in the NS group compared to the MS group.

Conclusion: The specificity of extrapyramidal to NS raises the intriguing question of whether specific inflammatory pathways involving TNFα play a role in the pathogenesis of Parkinson's disease and therefore may be a therapeutic target.

Disclosure: Nothing to disclose

PR1063

Clinical, neuropsychological and imaging characteristics of Alzheimer's disease patients presenting as corticobasal syndrome

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Background and aims: Corticobasal syndrome is a rare phenotype with diverse underlying pathologies, most commonly corticobasal degeneration (CBS-CBD) and Alzheimer's disease (CBS-AD). CSF biomarker analysis can confidently differentiate CBS-AD patients from other CBS patients. The aim of this study was to examine the clinical, neuropsychological and imaging differences of CBS-AD and CBS patients with other pathologies (CBS-non-AD).

Methods: A total of 17 CBS patients were included. They were divided in CBS-non-AD (n=12) and CBS-AD (n=5), after analysis of their CSF biochemical profile (elevated tau, phosphorylated tau and decreased beta-amyloid in CBS-AD patients). Clinical data included the presence of signs and symptoms. Neuropsychological tests included the MMSE, FAB, Clox1&2, Goldenberg apraxia, 5 word recall, as well as the NPI and GDS tests. Imaging data included a cortical atrophy visual scale, brainstem distance measurements as well as brainstem and corpus callosum planometry. T-test, x2 and Mann- Whitney were used as appropriate.

Results: CBS-AD patients were older (72.2 vs. 65.3 years, p=0.044), had lower GDS scores (3.0 vs. 6.0, p=0.0049) and had greater hippocampus surface asymmetry indexes (15.7 vs. 4.5, p=0.001) and superior colliculi (SC) widths (3.5 vs. 3.0, p=0.009) compared to CBS-non-AD patients. The two groups did not differ significantly in any of their clinical measures.

Conclusion: CSF analysis is pivotal in the ante mortem diagnosis of CBS-AD. CBS-AD patients are older, have more asymmetrical hippocampal atrophy and less pronounced SC width compared to CBS due to other etiologies.

Disclosure: Nothing to disclose

PR1064

Central pain processing in "drug-naïve" pain-free patients with Parkinson's disease

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Background and aims: Previous behavioural and neurophysiological studies have reported a reduced pain threshold in Parkinson's disease (PD) patients with or without pain symptoms. We aimed to investigate whether central pain processing is altered in "drug-naïve" pain-free PD patients.

Methods: Using event-related fMRI, functional response to forearm heat stimulation (FHS) at two different intensities (41° and 53°C) was investigated in 20 pain-free dnPD patients, compared with healthy controls (HCs). Each subject was asked to rate verbally the intensity of pain induced by the experimental stimulus by means of a numerical rating scale (NRS). Voxel-based morphometry was used to explore structural abnormalities. BOLD signal changes were also correlated to PD clinical features and behavioural responses.

Results: During low-innocuous FHS (41°C), no activation differences were shown between dnPD patients and HCs. During high-noxious FHS (53°C) a significantly increased activation in the left somatosensory cortex, left cerebellum (lingula) and right low pons was observed in dnPD patients compared to HCs. No statistically significant difference in experimental pain perception was detected between dnPD patients and HCs. During high-noxious FHS, a significant negative correlation was found between BOLD signal change in the right low pons and NRS scores only in dnPD patients. No structural abnormalities were detected.

Conclusion: Our findings suggest that a functional remodulation of pain processing pathways occurs even in the absence of clinically overt pain symptoms in dnPD patients. These functional changes may represent an additional recruitment of descending pain modulatory systems to meet analgesic demands and to maintain proficiency in an early stage of the disease.

Disclosure: Nothing to disclose

PR1065

Resting-state brain networks in patients with Parkinson's disease and impulse control disorders

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Background and aims: Evidence from previous brain metabolism, functional and morphometric imaging studies have consistently demonstrated a dysfunction within the meso-cortico-limbic-striatal circuit in Parkinson's disease (PD) patients with Impulse control disorders (ICD). We aimed to investigate resting-state neural networks connectivity changes in PD patients with and without ICD.

Methods: Fifteen patients with PD with ICD (ICD+), 15 patients with PD without ICD (ICD-) and 24 age and sex-matched healthy controls were enrolled in the study. Patients were screened for ICD by the Minnesota Impulsive Disorders Interview (MIDI). Whole brain structural and functional imaging was performed on a 3T GE MR scanner. Statistical analysis of functional data was completed using BrainVoyager QX software. Voxel-based morphometry (VBM) was used to test whether between-group differences in connectivity were related to structural abnormalities.

Results: PD patients with ICD showed an increased connectivity within the salience and default-mode networks, as well as a decreased connectivity within the central executive network (p<0.05 corrected). ICD severity was correlated with both salience and default mode networks connectivity changes only in the ICD+ group. VBM analysis did not reveal any statistically significant differences in local GM between ICD+ and ICD- patients and between all patients and HC (p<0.05. FWE).

Conclusion: The presence of a disrupted connectivity within the three core neurocognitive networks may be considered as a potential neural correlate of ICD presence in patients with PD. Our findings provide additional insights into the mechanisms underlying ICD in PD, confirming the crucial role of an abnormal prefrontal-limbic-striatal homeostasis in their development.

Disclosure: Nothing to disclose

PR1066

IGF-1 levels are associated with CSF pathology and executive dysfunction in de novo Parkinson's disease patients

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Background and aims: IGF-1 has been shown to harbor an important role for plasticity, neuronal survival and differentiation within the nervous system. IGF-1 has been linked with an increased risk of developing dementia in middle-aged population. The aim of our study was to investigate whether serum insulin-like growth factor-1 (IGF-1) is associated with clinical-neuropsychiatric, imaging and CSF markers of PD pathology in patients with early, drug-naïve Parkinson's disease (PD).

Methods: Using the Parkinson's Progression Markers Initiative database, a total of 388 participants were identified and included in this study. Serum IGF-1 was measured for all participants included in the study. The relationship between serum IGF-1 levels and clinical scales, neuropsychological battery, and imaging and non-imaging markers of PD pathology was evaluated.

Results: Lower IGF-1 serum levels were correlated with older age (r=−0.20, P<0.001), higher CSF tau levels (r=−0.24, P<0.001), worse Benton Judgment of Line Orientation test scores (r=0.12, P<0.05) and worse Symbol Digit Modalities Scores (r=0.17, P<0.001). No associations were found between serum IGF-1 and other clinical (e.g. UPDRS-III) and non-clinical biomarkers (e.g. DAT uptake).

Conclusion: Our findings demonstrate that lower IGF-1 levels are associated with an increased burden of CSF tau pathology and executive dysfunction in de novo PD patients and suggest a potential pathway which may contribute to cognitive impairment early in PD.

Disclosure: Nothing to disclose

PR1067

Immunofluorescence characterization of skin nerve misfolded α-synuclein in different synucleinopathies: A confocal study

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Background and aims: Intraneural misfolded α-synuclein (syn) characterized different synucleinopathies such as pure autonomic failure (PAF), idiopathic Parkinson disease (IPD) and dementia with Lewy Bodies (DLB). The aim of this study is to characterize by immunofluorescence the skin intraneural α-synuclein (syn) deposits in PAF, IPD and DLB to ascertain conformation-specific differences which may justify a different clinical phenotype.

Methods: We identified a total of 21 skin intraneural abnormal syn deposits in PAF, 22 in IPD and 40 in DLB. Ten healthy subjects were used controls. Skin biopsy was performed on C7 paravertebral, thigh and leg sites. To characterize syn deposits we used antibodies against α-synuclein core (NAC) and C-terminal α-synuclein epitopes such as phosphorylation at serine 129 (pS129) and tyrosine 125 (pY125), nitration at tyr125-133 (nY125-133) and advanced glycation end products (AGEs). Furthermore the mature amyloid α-synuclein fibrils were characterized by using a non-commercial antibody (Syn-F).

Results: Antibody raised against pS129 disclosed abnormal skin nerves syn deposits in all patients and never in the control group. Abnormal deposits were often (80-90% of all analysed deposits) also stained by the Syn-F antibody, by the NAC antibody (around 40%) and nY125-133 antibody (5%). Deposits were not stained by antibodies against pY125 and AGEs. IPD, PAF and DLB showed a similar immunofluorescence characterization of syn deposits.

Conclusion: Phosphorylation at serine 129 was the most sensitive and specific epitope to identify skin nerves abnormal syn deposits for the in vivo diagnosis of synucleinopathies. Skin syn neuritis showed no immunofluorescence differences in PAF, IPD and DLB suggesting a similar conformation.

Disclosure: Nothing to disclose

PR1068

Botulinum Neurotoxin (BoNT) for treatment of functional (psychogenic) jerky movement disorders: A randomized placebo-controlled clinical trial

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Background and aims: At least 2–9% of patients seen in movement disorder clinics suffer from functional movement disorders and a substantial part has jerks. Botulinum neurotoxin (BoNT) has emerged as a useful therapy for several hyperkinetic movement disorders. Our objective was to assess the effectiveness of botulinum neurotoxin (BonT) in patients with functional jerky movement disorders

Methods: 48 patients with invalidating functional jerky movement disorders, present for at least one year were included in a double-blind randomized placebo controlled of 16 weeks. The primary endpoint was reached patients showed minimal to major improvement (score 1,2 or 3) on the Clinical Global Impression (CGI)-scale. This was based on videotaped sessions, assessed by two investigators blinded to the allocated treatment. Hereafter all patients received BoNT treatment during one year in order to evaluate the long-term effect. Blinded assessment was repeated at the end.

Results: In the treatment group 16 of 25 (64%) patients reached the primary endpoint, opposed to 13 of 23 patients (57%) in the placebo group. No significant difference was detected. In the open-label follow-up phase 35 of 44 (80%) of patients improved (4 patients were lost to follow-up). Secondary outcome measures including psychiatric co-morbidity, disability and quality of life failed to reach significance for the trial phase (botulinum vs. placebo) as well as the follow-up compared to baseline.

Conclusion: Preliminary results show no significant effect of BoNT on functional (jerky) movement disorders. However the open label follow-up phase showed that the majority of patients improved on motor symptoms. (Netherlands Trial Registry 2478).

Disclosure: Nothing to disclose

Movement disorders 3

PR1069

Substantia nigra area evaluated by neuromelanin-sensitive MRI as an imaging biomarker of disease progression in Parkinson's disease

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Background and aims: A specific T1-weighted magnetic resonance imaging (MRI) sequence has been shown to detect substantia nigra (SN) neuromelanin (NM) signal changes that accurately discriminate Parkinson's disease (PD) patients from controls, even in early disease stages. However, it is unclear what happens to these SN changes in later disease stages.
Methods: A comparative cross-sectional study was performed, analyzing SN-NM MRI signals in late stage PD patients (LSPD) (Schwab and England Activities of Daily Living Scale score <50 or Hoehn Yahr Stage [HY] >3), comparing them with other disease stages, i.e. de novo, 2-5 year PD and controls. For all groups SN-NM signal area and contrast ratio (CR) values for the internal and lateral SN regions were obtained with semi-automated methods.
Results: 13 LSPD, 12 de novo patients with PD, 10 PD patients with a 2-5 year disease duration, and 10 controls were included. NM signal area was significantly decreased in de novo PD compared to LSPD (P-value=0.005; sensitivity: 75%; specificity 92% and AUC: 0.86). In the lateral SN region, a decrease in the CR was detected in all PD groups compared to controls; despite not reaching statistical significance, a slight increment was observed comparing LSPD to 2-5 year PD. NM signal area significantly correlated with HY (R=-0.37; P<0.05) and MDS-UPDR part II (R=-0.4; P <0.05) while a weak correlation was found with MDS-UPDRS part III (R=-0.26; P: 0.1).

Conclusion: SN area evaluated by NM-sensitive MRI may be a promising biomarker of nigral degeneration and disease progression in PD patients.
Disclosure: Nothing to disclose

PR1070

Excessive daytime sleepiness in Parkinson's disease – a 10-year longitudinal study

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Background and aims: The aim of the study was to investigate the evolution of excessive daytime sleepiness (EDS) over time in Parkinson´s disease (PD).
Methods: Thirty patients with PD below the age of 64 years were randomly selected from a movement disorders clinic in Stockholm. At inclusion, disease duration ranged between 0.5 to 20 years and the motor PD symptoms were classified as mild to moderate. Seventeen patients completed the 10 year follow-up. Drop outs were mostly explained by cognitive dysfunction and death. Patient underwent annual visits for clinical assessments of their PD status, medication, co-morbidities and an interview about their sleep habits and occurrence of EDS. Patients also completed self-reported scales about EDS (the Epworth Sleepiness scale; ESS), sleep, fatigue, depression and anxiety.
Results: Fifteen patients were classified to suffer from EDS at baseline (ESS scores >10). ESS scores remained relatively stabile over 10 years (mean, 9.38; range, 1-18) compared to baseline (mean, 10.17; range, 0-21), whereas motor symptoms (UPDRS motor scores) deteriorated from 13.03 (range, 3-30) to 28.35 (range, 15-47).
Conclusion: EDS did not worsen over 10 years, although other PD variables deteriorated. EDS seems to be a complex non-motor symptom that is unrelated to worsening of motor symptoms in PD.
Disclosure: Nothing to disclose

PR1071

CSF levels of biological markers of neurodegeneration in patiens with Lewy Body Disease (LBD) and Progressive Supranuclear Palsy (PSP)

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Background and aims: The differential diagnosis of parkinsonian syndrome in its initial stadium is difficult. In some cases, tauopathy as progressive supranuclear palsy (PSP) with parkinsonian phenotype (PSP-P) might resemble any phenotype of Lewy body disease (LBD) and vice versa. Our study aimed to find a connection between CSF levels of pathological proteins or their compounds and clinical manifestation of neurodegenerative disease.

Methods: CSF levels of β−amyloid42 a tau protein were assessed in 42 patients with clinical manifestations of neurodegenerative diseases (21 patients with LBD, 21 with PSP) and 21 subjects as a control group without neurodegenerative disease (CG).

Results: Average CFS levef of β−amyloid42 was 580 (259-1140) in LBD, 696 (285-1068) in PSP and 877 (250-1282) in CG. The diference between patiens suffering from PSA or LBD and patiens without neurodegenerative disorder was statistically not significant but there is noticeable trend of lower CSF levels of β−amyloid42 in neurodegenerative group than in CG. It seems that the more severe the cognitive deficit is the lower CSF level of β−amyloid42 is found. Average CFS levef of tau protein was 230 (132-772) in LBD, 246 (113-961) in PSP and 247 (95-511) in CG. CSF levels of tau protein were similar in patiens with PSP, LBD and CG.

Conclusion: β−amyloid42 with tau protein CSF levels could not serve as a potential tool for the differential diagnosis of atypical parkinsonian syndromes. It is necessary to use more sensitive and more specific reciprocal protein ratios, i.e. tau protein vs. alpha-synuclein.

Disclosure: Nothing to disclose

PR1072

White matter microstructural damage as predictor of cognitive decline in Parkinson's disease

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Background and aims: Many people with Parkinson's disease (PD) will eventually develop cognitive impairment as the disease progresses. This study investigated patterns of cortical and white matter (WM) changes associated with progression to mild cognitive impairment (MCI) or dementia in patients with PD.

Methods: We enrolled 84 PD patients and 41 healthy controls. At study entry, all subjects underwent clinical and cognitive evaluations, and MRI including 3D T1-weighted and diffusion tensor (DT) MRI. Patients were followed clinically and neuropsychologically for 2 years and classified as cognitive progressors (from normal cognition to MCI, or from MCI to dementia) or non-progressors. Measures of cortical thickness and WM tract microstructure were obtained by surface-based morphometry and probabilistic tractography, respectively.

Results: Thirty-one patients were classified as cognitive progressors. Compared with controls, both PD groups did not show cortical thinning; non-progressors showed microstructural changes in the cerebellar peduncles, while progressors had alterations in corpus callosum, cingulum, corticospinal and peduncolopontine tracts relative to controls. Progressors did not show significant cortical thinning compared to non-progressors. Conversely, they demonstrated a greater damage of the genu and body of the corpus callosum, cingulum, middle cerebellar and superior cerebellar peduncles (SCP), inferior longitudinal fasciculus, corticospinal tract bilaterally, as well as left superior longitudinal fasciculus and right uncinate fasciculus.

Conclusion: Our results suggest that the presence of microstructural WM alterations may be associated with the development or worsening of cognitive deficits in PD patients over two years. DT MRI offers new tools to identify PD patients at-risk for cognitive impairment.

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PR1073

Functional connectome changes predict cognitive decline in Parkinson's disease

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Background and aims: To investigate the functional connectome alterations associated with cognitive deterioration in patients with Parkinson's disease (PD).
Methods: We enrolled 87 PD patients and 41 healthy controls. At study entry, all subjects underwent clinical and cognitive evaluations, and MRI including resting-state functional MRI. Patients were followed clinically and neuropsychologically for 2 years and classified as cognitive progressors (from normal cognition to MCI, or from MCI to dementia) or non-progressors (stable cognition over two years). Differences in regional functional networks among groups were investigated using network-based statistic (NBS).
Results: Thirty-one patients were classified as cognitive progressors (22 without [NCOG-evo] and 9 with MCI [MCI-evo] at baseline), 56 patients as non-progressors (23 without cognitive impairment [NCOG-noevo] and 33 with MCI [MCI-noevo]). Compared with controls, NCOG-noevo patients did not show alterations. NCOG-evo and MCI-noevo groups showed decreased functional connectivity covering a large fronto-temporo-parietal network including cingulate cortex, primary sensorimotor cortices, superior temporal and supramarginal gyri and the insula. MCI-evo patients showed similar alterations with more extensive involvement of frontal and temporal nodes. NCOG-evo, MCI-noevo and MCI-evo showed the same alterations present in the comparison with controls when compared to NCOG-noevo.
Conclusion: The presence of functional connectome alterations at baseline is associated with the development or worsening of cognitive deficits in PD patients over two years. The study of functional connectome might open new perspectives in the identification of PD patients at-risk for cognitive impairment.
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PR1074

Treatment of patients with intractable dystonia: Long-term observation of motor, functional, cognitive, and affective outcomes of pallidal deep brain stimulation

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Background and aims: Deep brain stimulation (DBS) of globus pallidus internus (GPi) is used in treatment of dystonia patients with widespread and severe hyperkinetic movements, insufficiency of pharmacological treatment, marked impairment in daily activities, self-service, and quality of life. We aimed to evaluate comprehensively long-term outcomes of DBS-GPi in large cohort of primary dystonia patients.
Methods: We assessed 86 patients with pharmacoresistant dystonia: 31 patients suffered isolated generalized dystonia; 34 isolated segmental dystonia; 21 isolated cervical dystonia. Age of onset ranged from 3 to 63 years; mean disease duration was 11.8±10.6 years; mean age at DBS-GPi surgery 37.3±14.5 years. Motor and functional outcome was analyzed using Burke-Fahn-Marsden rating scale, TWSTRS, and Global outcome scale. We assessed quality of life with SF-36 questionnaire. Quantitative neuropsychiatric and neuropsychological testing was performed. Postoperative follow-up ranged from 3 to 12 years.
Results: Following three-year DBS-GPi, in patients with generalized and segmental dystonia, motor improvement was 62.9±16.8%, disability reduction 62.3±21.0% (BFMDRS). In cervical dystonia, motor and disability amelioration was 55.5±22.1% and 68.3±28.9%, respectively (TWSTRS). 54% of patients had excellent, and 35% had good functional outcome in long-term follow-up (GOS). Major negative predictive factor for DBS-GPi efficacy was the longer disease duration. Physical and mental components of QOL were improved. Unlike preserved neuro-psychological functions, neuropsychiatric state changed controversially. We observed overall decrease in depression and OCD, no principal changes in anxiety, and increment in apathy.
Conclusion: In isolated dystonia, DBS-GPi shows reliable motor and functional efficacy in long-term follow-up. Procedure is safe regarding cognition. QOL improves, although remains influenced by affective disturbances.
Disclosure: Nothing to disclose

PR1075

Non-motor symptoms in patients with cervical dystonia treated with deep brain stimulation of the globus pallidus internus

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Background and aims: Even though deep brain stimulation of globus pallidus internus (GPi-DBS) is now a well-established treatment of refractory cervical dystonia (CD), there is a lack of studies on the effect of GPi-DBS on the non-motor symptoms (NMS) in these patients.

Methods: Twenty-four bilaterally operated GPi-DBS (14 females; mean age 63.8±7.8y) and 22 unoperated CD patients (17 females; mean age 60.2±10.2y) matched by general characteristics, were recruited. Dystonic symptoms were assessed by using BFMDRS and TWSTRS. The NMS were assessed by using part one of MDS-UPDRS (items 1.1 to 1.5 and items 1.7 to 1.13). The EuroQol/EQ-5D was used to assess quality of life.

Results: Dystonia improved significantly in the DBS group pre vs. post operation (BFMDRS 12.0±2.4 vs. 6.8±1.1, p=.038; TWSTRS 22.1±4.3 vs. 12.5±5.9, p=.007). The BFMDRS and TWSTRS scores of non-DBS patients were 5.4±1.9 and 13.7±4.7 respectively. Operated patients reported less anxiety (item 1.4: 0.35±0.75 vs. 0.91±1.28, p=.005), less pain (item 1.9: 0.95±1.01 vs. 1.65±1.30, p=.028; TWSTRS pain score: 6.5±6.0 vs. 6.8±4.3, p=.07), and less sleep problems (item 1.7: 1.1±1.2 vs. 1.5±1.6, p=.005), but not depression (item 1.3: p=.187). The EuroQol/EQ-5D score was lower in operated patients (4.7±0.8 vs. 5.6±1.3, p=.004) indicating improved quality of life.

Conclusion: The significant differences between GPi-DBS and matched unoperated CD patients regarding anxiety, pain, sleep and quality of life indicate a beneficial effect of GPi-DBS on these NMS in CD. Prospective studies are needed to assess the effect of GPi-DBS on NMS in dystonia.

Disclosure: Nothing to disclose

PR1076

Prognostic indicators of survival in 136 multiple system atrophy patients

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Background and aims: The mean survival in multiple system atrophy (MSA) ranges from 6.2 to 10 years. Various clinical factors have been reported as predictive of shortened survival, showing conflicting results.

Aim of this study was to determine the predictive value of different clinical factors on shortened survival in a cohort of MSA patients.

Methods: We retrospectively identified patients with a final clinical diagnosis of MSA referred to our Department between 1991 and 2014 and evaluated at least once a year during the disease course. Clinical data were collected from medical records and updated at every follow-up visit. Survival data were defined based on time to death from the disease onset and calculated using Kaplan-Meier curves. To identify variables associated with MSA survival, univariate and multivariable Cox regression analyses were performed.

Results: A total of 136 MSA patients were included (88 males; 68 MSA with predominant Parkinsonism), 113 were deceased at the time of the study. On Kaplan-Meier curve the median disease duration was 7.84 years. Neither MSA subtype, sex, age at disease onset nor presence of stridor were significantly associated with survival in the univariate Cox regression analyses. The autonomic disease onset and the autonomic onset with orthostatic hypotension were associated with shortened survival both in the univariate and multivariable models (HR=1.70, p=0.013 and HR=1.74, p=0.019 respectively).

Conclusion: The study showed that autonomic disease onset and, in particular, the onset with orthostatic hypotension predicted unfavourable survival in MSA patients. These results could be useful in optimizing therapy and clinical management.

Disclosure: Nothing to disclose

PR1077

Hypertension and Parkinson's disease

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Background and aims: Hypertension (HT) has been associated with Parkinson's disease (PD) but the link between these two pathologies remains unknown. In this study we compared clinical burden, neuropsychological features, CSF and imaging pathology in early untreated PD patients with and without HT

Methods: Using the Parkinson's Progression Markers Initiative (PPMI) database, we evaluated motor and non-motor symptoms, neuropsychological features, CSF alpha-synuclein, total tau, p-tau and Aβ1-42 and striatal dopaminergic [123I]FP-CIT SPECT uptake in early untreated PD patients with and without HT. Region of interest (ROI) and Voxel-based analyses were performed by using Analyze 12.0 and SPM 12.0, respectively. We used occipital cortex as reference region for ROI analysis.

Results: Compared to PD patients without HT, PD patients with HT showed worse motor symptoms (UPDRS III $P<0.01$; UPDRS III subscores for bradykinesia $P<0.01$ and rigidity $P<0.05$) and loss of [123I]FP-CIT uptake in the most affected posterior putamen ($P<0.001$). In the whole population, higher systolic (SBP) and pulse blood pressure (PBP) correlated with worse motor symptoms (r= 0.39; p=0.005 for SBP; for r=0.36 ; p=0.01 for PBP) and greater loss of posterior putamen [123I]FP-CIT uptake (r=-0.329; p=0.02 for SBP; for r=-0.356 ; p= 0.01 for PBP).

[123I] FP-CIT (DaTscan™)

Parkinson with HT
77 aa F

Parkinson without HT
74 aa F
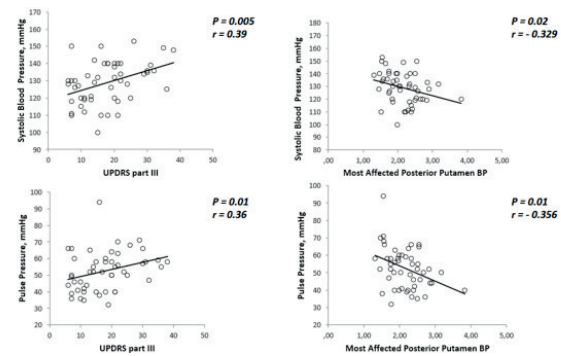
Conclusion: Our findings demonstrate that HT is associated with a more severe PD phenotype including increased dopaminergic pathology, and suggest that an optimal management of HT may help with PD symptoms.

Disclosure: Nothing to disclose
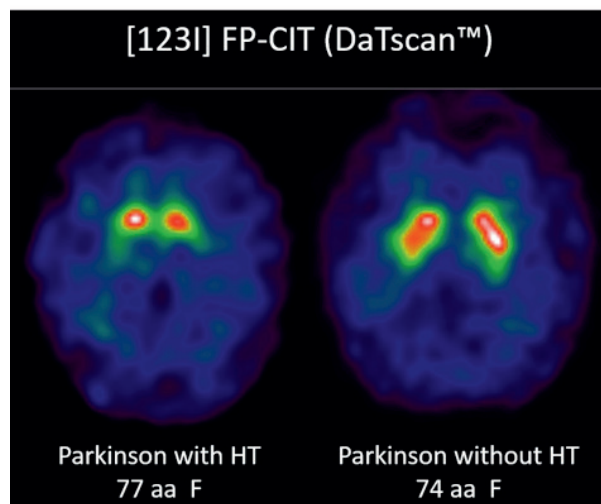
MS and related disorders 1

PR1078

Safety of IV pulse methylprednisolone therapy during breastfeeding in patients with multiple sclerosis

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Background and aims: Approximately 20% to 30% of women with multiple sclerosis (MS) have relapsed within 6 months during post partum period. High-dose IV methylprednisolone has become first-line treatment for acute relapse. In this study, we aimed to investigate the transfer of methylprednisolone into human milk as well as estimating the relative infant doses to assess any unwanted effects in the breastfed infant.

Methods: Sixteen breastfeeding women with MS who were being treated with IV 1000 mg methylprednisolone were enrolled in the study. All patients agreed to give sample collections 1, 2, 4, 8 and 12 hours after completing infusion therapy. Two of the patients agreed to give additional milk samples prior to infusion for the 3 days. Methylprednisolone breast milk concentrations were quantified by LC-MS.

Results: The milk methylprednisolone concentrations were below detection limits just before infusion. Cmax at 1, 2, 4, 8 and 12 hour after infusion were 2.100 μg/ml, 1.659 μg/ml, 0.680 μg/ml, 0.174 μg/ml and 0.102 μg/ml, consecutively. The absolute infant dose was 98,98 μg/kg/day and the relative infant dose was 0.71% of the weight-adjusted maternal dose.

Conclusion: Our findings present low infantile exposure to concentrations of methylprednisolone in breast milk. The RID for methylprednisolone was lower than typically accepted RID. As IV methylprednisolone therapy is brief (3 or 5 days), infant exposure would be very low if mother could breastfeed 1 hour after the end of the infusion. Mothers may choose to wait 2 to 4 hours if physician or mother would like to further limits infant exposure.

Disclosure: Nothing to disclose

PR1079

Baseline hippocampal subfields differ in CIS patients converting to clinically defined-MS in 1 year

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Background and aims: The hippocampus is affected early in multiple sclerosis (MS). In relapsing-remitting MS, expansion of the subgranular layer of the dentate gyrus (DG) has been shown. We evaluated if the patterns of regional hippocampal volume differ in clinically isolated syndrome (CIS) patients who will convert to MS within one year.

Methods: Brain dual-echo and 3D T1-weighted scans were acquired from 35 CIS patients within 2 months from clinical onset and after 3 and 12 months. Fourteen healthy controls (HC) were also studied. Manual hippocampal segmentation was performed according to a standardized procedure, and global volumes derived. Radial distance (RD) distribution was assessed using 3D parametric surface mesh models.

Results: After one year, 18 CIS converted to clinically definite MS. Baseline T2, T1 and GD lesion load (LL) and the main demographic features did not differ between converter-CIS and not-converter-CIS. At baseline converter-CIS showed an increased RD of the left DG compared to not-converter-CIS (p<0.05), and of the right DG after 3 months (p<0.05), that positively correlated with GD and T2LL (p<0.05, R>0.5). Atrophy of the CA1 subfield of the left hippocampal tail was detected at baseline in converter-CIS. Converter-CIS patients showed higher rates of liquoral oligoclonal bands than not-converter-CIS (75% vs 56%, p<0.05).

Conclusion: The relative expansion of the DG observed in converter-CIS patients was correlated with the extent of inflammatory lesions and the presence of liquoral oligoclonal bands, suggesting that DG hypertrophy could mirror a persistent flogistic status of the central nervous system.

Disclosure: Nothing to disclose

PR1080

Pragmatic abilities in multiple sclerosis: An rs-fMRI study

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Background and aims: Along with a cognitive impairment, Multiple Sclerosis (MS) patients could experience deficits in pragmatic (the ability to understand the context-dependent aspects of meaning beyond structural components of language). Along with the classical model of language that involves Wernicke's and Broca's areas, increasing evidence outlines the role of the Geschwind's area (GA) for comprehension of global coherence of narratives and pragmatics. We evaluate relationships between pragmatic abilities and GA's functional connectivity (FC) in MS patients.

Methods: Resting-State fMRI data of 40 MS patients were analyzed by means of a seed-based analysis of the right and left GAs FC, separately. Results were correlated with pragmatic abilities as assessed through APACS (Assessment of Pragmatic Abilities and Cognitive Substrates). Significance level was set at p<0.008 (0.05/6, as six regions were used for the definition of GAs).

Results: Clusters of significant direct correlation were present between APACS scores and FC of the right GA seed with the paracinguale cortex (p=0.003). Similarly, a trend of significance was present for the left GA seed with the same cortical region (p=0.009).

Conclusion: FC between GA and paracingulate cortex is related to pragmatic abilities, confirming that language is not simply confined to left perisylvian areas but involves a more distributed network over both hemispheres. These results highlight that the paracingulate cortex is an important hub for pragmatic abilities. Considering the evidence on the role of both GA and the paracingulate cortex in theory of mind, our data also indicate the close connection between language and social cognition.

Disclosure: Nothing to disclose

PR1081

Optical coherence tomography angiography retinal vascular network assessment in multiple sclerosis

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Background and aims: Cerebral and retinal vasculature share similar features. Therefore we aimed to assess retinal vascular network through angio-optical coherence tomography (OCT) in multiple sclerosis (MS) patients and healthy controls (HCs), in order to verify the presence of vascular abnormalities in MS and to evaluate their correlation to disease features.

Methods: MS patients with and without history of optic neuritis (ON) and HCs were included. Each subject underwent evaluation of best corrected visual acuity, fundus examination, standard visual field (VF) testing, spectral domain (SD)-OCT and OCT angiography. Clinical history, Expanded Disability Status Scale (EDSS), Multiple Sclerosis Severity Score (MSSS) and disease duration were collected for each patient.

Results: Fifty patients and 46 matched controls were included. Twenty-three eyes of MS patients had ON. Vessel density percentage showed a reduction in eyes of MS patients when compared to controls. A statistically significant reduction in all SD-OCT and OCT angiography parameters was noticed both in eyes with and without ON when compared with control eyes. A reverse correlation was found between GCC parameters and MSSS (p=0.003) and between vessel density parameters and EDSS (p=0.007).

Conclusion: We report a vessel density reduction in retina of MS patients. Moreover, we highlighted a clinical correlation between the vessel density parameters and EDSS, suggesting that angio-OCT could be a good marker of disease and of disability in MS and that it could be used as a progression outcome in clinical trials.

Disclosure: Nothing to disclose

PR1082

Comparative clinical efficacy of alemtuzumab and ocrelizumab in patients with relapsing-remitting multiple sclerosis: Number needed to treat analyses

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Background and aims: In absence of head-to-head trials, number needed to treat (NNT) can be used to indirectly assess comparative efficacy.

Methods: Post hoc NNT analyses compared alemtuzumab 12 mg/day (baseline: 5 days; 12 months later: 3 days) and ocrelizumab (600 mg every 6 months). Alemtuzumab: CAMMS223/CARE-MS I pooled (NCT00050778/NCT00530348, N=786; treatment-naive patients) and CARE-MS II (NCT00548405, N=628; patients with inadequate response to prior therapy). Ocrelizumab: OPERA I and II (NCT01247324, N=821; NCT01412333, N=835). NNT was based on inverse of absolute risk differences versus SC IFNB-1a 44 µg 3×/wk (common comparator) for annualised relapse rate (ARR) and clinical disease activity (CDA; proportion with relapses or 6-month confirmed disability worsening [CDW]), and the Altman method for CDW. Lower NNT reflects greater efficacy.

Results: Baseline mean EDSS scores (CAMMS223/CARE-MS I: 2.0; CARE-MS II: 2.7; OPERA I: 2.9; OPERA II: 2.8) and MS duration (CAMMS223/CARE-MS I: 1.9 years; CARE-MS II: 4.5 years; OPERA I and II: 6.7 years each) varied. Alemtuzumab and ocrelizumab significantly reduced ARR and CDW versus SC IFNB-1a. NNTs versus SC IFNB-1a were lower with alemtuzumab than ocrelizumab to prevent 1 relapse (CAMMS223/CARE-MS I: 5; CARE-MS II: 4; OPERA I/II: 8 each), CDW in 1 patient (CAMMS223/CARE-MS I: 15; CARE-MS II: 13; OPERA I: 23; OPERA II: 21), and CDA in 1 patient (CAMMS223/CARE-MS I: 5; CARE-MS II: 6; OPERA I/II: 8 each).

Conclusion: Two-year analyses show fewer patients required treatment with alemtuzumab than ocrelizumab to prevent clinical events in SC IFNB-1a comparator studies. Further clinical experience will help confirm these findings.
Disclosure: Sanofi and Bayer HealthCare Pharmaceuticals.

PR1083

Cardiac profile of ozanimod: Overview of pharmacologic and clinical trial data

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Background and aims: Ozanimod is an oral, selective sphingosine 1-phosphate (S1P) receptor-1 (S1P1R) and receptor-5 (S1P5R) modulator in development for relapsing multiple sclerosis (RMS). Its increased receptor selectivity, pharmaceutical properties, and use of dose escalation may confer an improved cardiac profile for ozanimod compared with other S1P receptor modulators.

Methods: Preclinical and clinical data on the cardiac safety profile of ozanimod are reviewed. In the completed RADIANCE Part A phase 2 trial (NCT01628393), patients with RMS were randomized to once-daily ozanimod (0.5 or 1.0 mg) or placebo for 24 weeks (Cohen et al. Lancet Neurol. 2016;15:373).

Results: Ozanimod selectively binds to S1P1R and S1P5R (Table 1). Ozanimod does not engage S1P3R, which may play a role in cardiac conduction (Sanna et al. Mol Pharmacol. 2016;89:176). In a thorough QT/QTc study, ozanimod did not prolong the QTc interval, including at a supratherapeutic dose (2.0 mg) (Hartung et al. Mult Scler J. 2013;19:S1_P983). Ozanimod's high volume of distribution (Vd) (Table 2) allows lower systemic drug concentrations and may contribute to reduced first-dose heart rate effects. In RADIANCE Part A, dose escalation resulted in minimal reductions of heart rate compared with baseline over the first 6 hours of monitoring. Type II or 2:1 atrioventricular block, prolongation of QTc, and significant blood pressure elevations were not observed with ozanimod. The incidence of cardiac events was comparable for ozanimod and placebo.

Conclusion: To date, both ozanimod doses (0.5 and 1.0 mg) demonstrate an acceptable cardiac profile, which potentially differentiates ozanimod from other S1P receptor modulators.

EC$_{50}$ (nM)	S1P$_{1R}$ GTPγS	S1P$_{2R}$ GTPγS	S1P$_{3R}$ GTPγS	S1P$_{4R}$ β-arrestin	S1P$_{5R}$ GTPγS
Ozanimod	0.4	>10,000	>10,000	>7,865	11
Fingolimod	0.3	>10,000	0.9	345	0.5

Scott et al. *Br J Pharmacol.* 2016;173:1778.

Table 1. S1P receptor selectivity of ozanimod vs. fingolimod

	t$_{1/2}$, hr	T$_{max}$, hr	C$_{max}$, nM	V$_d$, L/kg
Ozanimod[1]	19	6	0.36	81.9
Fingolimod[2,3]	144–216	12–16	10.76	17.1

[1]Timony et al. *Neurology.* 2014;82(10 Suppl P1.211).
[2]David, et al. *Clin Pharmacokinet.* 2012;51(1):15-28.
[3]Novartis Pharmaceuticals Corporation. Fingolimod (GILENYA) prescribing information. East Hanover, NJ: Novartis Pharmaceuticals Corporation, 2016.

Table 2. Pharmacokinetic properties of ozanimod vs. fingolimod

Disclosure: The RADIANCE study was funded by Celgene.

PR1084

Unveiling the impact of B-cell depletion on the immune profile of MS patients by high-dimensional mass cytometry

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Background and aims: B-cell depleting therapies (BCDT) are emerging as promising options to tackle multiple sclerosis (MS) relapses and progression. The original rationale was to eliminate the precursors of pathogenic autoantibody-producing plasma cells. However, the rapid dynamic of clinical response and the unaltered level of patients' autoantibodies hinted for alternative mechanisms. Here, we aim to investigate the direct and indirect impact of BCDT on the immune profile of MS patients, in order to identify potential biomarkers to gauge treatment responses as well as possible novel therapeutic targets.

Methods: We employ the high-dimensionality of single-cell mass cytometry to extensively characterize the alterations in trafficking-, activation- and cytokine expression-profile of the major immune populations found in blood upon BCDT. To this, we designed 48-parameters panels and implemented means of unsupervised, algorithm-guided data analysis that allow the unbiased identification of MS-relevant immune signatures.

Results: B-cell depletion broadly impacts on the effector functions of different cell types. We have observed a reduction in the inflammatory cytokine profiles of T-cells and NK cells. In particular, a defined T-helper subpopulation containing GM-CSF and IFN-gamma coproducing cells was underrepresented in relapsing-remitting MS patients after treatment. These cells mostly express important migratory molecules for T-cell infiltration of the central nervous system, such as VLA-4.

Conclusion: In this study we employed the newly developed mass cytometry to profile the immune phenotype of MS patients. Moreover, we developed innovative algorithms to integrate them with patients' clinical features

to provide important information on BCDT mechanism of action and, prospectivly, a deeper insights into MS pathophysiology.
Disclosure: Nothing to disclose

PR1085

CSF kappa free light chains and neurofilaments in multiple sclerosis work up: A pivotal study.

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Background and aims: Oligoclonal IgG bands (OCBs) for intrathecal inflammation and CSF light neurofilaments (NFs) for axonal damage have been indicated as prognostic factors in multiple sclerosis (MS).

Methods: Since it remains unclear how OCBs status could relate to disease progression, we aimed to compare kappa free light chains index (KFLCi), a quantitative measure of B-cell activity, to CSF NFs, an established measure of damage, in a pivotal cohort of 20 OCBs positive patients, of whom 8 has clinical isolated syndrome (CIS), 14 relapsing remitting (RR), and 3 secondary progressive (SP) MS.

Results: We found the most elevated values of KFLCi in RR, and of CSF NFs in SP MS. Among patients with CIS, KFLCi was modestly high whereas NLs were the lowest among our cohort. Both markers were not significantly raised in those patients with gadolinium-enhancing lesions, or receiving a disease-modifying treatment within 2 years.
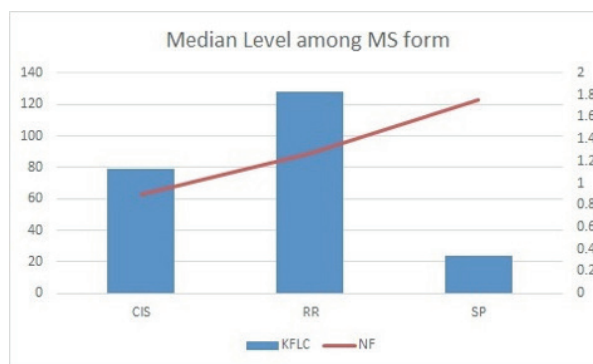
Conclusion: We confirmed KFLCi and CSF NFs as biomarkers of inflammation and degeneration in our pivotal MS group, but larger cohorts are needed to define a role in clinical decision-making.
Disclosure: Nothing to disclose

MS and related disorders 2

PR1086

Enhanced expression of IL-22 and GM-CSF by IL-17-producing cerebrospinal fluid T-cells in relapsing-remitting multiple sclerosis

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Background and aims: Multiple sclerosis (MS) is an autoimmune demyelinating disease of the central nervous system (CNS). The pathogenesis of MS involves both humoral and cellular immunity, with production of a large number of T-cell derived cytokines. The aim of this study was to analyze the cytokine profile of cerebrospinal fluid (CSF) T-cells in patients with relapsing-remitting multiple sclerosis (RRMS).
Methods: CSF samples were collected from 34 untreated RRMS patients and 20 age matched controls. Nineteen of the 34 RRMS subjects were experiencing a relapse. CSF T-cells were expanded in medium containing IL-2 and phytohemagglutinin for 10 days. Subsequently, cells were stimulated with PMA/ionomycin and intracellular production of IL-17A, IL-17F, IFN-γ, GM-CSF, IL-22, TNF-α, IL-4, IL-5, IL-10, IL-13, IL-2 and IL-21 was analyzed by flow cytometry
Results: Percentages of IL-17A, IL-17A/IL-22 and IL-17A/GM-CSF producing T-cells were higher in RRMS patients compared to controls (p<0.05). Percentages of T-cells producing IFN-γ were lower in RRMS patients (p<0.05). Patients in relapse showed higher percentages of CD4+ T-cells producing IL-5, GM-CSF and IL-13 (p=0.05) and lower percentages of CD8+ T-cells producing IL-2 (p<0.05) compared to patients not in relapse. We found a positive correlation between percentages of IL-13+ T-cells and the EDSS (r=0.5; p<0.05) in RRMS patients.
Conclusion: Differences in IL-17, IL-22, GM-CSF and IFN-γ production by CSF cells in RRMS vs. control subjects were observed. Notably, we observed a positive correlation between percentage of T-cells producing IL-13 and EDSS in RRMS patients.
Disclosure: Nothing to disclose

PR1087

An exploratory analysis of the risk of being restricted to wheelchair in patients with primary progressive multiple sclerosis in the ORATORIO trial

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Background and aims: Ocrelizumab is a humanised monoclonal antibody that selectively targets CD20+ B cells, and was shown to reduce clinical and magnetic resonance imaging (MRI) progression in patients with primary progressive multiple sclerosis (PPMS) in a Phase III clinical trial (ORATORIO). This analysis assessed the effects of ocrelizumab vs placebo on the risk of becoming wheelchair-bound, defined by reaching an Expanded Disability Status Scale (EDSS) score of ≥7.0.
Methods: This exploratory analysis of the ORATORIO intention-to-treat (ITT) population included 244 placebo-treated patients and 488 ocrelizumab-treated patients. We used Kaplan–Meier analyses to estimate the risk of 12- and 24-week confirmed progression to EDSS ≥7.0 in the ITT population and in patients with baseline EDSS ≤6.0 (placebo, n=219; ocrelizumab, n=424).
Results: In the ORATORIO study, strong trends were found showing a lower percentage of ocrelizumab- vs placebo-treated patients had confirmed 12- (5.1% vs 7.8%; hazard ratio [HR]: 0.58; P=0.074) and 24-week (4.7% vs 7.4%; HR: 0.59; p=0.091) progression to EDSS ≥7.0 in the ITT population. In patients with baseline EDSS ≤6.0, ocrelizumab significantly reduced the risk vs placebo of confirmed 12- (1.4% vs 4.1%; HR: 0.31; p=0.028) and 24-week (1.2% vs 4.1%; HR: 0.25; p=0.015) progression to EDSS ≥7.0. Additional results exploring specific transition to lower EDSS steps will be presented.
Conclusion: Ocrelizumab reduced the risk vs placebo of becoming wheelchair-bound, defined as confirmed transition to EDSS ≥7.0. These results are consistent with the established benefit of ocrelizumab in reducing overall disability progression in patients with PPMS.
Disclosure: Sponsored by F. Hoffmann-La Roche Ltd.

PR1088

The EXPAND study results: Safety and tolerability of siponimod in patients with secondary progressive multiple sclerosis

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Background and aims: Secondary progressive multiple sclerosis (SPMS) is a condition driven by compartmentalised inflammation and neurodegeneration in the central nervous system. Here, we present safety and tolerability results of the Phase 3 EXPAND study, evaluating siponimod versus placebo in patients with SPMS.

Methods: EXPAND is a randomised, double-blind, placebo-controlled study with an open-label extension. Patients were randomised 2:1 to once-daily siponimod 2mg or placebo (with a 6-day initial dose titration). Safety/tolerability for the double-blind part of the study are reported.

Results: Of 1651 randomised patients, 1645 comprised the safety population (siponimod, N=1099; placebo, N=546). Median age was 49 years and median EDSS 6.0. At least one treatment-emergent adverse event (TEAE) was reported for 88.7% and 81.5% of siponimod and placebo patients; in 7.6% and 5.1% of patients, these led to treatment discontinuation. Most common TEAEs (>10%, any group) were headache, nasopharyngitis, urinary tract infection, falls and hypertension. Serious TEAEs were reported in 17.9% and 15.2% of patients, respectively. Incidence of fatalities (0.4% vs. 0.7%), malignancies (1.9% vs. 2.6%) and infections (49.0% vs. 49.1%) was similar between treatment groups. Lymphopenia below 0.2x109/μL was observed in 2.7% vs. 0.2% of patients and Liver Function Test elevations ≥3xULN – in 5.6% vs. 1.5%. Other AEs of interest were: bradyarrhythmias (3.5% vs. 2.4%), hypertension (12.6% vs. 9.3) and macular oedema (1.8% vs. 0.2%). With dose titration during treatment initiation, bradyarrhythmic events were few. Mobitz II or higher degree atrioventricular blocks were not reported.

Conclusion: The safety profile of siponimod appears to be in line with other S1P receptor modulators.

Disclosure: This study was funded by Novartis Pharma AG, Basel, Switzerland. Detailed disclosures of each author will be included in the poster/oral presentation.

PR1089

Disability outcomes with teriflunomide: Results from the US and from Europe, Canada and Latin America in the real-world teri-PRO study

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Background and aims: Teriflunomide is a once-daily oral immunomodulator for relapsing-remitting MS. Disability outcomes, assessed using physician- and patient-reported measures, were secondary endpoints in Teri-PRO (NCT01895335), a global, real-world phase 4 study investigating effectiveness, safety, tolerability, and satisfaction with teriflunomide.

Methods: Patients with relapsing forms of MS received teriflunomide 14mg or 7mg (US only) for 48 weeks, per local labelling. Disability outcomes (Expanded Disability Status Scale [EDSS], MS Performance Scale [MSPS], Patient-Determined Disease Steps [PDDS]) for patients in the US, and in Europe, Canada, and Latin America (rest of world [ROW]), are presented.

Results: For US (n=545) and ROW (n=455) patients, mean (SD) ages were 50.6 (10.5) and 42.9 (10.1) years, and time since first MS symptoms was 14.7 (9.8) and 11.3 (8.9) years, respectively. Although mean (95% CI) baseline EDSS score for US patients (3.7 [3.6,3.9]) was higher than for ROW patients (2.2 [2.1,2.4]), following teriflunomide treatment, scores remained stable to Week (W)48 (US, 3.7 [3.5,3.9]; ROW, 2.4 [2.2,2.5]). This was also the case for PDDS scores. There were strong correlations between PDDS and EDSS scores at both timepoints: baseline/W48 rspearman=0.67/0.69 for US; rspearman=0.76/0.74 for ROW (all P<0.001). Baseline mean (95% CI) total MSPS score was also higher for US patients (15.1 [14.5,15.7]) than for ROW patients (8.9 [8.3,9.4]) and remained stable to W48 (US, 14.7 [14.0,15.3]; ROW, 9.0 [8.4,9.6]).

Conclusion: Disability, as determined by both physician- and patient-reported assessments, remained stable over the course of Teri-PRO, regardless of region and differences in baseline demographics and disability.

Disclosure: Study supported by Sanofi Genzyme.

PR1090

Optical coherence tomography, full-field visual evoked potentials and multifocal visual evoked potentials to monitor neurodegeneration and demyelination after acute optic neuritis.

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Background and aims: Visual evoked potentials (VEPs) and optical coherence tomography (OCT) are used to monitor optic neuritis (ON) evolution to assess demyelination and axonal loss. Multifocal VEPs represents a tool helping to characterize partial optic nerve damage. We applied these techniques to describe functional and structural damage occurring after ON.

Methods: 22 patients affected by acute ON (11 CIS, 11 RRMS) underwent OCT and VEPs (both full-field and multifocal) within 4 weeks after ON onset. Eight patients completed follow-up with OCT and VEPs repeated at 3,6 and 9 months.

Results: In ON eyes we found, 4 weeks after ON, good correlations between both high- and low-contrast visual acuity-VA and ff-VEPs amplitude (ρ=0.506, p=0.023 for HCVA; ρ=0.712, p<0.001 for LCVA). We also found good correlations between RNFL and GCC thickness and mf-VEPs latency (r=-0.539, p=0.021, r=-0673, p=0.002 respectively); ff-VEP latency showed instead a significant correlation only with GCC (r=-0.586, p=0.011). Considering patients who performed a complete follow-up monitoring, a significant global RNFL thickness decrease (m=-6.6 μm, p=0.014) and mf-VEPs amplitude recovery were observed over time (m=+30.2 nV, p=0.012). Furthermore mf-VEP amplitude at baseline showed a significant correlation with high-contrast HCVA at 9 months (ρ=0.576, p=0.025)

Conclusion: We found good correlations between clinical, morphological and functional parameters in the acute phase of ON and during its evolution. This represent a starting point to better define ON appropriate monitoring, with implications for clinical trials investigating neuroprotection and remyelination.

Disclosure: Part of this work was supported by Merck Serono S.A., Geneva, Switzerland. Merck Serono is the biopharmaceutical division of Merck KGaA, Darmstadt, Germany.

PR1091

Early switch to fingolimod to achieve 'No Evidence of Disease Activity' (NEDA) over 7 years in the TRANSFORMS Study

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Background and aims: No evidence of disease activity (NEDA) is being increasingly used as a comprehensive measure of treatment response for multiple sclerosis (MS). This study evaluated the long-term efficacy of fingolimod in annually achieving NEDA status.

Methods: A post-hoc analysis was performed on the 7-year data from TRANSFORMS core and extension studies. Separate analyses were performed on patients randomised to fingolimod 0.5 mg (N=429) from the start and those randomised to interferon beta-1a (IFN, N=431) and then switched to fingolimod in the extension. NEDA-3 was defined as the absence of magnetic resonance imaging activity (no active [new/enlarging] T2 lesions), relapses, and disability progression. NEDA-4 additionally included interval average yearly rate of brain volume change $\leq-0.4\%$. Odds ratios (ORs) and p-values were derived from logistic regression of NEDA. Patients without signs of disease activity but missing assessments were excluded.

Results: The analysis included 784 patients who completed Year 1. NEDA-3 and NEDA-4 were achieved by 43.3% (166/383) and 27.8% (106/381) patients, respectively, in the fingolimod group versus 30.3% (113/373) and 16.4% (61/371) patients, respectively, in the IFN group (NEDA-3: OR, 1.76; p=0.0002; NEDA-4: OR, 1.96; p=0.0002) in Year 1. Post switch to fingolimod, 50.2% (133/265) and 35.1% (92/262) patients achieved NEDA-3 and NEDA-4, respectively, at Year 2 (p<0.0001 versus Year 1 for both; n=588). Annual NEDA from years 3 to 7 ranged between 45.6% to 74.2% for achieving NEDA-3 and 24.4% to 53.2% for NEDA-4 in either group.

Conclusion: Early switch from IFN to fingolimod improved MS disease control, and benefit was sustained in the long-term.

Disclosure: This study was funded by Novartis Pharma AG, Basel, Switzerland. Detailed disclosure of each author will be included in the oral/poster presentation.

PR1092

Evaluation of No Evidence of Progression or Active Disease (NEPAD) in patients with relapsing multiple sclerosis in the OPERA I and OPERA II trials

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Background and aims: Incorporation of hand/arm function and walking assessments as proposed for the novel endpoint, no evidence of progression or active disease (NEPAD) increases the sensitivity for clinical disability worsening/progression compared with current definitions of no evidence of disease activity (NEDA) composites. The effect of ocrelizumab vs interferon beta-1a (IFN beta-1a) on the proportion of patients with NEPAD up to Week 96 was assessed in a post-hoc exploratory analysis of the pooled OPERA studies.

Methods: NEPAD was defined as having no evidence of progression (NEP; no 12-week confirmed progression of $\geq 1/\geq 0.5$ points on the Expanded Disability Status Scale (EDSS) if the baseline score was $\leq 5.5/>5.5$ points, respectively; no 12-week confirmed progression of $\geq 20\%$ on the timed 25-foot walk test and 9-hole peg test), no brain MRI activity (no new/enlarging T2 lesions and no T1 gadolinium-enhancing lesions), and no protocol-defined relapse. Brain MRI assessments were conducted at baseline and Weeks 24, 48 and 96.

Results: In the pooled OPERA studies, ocrelizumab (n=740) increased the proportion of patients with NEPAD at Week 96 by 82% compared with IFN beta-1a (n=753; 39.3% vs 21.5%; risk ratio [95% CI]: 1.82 [1.55, 2.14]; p<0.0001). The effect of ocrelizumab on NEPAD sub-components, i.e. the proportions of patients with NEP, no brain MRI activity and no relapse, and sensitivity analyses, will be presented.

Conclusion: Compared with IFN beta-1a, ocrelizumab increased the proportion of patients with NEPAD, a clinically expanded version of the NEDA outcome that incorporates hand/arm function and walking assessments.

Disclosure: Sponsored by F. Hoffmann-La Roche Ltd.

PR1093

Early clinical and MRI predictors of employment status in multiple sclerosis in 11 years of monitoring

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Background and aims: Multiple sclerosis (MS) often leads to premature worsening of employment status. The aim of this study was to identify early clinical and magnetic resonance imaging (MRI) predictors of employment status during long-term monitoring.

Methods: This prospective, longitudinal, observational cohort study, with over 11 years of follow-up, included 132 patients (78% females; at baseline: mean age: 31.0 ± 7.9; mean disease duration: 5.6 ± 5.3; median EDSS: 2.0) with early relapsing-remitting MS from the original Avonex-Steroids-Azathioprine (ASA) cohort. Average hours worked was monitored every 3 months. Cross-sectional and longitudinal regression analyses were used to identify the best MRI and clinical markers at the baseline of this study and their change during the first year for predicting proportional loss of hours worked due to MS over 11 years of monitoring. Univariate and multivariate models were estimated separately for clinical and MRI predictors and for their combinations.

Results: In the univariate analysis, the best MRI predictor of the proportional loss of hours worked over the subsequent years was normalized baseline gray matter volume (Nagelkerke's R squared (R2)=0.22). The best clinical predictor was MS duration (R2=0.12) and the strongest demographic marker was educational attainment (R2=0.14). In the multivariate model, the combination of independent clinical, MRI and demographic predictors explained up to 76% (R2=0.76) of variability of the proportional loss of hours worked over a follow up.

Conclusion: The results revealed significant early predictors of worsening of employment status in MS. Our fitted model consisting of clinical, MRI and demographic markers may refine the prediction of the employment status change.

Disclosure: The project was supported by the Czech Ministry of Education project PRVOUK-P26/LF1/4, RVO-VFN64165 and by the Czech Science Foundation GA CR 16-03322S, the ASA study was supported by Biogen Idec, funding for biostatistical support was provided by Novartis.

Muscle and neuromuscular junction disease 1

PR1094

Eculizumab improves fatigue in patients with refractory generalized myasthenia gravis in the REGAIN study

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Background and aims: REGAIN was a phase 3, multicentre, randomised, double-blind, placebo-controlled, parallel-group study of the safety and efficacy of eculizumab in patients with anti-acetylcholine receptor antibody–positive refractory generalised myasthenia gravis (gMG; N=125). Fatigue is a prominent and bothersome symptom in gMG. The REGAIN study marks the first use of the Neuro-QOL Fatigue scale in a clinical trial to assess fatigue in gMG.

Methods: The Neuro-QOL Fatigue scale is a reliable, validated, patient-reported assessment tool that has been used in other neurologic disorders. Assessments were performed at baseline and every 4 weeks during the 26-week treatment period. The Neuro-QOL Fatigue scale includes 19 items scored 1 to 5; total scores range from 19 to 95. An improvement of ≥ 5 points is a conservative estimate for a clinically meaningful change. Greater negative change from baseline indicates greater improvement.

Results: Based on the repeated-measures sensitivity analysis, patients receiving eculizumab showed greater improvement than those receiving placebo (change from baseline in total score at week 26 for eculizumab vs placebo was -16.8 [95% CI (-21.3, -12.3)] vs -7.9 [95% CI (-12.3, -3.5)]; P=.0061) (Figure 1). In patients treated with eculizumab, fatigue continued to improve after 4 weeks through the end of the study.
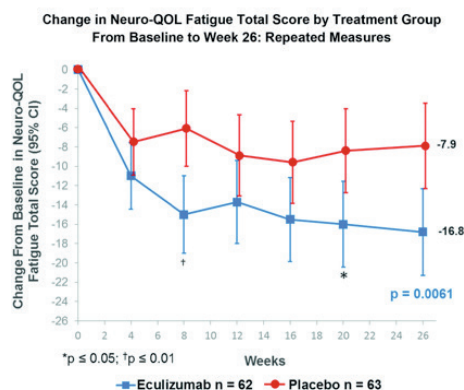
Figure 1. Change in Neuro-QOL Fatigue total score by treatment group over time from baseline to week 26. Least squares means are from a repeated measures analysis of change from baseline in Neuro-QOL Fatigue total score. Greater negative change from baseline indicates greater improvement.

Conclusion: Treatment with eculizumab resulted in significant improvements in Neuro-QOL Fatigue scores compared with placebo. Analysis of fatigue using the Neuro-QOL Fatigue scale, when added to the previously reported analyses of activities of daily living, muscle strength, and quality of life, supports the efficacy of eculizumab for patients with refractory gMG.

Disclosure: This study (NCT01997299) was sponsored by Alexion Pharmaceuticals (New Haven, CT, USA).

PR1095

Correlation of neuro-QOL with MG-ADL, QMG, and MG-QOL15 in assessing the spectrum of disease in patients with refractory generalised myasthenia gravis in the REGAIN study

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Background and aims: REGAIN was a phase 3, multicentre, randomised, double-blind, placebo-controlled study to assess the safety and efficacy of eculizumab in patients with anti-acetylcholine receptor antibody–positive refractory generalised myasthenia gravis (gMG; N=125). Each of the respective analyses (Myasthenia Gravis Activities of Daily Living [MG-ADL]), Quantitative Myasthenia Gravis [QMG] scale, Myasthenia Gravis Quality of Life [MG-QOL], and Quality of Life in Neurological Disease Fatigue [Neuro-QOL Fatigue]) was used to evaluate the overlapping and complementary symptoms that capture the totality of the burden of refractory gMG in the REGAIN study. In this analysis, the correlations between these assessment tools were calculated at week 26.

Methods: Fatigue was measured using the Neuro-QOL Fatigue scale. Activities of daily living were assessed by the MG-ADL scale. The QMG scale assessed muscle strength. The MG-QOL15 scale was used to assess quality of life. Correlation between scales was assessed using Pearson's r.

Results: There were close correlations between Neuro-QOL and MG-ADL, 0.63 (95% CI [0.51, 0.73]; P<.0001) (Figure 1); Neuro-QOL and QMG, r=0.57 (95% CI [0.44, 0.68]; P<.0001) (Figure 2); as well as between Neuro-QOL and MG-QOL15, r=0.75 (95% CI [0.66, 0.82]; P<.0001) (Figure 3).
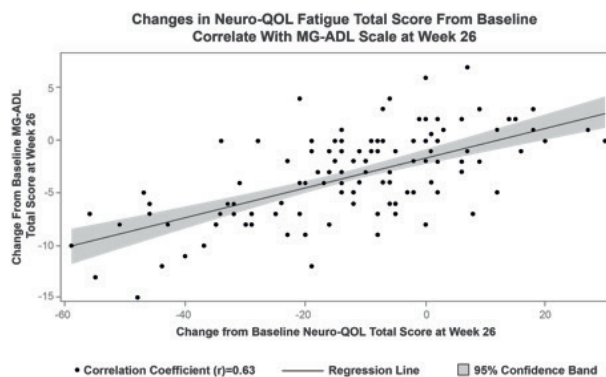
Figure 1. Changes in fatigue (Neuro-QOL) total score from baseline correlate with ADL and MG-ADL scale at week 26.
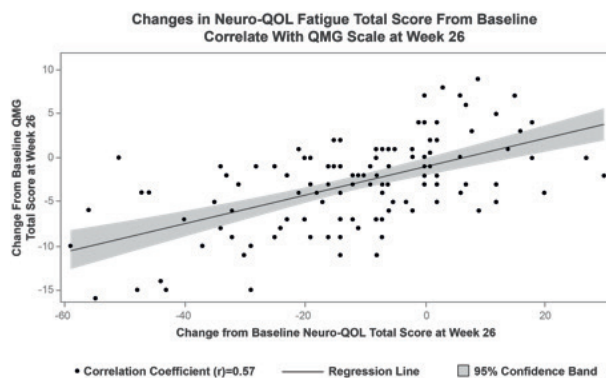
Figure 2. Changes in fatigue (Neuro-QOL) total score from baseline correlate with muscle strength and QMG scale at week 26.
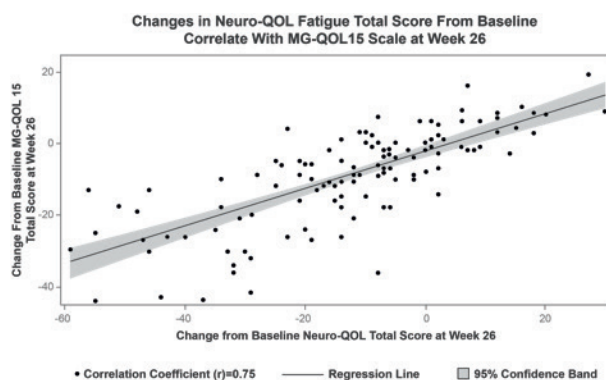
Figure 3. Changes in fatigue (Neuro-QOL) total score from baseline correlate with quality of life and MG-QOL15 scale at week 26.

Conclusion: Each of these assessment tools evaluates specific symptomatology that characterises refractory gMG. The Neuro-QOL Fatigue scale demonstrates a strong positive correlation with MG-ADL and MG-QOL15 and moderate positive correlation with QMG. Combined, these tools are sensitive and complementary for measuring the spectrum of impairment and burden in patients with refractory gMG.
Disclosure: This study (NCT01997229) was sponsored by Alexion Pharmaceuticals (New Haven, CT, USA).

PR1096

Neurological polyautoimmunity in myasthenia gravis

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Background and aims: Polyautoimmunity illustrates the existence of similar immunogenic mechanisms that lead to different clinical phenotypes. It occurs frequently in Myasthenia gravis (MG).
Methods: Analysis of 214 patients with MG, in follow-up between 1992 and 2016, for the co-occurrence of other neuroimmunological disorders. MG and the other diseases were defined based on clinical, electromyographic, imagiologic and serological criteria.
Results: Of 214 patients with MG, 25% (n=54) have another autoimmune disease; approximately 5% (n=11) have another immunomediated neurological disease: 3 of the CNS (2 NMO AQP4, 1 autoimmune encephalitis); 7 of the PNS (5 myositis, 1 Parsonage-Turner syndrome, 1 CIDP); 1 of the ANS (intestinal pseudo-obstruction syndrome). The majority (54.5%) of these patients are women and the average age of onset of myasthenic symptoms is 36 years. Ten patients have generalized MG. Anti-RACh antibodies were positive in 73%; there were other autoantibodies in relation with other autoimmune disease in 6/11 cases. The MG preceded or had concomitant appearance to other neuroimmunological disease in most cases (73%). 55% had been timectomized (3 thymic hyperplasia and 3 thymomas). The majority (73%) of patients had not yet been exposed to immunosuppression when the second disease emerged. The average time between onset of symptoms and the diagnosis of the second neurological disease was 1.27 years.
Conclusion: The possibility of autoimmune neurological comorbidity should be considered in all patients with MG, especially if patients present with unexpected neurological features in addition to those typical of MG.
Disclosure: Nothing to disclose

PR1097

Congenital myasthenic syndromes in Turkey

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Background and aims: Congenital myasthenic syndromes (CMSs) are a group of hereditary disorders affecting the neuromuscular junction. They usually start in the first year with fluctuating weakness in ocular, bulbar and extremity muscles. CMSs can be due to presynaptic, synaptic or postsynaptic defects. This differentiation, which is usually very difficult clinically, can be done by electrophysiological and molecular genetic tests.

Methods: Clinical, electrophysiological and genetic findings of 69 patients (36 female/33 male) from 50 unrelated families diagnosed with CMS at the Department of Neurology, Istanbul Faculty of Medicine were retrospectively evaluated. Genetic tests of 60 patients were performed between 1996 and 2016 by the laboratory of Dr. A. G. Engel at Mayo Clinic, USA.

Results: Most common CMS among our families was primary acetylcholine receptor deficiency (32/50) and the most common mutations were eIVS10+2T to G (12/50) and e1267delG (7/50) in CHRNE. This was followed by endplate acetylcholinesterase deficiency (5/50), DOK7 deficiency (3/50), GFPT-myasthenia (3/50), slow channel CMS (3/50), fast channel CMS (2/50), choline acetyltransferase (ChAT) deficiency (1/50) and desmin deficiency CMS (1/50). Most common mutation in endplate acetylcholinesterase deficiency was c.444G>A in COLQ (4/5 kinship) which was previously reported in families with Turkish origin only. We also report a new milder phenotype with upper extremity distal predominant involvement and autophagic vacuoles in muscle biopsy caused by homozygous c.686-2A>G mutations in GFPT1.

Conclusion: Mutations in CHRNE are the most common causes of CMS in our cohort. Our study provides data for creating a genetic testing algorithm for patients in Turkey.

Disclosure: Nothing to disclose

PR1098

Genetic landscapes in neuromuscular disorders: The influence of next-generation sequencing analysis

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Background and aims: Inherited neuromuscular disease (NMDs) are a large group of diseases involving muscles, motor neurons, neuromuscular junctions and nerves; within a given disease group genetic and clinical heterogeneity is the hallmark. The genetic diagnosis in rare diseases is now becoming mandatory for the inclusion in emerging therapeutic trials and the heterogeneous genetic landscape of NMDs raises challenges regarding the definition of a molecular diagnosis.

Methods: Within the EU Neuromics project we performed WES analysis in 5 families with congenital myopathy/dystrophy, 1 with spastic paraplegia, 2 with ataxia, 1 with Myofibrillar Myopathy, 1 with AV block and LGMD, and in 2 sporadic UCMD patients with no identified mutation in COL6 genes. We also studied two families with hereditary neuropathy and hereditary ataxia, orphan of genetic definition, with a clinical gene-panel approach

Results: WES analysis unraveled the genetic cause of 5 out of 10 families. We identified 3 known gene mutations (RYR1, ISPD and STIM1) and 2 novel causative genes, functionally validated. In the remaining families and COL6 patients, a few candidates were identified and functional assays are in progress. In the 2 families with hereditary neuropathy and hereditary ataxia we identified the causative mutation in known genes (ATP7A and AFG3L2).

Conclusion: The Next Generation Sequencing approach in NMDs patients is efficient in improving the diagnostic definition through clinical gene panel analysis (diagnostic field) and is also powerful for the identification of novel causative genes through WES (whole exome sequencing analysis, research field).

Disclosure: Nothing to disclose

PR1099

Patients with refractory myasthenia gravis are at increased risk for myasthenic crises, disease exacerbations, intensive care unit visits, and hospitalisations

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Background and aims: REGAIN was a phase 3, multicentre, randomised, double-blind, placebo-controlled study of the safety and efficacy of eculizumab in patients with anti-acetylcholine receptor antibody–positive refractory generalised myasthenia gravis (gMG) over 26 weeks. The objective of this analysis was to characterise the rates of exacerbations and myasthenic crises and the consequent need for hospitalisations and admissions to the intensive care unit (ICU) in the 2 years prior to enrollment in REGAIN.

Methods: Patients with refractory gMG in this study were required either to have failed ≥ 2 immunosuppressive therapies (ISTs) or to have failed ≥ 1 IST needing long-term intravenous immunoglobulin (IVIg) or plasma exchange (PLEX); patients also required evidence of ongoing functional weakness, defined as an MG Activities of Daily Living total score of ≥ 6.

Results: The mean duration of gMG prior to enrollment in REGAIN was 9.55 years in patients with refractory gMG (N=125; Table 1). Fifty-two percent had tried ≥ 3 ISTs; 79.2% and 48.0% had tried IVIg and PLEX (either chronically or acutely), respectively. The numbers of myasthenic crises and exacerbations in the 2 years prior to enrollment per 100 patient-years are presented in Figure 1. The numbers of ICU admissions and hospitalisations in the prior 2 years per 100 patient-years are presented in Figure 2.

Figure 1. Number of myasthenic crises and number of exacerbations per 100 patient-years, 1-2 and 0-1 years immediately before enrollment in REGAIN.

Figure 2. Number of admissions to ICU and number of hospitalisations per 100 patient-years, 1-2 and 0-1 years immediately before enrollment in REGAIN.

Conclusion: These data show that many years after diagnosis, patients with refractory gMG prior to enrollment in the REGAIN study continued to be at ongoing risk for exacerbations and myasthenic crises and consequent hospitalizations and admissions to the ICU.

Disclosure: This study (NCT01997229) was sponsored by Alexion Pharmaceuticals (New Haven, CT, USA).

Baseline Characteristics of Patients in the REGAIN Study

Characteristic	Total (N=125)
Mean age at diagnosis, years (min, max)	38.07 (5.9, 78.0)
Mean MG duration since diagnosis, years (min, max)	9.55 (1.0, 33.8)
Female, n (%)	82 (65.6)
Patients using 2 ISTs, n (%)	58 (46.4)
Patients using 3 ISTs, n (%)	39 (31.2)
Patients using ≥ 4 ISTs, n (%)	26 (20.8)
Patients who received IVIg, n (%)	99 (79.2)
Patients who received PLEX, n (%)	60 (48.0)

IST, immunosuppressive therapy; IVIg, intravenous immunoglobulin;

PLEX, plasma exchange.

Table 1. Baseline characteristics of patients in the REGAIN study

PR1100

Muscle fiber dysfunction contributes to muscle weakness in inclusion body myositis

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Background and aims: Inclusion body myositis (IBM) is the most common acquired muscle disorder in adults over 50 years old. It is characterized by progressive muscle weakness and marked atrophy, most prominent in the finger flexors and quadriceps. This study aims to investigate the causes of muscle weakness in IBM, in particular the contractile performance of residual muscle fibers.

Methods: We included 8 participants with IBM and 12 healthy controls. We measured functional performance and muscle strength. In all participants, muscle contractile capacity was measured in vivo, using quantitative muscle testing and MRI imaging, and ex vivo, using single fiber studies of the vastus lateralis and tibialis anterior muscle biopsies. Quadriceps specific force was calculated by correcting voluntary maximum force (N) for the contractile cross-sectional area (CCSA). CCSA was calculated by multiplying the total cross-sectional area by the muscle fraction on MRI.

Results: Voluntary maximum force generation of the quadriceps muscle was significantly reduced in IBM participants ($p<.001$). IBM patient had loss of contractile muscle mass due to fatty infiltration ($p=.006$) and intrinsic weakness of residual muscle tissue ($p=.003$). Muscle fiber specific force was reduced in IBM patients compared to healthy controls ($p=.036$).

Conclusion: In addition to loss of muscle mass due to fatty infiltration, the contractile performance of residual tissue is impaired in IBM due to muscle fiber weakness. Potential mechanisms for muscle fiber dysfunction are under investigation, and may be related to loss or damage of sarcomeric proteins as a result of inflammation and degenerative changes.

Neurogenetics 1

PR1101

Mitochondrial neurogastrointestinal encephalomyopathy: Novel pathogenic mutation in thymidine phosphorilase gene in a patient from Cape Verde

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Background and aims: Mitochondrial Neurogastrointestinal Encephalomyopathy (MNGIE) is a rare autosomal recessive disorder caused by mutations in the gene encoding the Thymidine Phosphorilase (TYMP). It is clinically characterized by severe gastrointestinal dysmotility, cachexia, palpebral ptosis, ophtalmoparesis, sensorimotor polyneuropathy and leukoencephalopathy.

Methods: Case report

Results: A 19-year-old female, born in Cape Verde islands from a consanguineous marriage, was admitted with a history of recurrent episodes of nausea, vomiting, diarrhoea and painful abdominal distension, since childhood. She had severe weight loss (≈15 Kg) over the previous year. In addition, she suffered from progressive weakness, causing impairment in climbing stairs and running, as well as decreased dexterity. There was no cognitive impairment. On examination, she developed cachexia (Body Mass Index=10.9), with bilateral symmetric ptosis, generalized muscle weakness and atrophy,areflexia, diminished nociception below knees, and reduced vibration and position sense in toes and fingers.

The diagnostic workup including muscle biopsy and nerve conduction studies, confirmed severe gastrointestinal dysmotility, sensory-motor demyelinating neuropathy associated with myopathy, leukoencephalopathy, and high levels of lactate in serum and CSF. The diagnosis of MNGIE was considered. Genetic screening of the TYMP gene identified two homozygous contiguous mutations (c. 1283G>A, c.1284 T>A), affecting the same codon (GGT>GAA). The patient died three months after admission from medical complications.

Conclusion: We report a novel homozygous TYMP gene mutation (c. 1283G>A), not yet described in MNGIE syndrome. The second mutation is a frequent polymorphism. Both, in association, result in amino acid change (p. Gly428Asp), being responsible for this rare neuromuscular disease.

Disclosure: Nothing to disclose

PR1102

An atypical presentation of Argininossuccinic aciduria

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Background and aims: Argininossuccinic aciduria (ASA), caused by deficiency of argininosuccinate lyase (ASL), is the second most common urea cycle disorder (UCD) and presents with heterogeneous clinical phenotypes. Late onset forms, despite fewer hyperammonemic episodes than in other UCD, have a greater risk for poor neurocognitive outcome, hypertension and liver disease. Usually, the typical biochemical profile (elevation of plasmatic or urinary argininosuccinic acid and in plasmatic citrulline) and molecular genetic testing are sufficient for the diagnosis.

Methods: Case report.

Results: A 50-year-old man was referred to our neurology department complaining from severe muscle cramps and irritability after protein rich meals, without association with physical activities or fasting. His medical history revealed asthma, hypertension and persistent creatine kinase (CK) levels elevation. Physical examination revealed a hepatomegaly, with normal neurological examination. Electromyography had no abnormalities. There was a slight increase in hepatic enzymes levels with normal ammonia levels. Acylcarnitine profile and alfa-glucosidase levels were normal. Citrulline plasmatic levels and argininossuccinic acid plasmatic and urinary levels were increased. The molecular genetic study of ASL gene identified a pathogenic homozygotic V178M mutation confirming the diagnosis of ASA. The patient began a protein restricted diet with clinical and biochemical improvement.

Conclusion: Despite the attenuated clinical course, the presence of clinical symptoms triggered or worsened by protein intake is common and can lead to diagnosis. Early diagnosis is important due to the possible clinical improvement associated with dietary adjustments. The high CK levels found in this patient are not directly explained by ASA but could be part of the attenuated adult phenotype.

Disclosure: Nothing to disclose

PR1103

The launch of the European Reference Network for Rare Neurological Diseases: New prospects for quality care and research in Europe

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Background and aims: Imagine if the best specialists from across Europe could join their efforts to tackle rare medical conditions that require highly specialised healthcare and a concentration of knowledge and resources. That's the purpose of the European Reference Networks (ERNs) and it's becoming a reality. In 2016 the European Commission has issued a call for the formation of ERNs for rare diseases.

Methods: The European Reference Network for Rare Neurological Diseases (ERN-RND) has been formed in response to the call and is a network of 32 Healthcare Providers from 13 EU member states. ERN-RDN builds on existing expert centres and mature networks dedicated to RND as well as established rare disease infrastructures such as Orphanet, EURORDIS and RD-Connect.

Results: The European Reference Network for Rare Neurological Diseases is one of the very first ERNs that have officially been approved by the Board of Member States on 15 December 2016.

European Reference Network for Rare Neurological Diseases

ERN RND
Initiative for European Reference Network for Rare Neurological Diseases

KEY WORDS
- Rare neurological diseases (RND)
- Reference network of approved European centers of expertise
- Focused on care of (RND) patients (diagnosis, evidence-based management and treatment)
- Patient centered
- Data collection and data based care

ABSTRACT
ERN-RND is a network of 32 Healthcare Providers from 13 EU member states. ERN-RDN builds on existing expert centres and mature networks dedicated to rare neurological diseases (RND) as well as established rare disease infrastructures such as Orphanet, EURORDIS and RD-Connect. Through coordination and knowledge transfer, ERN-RND shall establish a patient-centered network to address the needs of patients with RND of all age groups, with or without a definite diagnosis, by implementing an infrastructure for diagnosis, evidence-based management, treatment and collection of patient data. The network will develop, disseminate, implement and supervise best practice guidelines and care pathways to optimize patient care and facilitate training and capacity building in the field. A special effort will be aimed to member states with less developed infrastructure for caring for RND patients, where no current partners are located, or with only affiliated or collaborative partners. ERN-RND will inform planning of European and national health care in RND, facilitating translation of research activities into clinical practice and the development of future therapies. ERN-RND's strategic objectives for the first five year period are: 1. To increase by at least 20% the overall percentage of RND patients with a final diagnosis; 2. To improve care of RND patients, reaching at least a 20% improvement in established outcome measures; 3. To develop, share and implement care pathways and guidelines for all RND groups represented in ERN-RND; 4. To create, develop and enhance constituents' capacity to design, implement and supervise RND training, education and capacity building measures so that health care providers (HCP) of all EU member states actively participate in ERN-RND in the future; 5. To develop a comprehensive and data based European RND cohort to better understand these conditions and thus improve their management and help developing and testing treatments.

32 MEMBERS from 13 COUNTRIES (at present)
Countries present: Belgium, Bulgaria, Czech Republic, France, Germany, Hungary, Italy, Lithuania, Netherlands, Poland, Slovenia, Spain, UK (additional countries will follow)

Towns where members come from: Bruxelles, Leuven, Sofia, Prague, Bordeaux, Paris, Toulouse, Bonn, Lübeck, München, Tübingen, Ulm, Budapest, Pécs, Milan, Rome, Siena, Amsterdam, Groningen, Nijmegen, Rotterdam, Krakow, Ljubljana, Barcelona, London, Vilnius (additional centres will follow)

European Reference Network for Rare Neurological Diseases

DISEASE COVERAGE of ERN-RND
For the establishment of ERN-RND: 1) RARE NEURODEGENERATIVE DISEASES: movement disorders, cognitive and neurometabolic disorders like cerebellar ataxias, spastic paraplegias, Huntington's disease and choreas, dystonias, rare dementias, leukodystrophies and atypical Parkinson's diseases

For the disease expansion of ERN-RND: 2) RARE INFLAMMATORY and ONCOLOGICAL DISEASES and 3) VASCULAR DISEASES, MALFORMATIONS as well as further rare neurological diseases.

STRATEGIC AIMS
- To improve management of rare neurological diseases throughout the EU by sharing best practice and evaluation and development of consensus and evidence-based guidelines
- To facilitate diagnosis, care and therapy of rare neurological diseases by utilising TeleHealth approaches to share expertise and improve equity of access to expert opinions across the EU and by guiding access to quality assured diagnostic tests and care.
- To provide access to support and advice for those with ultrarare neurological diseases.
- To establish a European meta-registry for rare neurological diseases embracing existing and new patient registries to document natural history and patient outcomes and to facilitate future research
- To define outcome measures, including patient outcome measures, and key performance indicators and use these to define, and monitor best practice and implementation of guidelines across the network centers, through audit and benchmarking activities.
- To facilitate capacity building, training and education through courses, e-learning approaches and staff exchange programmes
- To empower patients with rare neurological diseases and their families/carers to play an active part in all of the above activities.

COLLABORATING ORGANISATIONS
- Existing European disease focussed networks and study groups such as: European Huntington 's Disease network, Ataxia Study Group, European Dystonia Network, Genetic PSP Study Group etc.
- BRAIN-TEAM (National care network for RND of France)
- European Federation of Neurological Associations and further national as well as disease focused patient organisations
- European Academy of Neurology
- European Paediatric Neurology Society
- European Brain Council
- European Molecular Genetics Quality Network, European Pathway Association
- RD Infrastructures: Orphanet, RD-Connect, EURORDIS

CONTACT INFORMATION
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Conclusion: As a consequence of the official approval, ERN-RND will begin to operate in the first quarter of 2017. The network is in a very good position to achieve its strategic objectives of the first five year period. These are: 1. To increase the overall percentage of RND patients with a final diagnosis; 2. To improve care of RND patients; 3. To develop, share and implement care pathways and guidelines ; 4. To create, develop and enhance RND training, education and capacity building measures; 5. To develop a comprehensive and data based European RND cohort to better understand these conditions and help developing and testing treatments.

Disclosure: Nothing to disclose

PR1104

A novel mutation in ABCD1 unveils different clinical phenotype in a family with adrenoleukodistrophy

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Background and aims: X-linked adrenoleukodistrophy (X-ALD) is the most common peroxisomal disorder. The disease is caused by mutations in the ABCD1 gene that encodes the peroxisomal membrane protein ALDP which is involved in the transmembrane transport of very long-chain fatty acids (VLCFA; >22).

Methods: In 2007, a 43-year-old patient developed progressive spastic paraparetic gait. Over the years, several brain and spinal magnetic resonance were normal. The laboratory tests revealed primary partial adrenal insufficiency. In 2015, his 9-year-old grandson referred to the pediatric endocrine clinic for obesity and raised TSH, his neurological examination was normal. Brain MRI revealed an unequivocal pattern of ALD. His 73- and 71-year-old aunts experienced unexplained walking difficulties at the age of 30 years which progressed to spastic paraparesis. Brain and spinal MR performed were negative. All patients presented fasting plasma levels of VLCFA significantly elevated. His mother and sister were asymptomatic.
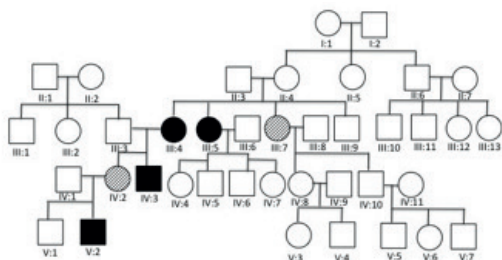
The cross inheritance of recessive X-linked adrenoleukodistrophy alleles in consanguineous pedigree

Results: The ABCD1 gene in the proband and family revealed a heterozygous single nucleotide variation in intron 4 (IVS4+2T>A; c.1393+2T>A). Sequencing analysis of cDNA showed an activation of a cryptic splicing site that leads to frameshift with premature stop codon in messenger-RNA transcript. The resulting ABCD1 protein lacks of C-terminal domain; the dysfunction of ALD protein induces an accumulation of VLCFAs in all tissues.

Conclusion: This is the first report of the IVS4+2 T>A mutation in intron 4 of the ABCD1 gene. We showed that, within individual kindreds with the same mutation, different phenotypes of the entire clinical and radiological spectrum of X-ALD since asymptomatic patient, could be detected.

Disclosure: Nothing to disclose

PR1105

A new phenotype of ethylmalonic encephalopathy

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Background and aims: Ethylmalonic encephalopathy (EE) is a rare mitochondrial disorder caused by mutations in the ETHE1 gene. ETHE1 codes for a mitochondrial sulfur dioxygenase which plays a crucial role in hydrogen sulfide (H2S) detoxification, recovering glutathione (GSH) in the process. There have been reports of clinical improvement of EE under treatment with N-Acetylcysteine (NAC), a GSH precursor. EE typically presents during early infancy, leading to death within the first decade. We present a case of EE in an adult patient and a treatment trial with NAC.

Methods: The diagnosis EE was first suspected after exome sequencing and confirmed by biochemical testing and ETHE1 Western-Blot from muscle. Oral NAC was administered in increasing dosage with a maximum dose of 70 mg/kg per day, under regular clinical assessment including 10m-walk-test, stair-climbing-test, Spastic paraplegia rating scale (SPRS) and biochemical parameters.

Results: The 29-year-old female patient had first manifested at the age of 15 years with spastic paraparesis. Exome sequencing revealed a homozygous ETHE1 mutation and biochemical analysis showed the characteristic biochemical profile of EE. Decrease of ETHE1 protein was confirmed by Western-Blot in muscle. The treatment trial with NAC was aborted after 8 months due to clinical deterioration fully reversible after ending NAC intake.

Conclusion: To our knowledge this is the first reported adult case of EE, showing a distinct, unusually mild phenotype, and proving unresponsive to NAC treatment. This case expands the known phenotype and prompts caution regarding NAC therapy in atypical EE.

Disclosure: Nothing to disclose

Neuroimaging 1

PR1106

Motor phenotype correlates of regional hypo-, normo- and hypercholinergic vesicle expression in Parkinson's disease

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Background and aims: There is increasing evidence for a cholinerigc role in motor abnormalities in Parkinson's disease (PD). Changes in cholinergic innervation occur in distinct brain regions differentially with decreases manifesting initially in posterior and increases in anterior cortices. We investigated the clinical significance of regionally differential cholinergic activity in PD.

Methods: PD patients (n=70, 52M; age: 67.0±6.6; HY stage: 2.4±0.5; underwent [18F]FEOBV vesicular acetylcholine transporter PET imaging. posterior (parieto-occipital) and anterior (frontal) cortical binding was determined. Cholinergic status was based on values<5th percentile of normative data (hypocholinergic), between the 5th and 95th percentile (normocholinergic) or exceeding the 95th percentile (hypercholinergic) status. UPDRS motor phenotyping was available for 67 subjects.

Results: There were 37 subjects with at least posterior hypocholinergic status (group A), 22 subjects with global normocholinergic status (group B) and 8 subjects with anterior hypercholinergic status without evidence of posterior hypocholinergic changes (group C). The distribution of tremor-dominant (TD), indeterminate (ID) and postural instability and gait difficulties (PIGD) subtypes across the three groups was significantly different ($\chi 2$=14.1, P=0.0087): Group A (n=37): TD n=14 (37.9%), ID n=7 (18.9%), PIGD n=16 (43.2%); Group B (n=22): TD n=14 (63.6%), ID n=0, PIGD n=8 (36.4%) & Group C (n=8): TD n=7 (87.5%), ID n=0, PIGD n=1 (12.5%).

Conclusion: There is a gradient of decreasing PIGD and increasing TD motor phenotype from hypo- to hypercholinergic status in PD. The TD motor phenotype is present in the majority of patients with anterior cortical hypercholinergic status.

Disclosure: NIH P50 NS091856 & The Michael J. Fox Foundation

PR1107

Dynamic changes of hippocampal subfields in CIS patients: A 2-year MRI longitudinal study

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Background and aims: To evaluate the patterns of regional hippocampal volume variations in clinically isolated syndrome (CIS) patients.

Methods: Brain dual-echo and 3D T1-weighted scans were acquired from 36 CIS patients within 2 months from clinical onset and after 3,12 and 24 months. Fourteen healthy controls (HC) were also studied. Manual hippocampal segmentation was performed according to a standardized procedure, and global volumes were derived. Radial atrophy distribution was assessed using 3D parametric surface mesh models.

Results: An increased radial distance (RD) in the DG was observed in the left hippocampus at baseline (p<0.01), 3 months (p<0.05) and, progressively decreasing, but not disappearing, at 12 and 24 months. A right DG expansion appeared at 3 months (p<0.01), and persisted until the second year. DG hypertrophy positively correlated with T2 and GD lesion load (LL) (p<0.05, R>0.5). Bilateral hippocampal atrophy was observed from the lateral and ventral CA1 subfield of the tail at baseline (p<0.05) and spreading to the subiculum, dorsal tail and head (p<0.01) at 12 and 24 months. At 24 months, global hippocampal volume significantly differed between CIS and HC (right p<0.05, left p=0.01). RD reduction was negatively correlated with T2 and T1 LL, especially at 12 and 24 months (p<0.01, R>-0.5).

Conclusion: Regional hippocampal volume abnormalities occur in CIS patients, with higher susceptibility to damage of CA1 and subiculum. Hippocampal volume abnormalities are dynamic and seem modulated by inflammation, as suggested by the correlation between DG expansion and inflammatory lesional measures.

Disclosure: Nothing to disclose

PR1108

Structural connectivity-defined thalamic sub-regions have different functional connectivity abnormalities in multiple sclerosis patients: Implications for clinical correlations

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Background and aims: Current findings on thalamic functional connectivity (FC) abnormalities in multiple sclerosis (MS) patients are largely discordant. Using a structural connectivity parcellation, we investigated sub-regional (SR) thalamic resting state (RS) FC alterations and their relationship with clinical and cognitive measures in MS patients.

Methods: MRI data from 187 MS patients and 94 healthy controls (HC) were used to parcellate the thalami into five SR, according to their structural connectivity profile. For each thalamic SR, a seed based RS FC analysis was performed. Correlations between thalamic RS FC and clinical/cognitive variables were assessed.

Results: Compared to HC, MS patients had an increased RS FC between all thalamic SR and the left insula. Except for temporal thalamic SR, all remaining SRs showed increased intra- and inter-thalamic RS FC in patients. MS patients also showed reduced RS FC between the frontal and motor thalamic SR and caudate nucleus and between the temporal thalamic SR and the ipsilateral thalamus, cingulate cortex, and cerebellum. Compared to cognitively preserved, cognitively impaired MS patients had higher thalamic RS FC with several temporal areas. In MS patients, lower RS FC between thalamic SR and caudate and cingulate cortex correlated with worst motor performance, whereas higher RS FC with the insula correlated with better motor performance.

Conclusion: The main thalamic SRs have different RS FC abnormalities in MS patients. Increased thalamic RS FC with the insula might have a compensatory role, whereas increased RS FC with temporal areas, observed in patients with cognitive impairment might reflect a maladaptive mechanism.

PR1109

Neuroimaging studies in familial forms of Parkinson's disease: A systematic review

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Background and aims: Between 5 and 15% of Parkinson's disease (PD) patients are carriers of genes linked with the development of PD. Studies on PD genetic carriers at an asymptomatic stage give a valuable opportunity to identify mechanisms underlying PD before the onset of motor symptoms. Here, we aim to systematically review the current status of MRI, PET and SPECT imaging in asymptomatic (aPD) and symptomatic (sPD) genetic carriers of PD.

Methods: MEDLINE, Web of Science, Cochrane and Scopus databases were searched for articles in all languages published up to 1st November 2016 using the key words "CHCHD2; DJ-1; DNAJC6; EIF4G1; GBA; LRRK2; parkin; PINK1; RAB39B; SNCA and VPS35" combined with "Neuroimaging", "MRI", "SPECT and "PET".

Results: A total of 143 MRI, 83 PET and 55 SPECT studies were identified and reviewed. aPD-parkin, PINK1 and LRRK2 carriers revealed a reduction of [18F]DOPA and [123I]-FP-CIT binding in the basal ganglia, suggesting a neurodegenerative process affecting the presynaptic dopaminergic terminals in the premotor stage of the disease. This alterations were not present in the basal ganglia of SNCA-aPD patients, whose tracer binding was similar to HC. MRI studies showed an increased grey matter volume in the caudate, putamen and globus pallidus of aPD-parkin and PINK1 carriers, and in the striatum of aPD-LRRK2 carriers. An overall reduced functional connectivity was present in all mutation carrying individuals, except from SNCA-aPD patients, whose MRI was indistinguishable from HC.

Conclusion: PET, SPECT and MRI are powerful tools for assessing and understanding the potential differences between asymptomatic and symptomatic stages of genetic PD.

PR1110

Non-motor symptom burden is associated with thalamic atrophy in Parkinson's disease

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Background and aims: Non-motor symptoms are common aspects of Parkinson's disease (PD) occurring in prodromal PD and greatly affecting the quality of life. The global impact of non-motor symptoms can be graded using the non-motor symptoms burden classification system and can be used to address the neural correlates of non-motor symptoms burden, which is an unmet need. Here, we investigated whether non-motor symptoms burden is associated with cortical and subcortical morphological changes in PD patients.

Methods: We studied 41 non-demented PD patients (24M, mean age: 64.0±9.3 years). Non-motor symptoms burden was assessed using the Non-Motor Symptoms Scale gradings (NMSS). Cortical thickness and subcortical nuclei volume analyses were carried out using the automated surface-based analysis package Free-Surfer (version 5.3.0). PD patients were divided into two groups according to the NMSS grading: mild to moderate (NMSS: 0-40) and severe (NMSS: ≥41) non-motor symptom burden.

Results: Thalamic atrophy was associated with worse NMSQ (r=−0.42, P=0.042) and NMSS (r=−0.47, P=0.014) total scores. The non-motor symptoms that drove this correlation were sleep/fatigue (r=−0.36, P=0.042) and gastrointestinal tract dysfunction (r=−0.36, P=0.042). When the PD patients were divided into two groups, we found that PD patients with severe non-motor symptom burden had significant thalamic atrophy compared to the group with mild to moderate non-motor symptom burden (P=0.048).

Conclusion: Our findings show that greater non-motor symptom burden is associated with thalamic atrophy in PD. Thalamus plays an important role in processing sensory information including visceral afferent from the gastrointestinal tract and in regulating states of sleep and wakefulness.

Disclosure: Nothing to disclose

PR1111

Clinical relevance of lesion mapping in vascular mild cognitive impairment

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Background and aims: Vascular mild cognitive impairment (VMCI) may have heterogeneous cognitive impairment and different brain lesion load. MRI-derived lesion probability map (LPM) allows the assessment of spatial patterns of focal pathology at group level. We aimed to assess the clinical relevance of brain lesion location and frequency of lesion occurrence in a large group of patients with VMCI

Methods: We included 110 VMCI patients from three centers, who were divided into four groups, according to cognitive impairment assessed with the VMCI-Tuscany neuropsychological battery (Table). We created LPM from FLAIR images (Figure) and performed voxelwise statistics with age, sex, center and slice thickness as covariates, with nonparametric permutation testing, using FSL (www.fmrib.ox.ac.uk/fsl).

Study patients	N=110, age= 74.3 +/- 6.6 years, 60 women
Fazekas scale (WM lesion severity)	grade 2 (n=52), grade 3 (n=58)
Groups	Amnestic/single-domain (n=9) Amnestic/multi-domain (n=76) Non-amnestic/single-domain (n=10) Non-amnestic/multi-domain (n=15)
Data source	Center 1 (n=75), Center 2 (n=19), Center 3 (n=16)
MR field strength	1.5 T (n=91), 3T (n=19)
FLAIR slice thickness	3 mm (n=16), 3.6 mm (n=75), 5 mm (n=19)
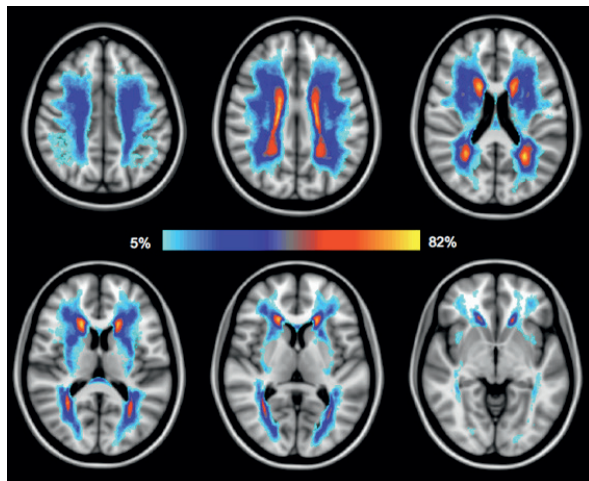
Results: In the whole VMCI group, higher lesion frequency along various regions of white matter (WM) tracts correlated (p<0.05, corrected) with lower global mental functioning, verbal memory, psychomotor speed and constructional praxis. In terms of between-group differences (p<0.01 corrected, analysis of variance), non-amnestic/multi-domain group had higher lesion frequency than both amnestic/multi-domain and non-amnestic/single-domain groups in the superior longitudinal fascicle, adjacent to the middle frontal gyrus. Moreover, non-amnestic/single-domain group had higher lesion frequency than amnestic/multi-domain group in the WM of the superior frontal gyrus and in the inferior fronto-occipital fascicle, adjacent to the frontal anterior cingulate gyrus.

Conclusion: In VMCI, higher frequency of lesion occurrence in strategic WM tracts is related with impairment of specific cognitive domains. Moreover, the involvement of WM fibers of the frontal lobe seems to characterize VMCI patients with nonamnestic type of cognitive impairment.

Disclosure: Nothing to disclose

PR1112

High-resolution ultrasound in Wartenberg's migrant sensory neuritis

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Background and aims: Wartenberg's migrant sensory neuritis (WMSN) is an infrequent spotty, pure sensory neuropathy. Nerve conduction studies (NCS) usually reveal a decrease of sensory nerve action potentials (SNAPs), but in the absence of a conclusive diagnostic test WMSN remains primarily a clinical diagnosis. High-resolution ultrasonography (HRUS) is an emerging adjunctive diagnostic technique in peripheral nerve disease, but has not been studied in WSMN. We examined the sonographic pattern of nerve involvement in WMSN and disease controls.

Methods: We performed a case-control study on newly diagnosed WMSN patients (n=8) and, as disease controls, patients with pure sensory axonal neuropathy (n=16) and pure sensory chronic inflammatory demyelinating disease ((CIDP) n=6)). All patients underwent routine diagnostic evaluations and an elaborate HRUS protocol.

Results: We found mild multifocal nerve enlargement in all 8 WMSN patients. The median nerve in the upper arm and the sural nerve were significantly larger in WMSN than in axonal controls (p=0,01 and p=0,04 respectively). In pure sensory CIDP sonographic enlargement was more extensive. Nerve conduction studies detected abnormalities in 5 of 8 WMSN patients (63%), in contrast to sonography, which detected enlargement in all 8 patients (100%). Furthermore sonographic enlargement was found even when clinical examination and NCS were normal.

Conclusion: Mild sonographic enlargement of multiple nerves can be found in WMSN. This pattern may help to discern it from sensory CIDP and axonal neuropathies, and could be of additional diagnostic value in establishing the diagnosis.

Disclosure: Nothing to disclose

Neuroimmunology 1

PR1113

No association of infection with reduced lymphocyte counts: Results from up to 6 years of teriflunomide treatment in patients with relapsing forms of MS (RMS) in the TOWER core and extension studies

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Background and aims: In TOWER (NCT00751881), teriflunomide reduced clinical disease activity vs placebo in RMS patients, with activity remaining low in the long-term extension. In the core study, lymphocyte count reductions occurred early, but remained within normal range. Here, we describe impact of teriflunomide on lymphocyte counts and infection rates in TOWER core and extension.

Methods: In TOWER extension, all patients received teriflunomide 14mg. Lymphocyte counts were obtained every 6 weeks until Week 24, then every 24 weeks. Lymphopenia, identified from 2 consecutive lymphocyte counts below lower limit of normal, was graded by Common Terminology Criteria for Adverse Events.

Results: In TOWER core, placebo-treated patients (n=385) and teriflunomide-treated patients (n=780) experienced Grade 1 (0.8%; 2.8%) and 2 (1.0%; 1.5%) lymphopenias infrequently. Infections occurred in placebo- and teriflunomide-treated patients with Grade 1 (33.3%; 50.0%) and 2 (75.0%; 16.6%) lymphopenias. No patients with Grade 1 lymphopenia, and only 1 (25%) placebo-treated patient with Grade 2 lymphopenia, experienced serious infections. Teriflunomide-treated patients in the combined core and extension studies (N=1031), with 2805 patient-years of teriflunomide exposure, experienced few Grade 1 (3.2%) or 2 (2.7%) lymphopenias; infections were reported in 54.5% and 42.9% of these patients, respectively, vs 52.3% of patients without lymphopenia. Serious infections only occurred in patients without lymphopenias (3.7%). No Grade 3 or 4 lymphopenias were reported.

Conclusion: TOWER core and extension patients infrequently experienced low-grade lymphopenia; no high-grade lymphopenia was reported. Rates of infections were similar in patients with or without lymphopenia, supporting the teriflunomide immunomodulatory mechanism of action and lack of effect on protective immunity.

Disclosure: Study supported by Sanofi Genzyme.

PR1114

Cancelled

PR1115

The diagnostic overlap of statin-induced necrotizing autoimmune myopathy with other idiopathic autoimmune myopathies

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Background and aims: Statin therapy is occasionally associated with the production of specific auto-antibodies against 3-hydroxy 3-methylglutaryl coenzyme-A reductase (anti-HMGCR) that may give rise to proximal muscle weakness, high creatine kinase (CK) levels and myofibrillar necrosis. These symptoms, in association with statin therapy, have established a new clinical entity known as statin-induced necrotizing autoimmune myopathy (SINAM), a subtype of immune-mediated necrotizing myopathy (IMNM). The clinical manifestations of INMN and idiopathic polymyositis (PM), and the histopathological criteria for both, may overlap significantly depending on the diagnostic criteria employed. Anti-HMGCR has been reported as specific for INMN that includes SINAM. The aim of this study was to discriminate unrecognized SINAM cases from among idiopathic autoimmune myopathies and to evaluate the usefulness of anti-HMGCR assessment.

Methods: A total of 30 subjects with original diagnosis of PM or IMNM underwent anti-HMGCR testing and structured quantitative revision of muscle biopsies. A history of any long-term statin therapy was taken.

Results: Twelve patients in the original group were anti-HMGCR positive (IMNM 5x, PM 7x). Seven of these had histories of long-term statin therapy, signs of myofibrillar necrosis, >10-fold increases in CK level, and all complied with the criteria for SINAM. Combined immunosuppression led to remission of clinical symptoms and decreases in CK levels in all of them.

Conclusion: Polymyositis is possibly an over-diagnosed entity and many IMNM cases may be concealed among PM patients, including those with SINAM. Where there is overlap of histopathological criteria for PM and IMNM, anti-HMGCR antibodies may be helpful in distinguishing IMNM(or SINAM) from PM, on the assumption of their specificity for IMNM.

Disclosure: Nothing to disclose

PR1116

Rapid and robust B-cell depletion in preliminary results of phase 2 multicenter study of Ublituximab (UTX), a novel glycoengineered anti-CD20 monoclonal Antibody (mAb), in patients with relapsing forms of multiple sclerosis (RMS)

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Background and aims: Patients with relapsing or primary progressive forms of multiple sclerosis have shown significant clinical improvement after B-cell depletion with an anti-CD20 antibody. UTX is a novel, chimeric mAb targeting a unique epitope on the CD20 antigen and glycoengineered to enhance affinity for all variants of $Fc\gamma RIIIa$ receptors, demonstrating greater antibody-dependent cellular cytotoxicity activity (ADCC) than rituximab.

Methods: TG1101-RMS201 is a 52-week, phase 2, placebo-controlled, multicenter study that is designed to assess the optimal dose and infusion time as well as safety/tolerability of UTX in RMS subjects. Radiological and clinical analysis are also performed. Optimal dosing is determined by B-cell depletion, defined as percentage of CD19+ B-cells present following UTX administration. This is calculated by gating the entire lymphocyte/myeloid population. Within this population, CD19+ CD3- cells were gated and% CD19+ B-cells was determined.

Results: To date, B-cell data from 23 subjects have been analyzed up to week 4 of the 52-week study, encompassing 2 infusions of UTX. Further, no SAEs have been reported, including subjects receiving rapid UTX infusions. Only patients whose B cells were within a normal range ($\geq 5\%$ of total lymphocytes) at screening were included in the study. At week 4 (1 week post second infusion), median B-cell depletion was 99% from baseline in UTX treated subjects, while placebo subjects maintained similar B-cell levels as compared to baseline.

Conclusion: Ublituximab, a novel glycoengineered anti-CD20 antibody, is well tolerated and demonstrates rapid and robust B-cell depletion. Unlike other anti-CD20s, ublituximab can be delivered in shorter infusions, providing a convenience benefit for patients.

Disclosure: This research is funded TG Therapeutics, Inc.

PR1117

Activation of peripheral immunity in Parkinson's disease favors a pro-inflammatory phenotype

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Background and aims: Parkinson's disease (PD) is characterized by both motor and non-motor features. Neuronal loss strikes not only the substantia nigra but also other widespread neuronal populations, from the bowel to the cerebral cortex. Surviving neurons show intraneuronal inclusions, whose main component is α-synuclein (α-syn) which exerts several functions, like the possible cross-talk with the immune system mightly relevant for therapeutic purposes.Characterize the role of peripheral adaptive immunity in an Italian cohort of PD patients

Methods: We enrolled 82 PD patients (49 men; mean age at onset 69.2 ± 8.7) and 47 healthy controls (HC, 25 men, mean age 66.9 ± 10). We obtained complete clinical-demographic data and samples of peripheral blood with WBC subtypes. We analysed T-cell surface antigens with flow-cytometric analysis (particularly Treg and Teff) and their cytokines production with ELISA. Moreover dopamine receptor (DR) expression was assessed with real-time PCR.

Results: PD patients showed a higher proportion of pro-inflammatory with lower proportion of anti-inflammatory lymphocyte subpopulations and (Th1: $100x106$ in patients vs $80x106$ in HC; Th2: $80x106$ in patients vs $40x106$ in HC $p=0,007$) higher pro-inflammatory cytokines production than in HC ($IFN\gamma$: 230 vs 50 pg/mL; $TNF\alpha$ 230 vs 100 pg/mL; $p<0,05$). DR expression on Treg was lower in PD patients (especially for DR2-like).

Conclusion: PD patients have a peripheral pro-inflammatory phenotype. Activation of adaptive immune response in periphery may prime the central effect of microglia, contributing to neurodegeneration in PD. The possibility that such cascade is triggered by α-syn acting as a peripheral antigen, is worth further investigation.

Disclosure: Nothing to disclose

PR1118

How green fluorescent neuritogenic T-cells enter the peripheral nerve in experimental autoimmune neuritis

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Background and aims: Autoimmune polyneuropathies are acquired inflammatory disorder of the peripheral nervous system (PNS) characterized by demyelination, inflammation and axonal degeneration. Although the precise pathogenesis remains uncertain T-cells recognizing self-antigens are believed to trigger the inflammatory reaction in the peripheral nerves. However, the route and time of entry into the PNS as well as autoimmune targets are still not described in detail.

Methods: Kinetics and localisation of neuritogenic cells we anaysed using T-cells from P255-78-peptide immunized rats to induce adoptive transfer experimental autoimmune neuritis (EAN). P2-reactive T-cells were retrovirally engineered to express GFP. This allowed antigen-specific T-cell tracking and localization by flow cytometry and immunohistology during disease course.

Results: We were able to induce autoimmune neuritis by transfer of P2-reactive T-cells expressing GFP. After transfer, these cell were detectable in liver, spleen, lymph nodes, lung, peripheral blood and the sciatic nerves with distinct kinetics. Endoneurial localisation of T-cells was detectable at day 5 after transfer, while T-cells were found in whole nerve homogenates at earlier time points. T-cell localisation in the PNS was not restricted to proximal roots but distributed homogenously within the peripheral nerve.

Conclusion: Our findings suggest that neuritogenic T-cells accumulate in the PNS early after disease induction. However, the massive infiltration into the endoneurium where T-cells cross the blood nerve barrier is rather late in the disease induction phase with no preferences to dorsal roots. Understanding the pathophysiological role of autoagressive T-cells in the PNS may help to improve therapeutic strategies.

Disclosure: Nothing to disclose

Neurorehabilitation

PR1119

Optogenetic modulation of sleep slow wave after focal ischemic stroke

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Background and aims: Disturbances of sleep are frequent after stroke and negatively affect outcome. Conversely, clinical and experimental studies suggest a favourable effect of sleep improvement/promotion post-stroke neuroplasticity and functional recovery.

Methods: AAV2DIO-EF1-ChR2-EYFP (VGAT-ChR2), AAV2DIO-EF1-ArchT-EYFP (VGAT-ArchT), AAV2DIO-EF1-EYFP (YFP, control), CamkII-ChR2-EYFP(CamKII-ChR2), CamkII-ArchT-EYFP (CamkII-ArchT) and CamkII-mCherry (mCherry, control) adeno-associated viruses (AAV) were injected into the layer V of the forelimb somatosensory cortex of Tg(VGAT)-IRES::Cre and wild type mice, respectively. Animals were chronically implanted with optical fibers and multiple tetrodes in ipsi-and contra-lateral cortical layer V. Stroke was induced by Middle Cerebral Artery Occlusion (MCAO). Tetrodes recording of brain cortical activity and optical stimulation were conducted 24h before and after the stroke.

Results: Immunohistochemistry analysis confirmed the presence of transfected cells within the layer V, forelimb somatosensory cortex, where stroke was induced. Amongst all stimulation protocols tested, we found that optical silencing of pyramidal cells in layer V of the cortex induced both LFP and single unit spike activity similar to a down-state of the neuronal network that correlates with a quiescent period of the recorded unit activity.

Conclusion: We show for the first time that optogenetical induction of down-states is possible in both transgenic and wild type mice. This modulation of sleep-like oscillation will now be used to test if and when in the post-stroke phase an enhancement of cortical down-states may positively affect neuroplasticity and functional recovery.

Disclosure: Nothing to disclose

PR1120

Motor recovery after stroke: The role of overground exoskeletons in shaping brain plasticity

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Background and aims: The use of neurorobotic devices in neurorehabilitation is reported to increase functional recovery and shape the sensory-motor plasticity (SMP) between the primary motor areas (M1) and the fronto-parietal network (FPN) connectivity. Aim of our study was to assess whether the overground exoskeleton Ekso would foster the recovery of FPN connectivity and SMP involved in deambulation, besides motor function.

Methods: We enrolled 10 patients affected by left hemiparesis due to ischemic stroke, randomly divided into two groups: the experimental group underwent Ekso whereas the control group (CG) performed conventional overground gait training (24 training sessions, 3 times a week for 8 weeks). All the patients were evaluated at the beginning and at the end of the treatment by using clinical (Tinetti-scale, 10MWT, 6MinWT) and neurophysiological (transcranial magnetic stimulation, EEG, and surface EMG) tools.

Results: As compared to CG, patients performing Esko showed a significant improvement in gait performance indices as revealed by surface EMG (p=0.01) and clinical scales (p=0.01), a recovery of the deterioration in prefrontal-SMA and SMA-centroparietal connectivity (both p=0.02), and a restoration of the equilibrium between the SMP patterns of the M1-leg areas (p=0.03). Noteworthy, the baseline plasticity and FPN connectivity were the most important factors in using Ekso fruitfully (r=0.9, p=0.03). Additionally, the clinical improvement significantly correlated with both the Ekso electrophysiological aftereffects (r=0.8, p=0.04).

Conclusion: Our pilot study provides new cues supporting the role of overground exoskeletons in improving gait performance and shaping brain plasticity, as demonstrated by the recovery of the prefrontal-SMA and SMA-centroparietal connectivity.

Disclosure: Nothing to disclose

PR1121

Evaluation of gait cortical motor control changes induced by the use of the regent multi-modal complex exoskeleton in neurorehabilitation of post-stroke patients

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Background and aims: In this work, we proposed a combination of fMRI in the sensorimotor passive paradigm imitating the support loading during walking with a functional connectivity analysis as a basically new approach to studying the mechanisms involved in the cortical control of locomotion.

Methods: In our study discusses the impact of a course of multimodal complex exoskeleton (MCE) in the reorganization of brain areas responsible for cortical control of locomotion, in 14 patients with post-stroke hemiparesis, mainly in the chronic stage of the disease. An original passive sensorimotor paradigm wherein a mechanical stimulator of plantar support zones is used to identify the brain regions that are activated during walking.

Results: In our study a processing of group data identified the primary sensorimotor area and supplementary motor areas (SM1+SMA), and inferior parietal lobules (IPL) on the right and left as sensorimotor cortical activation zones by fMRI before a course of MCE training. After a course of MCE training, we observed a decrease in activation zone of the IPL, especially in the healthy hemisphere, and an excessive increase in activation zone in the SM1+SMA areas. Changes in functional connectivity were revealed in special analyses performed before and after a rehabilitation course. Namely, activating interhemispheric connections between the secondary associative areas grew weaker, and a positive connection arose between the SM1+SMA areas and the IPL (an associative somatosensory area) in the affected hemisphere.

Conclusion: The findings can be interpreted as a decrease in inhibitory influences from the associative somatosensory area on the motor areas in the affected hemisphere.

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PR1122

Efficacy of the post-stroke arm function rehabilitation using Kinect-based virtual biofeedback system

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Background and aims: Successful recovery of upper limb motor function in post-stroke adult patients occurs only in 20% of cases. Motor training in virtual environment allows to create the necessary training space for motor skills relearning, as well as provide interactive biofeedback and intensify rehabilitation process.

Methods: 17 patients met the inclusion criteria (10 males; 7 females) at the age of 30 to 60 years and 3 to 12 months after stroke were included. Main group (n=10), received two weeks (30min, 6 days/week) of virtual biofeedback training on Kinect based system «Habilect». Control group (n=7) received equal time conventional therapy. Evaluation methods: Fugl-Meyer Assessment scale (FM), Action Research Arm Test (ARAT), 3D motion capture system.

Results: Main group patients showed improvements ($p<0.05$) in FM: arm and hand movements, and total score; ARAT: significant ($p<0.05$) improvement of pinch grip, gross movements and total score. Motion analysis showed significant increase in reaching movement speed and changes in the reaching synergy. The shoulder flexion torque decreased by 23% ($p<0.05$) with correlated elbow extension torque decreasing by 11% ($p<0.05$). Shoulder abduction torque decreased by 31% ($p<0.05$) and was correlated with shoulder flexion. In control group were found improvements ($p<0.05$) only in range of passive movements (FM).

Conclusion: Virtual biofeedback training is effective method for stroke rehabilitation that promotes arm function increasing, improves movement coordination and proved to be useful addition to the traditional methods of rehabilitation.

Disclosure: Nothing to disclose

PR1123

The role of stroke volume as a prognostic factor in early rehabilitation

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Background and aims: The objective of the study was to evaluate if the stroke volume measured in the first 24-48 hours after onset can represent an independent prognostic factor in early rehabilitation.

Methods: Fifty-nine patients with acute supratentorial ischemic stroke were included in a randomized, double-blind, placebo-controlled clinical study. The first group received Cerebrolysin 30 ml/day for 10 consecutive days, and the second group received placebo. All the patients performed early physical rehabilitation, two hours/day, for 10 consecutive days. The brain magnetic resonance imaging (MRI) was done in the first 24-48 hours after stroke, and at 30 days. Study medication and rehabilitation were initiated immediately after first MRI, no later than 48 hours after stroke onset.

Results: A significant statistical positive correlation was found between initial stroke volume, initial National Institutes of Health Stroke Scale (NIHSS) score and clinical scores at 30 days (NIHSS, modified Rankin Scale and Barthel Index), especially in the Cerebrolysin group (for NIHSS, Spearman correlation=0.81, P=<0.0001; for modified Rankin Scale, Spearman correlation=0.69, P=0.0002; for Barthel Index, Spearman correlation= -0.6, P=0.0003)

Conclusion: Initial stroke volume can represent a prognostic factor in early rehabilitation.

Disclosure: Nothing to disclose

PR1124

Serum microRNAs as biomarkers in myotonic dystrophy type 1 rehabilitation

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Background and aims: Myotonic dystrophy type 1 is one of the most common inherited muscular dystrophy in adulthood. Non invasive and reliable biomarkers are still needed in DM1. Indeed muscle biopsies although informative are of limited application because of their invasive nature and CK levels appear unreliable. In a preliminary study we identified a group of microRNAs that are deregulated in DM1 muscle. We investigated the use of microRNAs as circulating biomarkers for DM1 in a clinical setting and exploited sera collected during a rehabilitative protocol.

Methods: We analysed serum miR-1, miR-206, miR-133a and miR-133b by Real Time PCR in 10 DM1 patients (9male, 1 female).We used sera obtained before (T0) and after (T1) rehabilitation. The rehabilitation protocol has been recently published and consists in Functional Electrical Stimulation/lower extremity training or aerobic excercise for a period of 6-8 weeks.

Results: The overall tendency of miR-206, miR-1, miR-133a and miR-133b was to decrease.The decrease was variable in single patients and changed according to the single microRNA studied. Since most patients improved in functional parameters: 6MWT, muscle strength measured by MRC scale during rehabilitation this implies that there was an increase in functional muscle mass, that was also found in MRI imaging.

Conclusion: We hypothesise that microRNAs are valid tools to monitor the rehabilitation in DM1. MyomiRNA levels are modulated in DM1 skeletal muscles biopsies and that their extracellular presence might be due to a passive or active release. In alternative, microRNAs decrease might be directed to hypertrophyng or regenerating muscle, since they are negative regulators.

Disclosure: Nothing to disclose

PR1125
Cancelled

PR1126
Action observation training modifies the function and structure of the mirror neuron system in multiple sclerosis patients with right upper limb motor deficits

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Background and aims: We assessed the modifications of brain gray matter (GM) volumes, white matter (WM) architecture and mirror neuron system (MNS) activations following action observation training (AOT) in healthy controls (HC) and multiple sclerosis (MS) patients.
Methods: Forty-six right-handed HC and 41 right-handed MS patients with right-hand motor impairment were randomized into: 2 experimental groups (AOT-HC n=23; AOT-MS n=20) and 2 control groups (C-HC n=23; C-MS n=21). Training consisted of 10 sessions of 45 minutes in 2 weeks. AOT-groups watched 3 videos of daily-life actions alternated by their execution with the right-hand; C-groups performed the same tasks, but watched landscapes videos. At baseline and after 2 weeks (w2), functional scales, brain structural and fMRI scans during object manipulation with the right hand were obtained.
Results: At w2, all groups improved at functional scales. Compared with C-groups, AOT-groups had more improvements at right-hand strength measures. At w2: 1) no WM modifications occurred; 2) AOT-HC vs C-HC experienced increased volume of the superior frontal gyrus (SFG) and decreased volume of fronto-temporal areas; 3) AOT-MS vs C-MS had increased volumes of SFG, temporo-occipital areas and decreased volume of the supplementary motor area; 4) AOT-HC vs C-HC had higher activation of the pre-central gyrus and lower activation of the middle temporal gyrus, while AOT-MS vs C-MS had higher activation of the inferior frontal gyrus. Measures of functional improvement correlated with MRI modifications.
Conclusion: A 10-day AOT modifies GM structure and activations of motor network and MNS, promoting functional competence in HC and MS patients.

Neurotoxicology & Neurotraumatology & Spinal cord and root disorders 1

PR1127

Effect of second-tier therapies barbiturates and decompressive craniectomy in patients with severe traumatic brain injury and refractory intracranial hypertension on outcome

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Background and aims: There is still much debate on the treatment of patients with severe traumatic brain injury (TBI), in particular for refractory intracranial hypertension with often fatal outcome. Since second-tier therapies (barbiturate-coma and decompressive craniectomy) are not commonly applied, the effectiveness and disadvantages will be explored in this study.

Methods: Data analysis of an observational follow-up study of patients with severe TBI admitted to a level-one trauma centre. Only patients who fulfilled criteria for monitoring of intracranial pressure (ICP) defined by international guidelines with severe TBI admitted from 1996-2016 are included. Primary outcome was determined by Glasgow Outcome Scale Extended (GOSE-E) 12 months post-injury. Favorable outcome is defined by GOSE>4.

Results: Preliminary results: This study comprised 74 patients, with 34 patients in the barbiturate group and 40 patients in the surgical group. Outcome scores 12 months post-injury differ significantly between groups (p=0.020). Mortality was 82% in the barbiturate group versus 41% in the surgical group. Survivors of the barbiturate group all had favorable outcome. Favorable outcome in the surgical group was 32%. Age and gender distribution were not different between groups. Frequency of decreased Cerebral Perfusion Pressure was not different. Further evaluation of CT characteristics, ICP and admission variables will be presented to clarify their relation with outcome.

Figure 1: Outcome of last-tier therapies decompressive craniectomy and barbiturates depicted by GOS-E 12 months post-injury

Patient characteristics	Barbiturates	Decompressive craniectomy	p-value
Age – yr (SD)	29.9 (14.9)	35.1 (18.9)	0.445
Male no.	25 (74%)	28 (70%)	0.737
CT admission			0.001
Diffuse injury I	0%	0%	
Diffuse injury II	7%	14%	
Diffuse injury III (swelling)	75%	21%	
Diffuse injury IV (shift)	7%	11%	
Evacuated mass lesion V	7%	50%	
Non-evacuated mass lesion VI	4%	4%	
Focal/local edema	12%	16%	
Diffuse edema	88%	52%	
Both	0%	13%	
ICP			
Day max. ICP (SD)	5.6 days (2.8)	4.9 days (3.2)	0.393
Mean ICP (SD)	25.2 mmHg (6.5)	17.2 mmHg (5.0)	0.436
Mean CPP (SD)	65.7 mmHg (7.5)	71.5 mmHg (5.9)	0.437
ICP >20 mmHg * mean number / day	13.4 (5.5)	6.5 (5.8)	0.326
ICP <60 mmHg * mean number / day	6.7 (5.6)	2.4 (2.9)	0.326
Category opening pressure			0.721
<20 mmHg	40%	56%	
20-40 mmHg	40%	36%	
>40 mmHg	20%	8%	
ICP profile			0.811
Early (0-2 days)	17%	28%	
Intermediate (2-5 days)	27%	28%	
Late (>5 days)	56%	44%	

* frequency of event with duration of >5 minutes

Table 1: Patient and treatment characteristics of patients treated with second-tier therapies barbiturates or decompressive craniectomy

Conclusion: Treatment of patients with severe TBI and refractory intracranial hypertension showed that, treatment with barbiturates was associated with higher mortality, but with favorable outcome in survivors in comparison with decompressive craniectomy. This suggests that second-tier therapies can be applied under certain indications.

Disclosure: Nothing to disclose

PR1128

Acute methanol poisoning: A typical radiologic finding for an uncommon condition

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Background and aims: Although relatively uncommon nowadays, acute methanol poisoning is a serious intoxication generally occurring after accidental ingestion of homemade, methanol-contaminated beverages. Radiological findings are typical – bilateral basal ganglia haemorrhagic lesions and optic nerve oedema – and explained by the high susceptibility of these structures to methanol. With this case report the authors intent to highlight the importance of early radiologic findings for timely diagnosis and management.

Methods: Case Report

Results: A 28-year-old male, with a known history of regular ethanol consumption, was admitted to the ICU in coma. On examination, patient was unresponsive with fixed pupils, bilateral papilledema and generalized hypotonia with areflexia. Immediate arterial blood gases indicated a severe metabolic acidosis(pH6.9) with a high anion gap(28.4). During the first 24h, several seizures were reported. CT scan and MRI showed bilateral haemorrhagic lesions of the lenticular nuclei, with extensive areas of oedema extending to the white matter and compressing the brain stem. Supportive measures and renal replacement therapy were started, with clinical stabilization and acid-base correction over the next days. At discharge, patient was stable and neurological observation showed generalized hypertonicity with akinetic mutism and bilateral amaurosis. Later, we were able to identify a pattern of binge drinking of homemade alcoholic beverages during the three days preceding hospital admission.

Bilateral haemorrhagic lesions of basal ganglia with oedema

Bilateral haemorrhagic lesions of basal ganglia with oedema

Conclusion: In the emergency setting, clinical history and epidemiological context is not always available and the integration of laboratory and radiologic findings can be crucial for correct and early diagnosis, as in the case of acute methanol intoxication.

Disclosure: Nothing to disclose

Oedema of the optic chiasma

PR1129

Cranial nerve palsies and unilateral foot drop: Portugal's first confirmed case of type F botulism.

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Background and aims: Botulinum neurotoxin (BoNT) poisoning impairs synaptic transmission in the neuromuscular joint, usually presenting as an acute symmetrical descending flaccid paralysis, associated with autonomic dysfunction. Human cases have been caused by BoNT type A, B, E and rarely F.

Methods: Case Report

Results: A 53-year-old man reported vomiting a few hours after eating canned tuna. The next day he was admitted to the emergency department with diplopia, fixed dilated pupils, bilateral peripheral facial palsy, dysphagia, dysarthria, dry mouth and right foot dorsiflexion weakness. The patient quickly developed dyspnea and urinary retention and was transferred to the intensive care unit with suspected botulism food poisoning. Public health authorities were notified, serum and stool samples were sent to the National Health Institute Doutor Ricardo Jorge and trivalent antitoxin to BoNT (type A, B, and E) was administered. The patient continued worsening, requiring invasive mechanical ventilation for 8 days. BoNT type F and BoNT-producing Clostridium botulinum were detected in the stool samples. No exposure source was confirmed. The patient was discharged after 30 days, maintaining right foot dorsiflexion weakness and orthostatic hypotension. Three months later, he was asymptomatic with a normal neurological examination, however the EMG still showed decrement on repetitive nerve stimulation.

Conclusion: This was the first confirmed case of type F botulism in Portugal. Despite a good outcome, it raises concern over the unavailability of heptavalent BoNT (type A-F) antitoxin in European countries since the trivalent antitoxin appears to lack effectiveness in type F botulism.

Disclosure: All authors of this submission are co-authors of a poster, based on the same clinical case, titled "The first case of botulism type F in Portugal" (focusing on the microbiological and toxicological aspects of the case) to be presented at the conference "TOXINS 2017: Basic Science and Clinical Aspects of Botulinum and Other Neurotoxins", in Madrid, January 2017.

PR1130

Hexacarbon neuropathy

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Background and aims: Hexacarbon neuropathy occurs through industrial exposure or is caused by addictive inhalation. It's uncommon in developed countries but still exists, especially in industries with unventilated spaces.

Methods: Case report

Results: A 29-year-old female presented with progressive distal weakness which developed over a year. She had been working in a shoe factory for 11 years. Her first complains were numbness in hands and feet, with progression to moderate loss of all sensory modalities. A few months later she had difficulty in walking and then she developed hand weakness. She had lost 10Kg. Examination revealed mild muscle atrophy of hands and feet, grade 3/5 distal tetraparesis, generalized hyporeflexia with absent ankle jerks, hypoesthesia in a stocking-glove distribution, loss of vibratory sense and proprioceptive errors in the lower limbs. Electromyography demonstrated a severe axonal and demyelinating sensorimotor polyneuropathy. Nerve biopsy revealed a neuropathy with axonal swelling, in this context suggestive of a neuropathy due to hexacarbons. A rehabilitation program was initiated with almost complete recovery in 1 year. She changed work assignments and one year later the clinical picture developed again. This time, the electromyography revealed features of active denervation and partial conduction blocks. The patient recognized that she had been somehow exposed to glues once more, and after removal from exposure she improved again, maintaining a bilateral foot drop.
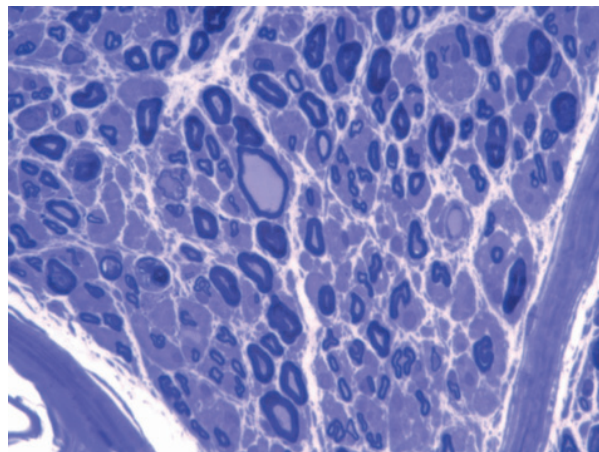
Optical microscopy of sural nerve biopsy showing axonal swelling (transverse section, toluidine blue stain)
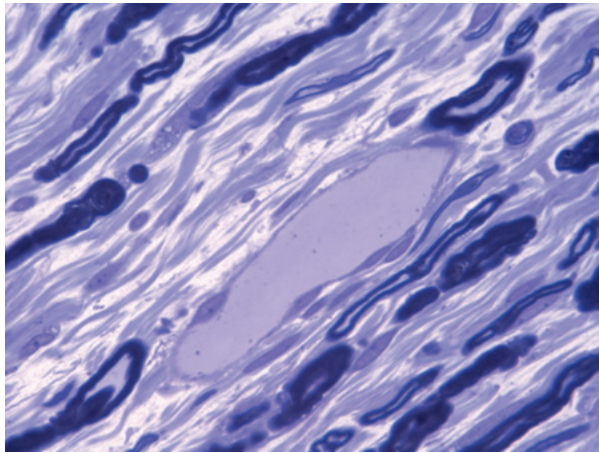
Optical microscopy of sural nerve biopsy showing axonal swelling (longitudinal section, toluidine blue stain)
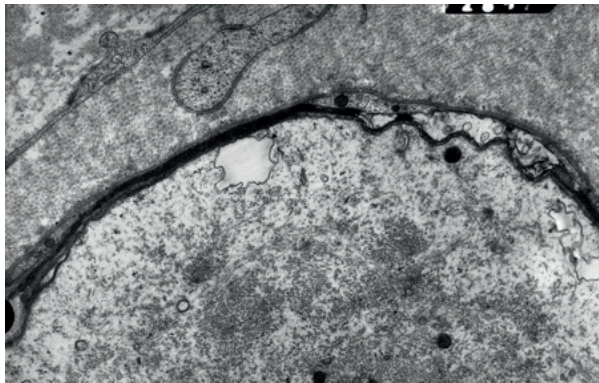
Electron microscopy of sural nerve biopsy showing axonal swelling filled with neurofilament accumulation

Conclusion: The improvement after cessation of exposure as well as the electrophysiological and pathological data are consistent with this etiology. The diagnosis implies a high index suspicion and a nerve biopsy since the findings are distinctive.

Disclosure: Nothing to disclose

PR1131

Spectrum of behavioural disturbances and after care in traumatic brain injury

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Background and aims: Behavioural disturbances are found in 40-60% of traumatic brain injury (TBI) patients and have considerable impact on daily life and level of recovery. The characteristics of behavioural disturbances in patients with various severity of injury are unclear. The purpose of this study is to specify characteristics of behavioural disturbances and pathways of care after discharge from the hospital.

Methods: This retrospective cohort study consisted of 226 patients, with mild TBI (mTBI; n=107) and moderate-to-severe TBI (mod/sevTBI; n=119). Inclusion criteria were: behavioural disturbances, age>16, treated at the UMCG outpatient department or rehabilitation centre between 2010-2015 and time of injury ≥2005. Data were collected from patient files. Functional outcome was determined with Differential Outcome Scale, Glasgow Outcome Scale Extended (GOSE) and Return to Work (RTW).

Results: mTBI patients mostly showed irritation (82%) and anger (49%), while mod/sevTBI patients mostly showed irritation (65%) and disinhibition (55%). Most (92%) patients returned home despite unfavourable GOSE outcome scores in 50% of patients. One in ten patients were (temporarily) admitted to nursing home or psychiatric institution due to behavioural disturbances. Half of the patients could not RTW. General practitioners (46%) and psychologists (22%) were the most common final care providers. Caregivers received help for dealing with limitations of the patient in 20%.

Conclusion: The spectrum of behavioural disturbances differs between mTBI and mod/sevTBI. Most patients eventually returned home, half of the patients have unfavourable outcome and could not RTW. Long-term care is also necessary for caregivers underlining the long-term impact of behavioural disturbances after TBI.

Disclosure: Nothing to disclose

Peripheral nerve disorders 1

PR1132

Revisiting the spectrum of Anti-MAG neuropathies in a large cohort of IgM-monoclonal gammopathy

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Background and aims: A sizeable number of patients with IgM monoclonal gammopathy (IgM-MG) also have anti-myelin associated glycoprotein (MAG) antibodies (anti-MAG-ab) associated with peripheral demyelinating neuropathies. The goal of this retrospective study was to unravel the spectrum and the prognosis of anti-MAG neuropathies in a large monocentric cohort of patients with IgM-MG.

Methods: We reviewed the neurological, neurophysiological and biological data from patients with IgM-MG identified by immunofixation between 2010 and 2015, for whom anti-MAG-ab were quantified by ELISA.

Results: Among 596 patients with IgM-MG (median IgM level of 4 g/L), 34 patients (22 males, mean age 69 years old [50-84]) had anti-MAG-ab, with levels over 10,000 BTU for 24 of them. Thirty-two patients suffered from pure distal sensory (62%) or sensory-motor (38%) neuropathy, often symmetric (72%) and sometimes painful (31%). Thirteen patients presented a typical clinical anti-MAG pattern, including ataxia and/or tremor. Nerve conduction studies at diagnosis showed a clear demyelinating profile for 25 patients, with a distal acquired demyelinating symmetric neuropathy (DADS) pattern for 16. Conversely, 7 patients were diagnosed with mild length-dependent axonal polyneuropathy, without features suggesting demyelination. None of them had other explanatory cause for their neuropathy. Initially, 27 patients had preserved walking capacity (3 needed help to walk). After a mean follow-up period of 68 months [3-243], the ambulatory score declined for 12 patients while it improved for 3.

Conclusion: Our study shows the wide spectrum of neuropathies with anti-MAG antibodies, from typical DADS pattern to moderate predominantly axonal sensory polyneuropathy. In the long term, prognosis remains variable despite therapeutic attempts.

Disclosure: Nothing to disclose

PR1133

One-year follow-up study in patients with Guillain-Barré syndrome

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Background and aims: Majority of patients with Guillain-Barré syndrome have a successful recovery, but in a number of them significant long-term consequences may negatively affect quality of life. We sought to analyze the outcome of the disease one year after the acute episode of GBS.

Methods: Among 82 patients diagnosed with GBS in seven tertiary centres in Serbia, Montenegro and Republic of Srpska during 2014, 57 subjects were retested after one year (62% males, mean age 57.3±16.0 years). Functional disability of patients was estimated based on the GBS Disability Scale (GDS) (score of 0 to 3 represented mild form of the disease, and score of 4 to 6 represented a severe form).

Results: Severe form of the disease was registered in 50% of patients at admission, 73% of patients at nadir, and 24% on discharge. After one-year follow-up period, 14% of patients had score 0 (no symptoms), 42% score 1 (minor symptoms), 24% score 2 (not able to run), 8% score 3 (walk with support), 3% score 4 (bedridden), and 8% score 6 (death). Paresthesias were present in 60% of patients, musculoskeletal pain in 40%, and fatigue in 21%. Factors associated with the worse functional outcome (GDS grade above 1) after one year were: age (p=0.05), preceding respiratory infection (p<0.05), and worse GDS on discharge (p<0.01).

Conclusion: One year after the onset of disease, significant number of GBS patients have neurological impairments including sensory symptoms, pain, fatigue and muscle weakness. These may significantly affect patients' everyday functioning and their quality of life.

Disclosure: Nothing to disclose

PR1134

Transthyretin familial amyloid polyneuropathy: A new clinical score for monitoring disease progression

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Background and aims: The Neuropathy Impairment Score (NIS – maximum: 244), a clinical score validated for the evaluation of diabetic polyneuropathy, has been widely used in monitoring neuropathy progression in patients with Transthyretin Familial Amyloid Polyneuropathy (TTR-FAP). Although NIS objectively assesses sensorial-motor neuropathy progression, it does not take into account autonomic dysfunction and organ involvement that occur in this disease. We propose a new clinical score for monitoring the multisystemic progression of TTR-FAP.

Methods: The Familial Amyloidotic Polyneuropathy Clinical Scale (FAPCS) evaluates: nutritional status, sensorial-motor and autonomic polyneuropathy, cardiac, renal and ocular involvement (maximum: 50). FAPCS and NIS were assessed in patients with TTR-FAP treated with Tafamidis, at baseline, 6, 12 and 24 months of treatment. The clinical data were obtained from the Transthyretin Amyloidosis Outcomes Survey (THAOS).

Results: Twenty-eight patients were longitudinally assessed, mean age of 43.4 (± 14) years, 14 male, and mean duration of disease of 2.5 (± 1.4) years. The mean baseline NIS was 12.6 (± 15.6) and baseline FAPCS was 9.1 (± 5.5). An increase of 1.8 (0.35% per year) in NIS scoring and of 2.5 (2.5% per year) in FAPCS was observed in two years of follow-up, suggesting no significant progression of disease.

Conclusion: The progression rate estimated with FAPCS was superior when compared with NIS in the same group of patients. We consider that application of the FAPCS in association with a validated scoring (NIS) can increase the sensitivity of these instruments in monitoring therapeutic efficacy.

Disclosure: Nothing to disclose

PR1135

Hyperacute Guillain-Barré syndrome

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Background and aims: Guillain-Barré syndrome (GBS) is characterized by development of maximal motor disability within four weeks. In the most surveys, 75% of GBS patients achieved their nadir within 2 weeks. If maximal incapacity is reached within a day or two, then it is marked as hyperacute GBS.

Methods: We retrospectively analyzed clinical and neurophysiological data from all GBS patients hospitalized in two neuromuscular centers during the last 5 years (2012-2016). There were more than 1 million inhabitants of our catchment area with 96 patients with GBS. Among these patients we have identified 7 patients (7, 3%) with hyperacute GBS (4 men, age 19-78 years).

Results: An antecedent infection was found in 5 of them (gastrointestinal symptoms in 2, acute respiratory signs in 3). A 19-year-old man has described physical overactivity. Time since the beginning to the nadir was 16-48 hours. All patients had severe qaudruparesis except one with disturbed consciousness. Four patients underwent mechanical ventilation. Plasma exchange was used in 6 and intravenous application of immunoglobulins in one case. Electro-physiological evaluation determined four acute demyelinizing lesions and three severe axonal loss (twice AMAN, once AMSAN). One patient died. In 2-9 years after acute stage two patients were wheelchair bounded, one was walking with cane and two have fatigue after longer walk.

Conclusion: Hyperacute GBS is an unusual and rare event with a variable prognosis. In our study, both demyelinating and axonal forms were found. Worse prognosis was observed in severe axonal damage. However, overall prognosis was favorable in most of cases.

Disclosure: Nothing to disclose

PR1136

Description of a series of Spanish patients carrying the HSPB1 p.r140g mutation

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Background and aims: Mutations in small heat-shock protein B1 (HSPB1) are a cause of distal hereditary motor neuropathy (dHMN) and Charcot-Marie-Tooth type 2 (CMT2). A family with a mixed phenotype that combines distal myopathy and neuropathy has been recently described in relation to the p.Asp129Glu HSPB1 mutation. We describe the clinical features of 17 patients belonging to five Spanish families diagnosed with an autosomal dominant (AD) CMT/dHMN who carry the HSPB1 p.R140G pathogenic sequence variation.

Methods: All patients carried the HSPB1 p.R140G change. They underwent neurological examination and electrophysiological studies with standard techniques. Muscle MRI was performed in eight patients and muscle biopsy in four patients.

Results: All families came from the same region of Spain. Age of clinical onset ranged between 5 and 72 years. Most patients had a typical dHMN or CMT2 phenotype. In one patient electromyography (EMG) showed features that were consistent with mixed myopathic and neurogenic pathology and in three patients there was motor unit hyperactivity. There was hyperCPkemia in six patients. Muscular biopsy showed myofibrillar aggregates and rimmed vacuoles in two patients. Muscular MRI showed fatty infiltration in lower limbs that followed a length-dependent pattern, being the soleus the most affected muscle in lower limbs.

Muscle biospies

Muscle MRI
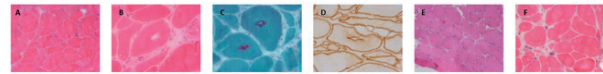
Conclusion: Our series of patients with HSPB1 mutations is one of the largest reported since now and includes the study of muscle samples of patients. Our results support that the HSPB1 p.R140G mutation can cause a mixed neuropathic and myopathic phenotype with typical features of a myofibrillar myopathy in muscle pathology.

Disclosure: Study funding: grants IIS La Fe 2015/0085, ISCIII (PI12/0946) and IRDiRC (IR11/TREAT-CMT).
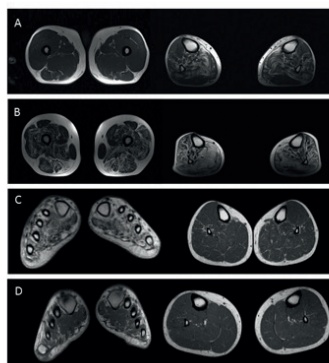
PR1137

Demyelinating polyradiculoneuropathy during bretuximab-based treatment

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Background and aims: Brentuximab vedotin (BV) is an anti-CD30 monoclonal antibody-drug conjugate approved for treating relapsed or refractory Hodgkin lymphoma and systemic anaplastic large cell lymphoma. Peripheral neuropathy is the most commonly reported adverse event with BV, reported in 56% of patients with no evidence of demyelinating polyradiculoneuropathy

Methods: Patients treated for hemopathy and diagnosed with peripheral neuropathy during BV treatment were retrospectively identified between January 2013 and January 2017 using the database of OncoNeuroTox (center for patients with neurological complications of oncologic treatments)

Results: Among 135 patients registered in OncoNeuroTox database with hemopathy and peripheral neuropathy, two patients presenting polyradiculoneuropathy while undergoing BV treatment for large B-cell lymphoma and Hodgkin disease. All patients had a sub acute clinical presentation with motor impairment, hypoesthesia and areflexia suitable with polyradiculoneuritis, within 6 months of BV. All patients had demyelinating signs on nerve conduction study with sensory and motor abnormalitis. All patients had albuminocytologic dissociation in CSF (0.8 and 0.5 of proteinorachia respectively with no cells). Both patients improved after BV discontinuation and immunomodulatort treatment (intraveinous immunoglobulin treatment for patient 1 and plasma exchange for patient 2)

Conclusion: Theses cases highlight that patients taking BV are at risk of developing subacute demyelinating polyradiculoneuropathy; a severe but treatable complication. Prompt recognition may improve the clinical and functional outcome of patients

Disclosure: Nothing to disclose

PR1138

Late-onset polyneuropathy and MME variants – a Norwegian study

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Background and aims: The inherited peripheral neuropathies are a genetically and clinically heterogeneous group of disorders that severely impair quality of life. Diagnostic molecular genetic testing is often successful in young individuals ie children and younger adults. However, among the largest group of affected individuals, those with adult-onset neuropathy, diagnostic genetic testing is usually negative. Difficulties identifying late-onset neuropathy genes might be explained by reduced penetrance and the involvement of additional factors such as life style and environmental exposure. However, recently the MME gene, a zinc-dependent membrane metalloendopeptidase, was linked to late-onset axonal polyneuropathy (Auer-Grumbach et al, 2016). The aim of this study was to investigate whether variants in MME are common among individuals with late-onset polyneuropathy in Norway.

Methods: The MME gene was added to an in-house peripheral neuropathy gene panel in September 2016. All individuals presenting with peripheral neuropathy referred to our hospital after September 2016 were examined for variants in the MME gene by next-generation sequencing.

Results: 46 individuals with various subtypes of peripheral neuropathies were tested. Three individuals (6%) carried possible disease causing heterozygous variants in MME. These included two loss-of function mutations classified as likely pathogenic and one missense mutation classified as uncertain pathogenic according to the ACMG criteria. The phenotype in all three was late-onset axonal neuropathy. An update on further testing will be given at the meeting.

Conclusion: Our preliminary findings indicate that MME mutations are also relatively common among Norwegian individuals with late-onset axonal neuropathy. Genetic testing of MME should be considered in adult-onset peripheral neuropathy.

Disclosure: Nothing to disclose

Sleep disorders 1

PR1139

Treatment of sleep disordered breathing after stroke - a systematic review and meta-analysis

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Background and aims: Sleep disordered breathing (SDB) is frequently seen after stroke and has been recognized as a potentially treatable risk factor, but the impact of its treatment on neurological parameters after stroke is still under investigation. This study aimed to estimate the feasibility and effectiveness of treating SDB after stroke or transient ischemic attack (TIA).

Methods: A systematic literature search using several databases and clinical trial registries was performed. Data from eligible trials assessing treatment options of SDB in adult patients after stroke or TIA was extracted and analysed. The main outcome measures were feasibility, evolution of neurological parameters, and cerebrovascular endpoints.

Results: Of the 27 studies included in the analysis (n=1781), 21 studies compared positive airway pressure (PAP) with usual care (CPAP n=17, other PAP n= 4), 2 compared CPAP with sham-CPAP. Four studies investigated alternative treatments. Feasibility of early (<7 days after stroke) and delayed (>7 days) PAP treatment could be demonstrated in all trials with a variable adherence to treatment, depending on stroke severity. The 10 randomized controlled trials using CPAP, included in the meta-analysis, were of variable methodological quality with heterogeneous study designs and outcome parameters. There was a trend towards improved neurological short-term outcome for stroke survivors who could tolerate PAP.

Conclusion: The systematic review confirms that treatment of SDB after stroke is feasible. Adherence to treatment is variable with good adherence to treatment being positively correlated with improved neurological outcomes. Short-term effects have not yet been sufficiently studied to allow stringent conclusions.

Disclosure: Nothing to disclose

PR1140

Effect of CPAP treatment for obstructive sleep apnea on long-term functional outcome in patients with ischemic stroke/TIA – a randomized controlled interventional trial (SAS-Care-2 Study)

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Background and aims: Obstructive sleep apnea (OSA) is frequent in ischemic stroke/TIA patients and may negatively affect functional outcome. Little is known about the effect of OSA treatment on the long-term outcome following ischemic stroke/TIA. We aimed to assess prospectively the effect of CPAP treatment for moderate to severe OSA on long-term stroke outcome.

Methods: Patients with ischemic stroke/TIA and OSA (AHI ≥20/h) 3 months after the acute event were included in an international multicenter trial (SAS-CARE-2). Sleepy patients (ESS ≥10) were directly assigned to CPAP treatment and non-sleepy patients (ESS <10) were randomized to either CPAP or no OSA treatment (CPAP-). Patients with AHI <20/h were followed observationally. Stroke outcome was determined by the modified Rankin Scale (mRS) at CPAP-initiation and after 6, 12, and 24 months.

Results: A total of 240 patients were included (61±9 years; 73% males; 82% stroke; BMI 27±5 kg/m2; baseline NIHSS 0.84±1.5; baseline mRS 0.8±0.8). Thereof 51 patients (21.3%) had OSA with AHI ≥20/h; 12 patients were sleepy (mean ESS 11.6±4.5) and 39 non-sleepy (mean ESS 5±2.6). 22 non-sleepy patients randomly received CPAP. At 12 months, change in mean mRS was significantly higher in randomized CPAP+ patients compared to CPAP- (-0.3±0.6 vs. 0.2±0.8; p=0.0429). There were no significant differences in mean mRS change at 6 and 24 months.

Conclusion: CPAP treatment started 3 months following acute stroke/TIA in non-sleepy OSA patients may improve stroke outcome 12 months after the event (however not at 24 months).

PR1141
Cancelled

PR1142
Coincident narcolepsy and multiple sclerosis

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Background and aims: Narcolepsy and multiple sclerosis (MS) are both suggested being immune-mediated CNS disorders including genetic and environmental factors. For narcolepsy, several observations suggest an immune-mediated process finally resulting in the loss of hypothalamic hypocretin-producing neurons. MS is a chronic inflammatory and heterogeneous disease of the CNS, which involves both innate and adaptive immune-mediated inflammatory mechanisms that ultimately contribute to demyelination and neurodegeneration. Rare cases of narcolepsy-like syndromes can be seen in the course of autoimmune disorders and symptomatic narcolepsy in MS or NMO has been described. Narcolepsy affects 0.026-0.05%, MS 0.06-0.15% of the population.

Aims: We aimed at identifying frequency and characteristics of coincident cases of narcolepsy and MS.

Methods: A pubmed literature and Bern sleep database search was performed. Articles were evaluated for completeness, content and relevance. In addition, published review articles were consulted for primary resources.

Results: In total, 23 cases (20 cases from publications and 3 from the Bern sleep database) could be identified. Three cases have been described only anecdotal. Selected 20 cases could be classified into two groups.

Group 1: Symptomatic cases (N=5) of solely excessive daytime sleepiness in MS due to a lesion in the hypothalamus.

Group 2: Narcolepsy and coincident MS (N=15). Narcolepsy presented with EDS and cataplexy. Patients were HLA-DQB1*0602 (N=9) positive and hypocretin-deficient (N=5).

Conclusion: Frequency of coincident cases in the published literature is lower than estimated. Coincident cases might occur incidentally, represent an overlapping form of MS and narcolepsy with a common pathophysiological background or might be secondary/symptomatic.

Disclosure: Nothing to disclose

PR1143
Prospective examinations in severe sleep apnea

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Background and aims: CPAP is the evidence based therapy of the obstructive sleep apnea syndrome (OSAS). Effective CPAP therapy deceases repetitive hypoxia, and progression of early atherosclerosis may decrease, consequently.

Methods: 41 patients with severe OSAS were examined (AHI: 60.5/h±16.1; DI: 45.8/h±23.4; age 53.9±10.2 years). Mean follow up time was 39.8±9.1 months. On the morning of diagnostic PSG cardiovascular questionnaire, laboratory tests and carotid ultrasound with CCA-IMT measurement were performed. These examinations were repeated during the follow up. 28 patients used CPAP regularly (CPAP users), while 13 patients could not get CPAP device (non-users). We compared parameters measured before and after CPAP therapy, and the results in CPAP users and non-users during the follow up.

Results: At the first examination mean age (p=0.125), risk factors, diagnostic PSG parameters, BMI (p=0.594), laboratory parameters, CCA-IMT (p=0.216) did not differ in CPAP users and non-users. PSG parameters were significantly better in CPAP users than non-users (AHI: 1.9±1.9 vs. 48.2±15.9/h, p<0.001; DI: 1.6±1.4/h vs 25.6±10.5/h, p<0.001) during follow up. Laboratory parameters and BMI did not differ in CPAP users and non-users during follow up, while the CCA-IMT was significantly lower in CPAP users than non-users (0.72±0.11 mm vs. 0.84±0.21 mm, p=0.027) after follow up time. CCA-IMT significantly increased in CPAP users and also in non-users during follow up time (0.64±0.1 vs 0.73±0.1; p<0.001 and 0.69±0.1 vs. 0.84±0.21 mm, p=0.004), but the progression of CCA-IMT was lower in treated group (0.1±0.12 mm vs. 0.2±0.23 mm; p=0.023)

Conclusion: CPAP therapy decreases progression of early atherosclerosis.

Disclosure: Supported by Hungarian Brain Research Program - Grant No. KTIA_13_NAP-A-II/6.

PR1144

Sleep and feeding behavior in the imprinted disorders Prader-Willi syndromes

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Background and aims: Prader-Willi syndrome (PWS) is a paternally imprinted disorder that leads to sleep and feeding alterations. It is usually characterized by hypothalamic dysfunctions. The lateral hypothalamus, and its neuronal population, melanin concentrating hormone (MCH) and orexin/hypocretin (OX) neurons are strongly implicated in the regulation of sleep-wake cycle and feeding behavior, we postulate that MCH and OX represent a key component in the pathophysiology of PWS.

Methods: To investigate whether the MCH (Precursor of MCH (Pmch) and its receptor MchR1) and OX systems (prepro-Orexin (Ppox) and its receptors OxR1 and OxR2), both involved in the regulation of sleep, are altered in PWS we perform total sleep deprivation for 6h. Gene expression analysis was performed in mice that carry a deletion of Snord116 gene (PWScrm+/p−) and wild-type (PWScrm+/p+) at three time points: in baseline (T0), after a sleep deprivation (T1) and after 2hr of sleep deprivation (T2) in different brain regions: hypothalamus (Hy); parietal cortex (PC) and frontal cortex (FC).

Results: MCH systems: At T1, an increase of Mchr1 was observed in PWScrm+/p- relative to PWScrm+/p+. At T2 the whole MCH system was found increased in PWScrm+/p- locally, in the Hy, compared to PWScrm+/p+. OX systems: At T0 Ppox and its receptors were increased in PWScrm+/p- relative to PWScrm+/p+. At T2, we found that Ppox in the hypothalamus and Ox1R and Ox2R in the FC and PC, were significantly altered in PWScrm+/p relative to PWScrm+/p+.

Conclusion: These preliminary results suggest that MCH and OX systems may be involved in the pathophysiology of PWS.

Disclosure: Nothing to disclose

PR1145

The role of histamine and melanin concentrating hormone neurons in Prader-Willi syndrome: A preclinical study

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Background and aims: Prader-Willi syndrome (PWS) is a paternally imprinted disorder that leads to sleep disturbances characterized by executive daytime sleepiness (EDS), rapid eye movement (REM) sleep alterations and cataplexy. Pitolisant, which is the first inverse agonist of histamine 3 receptor (H3R) to be introduced in the clinics for treating EDS and narcolepsy by increasing wakefulness. Here, we conducted a pre clinical study aimed at investigating the effect of pitolisant in PWS mice.

Methods: We studied the changes of sleep in mutant mice that carry a deletion of Snord116 gene (PWScrm+/p−), which is the best candidate for PWS. Specifically, we assessed EEG/EMG profiles, in PWScrm+/p− heterozygous mutants compared to wild-type littermates (PWScrm+/p+) at the baseline value (24h of recording) and 24h after either pitolisant or placebo administration. Pitolisant (20mg/Kg)/ placebo were administrated at the beginning of the light-off (active phase).

Results: By studying sleep in mice mutant PWScrm+/p−, we confirmed data already published from our group that REM sleep is significantly increased in PWScrm+/p− mice compered to PWScrm+/p+ mice. Interestingly, after pitolisant treatment REM sleep was significantly reduced in PWScrm+/p− mice during the dark phase (i.e., the 12h that immediately follow pitolisant/placebo injections) when compared with their baseline. Instead, REM sleep in PWScrm+/p+ was almost suppressed. No changes of sleep was observed in both groups during the light phase

Conclusion: Our preliminary results indicate that pitolisant by improving wakefulness may reduce EDS during the day in PWS. This suggest that pitolisant may represent, new therapeutic approach for PWS suffers that may ameliorate their quality of life

Disclosure: Nothing to disclose

Sunday, 25 June 2017

Ageing and dementia 2

PR2001

Estimates of health-care and societal costs as a function of pre-institutionalisation time in patients with Alzheimer's disease dementia

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Background and aims: To examine the costs of caring for community-dwelling patients with Alzheimer's disease (AD) dementia in relation to the time to institutionalisation.
Methods: GERAS was a prospective, non-interventional cohort study in community-dwelling patients with AD dementia and their caregivers. Using factors associated with time to institutionalisation identified from Cox proportional hazard models, parametric models were developed to estimate time to institutionalisation for all patients. Estimates of monthly total societal costs, patient health-care costs and total patient costs (health-care plus social care) before institutionalisation were developed as a function of the pre-institutionalisation time from the parametric models with a log-normal distribution.
Results: Of the 1495 patients assessed at baseline, 307 (20.5%) were institutionalised over 36 months. Patients with greater disease severity at baseline based on Mini-Mental State Examination scores had a higher risk of being institutionalised during follow-up (p<0.001). A faster time to institutionalisation was also associated with greater functional impairment in instrumental activities of daily living and worse behavioural disturbance at baseline and having a non-spousal informal caregiver. Total societal costs and total patient costs were significantly associated with pre-institutionalisation time. Total monthly societal costs increased by over 1000 pounds sterling (1166.1 euros) and total patient costs doubled during the five years before institutionalisation. Patient health-care only costs were not significantly associated with pre-institutionalisation time.
Conclusion: Total societal costs and total patient costs rise steeply as community-dwelling patients with AD dementia approach institutionalisation.
Disclosure: The GERAS study is fully granted by Eli Lilly & Co.

PR2002

Hypertension linked to Alzheimer's pathology

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Background and aims: Hypertension is regarded a modifiable risk factor for AD. Identifying candidates at risk for development of AD would help early intervention and may contribute in dealying AD symptoms. However, the precise mechanism that hypertension contributes to AD pathology has not been fully elucidated. The aim of our study is to investigate the presence of Alzheimer's Disease (AD) pathology in hypertensive (HTN) subjects by using [11C]PIB and [18F]FDG positron emission tomography (PET) for the quantification of beta-amyloid burden and cerebral glucose metabolism, respectively.
Methods: Using the Alzheimer's Disease Neuroimaging Initiative, a total of 229 non-degeneretive and non-demented, otherwise healthy participants were studied; of which 93 were HTN and 136 non-HTN. The presence of hypertension was screened by medical history and confirmed by two consecutive blood pressure measurements. Clinical, cognitive, and imaging evaluations were carried out in HTN and non-HTN subjects.
Results: HTN subjects showed lower [18F]FDG PET uptake in the temporal lobe (p<0.001) and higher [11C]PIB PET uptake in the occipital cortex (p<0.05) compared to the group of non-HTN subjects. We have on going investigations for associations with clinical measures and severity of hypertension.
Conclusion: Our preliminary findings indicate that hypertension is associated with temporal lobe hypometabolism and increased beta-amyloid pathology, and suggest that people with HTN may be at risk for developing AD.
Disclosure: Nothing to disclose

PR2003

LTP-like cortical plasticity in AD patients: A novel biomarker of disease progression

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Background and aims: AD diagnosis is performed according on clinical presentation and beta-amyloid or tau pathology, but there is poor sufficient accuracy in evaluating disease severity and predicting disease progression. Synaptic dysfunction represents a key driver of AD-related cognitive decline. Cortical plasticity mechanisms, especially Long Term Potentiation (LTP), can be assessed in humans with transcranial magnetic stimulation. Our aim is to establish the predictive value of LTP-like cortical plasticity as a prognostic biomarker of disease progression

Methods: We applied different neurophysiological protocols in a sample of 60 AD patients and 30 age matched healthy controls. ROC curve analyses evaluated the sensitivity and specificity of LTP biomarker and short-afferent inhibition (SAI), marker of central cholinergic activity, in discriminating AD patients from age-matched healthy controls.

Results: Area under curve was 0.90 for LTP, indicating excellent diagnostic accuracy of this biomarker, but only 0.64 for SAI. We performed univariate regression analyses for LTP, SAI, CSF biomarkers, APOE4, neuropsychological evaluation and demographic factors. Results showed that LTP was the only significant predictor of disease progression (p=0.02). Probability of disease progression significantly decreased with every point increase of LTP (p=0.04). ROC curve was also performed to evaluate the sensitivity of LTP biomarker in predicting cognitive decline in AD patients. We found AUC=0.71 indicating fair prognostic accuracy of this biomarker in discriminating among AD patients those with faster disease progression.

Conclusion: LTP impairment, but not other biomarkers, shows good predicting value on clinical progression.
LTP impairment can be considered as a biomarker of progression in AD patients.

Disclosure: Nothing to disclose

PR2004

Structural and functional brain connectome architecture in early onset Alzheimer's disease and the behavioral variant of frontotemporal dementia

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Background and aims: To investigate structural and functional brain network architecture in early-onset Alzheimer's disease (EOAD) and the behavioral variant of frontotemporal dementia (bvFTD).

Methods: Forty-two EOAD, 38 bvFTD, and 35 age-matched controls underwent 3D T1-weighted and resting-state functional MRI. Graph analysis and connectomics assessed global and local functional topological network properties, regional functional connectivity, and intra- and inter-hemispheric between-lobe connectivity.

Results: EOAD patients showed severe global functional network alterations relative to controls (lower mean nodal strength and local efficiency, and longer path length). BvFTD patients demonstrated a longer mean path length, predominantly in the frontal lobe. EOAD patients showed a longer mean path length relative to bvFTD patients in all cerebral lobes. At the regional level, compared to controls, EOAD patients showed widespread functional connectivity alterations linking temporal, medial and lateral parietal, and medial frontal nodes. BvFTD patients relative to controls were characterized by a more focal pattern of functional connectivity alterations including frontotemporal pathways and connections to the motor cortex and basal ganglia. EOAD patients showed reduced inter- and intra-hemispheric between-lobe connectivity, involving mainly temporal, frontal and parietal nodes. BvFTD patients were characterized by a reduced intra-hemispheric between-lobe connectivity linking temporal, frontal, and parietal nodes, and increased intra-hemispheric connectivity of parietal regions with basal ganglia and sensorimotor areas.

Conclusion: Disease-specific patterns of functional connectivity alterations were observed in EOAD and bvFTD. Graph analysis and connectomics may help elucidating pathophysiological differences between neurodegenerative dementia.

Disclosure: Italian Ministry of Health #GR-2010-2303035; Alzheimer's Drug Discovery Foundation #20131211.

PR2005

Sulcal opening in behavioural variant frontotemporal dementia: Comparison between automated and manual measures

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Background and aims: Evaluate the discriminating power and applicability of sulcal opening in the diagnosis of behavioural variant Frontotemporal dementia (bvFTD).

Methods: MRI of 23 patients with bvFTD and of 14 controls were compared. For each subject, 12 cortical sulci (olfactory, anterior and posterior cingulate, parietaloccipital, insula and temporal pole sulci, both sides) were reconstructed and automatically identified using Brainvisa software. Moreover, to test the applicability in clinical practice, visual rating scales for each sulcus were applied by two raters. Sulcal span and visual rating results for each sulcus were compared using Mann-Whitney U test and the area under receiver operating curve (AUC) was calculated.

Results: Using the automated method, bvFTD patients were found to have more opening in all sulci analized. Visual rating scales showed that bvFTD had more sulcal opening in olfactory and temporal pole both sides, left insula, right posterior cingulate and right pariealtoccipital. Similar AUC were obtained with the two methods, in particular the highest AUC for the automated method was the left anterior cingulate (0.814), whereas for the visual rating was the left temporal pole (0.828).

Conclusion: Both methods have demonstrated the utility of sulcal opening in the differentiation between bvFTD and controls. Despite differences most of the results obtained with the visual rating were confirmed with the automated method. Sulcal opening can be helpful for the diagnosis of bvFTD and visual rating scales can be an easy and economic way to assess it and can be used in the clinical setting to improve the diagnostic accuracy.

Disclosure: The current work was supported by AIRAalzh Onlus-COOP Italia

PR2006

Risk factors of Alzheimer's-related epileptic seizures and effect of epileptiform discharges on the progression of cognitive decline

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Background and aims: Evidence suggests that patients with Alzheimer's disease (AD) have a higher chance to have epileptic seizures. However, only a few studies observed the risk factors for developing seizures and the impact of spike activity on the progression of dementia. The aim of our study was to examine AD patients using long-term EEG recording, to identify the risk factors for seizures and to estimate the effect of epileptic discharges.

Methods: We selected 42 patients meeting the criteria for probable AD and followed them during 2 years. The patients underwent rigorous clinical investigation including long-term (24hours) EEG monitoring and repeated detailed neuropsychology.

Results: We identified epileptiform discharges in 52% and epileptic seizures in 23% of AD patients. Early onset of cognitive decline, long duration of dementia, severe stage of the disease and high number of educational years were correlated positively to the incidence of epileptic seizures. Patients with epileptiform discharges showed more prominent decline in the neuropsychological results during the 2-year follow-up

Conclusion: Epilepsy is a common comorbidity of AD. Epileptic seizures are predominantly occur in highly educated AD patients with early onset dementia at the severe stage of the disease. Epileptiform discharges could accelerate the progression of AD, so accurate assessment of AD-related epilepsy is essential because antiepileptic drugs might represent a new therapeutic strategy in AD.

Disclosure: Our research was supported by the National Brain Research Program (KTIA_NAP_13-1-2013-0001) and MET Hungary Ltd. There are no conflicts to disclose.

PR2007

Cerebral peri/para-vascular spaces in MRI in active young and aged individuals

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Background and aims: Recently, peri/paravascular spaces (PVS) are interested in the communication pathways of the interstitial fluid and cerebrospinal fluid in the brain. The enlarged PVS (ePVS) may be derived from obstruction of PVS with amyloid deposition in the cerebral arterial wall. However, it remains unclear about the prevalence of the ePVS in normal population. Here, age-related changes of the enlarged PVS were examined in a large number of normal individuals using MRI.

Methods: This study enrolled 784 individuals with active daily life, who came to ask brain check with MRI; 333 individuals with 3T-MRI and 451 individuals with 1.5T-MRI. A single neurosurgeon assessed the severities of ePVS in the basal ganglia (BVRS) and subcortical white matter (SPVS), periventricular hyperintensity (PVH), deep white matter hyperintensity (DWMH), microbleeds and atrophy. Their frequencies and correlations were statistically analysed with the free software "R".

Classification of peri/para-vascular spaces
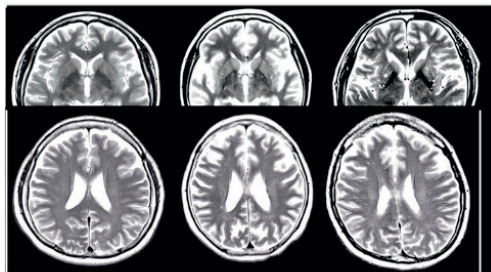
Results: Their mean age was 54 years ranging from 23 to 83 years. The lowest severity was most frequent in all of items except for SPVS, where the highest severity was most frequent. Frequencies of the high severities increased in the aged groups above 50 years in all except for the SPVS, where the highest severity was noted even in the youngest group and it increased with ages. High correlation was noted both in 3T and 1.5T.

Frequencies of high severity MRI changes and age distribution

age distribution: 1) 23-39, 2) 41-50, 3) 51-60, 4) 61-70, 5) 71-88
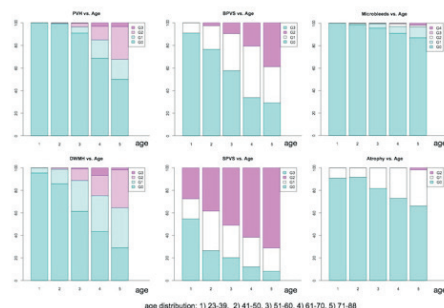
Conclusion: Present study revealed high severity SPVS were observed even in young normal individuals. This may be correlated with long interval between amyloid deposition and onset of dementia.

Disclosure: Nothing to disclose

PR2008

Time trend in opioid use among elderly with and without dementia

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Background and aims: Recently we reported that opioids were frequently used by elderly with dementia (Jensen-Dahm 2014). However, reasons for the frequent use of opioids among Danish elderly with dementia were unknown. One way to explore this is to examine changes in prescription patterns over time. The aim of this study was to investigate time trends of opioid drug use in patients with dementia in Denmark from 2000-2012.

Methods: Population-based observational study with time-series of cross-sectional studies conducted by use of Danish nationwide registers including the entire elderly population (age≥65) of Denmark. The registries were used to identify patients with dementia and users of opioids from 2000 to 2012.

Results: Prevalence of opioid use increased by 39% (from 24.2% to 33.5%) among elderly with dementia and 17% among elderly without dementia (from 14.9% to 17.4%) from 2000 to 2012. The higher increase in prevalence of opioid use among elderly with dementia was mainly due to an increase in strong opioids (dementia: from 11.7% to 23.3%; no-dementia: from 5.9% to 7.3%), in particular buprenorphen and fentanyl.

Conclusion: From 2000 to 2012 use of opioids among the elderly population increased, but particularly among elderly with dementia despite a higher prevalence in 2000. During the same time period use of antipsychotics decreased (Nørgaard 2016). The time-dependent association with a decrease in antipsychotics may suggest that opioids to some extent have replaced antipsychotics in managing neuropsychiatric symptoms, despite lack of evidence for effect of opioids (Cochrane 2015). Future research should focus on potential risks associated with increased use of opioids.

Disclosure: Nothing to disclose

PR2009

Grey matter network de-integration as predictor of cognitive dysfunction with aging

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Background and aims: Aging is associated with loss of grey matter and cognitive decline. It was shown that morphological characteristics of a given brain area co-vary with the characteristics of other areas forming inter-dependent networks. We aimed to identify networks that lose grey matter integrity with advancing age, investigate if age-related de-integration of networks is associated with cognitive dysfunction, and whether these networks better predict cognitive dysfunction than whole brain volume.

Methods: T1-weighted anatomical MRI scans of 257 subjects between 20 and 87 years were used to study structural grey matter network de-integration with increasing age. After segmentation, networks were identified based on structural covariance among subjects using independent component analysis. Hierarchical multiple regression analysis was used to examine the association between age and grey matter de-integration, cognitive functions and fine motor skills.

Figure 1. Supratentorial structural covariance networks of healthy elderly. Box-whisker plots indicate grey matter integrity per decade, p-value indicates significance of age as predictor (adjusted for sex and education, and corrected for multiple comparisons; FDR, q=0.05).

Results: Ten supratentorial and four infratentorial grey matter networks showed integrity change with advancing age (Figure 1a-j). The cuneal network (R2=0.443, p=0.034), the dorsal anterior cingulate (R2=0.419, p=0.019), the amygdala-hippocampus (R2-range=0.358-0.516, p-range=0.002-0.044), the temporal (R2-range=0.371-0.524, p-range=0.004-0.014), the fronto-parietal (R2=0.420, p=0.008), the opercular (R2range=0.366-0.368, p-range=0.011-0.012), and the sensorimotor network (R2=0.382, p=0.001) showed associations with memory, executive functions and fine motor abilities. Whole brain volume did not add information (p>0.071) above the explanation by the de-integrating grey matter networks.

Conclusion: We suggest that brain aging occurs in networks rather than single independent areas, that the influence of age on networks is selective and not global, that network de-integration selectively affects memory, executive functions and fine motor skills, and that network de-integration outperforms whole brain volume.

Disclosure: This study was funded by the Austrian Science Fund (FWF, KLI 546-BBL).

Autonomic nervous system 2

PR2010

Vanilla-stimulation suggests subtle central autonomic dysfunction in patients with a history of mild traumatic brain injury

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Background and aims: Cardiovascular autonomic effects of odorous stimulation are unknown in patients with a history of mild traumatic brain injury (post-mTBI-patients). We evaluated effects of Vanilla-stimulation on cardiovascular autonomic modulation in post-mTBI-patients.

Methods: We monitored respiration, RR-intervals (RRIs), systolic and diastolic blood pressure (BPsys, BPdia) in 17 healthy persons (30.0±11.5 years; 8 women) and 14 post-mTBI-patients (38.3±12.9 years; 3 women) at rest and during three series of six 1-second Vanilla stimuli. After stimulation, participants rated "Pleasantness" and "Familiarity" on a scale from 1 to 9. We calculated RRI-standard-deviation (RRI-SD), RRI-coefficient-of-variation (RRI-CV), RRI-low-frequency (LF: 0.04-0.15 Hz)-powers and normalized LF-powers (RRI-LFnu), BPsys-LF-powers, RMSSD, RRI-high-frequency (HF: 0.15-0.5 Hz)-powers, normalized HF-powers (RRI-HFnu), RRI-LF/HF-ratios, and baroreflex sensitivity (BRS). We compared data at rest and during stimulation with paired t-test (normal distribution) or Wilcoxin signed-rank test (non-normal distribution) and used Spearman rank correlation for correlation analysis (significance: P<0.05).

Results: During Vanilla-stimulation, BPsys (129.9±9.7 mmHg vs. 126.8±10.8 mmHg) and BPdia (68.3±6.8 mmHg vs. 66.1±7.4 mmHg) decreased and RRI-HF-powers (1178.5±1302.3 ms2 vs. 1524.5±1887.1 ms2) increased significantly in healthy persons but not in post-mTBI-patients. Pleasantness correlated positively with RRI-HF-powers, RRI-HFnu, RMSSD and BRS, but negatively with RRI-LFnu, RRI-LF/HF-ratio and BPsys-LF-powers; Familiarity correlated positively with RRI-HF-powers and RRI-HFnu but negatively with RRI-LFnu in healthy persons but not in post-mTBI-patients.

Conclusion: In healthy persons, Vanilla-stimulation increased parasympathetic modulation and decreased sympathetic modulation depending on the subjective perception of Pleasantness and Familiarity. Absence of such responses and lack of an association between autonomic changes and subjective valence of olfactory evaluation in the post-mTBI-patients suggests central autonomic dysfunction.

Disclosure: Nothing to disclose

PR2011
Cancelled

PR2012

Fingolimod discontinuation restores cardiovagal gain in patients with relapsing-remitting multiple sclerosis

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Background and aims: Fingolimod-therapy has vagomimetic-effects in relapsing-remitting multiple sclerosis (RRMS) patients. However, long-term effects of Fingolimod-treatment and Fingolimod-discontinuation on the cardiovagal gain (CVG) remain unclear. Therefore, we evaluated the effects of Fingolimod-discontinuation on CVG in RRMS patients.

Methods: In 19 RRMS patients (13 women and 6 men, mean age 33.7±10.2 years), we recorded RR-intervals (RRIs) and systolic blood pressure (BPsys) during Valsalva maneuver (VM), before and 6 months after continuous Fingolimod-treatment (0.5mg/day), and - for a third time - in 8/19 RRMS patients (7 women and 1 man, mean age 35.8±10.1 years) who had discontinued Fingolimod after 6 months, after additional 10.39±4.78 months. We quantified CVG from the slope of the relationship between RRIs and BPsys during early phase II of the VM. We compared date by repeated measurements of ANOVA and post-hoc paired t-testing (significance: p<0.05).

Results: In the 19 RRMS patients, CVG was significantly lower after 6 months of Fingolimod-therapy than before Fingolimod-initiation (4.8±3.1 vs. 2.2±1.2ms/mmHg; p=0.001). In the 8/19 RRMS patients who had discontinued Fingolimod after 6 months, CVG also was lower at 6 months of Fingolimod-treatment than before Fingolimod-initiation (6.4±3.6 vs 2.6±1.4 ms/mmHg, p=0.022), however CVG had re-increased after Fingolimod-discontinuation (2.6±1.4 vs 5.7±3.3 ms/mmHg, p=0.039) and no longer differed from values before Fingolimod-initiation (6.4±3.6 vs 5.7±3.3 ms/mmHg, p=0.594).

Conclusion: As a long-term effect, Fingolimod-therapy significantly decreases CVG which may result from central autonomic network readjustment in order to counter-regulate vagomimetic Fingolimod-effects. Yet, this effect is not lasting but fully reverses upon Fingolimod-discontinuation within ten months after Fingolimod-discontinuation.

Disclosure: This study was partly supported by Novartis Pharma, Germany.

PR2013

Heart rate variability decreases after 3 months of sustained treatment with fingolimod in patients with multiple sclerosis: A prospective clinical trial

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Background and aims: To prospectively investigate short- and mid-term changes of heart rate variability (HRV) in patients with relapsing-remitting multiple sclerosis (RRMS), being started on fingolimod.

Methods: Patients (n=33) with RRMS starting treatment with fingolimod underwent a time-domain-based analysis of HRV (breathing at rest, deep breath, and in response to the Valsalva maneuver) shortly before, 4.5 hours and 3 months after first intake. Blood pressure changes after the Valsalva maneuver were used as a marker of the sympathetic noradrenergic system. We used a non-invasive continuous beat-to-beat heart rate and blood pressure monitoring. Additionally, the Fatigue Severity Scale and the refined and abbreviated Composite Autonomic Symptom Score were applied.

Results: Significant changes in HRV in RRMS patients, following treatment with fingolimod, were detected. After an initial increase in HRV, 4.5 hours after the first intake of fingolimod, a substantial decrease in HRV occurred after 3 months on continuous treatment.

Conclusion: Treatment with fingolimod in RRMS patients significantly decreases HRV after 3 months. Our findings might have implications for the long-term cardiac safety of fingolimod treatment, especially in patients with cardiovascular risk factors. Treatment with more selective sphingosine 1-phosphate receptor agonists might be more favorable in this population. Long-term effects (> 3 months) of fingolimod on HRV in RRMS patients remain to be investigated.

Disclosure: This study was funded by a grant from the clinical trials department of the cantonal hospital St. Gallen. The Department of Neurology, Cantonal Hospital St. Gallen, Switzerland has received financial support from Novartis Switzerland. The submitted work is not related to these agreements. The authors of this study have not received financial support related to the submitted work.

PR2014

Autonomic challenges suggest that Fingolimod induced cardiac autonomic changes might be reversible

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Background and aims: Long-term Fingolimod-therapy may alter cardiac autonomic modulation in patients with relapsing-remitting multiple sclerosis (RRMS). Whether these autonomic effects still persist after Fingolimod-discontinuation is unknown. This study therefore aimed to assess cardiovascular autonomic responses to autonomic challenge in patients with relapsing-remitting multiple sclerosis (RRMS) during Fingolimod-therapy and after Fingolimod-discontinuation.

Methods: In 10 RRMS-patients (mean age 35.8 ± 10.1 years) who were on Fingolimod-therapy for a median of 17.3 (interquartile range10.9-20.9) months but then discontinued treatment, we monitored monitored RR-intervals (RRI), systolic, diastolic blood pressure (BPsys, BPdia), and respiration (RESP) during metronomic deep breathing (MDB), Valsalva-Manoeuvre, and active standing-up. Measurements were performed before and after six months of continuous Fingolimod-therapy, and 11.6 (7.6; 16.6) months (median; lower, upper quartile) after Fingolimod-discontinuation. We calculated expiratory-inspiratory-ratios (E/I-ratios) during MDB, Valsalva ratios (VRs), and 30/15-RRI-ratios upon standing-up. Values were compared between different time-points (Friedman test, with post-hoc Wilcoxon-test, significance: $p<0.05$).

Results: E/I-ratios significantly decreased after six months of Fingolimod-therapy (1.42 ± 0.18 vs. 1.23 ± 0.15, p=0.015) but significantly increased after Fingolimod-discontinuation (1.23 ± 0.18 vs. 1.40 ± 0.31, p=0.023). Similarly, VRs and 30/15-RRI-ratios both significantly decreased after six months of Fingolimod-therapy (VRs: 1.75 ± 0.33 vs. 1.40 ± 0.13, p=0.002; 30/15-RRI-ratios: 1.49 ± 0.29 vs. 1.16 ± 0.13, p=0.010) but significantly increased after Fingolimod-discontinuation (VRs: 1.40 ± 0.13 vs. 1.74 ± 0.35, p=0.005; 30/15-RRI-ratios: 1.16 ± 0.13 vs. 1.33 ± 0.25, p=0.022).

Conclusion: Long-term Fingolimod-treatment dampens cardiovagal responses to autonomic challenges. After Fingolimod-discontinuation, the cardiovagal responses to challenge maneuvers could recover. These results suggest that the effects of Fingolimod on cardiac autonomic modulation may be reversible.

Disclosure: This study received partial financial support from Novartis Pharma, Germany.

Cerebrovascular diseases 3

PR2015

Clinical patterns in cerebral reperfusion syndrome after carotid artery recanalization

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Background and aims: Carotid artery recanalization is usually indicated when a >70% carotid artery stenosis is the cause of an ischemic stroke. A potential risk in these patients, for both procedures carotid- endarterectomy (CEA) and carotid artery stenting (CAS) is the cerebral hyperperfusion syndrome.

Methods: We studied consecutive patients with internal carotid artery (ICA) stenosis who underwent a revascularization procedure from February 2005 to May 2016 in a tertiary level University Hospital. We recorded all neurological symptomatology after carotid revascularization (NSACR) not attributable to recurrent ischemia. Neurological clinical events must be described as a new symptomatology.

Results: Data from 1029 consecutive patients were analyzed. 83 patients were included following the criteria described above: 58/83 (69.9%) male and 25/83 (30.1%) female. Of these patients, 47/83 (56.6%) underwent CEA, 34/83 (41%) underwent CAS and 2/83 (2.4%) underwent carotid bypass. NSACR was reported in 83 patients: 32/83 patients (38.5%) presented headache, 11/83 patients (13.2%) visual hallucinations, 11/83 patients (13.2%) seizures, 26/83 patients (31.3%) confusional episodes and 26/83 patients (31.3%) focal neurological deficit. In the majority of the patients, complementary studies (cerebral parenchymal and neurovascular studies) were normal pointing toward a complex physiopathological mechanism.

Conclusion: A wider range of neurological symptoms and clinical findings than previously described are associated with CHS. Despite the present knowledge of this syndrome the exact physiopathological mechanism remains unknown.

Disclosure: Nothing to disclose

PR2016
Cancelled

PR2017

Intravenous thrombolysis for acute ischemic stroke outside office hours

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Background and aims: Previous studies have suggested that outcome after intravenous thrombolysis (IVT) for acute ischemic stroke (AIS) is worse for patients admitted outside office hours. Longer door-to-needle times (DNT) could potentially explain this difference. We examined this hypothesis in a well-organized acute stroke care region in the Netherlands comprising of 13 hospitals.

Methods: Retrospective, observational study of consecutive patients with AIS who received IVT between January 2009 and December 2015. Office hours was defined as admittance to the ER during weekdays between 8 a.m. and 5 p.m. Primary outcome was DNT. Secondary outcomes were in-hospital mortality and symptomatic intracranial hemorrhage (sICH). In multivariate analysis we adjusted for potential confounding variables.

Results: Of 3,154 patients treated with IVT, 1,869 (59.3%) presented outside office hours. More men were presented outside office hours (56.5% vs. 51.4%, p<0.001). DNT was slightly longer outside office hours (median 35 vs. 33 minutes, p= 0.011). In-hospital mortality (7.3% vs. 7.8%, p=0.59) and symptomatic ICH (4.5% vs. 4.2%, p=0.68) did not differ between groups. After adjustment, there was no association between DNT and admittance outside office hours (DNT <30 minutes OR 1.14, 95% CI 0.98–1.33; DNT <60 minutes OR 0.82, CI 95% 0.66–1.02. The risk of in-hospital mortality and sICH also did not differ between groups in multivariate analysis.

Conclusion: In our acute stroke care region, patients with AIS who presented outside office hours did not have longer DNTs, higher risk of complications, or higher mortality rates, than patients who presented during office hours.

Disclosure: Nothing to disclose

PR2018

Utility of CHADS2, CHA2DS2VASC, logistic EUROSCORE and EUROSCORE II predicting post-operative stroke and atrial fibrillation after cardiopulmonary bypass

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Background and aims: Some authors affirm that CHADS2 and CHA2DS2VASC scores are useful risk assessment tools for stroke after cardiovascular events, even in patients without atrial fibrillation. We pretend to confirm validity of these scales on predicting stroke and post-operative atrial fibrillation (POAF) after cardiac surgery.
Methods: We included 823 patients undergoing cardiac surgery under cardiopulmonary bypass: 672 with normal sinus rhythm (Group A) and 151 with pre-operative AF (Group B). We administered CHADS2, CHA2DS2VASC, surgical logistic EuroSCORE and EuroSCORE II and considered multiple vascular risk factors.
Results: Pre-operative CHA2DS2VASC, logistic EuroSCORE and EuroSCORE II were significantly increased in group B patients. Stroke rate was 2.4% in Group A and 2.6% in Group B. POAF was diagnosed in 15.8% of patients in Group A. In multivariate analysis age older than 70 years and worse pre-operative functional class were incremental risk factors for POAF. Pre-operative peripheral arteriopathy (p: 0.0016, OR: 4.80 (1.81-12.7)), was identified as a risk factor for post-operative stroke in Group A and diabetes mellitus in group B (p: 0.043, OR: 8.06 (1.96-51.24)). We found no significant relationship between preoperative CHADS2 and CHA2DS2VASC scores and post-operative stroke or POAF. Pre-operative logistic EuroSCORE predicted adequately the occurrence of post-operative stroke.
Conclusion: Peripheral vascular disease was the main risk factor for post-operative stroke after cardiac surgery in our series. CHADS2 and CHA2DS2VASC scores were ineffective predictors of stroke or POAF in our population. Scores measuring variables related with surgical procedure, such as logistic EuroSCORE, were more effective in predicting post-operative stroke.
Disclosure: Nothing to disclose

PR2019

The association between estradiol/testosterone ratio and acute cerebral infarction

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Background and aims: Sex hormones may be associated with higher incidence of clinically significant stroke or stroke related events. In observational studies lower testosterone concentrations are associated with frailty, adverse cardiovascular risk factors, and vascular disease. Estradiol was shown to be neuroprotective as well as anti-inflammatory in animal models of ischemic stroke with unclear mechanism. The aim of this study is to assess the role of estradiol/testosterone (E/T) ratio in acute ischemic stroke.
Methods: Between January 2011 and December 2015, a total of 196 patients with acute cerebral infarction or transient ischemic attack, and 192 control subjects were included in this study. Sex hormones were obtained in the patient and control groups. We analyzed clinical and E/T ratio of these patients.
Results: In men, compared with control group, E/T ratio and estradiol/free testosterone (E/T free) ratio were significantly elevated in the stroke patient group. (P=0.035). On the contrary, there were no evidence for an association between ischemic stroke and E/T, E/T free ratio in women.
Conclusion: In men, higher E/T or E/T free ratio were associated with ischemic stroke. These findings support the hypothesis that increased estradiol and reduced testosterone were associated with ischemic stroke, particularly in men. Thus, additional studies are warranted to explore potential mechanisms underlying this relationship and to assess whether hormonal interventions would selectively modify stroke risk.
Disclosure: Nothing to disclose

PR2020

Smoker's paradox in acute stroke: The past and the present

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Background and aims: Our aim was to investigate the association between smoking and the course of stroke accounting for gradual improvement of care over the years.

Methods: We analysed consecutive acute stroke patients admitted to our center between June 1995 and December 2015. Data were prospectively collected in a detailed registry. Patients smoking tobacco at least occasionally within the last 5 years were classified as current smokers. Comparisons were made separately in two periods: years 1995-2005 (n=2415) and 2006-2015 (n=2711).

Results: The proportions of never smokers, past smokers and current smokers have significantly changed from 1995-2005 to 2006-2015 (59.6%, 14.2%, 26.1% vs 55.0%, 20.0%, 25.0%, $p<0.001$). Hospital mortality was highest among never smokers in years 1995-2005 (21.7%, 14.7%, 15.9%) and lowest among current smokers in 2006-2015 (14.2%, 12.9%, 6.3%). The proportion of patients independent at discharge was lowest among never smokers both in 1995-2005 (37.8%, 49.9%, 50.9%) and 2006-2015 (38.5%, 49.9%, 54.6%). After adjustment for gender, age, previous disability, history of stroke, hypertension, atrial fibrillation, diabetes, congestive heart failure and stroke severity, never smokers in comparison to current smokers did not have increased odds of hospital death (0.96 in 1995-2005, 0.96 in 2006-2015) and being discharged as dead or dependent (0.96 and 0.79, respectively).

Conclusion: Over the last two decades stroke outcome in never smokers continues to be less favorable than in current smokers. However, it seems to depend mostly on coexisting conditions.

Disclosure: Nothing to disclose

PR2021

Stroke: A difficult diagnosis in nursing home residents

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Background and aims: Stroke has become a treatable condition with increasing evidence of treatment benefits also in the old and very old. However, stroke-mimicking conditions in geriatric patients are especially prevalent, causing incorrect suspicion and consecutive burden to these patients and emergency room (ER) resources. We therefore aimed to examine the dimension of this problem by investigating ER admissions from nursing homes (NH) for suspected stroke.

Methods: We retrospectively identified all NH-residents admitted to the neurological ER of our primary and tertiary care hospital between 2013 and 2015 (n=419) and reviewed their referrals for suspected stroke (excluding TIA patients). Patients were further divided into those with the final diagnosis of confirmed stroke or stroke mimics.

Results: Of 127 NH-residents (mean age: 78±14 years, polypharmacy rate: 77%) referred to our neurological ER for suspected stroke, only 43 (34%) had a confirmed stroke (ischaemic: n=35; haemorrhagic: n=8) and 84 demonstrated stroke-mimicking conditions. Infectious diseases (24%) and epileptic seizures (21%) were the most prevalent mimics. Only one patient received intravenous thrombolysis followed by mechanical thrombectomy. Prehospital delay (47%) and multimorbidity-associated contraindications (33%) were the main reasons for withholding recanalization therapy.

Conclusion: In our region, referrals from NH for suspected stroke have a high false positive rate and occur delayed, which most often precludes specific treatment in addition to multimorbidity. These problems may also exist in other centers and highlight the need for targeted educational and organizational efforts.

Disclosure: Nothing to disclose

PR2022

Comparison of prognostic value of different clinical scales for predicting early lethal outcome after acute spontaneous supratentorial intracerebral hemorrhage

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Background and aims: Identification of vital prognosis in patients with acute spontaneous supratentorial intracerebral hemorrhage (ASSICH) using clinical parameters is very important and relevant in modern angioneurology and can help the practicioners to improve treatment approaches. Therefore we decide to verify the clinical scale with the largest prognostic value for predicting early lethal outcome (ELO) after ASSICH.

Methods: 97 patients (mean age 64.0 ± 1.3 years) were studied within first 72 hours after clinical onset of ASSICH. Clinical examination included evaluation by National Institute of Health Stroke Scale (NIHSS), Glasgow Coma Scale (GCS), Full Outline of UnResponsiveness scale (FOUR) and Essen-ICH scale. Comparison of prognostic values of FOUR, GCS, NIHSS, Essen-ICH scale for predicting ELO after ASSICH was done using comparative ROC-analysis.

Results: From 97 stroke patients, 22 (22.7%) were died during 21 days from the ASSICH clinical onset. Predictors of ELO were verified: FOUR score on the 1st day from the clinical onset of AISS ≤ 13 (Se=86.4%, Sp=86.7%) and FOUR score on the 2nd day from the clinical onset of AISS ≤ 12 (Se=100.0%, Sp=90.7%). On the 1st day from the clinical onset of AISS FOUR score has the largest area under the curve (AUC=0.91) for predicting ELO, than GCS score (AUC=0.82), NIHSS score (AUC=0.85), Essen-ICH score (AUC=0.83) (fig. 1). These differences were found also for scores on the 2nd day from the clinical onset of ASSICH.

Conclusion: Full Outline of UnResponsiveness scale might be a powerful tool for predicting ELO after ASSICH and improving effectiveness of treatment.

Disclosure: Nothing to disclose
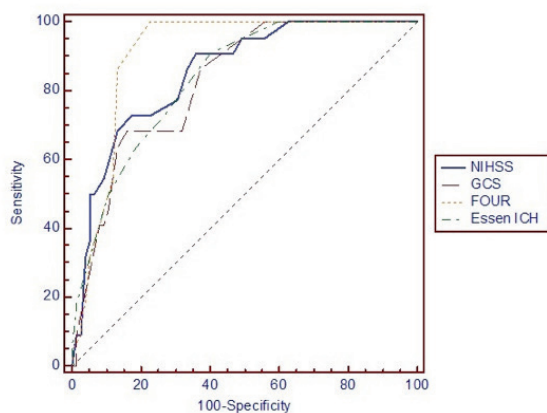
Fig. 1. Comparison ROC-analysis of different clinical scales.

Cognitive neurology/neuropsychology 2

PR1031

Social cognition disorders in Alzheimer's disease and frontotemporal dementia

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Background and aims: Social cognition domains are often impaired in neurodegenerative dementias. Up to date, the prevalence of such disorders in clinical settings is, however, still underestimated.

Methods: In this study, we enrolled 138 dementia (i.e., 90 frontotemporal dementia-FTD and 48 typical Alzheimer's disease-AD) and 25 Mild Cognitive Impairment (MCI) patients. The FTD group included behavioral variant (bvFTD; n=48) and primary progressive aphasia (PPA; n=42) patients. The standardized Italian versions of the Ekman 60-Faces Test and the Story-based Empathy Task-SET, respectively assessing recognition of basic emotions and attribution of emotions and intentions, were administered to patients.

Results: Compared to the other groups, socio-affective deficits were more frequent in bvFTD $(X2(3)=22,45,p<0.001)$. Of note, impaired socio-emotional performances were present in the 40% of AD and PPA as well as in a subset of MCI patients (i.e., 20%). Correlation analyses revealed significant association between performances at the emotion recognition and attribution of emotions and changes in social behaviors as reported by caregiver questionnaires.

Conclusion: The use of standardized socio-emotional tasks in clinical settings owns a crucial value in order to early detect social cognitive disorders in neurodegenerative patients. Socio-affective disorders are indeed not only main symptoms of bvFTD but may also be cognitive features of typical AD or PPA patients. The presence of socio-emotional alterations in non-bvFTD subjects suggests caution because they might represent a necessary but not sufficient cognitive feature in distinguishing bvFTD from other neurodegenerative patients.

Disclosure: Nothing to disclose

PR2023

Decreased level of consciousness in thalamic hemorrhage patient

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Background and aims: Widespread loss of cerebral connectivity is assumed to underlie the failure of brain mechanisms that support communication and purposeful behaviour following severe brain injury. Recent studies showed preservation of large-scale cerebral networks in minimally conscious state (MCS) patients (Adams, 2000).

Methods: We present stroke patient who was in MSC after hypertensive thalamic hemorrhage without diffuse cortical damage (Fig.1) with patterns observed on resting-state fMRI and TMS-EEG similar to consciousness state.

Results: Patient B., female, 31 y.o. had 18 CRS-R score 1 year after left thalamic hemorrhage with fluctuating consciousness level. She improved gradually with spontaneous eye opening and simple commands following although communication was limited to yes/no answers on voices recognition. We used rs-fMRI to investigate the default mode network (DMN; Vanhaudenhuyse, 2010) residual signal and found out activation in precuneus, bilateral temporo-parietal junctions and medial prefrontal cortex that was similar to healthy controls (Fig.1). TMS-EEG showed high perturbational complexity index (PCI; Casali, 2014) of 0.383 (>0.31, which is considered as cutoff level between unconscious and the conscious conditions; Casarotto, 2016), that corresponds to high complexity of TMS cortical response, same as in healthy controls (Fig. 2, 3).
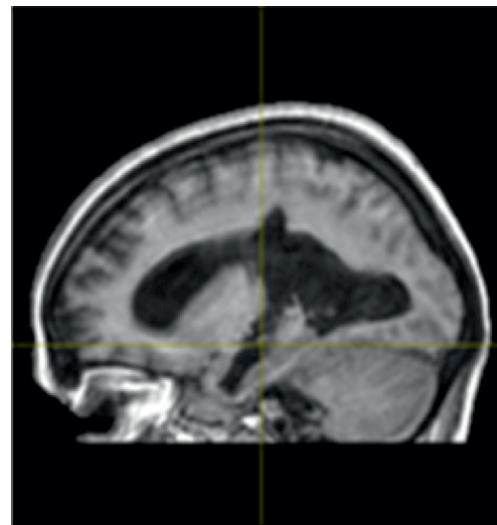
Fig.1. Structural MRI
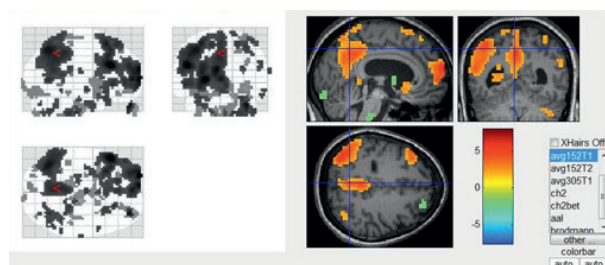
Fig.2. RS fMRI data.

Conclusion: By means of novel methods of consciousness detection, based on assessment of cortical activity and cerebral networks, patient appears to be conscious. We hypothesize that isolated dysfunction of thalamo-cortical interactions caused by thalamic damage lead to clinically seen reduced level of consciousness.

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Disclosure: Nothing to disclose

PR2024

Associated and predictive factors of cognitive impairment in Patients with Parkinson's disease (PwPD)

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Background and aims: Cognitive impairment (CI) is the common non-motor symptom in PwPD and determine patients and their relatives life quality[Rebecca Gilbert,2015]. Aim is to examine symptoms associated with CI in PwPD, and to identify risk factors for their future occurrence for prevention and treatment.

Methods: Analyses were performed in data of the Siberian region, Russia, a 5-year hospital-based longitudinal study of over 366 PwPD examined annually. Clinical assessments were conducted using the Montreal Cognitive Assessment(MoCA-test), UPDRS, H&Y Scale, Beck depression inventory II, HADS, Apathy Scale, PD Sleep Scale, Epworth Sleepiness Scale, Scale for Outcomes in PD for Autonomic Symptoms, PDQ-39. Cross-sectional analyses were conducted to evaluate differences between patients with/without CI at baseline, while linear-mixed models using all data were used to identify factors associated with longitudinal changes in MoCA-test scores.

Results: At baseline 24.3% PwPD had CI, while 28.9% PwPD without developed it at some point during follow-up. In about half of these latter group of PwPD, CI was a persistent phenomenon, the other half had relapsing-remitting course. Female, older age, older PD debut, higher disability scores(UPDRS), more severe motor fluctuations, autonomic and cognitive dysfunction, apathy, depression, poorer nighttime sleep, excessive daytime sleepiness were associated with lower MoCA scores. Lower baseline MoCA score, depression, higher levodopa dosage, poorer nighttime sleep and excessive daytime sleepiness were risk factors for future CI.

Conclusion: Monitoring for CI is important in patients with risk factors to get it in future. CI in PD can be more disabling than PD movement symptoms. It's important to recognize and treat it.

Disclosure: Nothing to disclose

PR2025

Clinical, demographic and etiological characteristics of 193 patients attending a cognitive clinic in Ireland

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Background and aims: Cognitive neurology clinics excel in assessing and managing amnestic and non-amnestic cognitive disorders. Few data exist regarding evaluating the outcome of such specialist clinics.

Objective: To perform a descriptive analysis of the demographics and diagnoses of patients presenting over a three year period to the cognitive neurology clinic at Saint James's Hospital, Dublin, Ireland.

Methods: We identified 193 patients by searching the medical records of the cognitive clinic of our tertiary university hospital. Participants of this observational, retrospective, single cohort study were seen for evaluation of cognitive symptoms between January 2013 and December 2015. All patients were consecutive, new referrals to the clinic. All available clinical, radiological, laboratory and pathological data were reviewed and constituted the main outcome measures.

Results: 193 patients presented to the clinic during the inclusion period. Of those 101 (52%) were males and 108 (59%) were from Dublin. 31%, 29% and 21% of referrals were made by General practitioners, Neurologists and the Memory clinic respectively. 62% had neurodegenerative disorders. Diagnoses varied but despite extensive evaluation the aetiology was not determined in 7 patients (4%). Final diagnosis was refined or changed in 41% of cases. Regarding early-onset cases (below 65), 28.8%, 16.8%, 12.1% and 9.8% were due to AD/MCI, Frontotemporal dementia, anxiety and excess alcohol respectively.

Conclusion: Cognitive symptoms can be due to a broad variety of aetiologies, (some are potentially treatable). Cognitive clinics provide a reach source of epidemiological data for health service planning.

Key words: Cognition, Neurodegeneration. Health service

Disclosure: Nothing to disclose

PR2026

Predict cognitive decline with clinical markers in Parkinson's disease

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Background and aims: Over the course of the disease about 80% of Parkinson's disease (PD) patients will develop cognitive impairment (CI) but predictive factors associated with cognitive decline are still under investigation. Here, we investigated which clinical-ready and cost-effective markers are predictive of CI in PD in a cohort of 294 patients with early de novo PD from the Parkinson's Progression Markers Initiative database.

Methods: Cognitive decline was defined as MoCA <26 at Level 1 diagnosis and as MoCA <26, in presence of clinical cognitive decline and at least 2 neuropscholoigical test impaired at Level 2 diagnosis. The variables with a validated cut-off were divided into normal/abnormal, while the other variables were divided into deciles.

Results: At three years follow-up, 122/294 PD (41.5%) patients had a cognitive decline at Level 1, of which 53/122 (43.4%) received a confirmed diagnosis at Level 2. We found that age of onset, MDS-UPDRS Part-III, Hopkin's Learning Verbal Test-Revised Recall, Semantic Fluency Test, Symbol Digit Modalities Test were all predictors of cognitive decline. We found that grouping patients by using these variables allow identifying 63.6–86.7% of subjects developing CI.

Conclusion: Our findings show that these clinical-ready and cost-effective measures have the ability to identify PD patients with the highest risk for CI and therefore, provide with an opportunity for early detection of potential candidates for novel neuroprotective treatments.

Disclosure: Nothing to disclose

PR2027

Decreased pattern separation performances suggest dentate gyrus dysfunction in patients with early multiple sclerosis

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Background and aims: Hippocampal dependent memory impairment is frequent and occurs early during the course of multiple sclerosis (MS). While mechanisms responsible for episodic memory dysfunction in patients with MS remain largely unknown, dentate gyrus structure has been suggested as particularly vulnerable at the early stage of the disease. If true, we hypothesized that the pattern separation component of episodic memory (a function known to be critically dependent to dentate gyrus function) would be impaired in patients with early MS (PweMS).

Methods: Thirty eight participants (19 PweMS and 19 healthy controls matched on age, gender and education level) were tested with a behavioral pattern separation task (Mnemonic Similarity Test) and also for information processing speed (Computerized Speed Cognitive Test) and visuospatial episodic memory (Brief Visuospatial Memory Test revised).

Results: We report a significant decrease of pattern separation performances in PweMS compared to healthy controls (27.07 vs 40.01, p=0.028, d=1.02) together with a significantly higher pattern completion rate (56.11 vs 40.95, p=0.0021, d=1.07) while no difference was found among groups for information processing speed and "global" visuospatial episodic memory regarding learning, long term recall or recognition.

Conclusion: Our results argue for early dentate gyrus dysfunction during the course of the disease and suggest that behavioral pattern separation task can detect subtle memory decline in MS.

Disclosure: This study was supported by the ARSEP Fondation, Bordeaux University Hospital, TEVA laboratories and by public grants from the French Agence Nationale de la Recherche within the context of the Investments for the Future program referenced ANR-10-LABX-57 named TRAIL and ANR-10-LABX-43 named BRAIN.

PR2028
Cancelled

PR2029

The influence of hands-free cellphone conversation on selective attention, perceptual speed and time movement anticipation required for driving performance

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Background and aims: Attention, perception and time/movement anticipation are essential cognitive abilities for safe driving and their impairments are predictive of traffic crash. The objective of this work was to determine the effects of conversing with hands free cell-phone on these abilities of drivers.

Methods: Twenty four University students participated in a crossover Randomized Controlled Trial study. Participants were assigned into two groups. In one of the groups, participants passed the following tests, then took rest for 60 minutes and then took the tests again while talking to hands-free cell phone. Participants of the other group first passed the tests while talking to hand-free cell phone and then after a rest for 60 minutes, passed the same tests without conversing. Participants of each group were shifted to the other group, after 7-10 days.

The tests used in this study were as follows: selective attention (Cog), perceptual speed (ATAVT) and time movement anticipation (ZBA) tests, by using the Vienna test system (VTS) driving simulator. Linear regression was used for analysis and the clustered structure of the data was taken into account.

Results: Conversation with hands free cell-phone affected Mean Time Correct Rejection (P-value=0.05) and Sum Hits (P-value< 0.001) in COG test. The Median Deviation Time (ZBA test) was increased while talking to hands-free cell phone (P-value=0.01). There was not a significant association between perceptual speed (ATAVT test) and conversing with hands free cell-phone.

Conclusion: Hands free cell-phone conversation while driving deteriorates selective attention and time/movement anticipation that are required for safe driving.

Disclosure: Nothing to disclose

Epilepsy 2

PR2030

Distribution of findings in 831 patients supposed of having pharmacoresistant epilepsy submitted to non-invasive presurgical evaluation

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Background and aims: Comprehensive epilepsy centers help in differentiating between nonepileptic and epileptic seizures, classification of epileptic types and syndromes, in determining etiology of epilepsy, with primary goal to select patients with pharmacoresistant epilepsy who could benefit from resective surgery of epileptogenic zone.

Methods: 831 patients treated at the Epilepsy Center, Clinic of Neurology, Belgrade, between June 2010 and December 2015, were retrospectively analyzed. Patients underwent five-day video-EEG telemetry (83 patients more than 5 days of recording), MRI (812 patients), neuropsychological tests (747), PET (266) and SPECT (23). Analysis of collected data was conducted in Patient management Conferences in our Clinic.

Results: From the cohort of 831 patients, we defined 608 (73%) with focal epilepsy. The rest were patients with idiopathic generalized epilepsy (8%), nonepileptic seizures (13%), and in 6% of cases the diagnosis was not determined. No seizures were recorded in 19% (even though the clinical presentation was indicative of focal epilepsy). Twenty-nine percent of patients (with refractory focal epilepsy) were not amendable for surgery without invasive presurgical procedures. Vagal nerve stimulator was implanted in 10 patients (1%). We selected 195 (24%) patients for resective surgery. Surgery was performed in 111 (14%) and denied by 85 patients (10%). Resective surgery was successful (more than 2 years seizure free) in 89 patients (80%).

Conclusion: Noninvasive video-EEG telemetry can determine the indication for epilepsy surgery in near 25% of evaluated patients, while in the rest of patients can help determine the correct diagnosis of paroxysmal neurological disorder.

Disclosure: Nothing to disclose

PR2031

Prevalence of non-epileptic psychogenic crisis in adult patients with refractory epilepsy in the Regional Hospital of High Specialty, León, Guanajuato, México.

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Background and aims: Epilepsy affects 0.5% to 1% of population, with refractory epilepsy (RE) proportion of 20-30%, psychogenic nonepileptic seizures (PNES) are paroxysmal changes in responsiveness, movements, behavior resembling seizures but lack a neurobiological origin and electrophysiological changes. PNES are result of psychological alteration, most of PNES are codified as somatoform disorders - Diagnostic and Statistical Manual of Mental Disorders-.

Aim: to know patients demographic characteristics with PNES and RE to have additional tools to diagnosis and management.

Methods: We conducted a retrospective analysis of 116 patients with RE (March 2011-August 2015) at HRAEB Epilepsy Clinic, recording demographic/clinical variables. PNES was defined as absence of EEG changes with behavioral manifestations and correspondence of clinical phenomena with a previous event witnessed by a family member. PNES were categorized by Griffith classification. Patients participated in clinical interviews with psychiatrists.

Results: We identified 28 PNES patients (16-55 years), seizure types were: focal epilepsy (20), focal generalized (8). No neuroradiological findings were found (16 patients). 1 patient had mesial temporal sclerosis (MTS), 2 hippocampal atrophy, 9 had abnormal MRI (encephalomalacia, atrophy, demyelinating vascular lesions, arachnoid cyst, neurocysticercosis).

Characteristics of PNES patients (n = 28)	n (%)
Median age (range)	35.5 (16 – 55)
Gender	
Male	2 (7)
Female	26 (93)
Education	
Illiterate	4 (14)
Primary education	6 (21)
Secondary education	11 (39)
Preparatory	4 (14)
Higher education	3 (12)
Marital status	
Single	16 (57)
Married	12 (43)
Psychiatric disorders	
Conversion disorder with motor symptoms.	28 (100)
Conversion disorder plus	
Major depression	12 (43)
Generalized anxiety disorder	5 (18)
Personality disorder	1 (4)
Mental retardation	1 (4)
Post traumatic stress disorder	1 (4)
Organic affective disorder	1 (4)
More of the disorder	16 (57)
Antiepileptic drug	
Monotheraphy	11 (39)
Polytheraphy	17 (61)

Characteristics of PNES patients

Conclusion: Patients were predominantly female, 10: 1 ratio. PNES women probably reflects the underlying biological/psychosocial factors congruent with other reports. Men PNES suggest a lower sexual abuse, employment rates, less acceptance of diagnosis and higher rates of emotional maladjustment than women. Both differences based on sex (biological) and gender (socio-cultural) can affect not only the prevalence of a disease, but also the presentation, diagnosis/results. Age/education level of patients did not seem to influence.

Disclosure: Nothing to disclose

PR2032
Cancelled

PR2033
Isolated self-limited aphasic syndrome: When should we suspect an epileptic origin?

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Background and aims: Epileptic aphasia is described as a rare cause of isolated self-limited aphasic syndrome (ISAS), being stroke the most important and frequent etiology to consider within the acute ill patient. There are not clinical criteria to differentiate between vascular and epileptic etiology of ISAS episodes. Our objective was to characterize the clinical, neuroimaging and electrophysiologic findings within the vascular or epileptic ISAS.

Methods: 61 patients with ISAS were identified between September 2015 and May 2016 at our institution. We analyzed clinical variables, neuroimaging and electroencephalography (EEG) studies.

Results: 69% of the patients were women, mean age 75.6 ± 12.3 years. 29 patients got final diagnostic of epileptic-AIAS, and 76% of them had had similar previous episodes. Epileptic-ISAS patients had more previously similar episodes than vascular-ISAS patients [median 4 episodes (IQR:3-5) vs 1 (IQR:1-1.75); p<0.001]; and it also had lower duration of the episode[median 10 minutes (IQR:5-80) vs 30 (IQR:12.75-146); p=0.023]. 38% of the acute ill patients with final epileptic-ISAS diagnosis had an urgent-EEG, but 37% of those EEG were normal. Continuous EEG-monitorization confirmed the diagnosis of epileptic ISAS in those whose initial-30 min EEG study was normal. There were not significant differences in age, sex or cardiovascular risk factors.

Conclusion: Our results suggest that epileptic-ISAS is quite under-diagnosed in the Emergency department. There are not many clinical keys to approach into the correct diagnosis. Urgent-EEG and more neuroimaging studies availability would permit an accurate diagnosis and to start a specific and early treatment.

Disclosure: Nothing to disclose

PR2034
Pseudopheochromocytoma as a potential side effect of VNS in refractory epilepsy: A case report.

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Background and aims: We describe the first case to our knowledge of pseudopheochromocytoma as a potential side-effect of vagus nerve stimulation (VNS).

We report the case of a 34-year-old man with a history of autism, mental retardation and refractory focal epilepsy. Treatment with VNS was initiated at age 28, with good response. 9 months later, he experienced 2 episodes with brief cardiorespiratory arrest (near-SUDEP), following clusters of generalized tonic-clonic seizures. Optimization of antiepileptic drug treatment and VNS stimulation parameters resulted in improved seizure control. In the course of these adjustments he began to experience episodes of lethargy, sweating, siallorhea and tachycardia. Endocrinological investigations confirmed a biochemical diagnosis of pheochromocytoma. Interestingly, subsequent repeated whole body PET-CT, structural heart and bladder imaging, and I-123 MIBG imaging failed to demonstrate a causative localization. This in turn gave rise to the hypothesis of a VNS effect.

Methods: A 24-hour urinary catecholamine collection was performed prior to, and 24 and 48h after turning off VNS. Plasma metanephrins were determined 48h after turning off VNS, and compared to previous measurements.

Results: During VNS, metanephrins were up to 4 times upper normal limit, whereas they normalized upon turning VNS off. (see graphs)
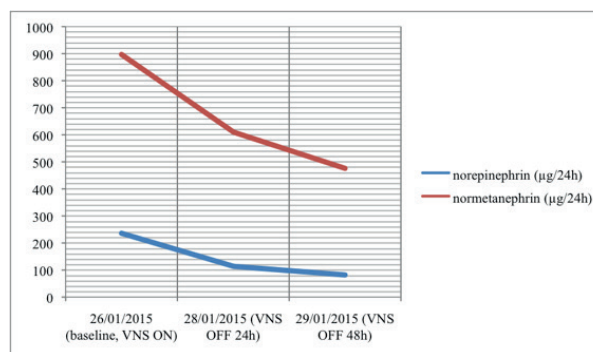
24h urine collection: 26/01/2015 (ON; VNS parameters: 1.75 mA-30 Hz-500 µs-30" on/10' off): norepinephrin 236 µg, normetanephrin 879 µg. 28/01/2015 (OFF 24h): norepinephrin 115 µg, normetanephrin 610 µg. 29/01/2015 (OFF 48h): norepinephrin 82 µg, normetanephrin 476 µg. Upper limit normal values: norepinephrin: 80 µg, normetanephrin: 650 µg
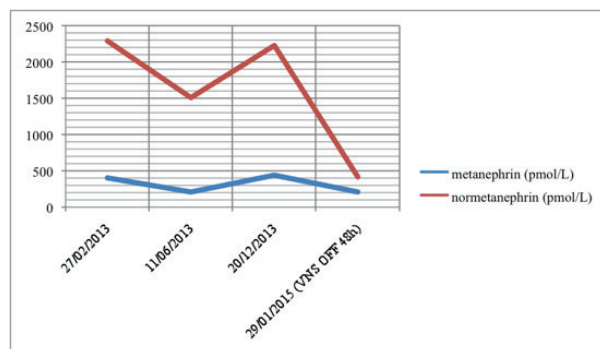
Plasma metanephrins: 11/06/2013: metanephrin 215 pmol/L, normetanephrin 1512 pmol/L. 20/12/2013: metanephrin 440 pmol/L, normetanephrin 2224 pmol/L. 29/01/2015: metanephrin 209 pmol/L, normetanephrin 417 pmol/L. Upper limit normal values: metanephrin: 295 pmol/L. normetanephrin: 495 pmol/L

Conclusion: Since thorough, repeated imaging identified no pheochromocytoma, a diagnosis of VNS-induced pseudopheochromocytoma was made. Taking animal research into account, we hypothesize that this effect arises through an afferent (central) pathway. Of interest, VNS is still successfully continued in this patient, while his pseudopheochromocytoma is treated with phenoxy-benzamine. We suggest further research to verify whether VNS affects peripheral catecholamines.

Disclosure: Nothing to disclose

PR2035

Serum metalloproteinases 2 and 9 levels after generalized tonic-clonic seizures indicate increase of blood-brain barrier permeability.

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Background and aims: The blood-brain barrier (BBB) permeability is changed during epileptic discharges in the brain. It is suggested that inflammation and BBB activation create a milieu for increased neuronal excitability. Metalloproteases 2 and 9 play an important role in the BBB maintenance and might be involved in seizures propagation. The aim of the present study was to investigate changes in the expression of MMP2 and 9 and their inhibitory proteins in serum after generalized tonic-clonic seizures.

Methods: We examined 50 patients hospitalized after generalized tonic-clonic seizures. The control group consisted of adult patients and healthy volunteers without epilepsy. Recent stroke, infection, inflammatory disease, tumor were considered as exclusion criteria. The blood sample were taken from patients 1 h, 24h and 72h after seizures, and once from the control group. The serum level of metaloproteinase 2 and 9, TIMP-1 and 2, thrombomodulin, thrombospondine – 1 and α2-macroglobulin were measured using ELISA kits (R&B system).

Results: The levels of MMP9, MMP9/TIMP1 ratio were significantly increased 1 and 24h after seizures, and then returned to the control level. MMP2 and MMP2/TIMP2 ratio were also changed. There were no significant changes in thrombomodulin and α2-macroglobulin. The expression of thrombospondine-1 decreased 1h after seizures and then slowly increased.

Conclusion: The changes of MMP 2 and 9 levels indicate increased permeability of blood-brain barrier. This increased permeability lasted about 24 hours and then started to stabilize by increasing activity of TIMP 1 and 2 and thrombospondine-1. The following study is needed to show if MMP influences seizures activity.

Disclosure: Nothing to disclose

PR2036

Cytokine expression in brain tissue of mesial temporal lobe epilepsy

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Background and aims: Epileptic Seizures are associated with a profound change in gene expression. Microarray studies have demonstrated that inflammatory response is one of the most upregulated processes during epileptogenesis. Experimental and clinical studies have shown a pro-inflammatory cytokines upregulation in brain tissue of Mesial Temporal Lobe Epilepsy Patients with Hippocampal Sclerosis (MTLE-HS). This higher expression is associated with neuronal damage and more frequent and severe seizures. Nevertheless, information on anti-inflammatory responses in MTLE-HS is scarce. Our aim was to quantify pro and anti-inflammatory molecules expression – IL-1β, IL-6, TLR-4 and IL-10- in MTLE-HS patients.

Methods: Gene expression was quantified in brain tissue samples (hippocampus and neocortical adjacent region) collected from 23 MTLE-HS patients and 8 cadaveric controls.

Results: IL-1β and TLR-4 were upregulated in both hippocampus ($p=0.001$) and neocortical ($p=0.005$ and $p=0.0003$, respectively) region of MTLE-HS patients comparing to controls. Although IL-6 expression was also 2 fold higher in MTLE-HS patient, no statistically significant difference was observed. IL-10 brain expression in hippocampus and neocortical adjacent region was similar in patients and controls.

Conclusion: Our results corroborate previous findings indicating that pro-inflammatory molecules, particularly involved in IL-1β pathway, may participate in seizure development and progression. It is argued that the epileptogenic role of pro-inflammatory cytokines is due not only to a neurotoxic effect but alsoto an interference with neurotransmission. The fact that the anti-inflammatory cytokine IL-10 expression is similar in patients and controls suggests that regulation of inflammatory response is impaired in MTLE-HS patients contributing to propagation of seizures in the cortical region.

Disclosure: Nothing to disclose

Headache and pain 2

PR2037

Clinical characteristics associated with the initial visits to emergency department in patients with migraine: A headache clinic-based study

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Background and aims: Migraine attack is a common cause of the visits to emergency department (ED). The aim of this study is to investigate clinical characteristics associated with the initial visits to ED for migraine.

Methods: This was a cross-sectional study using an outpatient headache-clinic registry from September 2014 to August 2015. Consecutive first-visit migraine patients aged ≥ 19 years were dichotomously classified according to visiting patterns: referral from ED vs. direct visit to outpatient headache clinic groups (ED vs. OHC groups). Logistic regression analysis was conducted to evaluate the association of clinical characteristics of migraine patients referred from ED.

Results: Of 257 patients (mean age: 43.6±13.8 years, female: 76.7%) in this study, 38 (14.8%) were referred from ED during a 1-year period. Univariate analysis found that headache intensity (0–10 NRS), vomiting, and vestibular symptoms were associated with ED group, compared to OHC group. In a multivariate-adjusted model, the odds ratios (95% CI) of headache intensity, vomiting, and vestibular symptoms for ED group were 1.31 (1.06–1.63), 2.60 (1.20–5.66), and 4.29 (1.84-10.00), respectively.

Conclusion: Patients of ED group were likely to have more severe headache intensity, vomiting, and vestibular symptoms. This finding suggests that disabling characteristics of severe headache intensity or troublesome associated symptoms could be independent predictors for the initial visits to ED among migraine patients.

Disclosure: Nothing to disclose

PR2038

Wearing-off effect of onabotulinumtoxina in chronic migraine: Evaluation in a series of 117 patients

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Background and aims: OnabotulinumtoxinA (OnabotA) is considered an effective preventive therapy for around 80% of Chronic Migraine (CM) patients. PREEMPT protocol established the injection of OnabotA every 12 weeks, but in real-life setting duration of effect is, in some patients, below this period. We aimed to analyze the response to OnabotA, including characteristics of a wearing-off effect in a series of CM patients.

Methods: We included 117 CM patients (102 females, 15 males), who completed at least 2 OnabotA procedures. Monthly headache and migraine days before and after OnabotA injections were recorded in a diary. Patients were considered as responders when a reduction of migraine days by at least 50% was achieved, and, among them, wearing-off responders when effect was observed only during the first two months after the procedure.

Results: Mean age at first procedure was 41± 11.7 years (18-71). Latency between migraine onset and inclusion was 26.6±12.7 years (2-61), and between CM onset and inclusion 39.5±44.8 months (6-240). 93 patients (79.5%) were classified as responders, and, among them, 25 (26.8%) as wearing-off responders. Latency between migraine onset and OnabotA therapy was longer among no responders (28.6±16.1 vs 22.2±11.3 years, p:0.029). We found no differences when comparing wearing-off and rest of responders.

Conclusion: A wearing-off response to the first procedures of OnabotA is not infrequent in CM patients. We recommend considering this type of response in order to evaluate characteristics of this population and to establish adequate strategies to improve it during subsequent OnabotA procedures.

Disclosure: Nothing to disclose

PR2039

Efficacy of erenumab (AMG 334) in patients with chronic migraine in North America and Europe: Subgroup analysis of a phase 2, randomised, double-blind, placebo-controlled study

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Background and aims: Erenumab, a fully human monoclonal antibody, targets the calcitonin gene-related peptide (CGRP) receptor. In a 12-week, phase 2 study of patients with chronic migraine (CM), erenumab treatment resulted in significant and clinically meaningful reduction in the number of monthly migraine days (MMD) versus placebo, with a safety profile comparable to placebo. Here, we present results of the regulatory phase 2 study stratified by region (North America and Europe).

Methods: Patients (N=667; aged 18-65 years inclusive) with CM (≥15 headache days/month; ≥8 migraine days/month) were randomised (3:2:2) to receive subcutaneous erenumab 70mg, 140mg or placebo, with randomisation stratified by region and medication overuse. In this subgroup analysis efficacy endpoints were change in MMD, ≥50% reduction in MMD, change in monthly acute migraine-specific medication treatment days and change in cumulative monthly headache hours. All assessments compared the weeks 9-12 to baseline.

Results: At week 12, there were greater reductions in MMD and acute migraine-specific medication treatment days as well as more patients achieving ≥50% reduction in MMD with erenumab 70mg and 140mg doses versus placebo in patients from both North America and Europe (Table). Moreover, a numerical reduction in cumulative monthly headache hours was observed with erenumab 70mg and 140mg compared with placebo in patients from both regions.

Measures	North America			Europe		
	Placebo (N=135)	Erenumab 70mg (N=91)	Erenumab 140mg (N=87)	Placebo (N=146)	Erenumab 70mg (N=97)	Erenumab 140mg (N=100)
MMD at baseline, mean (SD)	18.13 (4.65)	18.17 (4.26)	17.71 (4.71)	18.34 (4.80)	17.72 (4.46)	17.85 (4.67)
ΔMMD, LSM (95% CI) at week 12	-4.92 (-5.93, -3.92)	-7.31 (-8.51, -6.11)	-6.75 (-7.98, -5.53)	-3.50 (-4.43, -2.57)	-6.00 (-7.15, -4.85)	-6.49 (-7.61, -5.38)
≥50% reduction in MMD, responder rate (%) at week 12	26.7	41.8	47.1	20.5	38.1	36.0
≥50% reduction in MMD, adjusted odds ratio (95% CI) (erenumab vs placebo) at week 12	-	1.98 (1.12, 3.48)	2.45 (1.39, 4.32)	-	2.42 (1.36, 4.31)	2.24 (1.25, 3.99)
Monthly acute migraine-specific medication treatment days at baseline, mean (SD)	6.72 (6.80)	6.64 (7.14)	7.48 (6.95)	11.92 (7.36)	10.76 (6.74)	11.58 (6.56)
ΔMonthly acute migraine-specific medication treatment days, LSM (95% CI) at week 12	-1.52 (-2.11, -0.94)	-2.84 (-3.54, -2.14)	-3.53 (-4.25, -2.81)	-1.60 (-2.32, -0.88)	-3.93 (-4.81, -3.04)	-4.59 (-5.45, -3.73)
Cumulative monthly headache hours at baseline, mean (SD)	248.38 (129.85)	246.41 (135.02)	214.69 (124.00)	223.16 (121.65)	202.22 (114.80)	215.38 (123.71)
ΔCumulative monthly headache hours, LSM (95% CI) at week 12	-58.50 (-74.97, -42.02)	-73.22 (-92.97, -53.47)	-63.41 (-83.67, -43.16)	-52.53 (-67.64, -37.43)	-57.76 (-76.45, -39.07)	-83.02 (-101.14, -64.90)
CI, confidence interval; LSM, least squares mean; MMD, monthly migraine days; SD, standard deviation						

Table: Outcome measures by region

Conclusion: Similar efficacy of erenumab was observed in patients with CM in both North American and European Union subgroups.

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PR2040

Migraine is associated with intracranial carotid artery calcification: The Rotterdam Study

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Background and aims: Migraine has been associated with increased risk of cardiovascular disease such as stroke and coronary heart disease. The question remains whether migraine is associated with intermediate markers of cardiovascular disease. We investigate whether migraine is associated with carotid intima media thickness (cIMT) and arterial calcification.

Methods: Migraine was assessed by questionnaire in 6961 participants of the Rotterdam Study. Mean cIMT was assessed by ultrasound of the common carotid artery, carotid bifurcation and the internal carotid artery. 6157 participants had data on both migraine and cIMT. Arterial calcification of the coronary arteries, aortic arch, and extracranial and intracranial carotid arteries was assessed by computed tomography. 1856 participants had data on migraine and arterial calcification. Analyses were performed using linear regression with adjustment for age, sex and cardiovascular risk factors.

Results: Migraine was associated with lower mean cIMT (unstandardized beta coefficient -0.01 (95% CI -0.02, 0.00)) and lower intracranial carotid artery calcification score (-0.19 (-0.29, -0.08)). There was no association with coronary artery, aortic arch or extracranial carotid artery calcification.

Conclusion: Migraine is associated with lower cIMT and lower arterial calcification in the intracranial carotid artery, but is not associated with calcification in the other arterial vessels. More studies are needed to investigate the underlying mechanisms and clinical implications of these findings.

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PR2041

Demographic and clinical characteristics of migraine patients in Denmark

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Background and aims: We examined demographic and clinical characteristics of patients with migraine in Denmark according to their initial migraine treatment.

Methods: Using Danish registry data from hospital diagnoses of migraine and outpatient dispensations for migraine-specific treatments (triptans, ergots, pizotifen, clonidine), we assembled a cohort of incident migraine patients aged ≥18 years, in 2005-2013. The date of migraine onset was the date of the first-recorded diagnosis or the second dispensation. We classified the initial migraine treatment as 'no treatment'; 'acute only'; 'prophylactic only'; and 'both acute and prophylactic' and described the distributions of sex, age, comorbidities and comedications overall and by initial migraine treatment (Table 1).

Results: Among the 114,308 migraine patients, 80% were women, median age 43 years (interquartile range=34-53 years). The initial migraine treatments received were: acute only (N=85,729, 75.0%); prophylactic only (N=15,318, 13.4%); and both acute and prophylactic (8,753, 7.7%); 4,508 (3.9%) migraine patients had no record of treatment. Initiators of prophylactic treatment - with or without acute treatment - were more likely than initiators of acute treatment only to be women (91% and 82% vs. 79%), to be older (median age, 53 years and 51 years vs. 41 years), and to have a history of diabetes (3.4% and 4.8% vs. 1.9%), hypertension (23% and 28% vs. 6.8%), or chronic obstructive pulmonary disease (14% and 18% vs. 11%) (Table 2).

Table 2. Demographic and clinical characteristics of patients with incident migraine according to initial migraine treatment received, Denmark, 2005-2013

Characteristic	No treatment N=4,508	Acute treatment N=85,729	Prophylactic N=15,318	Both acute and prophylactic N=8,753	All migraine patients N=114,308
Sex, n (%)					
Men	1,512 (33.5)	18,231 (21.3)	1,343 (8.8)	1,552 (17.7)	22,638 (19.8)
Women	2,996 (66.5)	67,498 (78.7)	13,975 (91.2)	7,201 (82.3)	91,670 (80.2)
Age, median (Q1-Q3), years	36.3 (28.0 – 47.1)	40.7 (32.3 – 49.3)	53.3 (49.0 – 60.0)	50.8 (40.5 – 60.1)	43.3 (33.7 – 52.6)
Age group, n (%)					
18-<30 years	1,387 (30.8)	16,844 (19.6)	512 (3.3)	889 (10.2)	19,632 (17.2)
30-<40 years	1,287 (28.5)	24,218 (28.2)	733 (4.8)	1,220 (13.9)	27,458 (24.0)
40-<50 years	921 (20.4)	24,708 (28.8)	3,316 (21.6)	2,022 (23.1)	30,967 (27.1)
50-<60 years	526 (11.7)	12,770 (14.9)	6,928 (45.2)	2,415 (27.6)	22,639 (19.8)
≥60 years	387 (8.6)	7,189 (8.4)	3,829 (25.0)	2,207 (25.2)	13,612 (11.9)
Comorbidity, n (%)					
Diabetes	85 (1.9)	1,596 (1.9)	519 (3.4)	423 (4.8)	3,681 (3.2)
Hypertension	318 (7.1)	5,857 (6.8)	3,531 (23.1)	2,449 (28.0)	11,775 (10.3)
Obesity	197 (4.4)	3,957 (4.6)	695 (4.5)	574 (6.6)	5,354 (4.6)
COPD	460 (10.2)	9,209 (10.7)	2,209 (14.4)	1,536 (17.5)	13,269 (11.6)
Chronic kidney disease	21 (0.5)	251 (0.3)	87 (0.6)	80 (0.9)	430 (0.4)
Autoimmune disease	100 (2.2)	2,386 (2.8)	538 (3.5)	410 (4.7)	3,392 (3.0)
Liver disease	23 (0.5)	368 (0.4)	107 (0.7)	87 (1.0)	578 (0.5)
Medication use, n (%)					
Anti-asthma medications	1,198 (26.6)	23,416 (27.3)	4,819 (31.5)	2,971 (33.9)	32,090 (28.1)
Cardiovascular medications	885 (19.6)	19,226 (22.4)	7,356 (48.0)	5,271 (60.2)	32,263 (28.2)
Beta-blockers	337 (7.5)	7,343 (8.6)	2,712 (17.7)	2,937 (33.6)	13,249 (11.6)
Antidepressants	679 (15.1)	15,263 (17.8)	3,682 (24.0)	2,717 (31.0)	21,977 (19.2)

COPD = chronic obstructive pulmonary disease; Q1 = first quartile; Q3 = third quartile

Table 2.

Conclusion: For three-quarters of the patients with incident migraine, the initial migraine treatment was acute treatment only. Use of prophylactic medications was associated with older age and higher comorbidity.

Disclosure: This project was partially funded by a grant from Amgen Inc., issued to and administered by Aarhus University, Aarhus, Denmark.

Table 1. Acute and prophylactic migraine medications used to assess treatment patterns

Specific acute treatment	
Triptans	sumatriptan, naratriptan, zolmitriptan, rizatriptan, almotriptan, eletriptan, frovatriptan
Ergots	dihydroergotamine, ergotamine, ergotamine, combinations, ergotamine, combinations with psycholeptics
Nonspecific acute treatment	
Opioids (tramadol), non-steroidal antiinflammatory drugs, aspirin, paracetamol, caffeine, metoclopramide, ondansetron	
Specific prophylactic treatment	
Pizotifen, flunarizine, methysergide, clonidine	
Nonspecific prophylactic treatment	
Beta-blockers	Metoprolol, propranolol
Antidepressants	Amitriptyline, mirtazapine
Anticonvulsants	Topiramate, valproic acid, lamotrigine
Antihypertensives	Lisinopril, candesartan
Other	Botulinum toxin

Table 1.

PR2042

Migraine and pregnancy outcome: A Danish population-based prevalence study

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Background and aims: Migraine is a common headache disorder affecting primarily women of reproductive potential. Pregnancy often ameliorates migraine, but the disease persists in up to 8% of pregnant women. We examined association between migraine and pregnancy outcome.

Methods: Using data linked from Danish population-based registries, we identified, in 2005-2013, pregnancies with migraine and a reference cohort of pregnancies without migraine, matched (up to 10:1) on age and on conception year. Presence of migraine was determined based on hospital diagnoses or migraine-specific medications. We estimated prevalence ratios (PR [95% confidence intervals, CI]) for early foetal death and major birth defects and, among pregnancies carried to ≥22 gestational week, PRs for placental abruption, preeclampsia/eclampsia, and stillbirth.

Results: There were 22,915 pregnancies with migraine and 229,064 matched pregnancies without migraine. Pregnancies with and without migraine had similar distributions of age at conception and pregnancy outcomes leading to cohort inclusion. Pregnant women with migraine were more likely than pregnant women without migraine to have a history of depression, hypertension, and prescription medication use (Table 1). Migraine in pregnancy was not associated with early foetal death (Table 2) or other adverse pregnancy outcome except pregnancy-associated hypertensive disorders (adjusted PR [95% CI] 1.31 [1.22–1.41]), driven primarily by preeclampsia/eclampsia (1.30 [1.19–1.42]) (Table 3).

Table 2. Association between migraine and early foetal death, all pregnancies

Outcome		Pregnancies without migraine 229,064	Pregnancies with migraine 22,915
Miscarriage	Number of events	23,764	2,578
	Prevalence, %	10.37	11.25
	Crude PR (95% CI)	1	1.10 (1.05–1.15)
	Adjusted PR (95% CI)*	1	1.06 (1.02–1.11)
Elective pregnancy termination, first trimester	Number of events	33,114	3,270
	Prevalence, %	14.46	14.27
	Crude PR (95% CI)	1	0.98 (0.94–1.03)
	Adjusted PR (95% CI)*	1	0.91 (0.87–0.95)
Elective pregnancy termination, second trimester	Number of events	876	83
	Prevalence, %	0.38	0.36
	Crude PR (95% CI)	1	0.95 (0.76–1.19)
	Adjusted PR (95% CI)*	1	0.91 (0.72–1.14)

CI confidence interval; PR prevalence ratio

*Adjusted for maternal history of diabetes, hypertension, depression, asthma, infertility, history of pregnancy hypertension, parity, history of spontaneous abortion, history of elective abortion, history or ectopic or molar pregnancy, history of giving birth to a child with malformation, and maternal age as restricted cubic spline with 5 knots.

Table 2

Table 3. Association between migraine and pregnancy complications/stillbirth among pregnancies at ≥22 gestational weeks

Outcome		Pregnancies without migraine N=114,916	Pregnancies with migraine N=15,924
Placenta previa	Number of events	599	92
	Prevalence, %	0.52	0.58
	Crude PR (95% CI)	1	1.11 (0.88–1.39)
	Adjusted PR (95% CI)*	1	1.05 (0.84–1.32)
Placental abruption	Number of events	551	84
	Prevalence, %	0.48	0.53
	Crude PR (95% CI)	1	1.10 (0.87–1.39)
	Adjusted PR (95% CI)	1	1.02 (0.81–1.29)
Pregnancy-associated hypertension disorders	Number of events	5,702	1265
	Prevalence, %	4.96	7.94
	Crude PR (95% CI)	1	1.65 (1.54–1.77)
	Adjusted PR (95% CI)*	1	1.31 (1.22–1.41)
Preeclampsia/eclampsia	Number of events	3,274	679
	Prevalence, %	2.85	4.26
	Crude PR (95% CI)	1	1.52 (1.39–1.66)
	Adjusted PR (95% CI)*	1	1.30 (1.19–1.42)
Stillbirth (week 22+)	Number of events	372	59
	Prevalence, %	0.32	0.37
	Crude PR (95% CI)	1	1.15 (0.86–1.53)
	Adjusted PR (95% CI)*	1	1.09 (0.82–1.44)

CI confidence interval; PR prevalence ratio

*Adjusted for maternal history of diabetes, hypertension, depression, asthma, infertility, history of pregnancy hypertension, parity, history of spontaneous abortion, history of elective abortion, history or ectopic or molar pregnancy, history of giving birth to a child with malformation, and maternal age as restricted cubic spline with 5 knots.

Table 3

Conclusion: Pregnant women with migraine have higher chronic morbidity than pregnant women without migraine. Pregnancies in migraine patients are more likely to be affected by pregnancy-associated hypertensive disorders. The data did not support association between migraine and other adverse pregnancy outcomes.

Table 1. Characteristic of pregnancies with and without migraine

Maternal characteristic	Pregnancies with migraine N=22,915	Matched pregnancies without migraine N=229,064	All pregnancies N=251,979
Age at conception, years, n (%)			
<25	1,905 (8.3)	18,032 (7.9)	19,937 (7.9)
25-35	11,557 (50.4)	116,670 (50.9)	128,227 (50.9)
>35	9,453 (41.3)	94,362 (41.2)	103,815 (41.2)
Current pregnancy outcome, n (%)			
Miscarriage	2,578 (11.3)	23,764 (10.4)	26,342 (10.5)
First-trimester elective termination	3,270 (14.3)	33,114 (14.5)	36,384 (14.4)
Second-trimester elective termination	83 (0.4)	876 (0.4)	959 (0.4)
Livebirth	16,912 (73.8)	170,621 (74.5)	187,533 (74.4)
Stillbirth	72 (0.3)	689 (0.3)	761 (0.3)
Preconception morbidity, n (%)			
Hospital diagnosis of essential hypertension	358 (1.6)	1,291 (0.6)	1,649 (0.7)
Hospital diagnosis of diabetes	121 (0.5)	1,253 (0.5)	1,374 (0.5)
Hospital diagnosis of depression	263 (1.1)	1,099 (0.5)	1,362 (0.5)
Hospital diagnosis of asthma	1,037 (4.5)	6,176 (2.7)	7,213 (2.9)
Preconception medication use, n (%)			
Antihypertensives	1,544 (6.7)	4,515 (2.0)	6,059 (2.4)
NSAIDs	15,196 (66.3)	96,860 (42.3)	112,056 (44.5)
Antidiabetic agents	681 (3.0)	5,852 (2.6)	6,533 (2.6)
Antidepressants	5,130 (22.4)	27,305 (11.9)	32,435 (12.9)
Anti-asthma medications	3,791 (16.5)	27,977 (12.2)	31,768 (12.6)
Reproductive history before current pregnancy, n (%)			
Pregnancy-associated hypertensive disorders	1,046 (4.6)	7,520 (3.3)	8,566 (3.4)
Preeclampsia or eclampsia	712 (3.1)	5,353 (2.3)	6,065 (2.4)
Gestational diabetes	327 (1.4)	3,133 (1.4)	3,460 (1.4)
Subfertility	3,085 (13.5)	29,905 (13.1)	32,990 (13.1)
Livebirth	13,061 (57.0)	130,175 (56.8)	143,236 (56.8)
Elective termination	4,619 (20.2)	43,168 (18.8)	47,787 (19.0)
Miscarriage	4,068 (17.8)	37,906 (16.5)	41,974 (16.7)
Stillbirth before	124 (0.5)	1,477 (0.6)	1,601 (0.6)
Ectopic pregnancy	515 (2.2)	4,012 (1.8)	4,527 (1.8)
Molar pregnancy	61 (0.3)	496 (0.2)	557 (0.2)
Pregnancy with foetal abnormality	679 (3.0)	4,822 (2.1)	5,501 (2.2)

NSAID non-steroidal antiinflammatory drug

Table 1

Motor neurone diseases 1

PR2043

Tracking longitudinal evolution of amyotrophic lateral sclerosis using multimodal MRI

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Background and aims: Identifying prognostic predictors in amyotrophic lateral sclerosis (ALS) is important for both clinical practice and design of treatment trials. This study explored longitudinal clinical, cognitive, and structural brain changes in patients with ALS.

Methods: We enrolled 45 ALS patients and 40 healthy controls. Patients were followed prospectively with clinical and neuropsychological evaluations, and MRI scans were obtained every 3 to 6 months, for a maximum follow up of 1 year. Longitudinal linear models assessed clinical and cognitive changes over time. Cortical thickness and tract-based spatial statistics analyses assessed progressive grey matter (GM) and white matter (WM) damage, respectively.

Results: Over 1 year, motor decline in ALS patients was paralleled by a significant deterioration of global cognition and several executive-attentional measures. At study entry, ALS patients showed widespread cortical thinning of frontal regions and WM damage to the corticospinal tracts, motor callosal fibers, and superior longitudinal fasciculus bilaterally. Longitudinal analysis revealed significant progression of GM and WM damage after 9 months, involving the premotor cortex, the genu of the corpus callosum, bilateral prefrontal WM, and the right corona radiata and internal capsule. At 1 year follow-up, WM damage further extended to the left hemisphere and to posterior brain regions.

Conclusion: We found a significant progression of brain damage in ALS patients, evolving as a widespread structural network degeneration. Our results suggest that MRI provides a powerful tool to track in vivo the disease spreading evolution related to pathological propagation in ALS.

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PR2044

Antisense oligonucleotides-based therapy as a promising therapy for amyotrophic lateral sclerosis

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Background and aims: Familial amyotrophic lateral sclerosis (fALS) accounts for 5-10% of all ALS cases and represents a useful model for studies of ALS pathogenesis and therapy. Antisense oligonucleotides (ASOs) are short oligonucleotidic sequences interfering with RNA processing in order to decrease the gene expression of the target protein. In this work, we tested ASOs with morpholino (MO) in SOD1 and C9ORF72, the most frequent ALS genetic mutations, animal and human models.
The treatment in a SOD1 transgenic mouse demonstrated to improve motor functions and disease course and to exert neuroprotective and anti-inflammatory effects as it was showed by neuropathological analysis. The efficacy of MO therapy was also confirmed in human induced pluripotent stem cell (iPSC)-derived motorneurons.

Methods: Motorneurons were differentiated from iPSC derived from patients carrying SOD1 and C9ORF72 mutations. After electroporation with MO, these cells were evaluated for survival and expression of pro-apoptotic markers and RAN products. In vivo, SOD1G93A mice were sistemically and intracerebroventricularly treated with MO at the onset of the symptoms.

Results: A longer survival and reduced expression of pro-apoptotic molecules were demonstrated in SOD1 iPSC-derived motorneurons. On the other side, C9ORF72 iPSCs revealed a reduction of RAN products. These results were reproduced also in animal models and supported by histopathological analysis which confirmed a preservation of motorneurons and a decrease of glia reaction.

Conclusion: This work confirmed the potentiality of ASOs as a novel therapy for ALS, particularly for genetic forms caused by SOD1 and C9ORF72 mutations.

Disclosure: Nothing to disclose

PR2045

Metabolic correlates of ApoE genotype in ALS: A 18FDG-PET study

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Background and aims: The presence of the ε2 allele of ApoE lowers the risk and delays the onset of Alzheimer's disease (AD), while the ε4 isoform increases the risk of dementia by ～3-fold in heterozygous carriers and 12-fold in homozygous carriers. Conversely, we found in a population-based ALS series, collected through the Piemonte and Valle d'Aosta Register for ALS, that ε2 allele provides an increased risk of FTD in ALS patients. In the present study we aimed at evaluating the metabolic correlates of the ApoE genotype in ALS patients.
Methods: The ApoE genotype (from ε2/ε2 to ε4/ε3) was regressed in 159 ALS patients against whole brain metabolism as assessed by 18FDG-PET. SPM8 Multiple Regression routine was implemented with age, sex, education and type of onset as covariates. Statistical significance threshold was set at $p < 0.005$ uncorrected.
Results: Higher metabolism positively correlated with ε2-lacking ApoE genotype in the followiong brain regions: bilateral frontal, prefrontal, orbitofrontal and anterior cingulate cortices as well as in the right thalamus. We found no significant negative correlation.
Conclusion: The presence of ε2 alleles in ALS patients was associated with a lower 18FDG uptake in brain areas tipically affected when a comorbid cognitive impairment is present. These data are in agreement with our previous report of a role of the ε2 isoform of ApoE in increasing the risk of frontal cognitive deficits in ALS patients.
Disclosure: Nothing to disclose

PR2046

Bulbar lateral amyotrophic sclerosis and progressive supranuclear palsy: Unusual association

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Background and aims: We describe a 75-year-old man with Lateral Amyotrophic Sclerosis (ALS) and Progressive Supranuclear palsy (PSP).
Methods: At age 69 the patient began to complain dysarthria and dysphagia and he presented to our tertiary ALS Centre. Familial and remote histories were negative for neurodegenerative diseases. Neurological examination showed dysarthria and dysphagia, tongue's fasciculation, bilateral Babinski sign and accentuated primitive reflexes. Muscular strength, trophism and tone were normal. Electromyography showed fasciculations in bulbar, cervical and lumbar districts. Transcranial magnetic stimulation showed a delay of the central conduction time both in upper and lower limbs. Brain Magnetic Resonance (MRI) was no remarkable. Neuropsychological evaluation showed an intact cognitive functioning. Genetic tests showed no mutations of FUS/TDP-43/SOD/GNR/C9orf72 genes. We diagnosed a sporadic ALS with bulbar onset. Two years later motor neuron symptoms were slightly worsen; neuropsychological exam demonstrated executive dysfunctions.
Results: Three years after diagnosis the patient complained postural instability with a propensity to fall. Clinical examination showed vertical supranuclear gaze palsy and axial and limbs rigidity, non responsive to L-Dopa treatment. MRI disclosed mild cortical, midbrain and mesencephalic atrophy, configuring the typical 'humming-bird' and 'morning glory' signs. The DTI sequences showed atrophy of corticospinal tract.
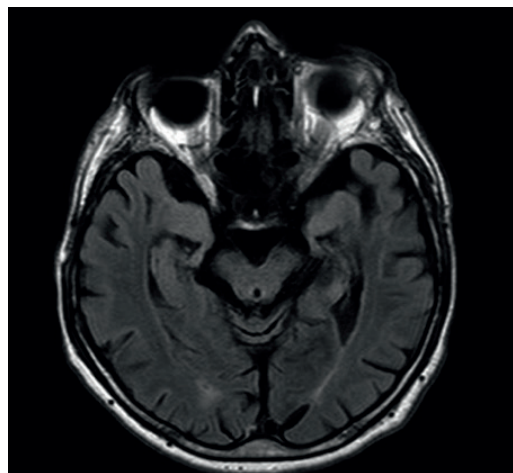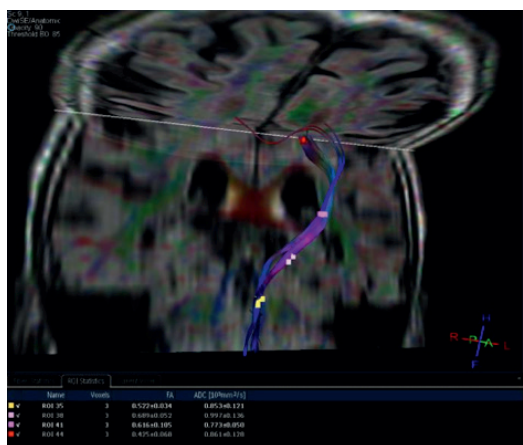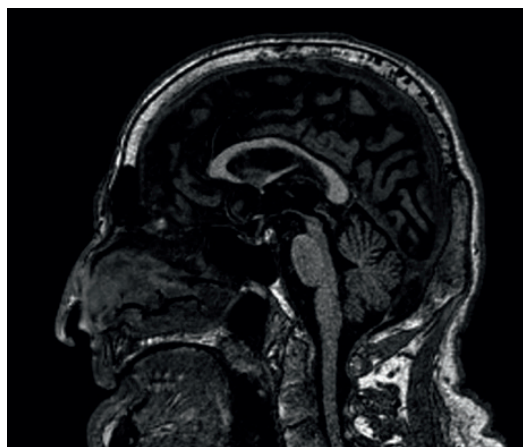
Conclusion: We believe our patient suffered from a defined MND and probable PSP, respectively in accordance with El Escorial and NINDS-SPSP Clinical Criteria. Although associations between ALS and other neurodegenerative disorders (FTD, parkinsonism-dementia complex) have been previously described, the coexistence of ALS and PSP is extremely uncommon and our patient is the first case of bulbar ALS and PSP.

Disclosure: Nothing to disclose

PR2047

Motor neurone disease in Sub-Sahara Africa: Case series from a Tanzanian referral hospital

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Background and aims: Motor Neurone Disease (MND) is a class of rare neurodegenerative disorders with largely unraveled aetiology. The clinical characteristics and distribution patterns of MND across Sub-Sahara Africa are basically unknown. One of the reasons is the historically determined emphasis on communicable disease research, leaving many non-communicable disease patterns in Sub-Sahara Africa to be elucidated.

Methods: We describe a series of MND patients from a tertiary referral centre in the United Republic of Tanzania. Amyotrophic Lateral Sclerosis cases had to be rated according to the original El Escorial criteria (Brooks 1994 without electromyography), as to date an EMG facility is unavailable in the research setting.

Results: A total of 116 patients with suspected MND (72 male, 44 female) were enrolled. ALS constituted 74% of the classified study population, likewise PBP 4%, PMA 15%, PLS 5% and Flail Arm/Leg 2% (n=113). In 52 of MND suspected patients, comprehensive clinical data were available: 42 patients were suspected of ALS (81%), eight patients PSMA (15%), and two patients the Flail Arm/Leg presentation (4%). Of 42 ALS-suspected patients, 18 (43%) could be classified as 'Definite ALS', another 18 patients (43%) as 'Probable ALS', and 6 patients (14%) as 'Possible ALS'. For 24 patients, HIV status was known: four patients were positive (17%) and the other 20 were negative (83%). Of these four HIV positive patients with ALS, three were 'Definite ALS' and one 'Probable ALS'.

Conclusion: This study shows that MND and all its subtypes occurs in Sub-Sahara Africa. Furthermore, HIV infection was more common in ALS patients.

Disclosure: Nothing to disclose

PR2048

Association between alcohol consumption and risk of ALS in the Euro-MOTOR case-control study

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Background and aims: Several studies reported an association between alcohol consumption and ALS, although findings remain inconsistent. The aim of this study is to evaluate this association through an international population-based case-control study performed in Ireland, The Netherlands and Italy.

Methods: Euro-MOTOR is a case-control study where incident ALS patients and controls matched by gender, age and area of residency were recruited in a population-based design. Logistic regression models adjusted for sex, age, cohort, education, leisure time physical activity and smoking were performed. All exposures were truncated at 3 years before date of survey, for both cases and controls.

Results: 1,557 ALS patients and 2,922 controls were enrolled in the study. Ever exposed to alcohol drinking, and red wine consumption in particular, were not significantly associated with ALS risk. A stratified analysis of ever exposed to alcohol by cohort revealed significant ORs in The Netherland and in Apulia, with opposite directions (respectively 0.58 and 2.44). With regard to red wine consumption, only in Apulia the high OR remained significant (the red wine consumption in this region represented 95% of total alcohol exposure). A significant decreased risks were found only for current alcohol drinkers (OR=0.80) in respect of never drinking people. Analysis of cumulative exposure to alcohol revealed significant decreased ALS risk only in the second quartile for both general alcohol (OR=0.74) and red wine (OR=0.76) intake.

Conclusion: The study showed conflicting results across countries, probably due to different socio-cultural environments and alcohol consumption habits between the three countries.

Disclosure: Nothing to disclose

PR2049

The protective role of diabetes on developing amyotrophic lateral sclerosis

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Background and aims: The literature on the association between diabetes and Amyotrophic Lateral Sclerosis (ALS) produced contrasting results. This study was developed in order to assess the role of diabetes on the risk of developing ALS.

Methods: The study population was represented by all residents in Turin (Italy) in 1995, already present at 1991 Census, older than 14 years (n=752,863), followed up for diabetes and ALS occurrence from 1996 to 2014. Presence of diabetes was ascertained through two Piedmont regional sources: the Diabetes Registry and the Drugs Prescriptions Archive, both active or of acceptable quality from 1996. The risk of ALS was estimated using the Piedmont and Valle d'Aosta ALS Registry (PARALS). The association of diabetes and antidiabetic drugs, considered as time-dependent variables, with ALS onset was estimated through Huber-White sandwich multivariate Poisson regression models adjusted for age, gender, education and marital status.

Results: During the follow-up, 447 subjects developed ALS, of whom 14 from the diabetes registry and 22 from antidiabetic drugs archive. Both diabetes diagnosed, and antidiabetic drugs prescribed, more than one year before ALS onset, approximately halved the risk of ALS. Among antidiabetic drugs, the association between ALS and metformin, which was the most prescribed drug, was similar to the risk estimated for overall antidiabetics.

Conclusion: The study results support a protective role of diabetes or antidiabetics toward ALS.

Disclosure: Nothing to disclose

PR2050

Dysregulation of miRNA expression in ALS induced pluripotent stem-cells-derived motor neurons

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Background and aims: Amyotrophic lateral sclerosis (ALS) is a fatal disorder characterized by progressive degeneration of motor neurons (MNs). Although the role of alterations in RNA metabolism has been increasingly recognized, the pathogenic mechanisms of the disease are almost unknown. According to previous studies, ALS-linked genes can affect microRNA (miRNA) processing and expression. MiRNAs are tissue-specific small molecules that regulate several biological processes and that may play an important role in the aetiology or progression of neurodegenerative disorders. The aim of this work is to test the hypothesis that altered expression of miRNAs is specifically present in ALS-MNs.

Methods: Thus, we investigated miRNA profile in induced pluripotent stem cells (iPSCs)-derived MNs of patients affected by sporadic and familial ALS, as compared to controls. We performed next generation sequencing (NGS) analysis of ALS-MNs in order to identify pathological alterations in miRNA expression profiles which were not found in the controls. Then, to assess the dysregulation in miRNA processing, we performed proteomic analysis on factors related to miRNA biogenesis, such as Drosha, Dicer and AGO2 proteins.

Results: We observed a decreased expression of 20 miRNAs in patients' cells, suggesting the presence of a global down-regulation of miRNAs in ALS. Through bioinformatic analyses, 278 target genes associated with miRNA downregulation were identified in ALS patients and gene expression analysis was performed to detect the molecular pathways in which they are involved.

Conclusion: Our findings suggest that dysregulation of miRNAs might play an important role in the MN degeneration. Moreover, miRNA biogenesis machinery may represent a therapeutic target for ALS.

Disclosure: Nothing to disclose

Movement disorders 4

PR2051

White matter tract alterations in Parkinson's disease patients with punding

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Background and aims: Punding is a peculiar behavioral phenomenon that affects about 7% of patients with Parkinson's disease (PD) and presents as an intense fascination with a complex, excessive, non-goal oriented and repetitive activity. Microstructural white matter (WM) abnormalities of sensorimotor and extramotor brain regions have been observed in early and cognitively normal PD patients, and in PD patients with cognitive impairment. In this study, we aimed at identifying patterns of microstructural WM changes in patients with PD-punding compared to matched PD patients without any impulsive-control behaviour (ICB) and healthy controls.
Methods: Forty-nine PD patients (21 PD-punding) and 28 controls underwent diffusion tensor MRI. Diffusion tensor MRI metrics of the main white matter tracts were assessed using a probabilistic tractography approach.
Results: Compared with controls, each PD group showed white matter microstructural alterations of the left pedunculopontine tract. PD-punding patients showed a further damage to the right pedunculopontine tract and uncinate fasciculus, genu of the corpus callosum, and left parahippocampal tract. On the other hand, relative to controls, PD no-ICB patients showed an increased mean diffusivity of the splenium of the corpus callosum.
Conclusion: PD-punding is associated with a disconnection between midbrain, limbic and white matter tracts projecting to the frontal cortices. These alterations may reflect repetitive behavior despite the lack reward which is typical of PD-punding patients. Diffusion tensor MRI is powerful in understanding the neural substrates underlying punding in PD.
Disclosure: Ministry of Education and Science Republic of Serbia (Grant #175090).

PR2052

Development of an apparatus for the quantitative assessment of pull test in Parkinson's disease

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Background and aims: Pull test is generally used for the assessment of postural instability in Parkinson's disease. However, pull test is a qualitative measurement and lacks objectivity. We planned to develop an apparatus for quantitative assessment of pull test in Parkinson's disease. In the present study, we applied this newly developed apparatus to healthy subjects.
Methods: Ten adult healthy men (23±3.7 y.o.) participated in the experiment. The subject was worn a vest, in which a lope was connected at the back. A basket was attached at the other end of the lope. By putting a heavy bob into the basket, the subject at standing position was pulled backwards unexpectedly (see Figure). A minimal weight for inducing stepping reaction (MWS) was measured. During the experiment, EMGs of both tibialis anterior muscle (TA) and soleus muscle (SOL) were recorded. All the experiment process was recorded with a video camera.
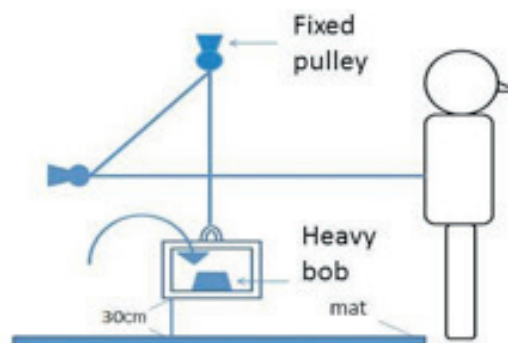
Results: All stepping reactions of the subjects were performed with right leg. Mean MWS was 1.73±0.73 kg. There was no statistical correlation between MWS and physical data obtained from the subjects (height, weight, foot size, etc.). In the experiment of MWS, the latency of EMGs in right and left TA were 85±19 msec and 93±36 msec, respectively. Integral amounts of EMG activity in both left and right TA were significantly correlated with MWS.
Conclusion: We were able to develop an apparatus and method for making a quantitative assessment of severity of postural instability in Parkinson's disease.
Disclosure: JSPS KAKENHI Grant (Grant-in-Aid for Scientific Research C) Number JP16K01510.

PR2053

Treat iron-related childhood-onset neurodegeneration (TIRCON) work package 1: International patient registry for Neurodegeneration with Brain Iron Accumulation (NBIA)

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Background and aims: NBIA is a group of rare genetic disorders characterized by progressive dystonia and pathologically increased iron levels in the brain. By the end of 2011, TIRCON (Treat Iron-Related Childhood-Onset Neurodegeneration) has been formed as an international consortium to improve medical care, explore therapeutic options and foster research in NBIA. Here we report results from TIRCON`s international registry, currently comprising 326 patients with genetically confirmed or clinically suspected NBIA.

Methods: The TIRCON registry has been designed as a multicenter, prospective, both cross-sectional and longitudinal study. Follow-up visits are scheduled on a yearly basis or as appropriate. Besides standard demographic data, several scales have been used to assess motor function (Barry–Albright Dystonia Scale, UPDRS Part III), activities of daily living (FIM), and quality of life (PedsQL). Data were analyzed using methods of descriptive statistics.

Results: Of the 326 patients, the largest subgroups were genetically established or clinically suspected Pantothenate kinase-associated neurodegeneration (PKAN, n=190) and Mitochondrial-membrane Protein-Associated Neurodegeneration (MPAN, n=48). The most frequent symptoms were gait disturbance (90.4%), swallowing problems (69.0%), cognitive impairment (57.2%), and dystonia (53.2%).

Conclusion: Here we present first results on genotype-phenotype correlations from the TIRCON registry. In a next step, the registry will be of great benefit to retrieve quantitative data on the longitudinal course of NBIA disorders. Moreover, the registry will be pivotal to design clinical trials and to facilitate recruitment.

PR2054

Double-blind, randomised, placebo-controlled study (TOLEDO) to evaluate the efficacy of apomorphine infusion in reducing OFF time in Parkinson's disease patients with motor fluctuations

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Background and aims: Open-label studies demonstrate that apomorphine infusion (APO) is effective in reducing OFF time, dyskinesias and levodopa dose in Parkinson's disease (PD) patients with severe motor fluctuations poorly controlled by conventional therapy but data from randomised, controlled studies are lacking. TOLEDO (NCT02006121) is the first prospective, randomised, controlled trial to investigate the efficacy of APO versus placebo in such patients.

Methods: Patients from 23 centres in 7 countries were randomised to receive APO during their waking time (16±2 hours) or placebo saline infusion using the same pump system for 12 weeks. Based on efficacy and tolerability, the infusion dose and concomitant oral treatment were adjusted during the first 4 weeks. The primary endpoint was the absolute change in OFF time based on patient diaries.

Results: Compared with placebo (n=53), APO (n=53) provided significantly greater reduction in OFF time between baseline (BL) and week 12 APO and a significantly greater improvement in ON time without troublesome dyskinesia (Table). The proportion of patients who responded to therapy, defined as ≥2 hours OFF time reduction from BL was significantly higher for APO than placebo at each visit. The beneficial effects of APO were reflected in the scores for Patient Global Impression of Change, which significantly favoured APO (Figure). APO was generally well tolerated with no unexpected adverse effects detected.

Change from baseline to Week 12	APO (n=53)	Placebo (n=53)	Treatment difference (95% CI)	p-value
Primary endpoint				
Absolute change in time spent OFF (hours/day), based on patient diaries	-2.47	-0.58	-1.89 (-3.16, -0.62)	0.0025
Pre-specified secondary endpoints				
Absolute change in time spent ON without troublesome dyskinesia (hours/day)	2.77	0.8	1.97 (0.7, 3.23)	0.0008
Number (%) of patients with response to therapy (OFF time reduction of ≥2 hours)	33 (62.3%)	15 (28.8%)	33.4% (15.48, 51.36)	0.0008

Table: Change from baseline to week 12 in primary and secondary endpoint parameters.
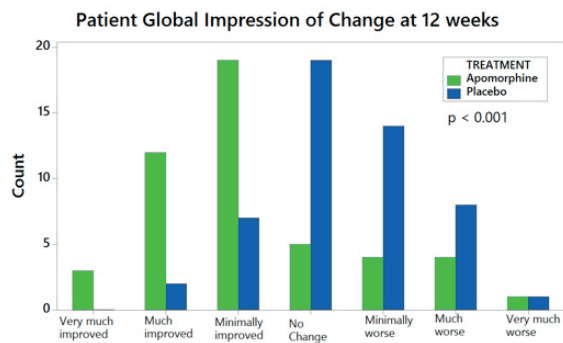
Figure: Patient Global Impression of Change at 12 weeks.

Conclusion: These results provide Level 1 evidence confirming the efficacy of APO for OFF time reduction and support its wider use in PD patients with a high need for effective treatment for motor fluctuations.

Disclosure: The TOLEDO Study was sponsored by Britannia Pharmaceuticals Ltd

PR2055

Non-motor and neuropsychological features of p.A53T α-synuclein mutation carriers compared to sporadic Parkinson's disease in a PPMI cohort.

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Background and aims: To evaluate the prevalence of non-motor symptoms in p.A53T α-synuclein (SNCA)-related PD patients as compared to sporadic PD (sPD) patients.

Methods: Non-motor symptoms were assessed in N=18 p.A53T SNCA-related PD patients, who participated in the Parkinson's Progression Markers Initiative (PPMI) by standardized questionnaires and validated scales (University of Pennsylvania Smell Identification Test [UPSIT], REM sleep questionnaire, Epworth sleepiness scale, SCOPA-AUT scale of autonomic dysfunction, Geriatric depression scale, PD Impulsive-Compulsive Disorders Questionnaire [QUIP]). The Montreal Cognitive Assessment (MoCA), the Hopkins Verbal learning test (HVLT), the Benton Judgement of Line Orientation test, the Letter Number Sequencing test (LNST), the Symbol digit Modalities test (SDMT) and semantic/phonemic verbal fluency assessment were administered. Data from the PPMI database from 18 age-, gender-, disease duration- and education-matched sPD patients were compared to the p.A53T-patients.

Results: UPSIT score in p.A53T related-PD was lower (p=0.001) and QUIP score was higher (p=0.002) compared to sPD. The frequency of depression, REM sleep behavior disorder, daytime sleepiness and dysautonomic symptoms, were not significantly different. The p.A53T-PD group presented lower scores in HVLT immediate recall (p=0.026), Benton test (p=0.001), LNST (p=0.002), SDMT (p=0.018) and semantic (p=0.043) or phonemic verbal fluency (p=0.002). No significant differences could be noted in the overall MoCa score, HVLT delayed recall and recognition.

Conclusion: The observed impairments in working memory, processing speed and visuospatial skills may reflect a selective cognitive dysregulation in PD patients carrying the p.A53T mutation as compared to sporadic PD patients.

Disclosure: This study has received funding from the Michael J. Fox Foundation (PPMI study).

PR2056

Caudate nucleus dopaminergic denervation is not correlated to neuropsychological assessment scores in a PPMI cohort of symptomatic p.A53T α-synuclein mutation carriers.

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Background and aims: The objective of this study was to assess striatal dopaminergic denervation in p.A53T α-synuclein (SNCA)-related PD patients as compared to sporadic PD (sPD) patients and to evaluate the neuropsychological features of each cohort.

Methods: DaTSCAN SPECT imaging binding rations and neuropsychological assessments from the Parkinson's Progression Markers Initiative (PPMI) database of 7 symptomatic p.A53T SNCA mutation carriers who underwent DaTSCAN at our site, were compared to those of 21 age-, gender- , disease duration- and education-matched sPD patients . The Montreal Cognitive Assessment (MoCA), the Hopkins Verbal learning test (HVLT), the Benton Judgement of Line Orientation test, the Letter Number Sequencing test (LNST), the Symbol digit Modalities test (SDMT) and semantic/phonemic verbal fluency assessment were administered.

Results: p.A53T mutation carriers had significantly lower left caudate nucleus binding ratio (p=0.01) and caudate / putamen signal ratio (Right side p=0.028, Left side p=0.018) as compared to sPD. The p.A53T-PD group presented lower scores in Benton test (p=0.045), LNST (p=0.001), SDMT (p=0.011) and phonemic verbal fluency (p=0.047). There was no significant positive correlation between DaTSCAN caudate nucleus binding ratios and neuropsychological tests scores in neither group.

Conclusion: PD patients harboring the p.A53T SNCA mutation show evidence of a more severe, albeit variable, dopaminergic nigrostriatal denervation, mainly involving the caudate nucleus. Although scores in certain neuropsychological tests were inferior in the p.A53T-PD cohort, no firm correlation between such scores and caudate nucleus dopaminergic denervation could be demonstrated.

Disclosure: This study was funded by the Michael J. Fox Foundation (PPMI study).

PR2057

Tremor characteristics in patients with cerebellar and/or brainstem lesions

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Background and aims: Cerebellar tremor is a generally accepted term for a slow, frequently irregular, intentional and/or postural tremor of usually less than 3-4 Hz frequency caused by a cerebellar lesion. In the literature there are only scarce data on quantitative parameters of such tremor. The aim of our study was to quantitatively characterise tremor in patients with cerebellar and/or brainstem lesions in different locations, and to assess their recovery.

Methods: 116 patients with cerebellar/brainstem lesions proved by MRI/CT were investigated. 36 patients were excluded because of concomitant diseases/drugs that might induce tremor. Tremor was recorded with biaxial accelerometry in resting-postural-intentional position. Affected CNS structures were identified on MRI scans by a neuroradiologist. Patients were divided into subgroups according to the location and pathomechanism of their lesion. 9 patients were followed-up for several months.

Results: None of the 80 patients had pathologic tremor at rest. 16/80 patients (27%) had pathologic postural±intentional tremor with low intensity, pathologic frequency dispersion and center frequency around 2 Hz, ipsilateral to the lesion. Isolated lesions affecting the same structure resulted in different tremor characteristics. All tremulous patients suffered from acute stroke/MS-shub/ malign tumour. Mesencephalon lesions did not affect tremor frequency but increased intensity. In 9 followed-up patients tremor became normal in 4-6 weeks.
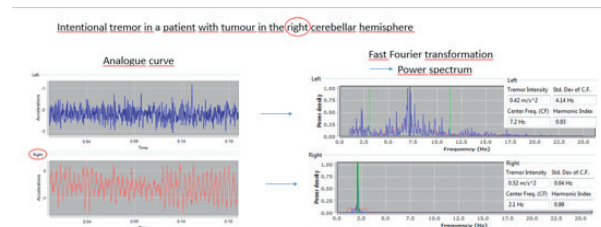
Typical curve of cerebellar tremor

Recovery of postural (PT) and intentional tremor (IT) in patients with cerebellar and/or brainstem lesions
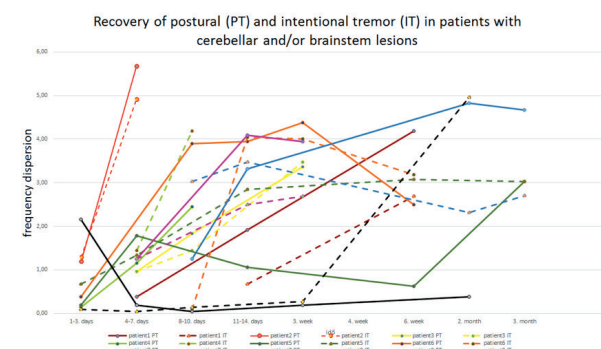
Tremor recovery

Conclusion: Tremor caused by acute cerebellar lesion has low intensity and a center frequency of about 2 Hz. We could not identify a specific structure which is responsible for cerebellar tremor generation. In contrast with tremor syndromes caused by neurodegenerative disorders, cerebellar tremor recovers in 4-6 weeks.

Disclosure: Nothing to disclose

PR2058

Increase of ghrelin levels after bilateral subthalamic nucleus deep brain stimulation in Parkinson's disease

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Background and aims: It is well known that deep brain stimulation of subthalamic nucleus (STN DBS) improves motor function in advanced Parkinson's Disease (PD). Recent studies have reported rapid weight gain in patients who underwent STN DBS. This phenomenon has been hypothesized to be linked with the bi-directional communication that occurs along the gut/brain axis and potential changes of hormone ghrelin signaling. The aim of this study was to evaluate the effect of STN DBS on plasma ghrelin levels.

Methods: Blood samples were collected from fasted 13 PD patients, with disease duration ranging from 5 to 22 years, before and 3 months after STN DBS implantation, and from 19 healthy controls. Patients and controls were fasting at least 12 hours. The levels of ghrelin in plasma were measured according to ELISA method. Ghrelin plasma levels were compared in the PD patients before and after surgery, and with healthy controls.

Results: Significant differences in fasting plasma ghrelin levels were found between the PD patients before and after STN DBS (mean: 173.8±62.1 pg/ml vs mean: 207.5 ±68 pg/ml, respectively) (p<0.0001), between healthy controls (mean: 260.30±87.83pg/ml) and the PD patients before DBS (p<0.001) and between healthy controls and PD patients after DBS (p<0.05).

Conclusion: This study has shown an increase of ghrelin levels in plasma 3 months after STN DBS. Further studies are warranted in order to assess the effect of STN DBS on changes of ghrelin and the role of ghrelin in the gut/brain hormonal axis.

Disclosure: Nothing to disclose

PR2059

Gut microbiota is associated with motor manifestations of Parkinson's disease

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Background and aims: Parkinson's disease (PD) - is a neurodegenerative disorder with a complex pathogenesis. Gastrointestinal tract is thought to be one of the first systems being involved, with an evidence of constipation that manifests decades before motor symptoms. One of possible reasons for intestinal dysfunction is change in gut microbiota, that has widespread modulatory influence and might trigger the neuropathologic process.

The aim was to determine the relationship between the composition of the intestinal microbiota and clinical manifestations of PD.

Methods: We examined 89 patients with a diagnosis of PD. Median age was 69 years (64; 67). Motor and nonmotor symptoms were examined using the UPDRS and Hoehn and Yahr scale. Fecal samples were collected; isolation of DNA was performed. Preparation of libraries and amplicon sequencing of bacterial 16S rRNA genes was performed on MiSeq device (Illumina). Filtering readings by quality and their taxonomic classification were carried out using QIIME version 1.9.0 software. Statistical analysis was done using IBM SPSS Statistics 23.1 software.

Results: We identified significant differences in the abundance of 7 bacterial genera between patients with different motor subtypes of the disease. Significant differences in alpha-diversity between patients with akinetic-rigid and mixed subtypes were evident - the richness of gut microbiome community was relatively diminished in akinetic-rigid subtype. About 40 genera (constituting 54.8% of the intestinal microbiota) demonstrated correlations with clinical manifestations of the disease.

Conclusion: These microorganisms might be involved in the pathogenesis of PD and require more research, considering potential methods of altering microbiome composition to improve disease management and outcome.

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PR2060

Primary familial brain calcifications: Results from a monocentric study and a novel XPR1 mutation

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Main clinical presentation at onset of patients with PFBC

Background and aims: Primary familial brain calcifications (PFBC), previously known as Fahr disease, is characterized by calcium deposition in basal ganglia, dentate nuclei and subcortical white matter. Clinical presentation includes parkinsonism, dementia or psychiatric disturbances. Four causative genes (SLC20A2, PDGFB, PDGFRB, XPR1) have been discovered so far. To analyze the clinical, radiological and genetic spectrum of a group of patients with PFBC and report on a novel XPR1 mutation.

Methods: All brain CT scans of in- and outpatients patients referred to the Neurology Department of Maggiore Hospital, Novara between 2008 and 2016 and consistent with PFBC, according to Nicolas et al (Brain 2013) were reviewed . Clinical data of patients were collected. Secondary causes of PFBC were ruled out and subsequent genetic analyses performed.

Results: About 13,000 cerebral CT were reviewed. 28 (0.2%) were consistent with PFBC, of which 8 were due to secondary causes (especially hypoparathyroidism). 20 patients underwent genetic analyses with NGS revealing in 7 of them (35%) mutations in PDGFRB (5%) (c.676C>T), SLC20A2 (25%) (c.1765G>A; c.1463A>G; IVS-8 A>G; c.338C>G) and XPR1 (10%) (c.697A>T in two unrelated patients). Clinical and radiological data are summarized in table 1.

Conclusion: PFBC represents a rare genetic condition. Aside from movement disorders, cognitive impairment and psychiatric symptoms, nonspecific symptoms can be present. We identified a novel mutation in XPR1 (c.697A>T) in two unrelated patients with different clinical presentation (mild cognitive impairment and vertigo). The negative results in about 70% of our cases indicates that other genes may be involved in PFBC pathogenesis.

Disclosure: Nothing to disclose

	SLC20A2				
Pt no.	Current age	Mutation	Family history	Symptoms at onset	CT calcification distribution
1	82	c.1765G>A	Positive	Visual hallucinations	Lenticular and dentate nuclei
2	61	c.1463A>G	Negative	Memory deficits	Globi pallidi
3	69	IVS-8 A>G	Negative	Parkinsonism	Lenticular and dentate nuclei
4	66	c.338C>G	Negative	Focal chorea (hand)	Putamen, thalamus, caudate and lenticular nuclei
	PDGFRB				
1	32	c.676C>T	Negative	Paroxysmal kinesigenic dystonia	Caudate, lenticular nuclei, thalamus and dentate nuclei
	XPR1				
1	82	(c.697A>T)	Negative	Mild cognitive impairment	Lenticular nuclei
2	49	(c.697A>T)	Negative	Vertigo	Lenticular nuclei

Anamnestic, clinical, radiological and genetic data of patients with genetically determined PFBC

PR2061

Longitudinal cortical thickness changes in GBA-positive relative to GBA-negative Parkinson's disease patients with hemiparkinsonism

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Background and aims: Glucocerebrosidase gene (GBA) mutations are the greatest genetic cause of Parkinson's disease (PD). Compared with noncarriers, heterozygous GBA-PD patients are characterized by an earlier age-of-onset, a better response to L-Dopa and an increased likelihood to experience cognitive symptoms, neuropsychiatric disturbances, and autonomic dysfunction. This study investigated the longitudinal changes of the cortical grey matter in PD patients with hemiparkinsonism, with (GBA-positive) and without (GBA-negative) GBA mutations.

Methods: Eleven GBA-positive PD patients with hemiparkinsonism (Hoehn and Yahr 1.0 or 1.5) were compared with 24 GBA-negative PD patients matched for age, sex, disease duration and severity. Patients underwent clinical and neuropsychological evaluations and MRI scans at baseline and once a year for 3 years. 25 healthy controls underwent evaluations at baseline. The pattern of cortical thinning was investigated in PD patients relative to healthy controls at baseline. Longitudinal cortical changes were assessed in the GBA-positive and GBA-negative PD patients.

Results: At baseline, GBA-positive PD patients showed a greater left side predominant cortical atrophy in motor, frontal, temporal and occipital areas relative to both healthy controls and GBA-negative subjects matched for disease duration and severity. Overtime, the GBA-negative group showed a higher rate of cortical thinning relative to GBA-positive patients; however, the pattern of cortical thinning in GBA-negative cases did not reach the severity shown by GBA-positive patients after 3 years.

Conclusion: GBA-positive PD patients showed a greater and earlier cortical thinning relative to GBA-negative cases with the same disease duration and severity.

Disclosure: Ministry of Education and Science Republic of Serbia (Grant #175090).

PR2062

Longitudinal cortical thickness changes in early Parkinson's disease patients with impulsive compulsive behaviors

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Background and aims: Numerous cross-sectional studies showed that occurrence of impulsive-compulsive behaviors (ICBs) in Parkinson's disease (PD) is related to subtle changes in fronto-striatal and mesolimbic circuits. This study evaluated longitudinal changes of the cortical grey matter in very early PD patients with ICBs.

Methods: We included 110 patients in the initial stage of PD (Hoehn Yahr 1-1.5) which were followed-up regularly each year, clinically and neuropsychologically and with brain MRI. Twenty patients were diagnosed with at least one ICB on the initial exam or during follow-up (PD-ICB). From the initial cohort we matched 35 patients who did not develop ICBs (PD-noICB) for age, education, motor severity and cognitive status. We assessed cortical thickness in PD patients relative to 35 healthy controls at baseline. Pattern of longitudinal cortical thinning was assessed in PD-ICB and PD-noICB.

Results: At baseline, we did not show significant differences between patients' groups and controls. Over time, both PD-ICB and PD-noICB patients showed widespread cortical thinning involving temporal, parietal and frontal regions, more prominent to the left. When analyzing the interaction of group effect over time, significant cortical thinning in PD-ICB group relative to PD-noICB was shown in medial orbitofrontal region of the right hemisphere, and additionally few smaller clusters in rostral middle frontal and superior frontal regions of the right hemisphere.

Conclusion: Our data suggest importance of damage to the regions involved in inhibitory control for the development of ICBs in PD; specifically of the right orbitofrontal region.

Disclosure: Ministry of Education and Science Republic of Serbia (Grant #175090).

PR2063

Affective disorders and microbiome in patients with Parkinson's disease

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Background and aims: Affective disorders are significant part of nonmotor manifestations of Parkinson's disease (PD) that have a pronounced negative impact on quality of life. Extensive studies are performed in the field of microbiota influence on the mood and anxiety. However, data concerning association of microbiota composition and the spectrum of affective dysfunction in PD is scarce.

The aim is to study taxonomic diversity of the gut microbiota in PD patients with different levels of anxiety and depression.

Methods: 51 patient with PD participated in the study. The mean age was 69.5 ± 8.6 years. Affective state was studied using Beck's Depression Inventory (BDI) and the Hospital Anxiety and Depression Scale (HADS). Assessment of the microbiota composition in fecal samples was performed using bacterial 16s rRNA sequencing, bioinformatics and statistical analysis.

Results: Alpha-diversity of gut microbiota in patients with mild anxiety was higher than in patients without evident anxiety (52.14 ± 3.59 and 47.85 ± 6.89 respectively; $T=2.35; p<0.05$). The alpha-diversity index was highest in patients with mild anxiety and was decreasing in patients with moderate to severe levels (52.14 ± 3.59 and 48.26 ± 4.33 respectively; $T=2.29; p<0.05$). Gut microbiome of patients with moderate to severe anxiety was characterized by higher prevalence of Clostridium clariflavum when compared to patients with normal levels of anxiety. Patients with moderate depression were characterized by significantly higher abundance of Christensenella minuta, Clostridium disporicum and Oscillibacter valericigenes than patients with mild depression or with normal scores.

Conclusion: Our findings show that significant differences in microbial diversity and the abundance of certain species exist between patients with different levels of anxiety and depression.

PR2064

MRI guided focused ultrasound for movement disorders: A report of 50 consecutive cases in a single center

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Background and aims: VIM Thalamotomy is effective in alleviating medication resistant tremor. MRI guided focused ultrasound (MRgFUS) is an innovative technology that enables thalamotomy via thermal ablation through an intact skull.

Methods: Patients with severe medication resistant tremor underwent unilateral VIM thalamotomy using MRgFUS. Effects on tremor in essential tremor (ET) patients were evaluated by the Clinical Rating Scale for Tremor (CRST), in Parkinson's disease (PD), ET-PD (ET patients which developed PD years later) and MSA by the Unified PD Rating Scale (UPDRS). Quality of life was measured by the Quality of Life in ET Questionnaire (QUEST) and by the PD Questionnaire (PDQ-39).

Results: Fifty patients, 26 ET, 20 PD, 3 ET-PD and 1 MSA patient underwent MRgFUS. Mean age was 67.7 ± 8.6 years (range, 46-87). Tremor stopped in the treated arm in all patient immediately following treatment. Co-existing head, chin and leg tremor improved as well. At one month post-treatment, ET patients' CRST score decreased from 38.9 ± 11.3 to 9.6 ± 8.1 ($p<0.001$) and QUEST scores decreased from 45.9 ± 17.4 to 14.1 ± 19.8 ($p<0.001$). In PD patients UPDRS-motor part decreased from 26.6 ± 8.1 to 15.9 ± 10.2 ($p=0.009$) and PDQ39 decreased from 42.1 ± 17.7 to 27.0 ± 13.5 ($p=0.008$). During follow up tremor reappeared in ten patients (3 ET, 4 PD, 2 ET-PD and 1 MSA patients). Adverse events included unsteady feeling, gait ataxia, unilateral taste disturbances and hand ataxia. that lasted up to 3 months.

Conclusion: MRgFUS VIM thalamotomy to relieve medication resistant tremor was safe and effective. Large randomized studies are needed to assess prolonged efficacy and safety.

Disclosure: Nothing to disclose

PR2065

Meta-analysis of mortality following Subthalamic and Pallidal deep brain stimulation for patients with Parkinson's disease

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Background and aims: Subthalamic nucleus (STN) and Globus Pallidus internus (GPi) are two common targets for the Deep Brain Stimulation (DBS) in Parkinson's disease. This meta-analysis aims at comparing mortality after STN DBS and GPi DBS for patients with advanced PD.

Methods: We searched PubMed through November, 2016 for prospective controlled studies comparing STN DBS and GPi DBS for PD patients. Records were screened and data of mortality were extracted from CONSORT flow diagrams or within the text. Mortality rates were pooled as risk ratio (RR) between the two groups in a fixed effect model meta-analysis. We introduced stratification analysis according to the follow up duration. Heterogeneity was measured by I-square and Chi-Square tests.

Results: Four studies (7 full text articles) were included in the final analysis with a total of 479 patients (STN 253 patients, and GPi 226 patients). Follow up duration ranged from 6 months in COMPARE trial to 6 years in the study of DBS group 2001. The overall risk ratio favored GPi DBS than STN DBS with RR 3.64 (95% CI [1.68 to 7.87], Figure 1). Stratification analysis showed a significant difference in mortality between the two groups in the subgroups beyond 3 years (Figure 2). Pooled studies were homogenous.

Conclusion: Death was more common after STN DBS than GPi DBS in PD patients. But most of death cases were due to postoperative complications and were not related directly to stimulation. Our results highlight the importance of considering postoperative complication while choosing surgical target for PD patients.

Figure 1 shows overall RR of mortality in the STN DBS vs. GPi DBS groups
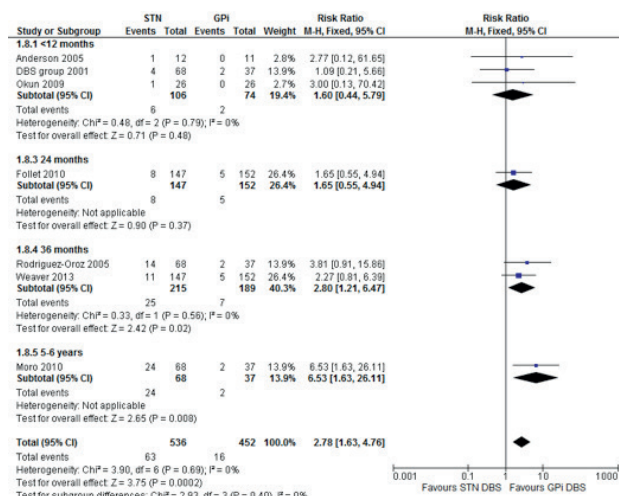
Figure 2 shows stratification analysis of the pooled RR of mortality rates according to the follow up duration

Disclosure: Nothing to disclose

PR2066

Differential responses in somatosensory and motor task-related functional imaging after initial and long-term botulinum toxin treatment in cervical dystonia patients

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Background and aims: Clinical effect of botulinum toxin (BoNT) on dystonia is assumed to be mediated by dynamic changes at multiple levels of the sensorimotor system, from the neuromuscular junction up to the cerebral cortex. It was reported mostly by studies using neurophysiological and imaging methods in focal dystonia. Although the first BoNT injection is effective, the clinical picture in cervical dystonia (CD) often changes during continuous BoNT treatment. This results in some cases in the need to change the BoNT injection pattern by clinicians. Aim of this study is to compare the response of sensorimotor networks to BoNT-A therapy in naïve and repeatedly-treated CD patients.

Methods: Six CD patients were examined with whole-brain functional MRI during electrical stimulation of the median nerve at the wrist and during a skilled hand motor task before and 4 weeks after the BoNT-A injection to the dystonic neck muscles. The first pair of these examinations was performed before and after the first BoNT-A injection. Next pair was performed in the same subjects after 5 years of regular and effective BoNT-A treatment.

Results: In electrical stimulation, effective BoNT-A treatment resulted in differential response to somatosensory

stimulation in the contralateral precentral and postcentral gyrus. The first BoNT-A injection led to activation increase in all subjects, whereas the activation decreased after BoNT-A injection in long-term treatment.

Conclusion: In agreement with sustained good clinical outcome, changes in hand motor related activation remained stable throughout the follow-up. However, differential response to electrical stimulation may reflect gradual changes in sensorimotor integration during continuous BoNT-A treatment.

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PR2067

In-vivo evaluation of tau and amyloid pathology in Corticobasal Syndrome

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Background and aims: To assess in-vivo, with molecular imaging the brain distribution of tau aggregates ([18F] AV1451 PET) and β-amyloid depositions ([18F]AV45 PET) in patients with Corticobasal Syndrome (CBS).

Methods: Six CBS patients (3M; mean age ±SD: 71.3±7.4 years; mean disease duration ±SD: 5.2±2.9 years) and 6 healthy controls (3M; mean age ±SD: 72.5±6.5 years) underwent one [18F]AV1451 PET, one [18F]AV45 PET scan and one 3-T MRI scan. Image processing was carried out using MIAKAT™. Standardised uptake value ratio (SUVR) were generated for [18F]AV1451 and [18F]AV45 relative to cerebellum grey matter.

Results: CBS patients showed 10-30% increases in cortical [18F]AV1451 uptake compared to the group of healthy controls consistent with increased tau deposition. In CBS patients, [18F]AV1451 SUVR were significantly increased in the medial frontal cortex (+10%; P<0.05), posterior medial frontal cortex (+13%; P<0.05), supplementary motor area (+21%; P<0.05), precentral gyrus (+17%; P<0.05), parietal lobe (+21%; P<0.05), parietal lobule (+30%; P<0.01), postcentral gyrus (+17%; P P<0.05), precuneous (+22%; P<0.05), cuneus (+22.2%; P<0.05), occipital fusiform gyrus (+26%; P<0.01) and lingual gyrus (+15%; P<0.05). Asymmetrical tau deposition with greater [18F]AV1451 retention contralateral to the most affected side was observed in CBS patients. Cortical and subcortical

[18F]AV45 uptake was within normal levels in CBS patients.

Conclusion: Cortical aggregates of tau pathology are present in CBS patients with low amyloid burden. PET imaging of tau aggregates can aid in early diagnosis of CBS before extensive neuronal loss and clinical symptoms become evident and can serve as an indicator of treatment efficacy.

Disclosure: Nothing to disclose

PR2068

Influence of onset age on the spectrum and progression of non-motor symptoms in Parkinson's disease: A prospective study from the Siberian region, Russia

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Background and aims: Non-motor symptoms (NMS) dominate in the clinical picture of Parkinson's disease (PD) contributing to severe disability, impaired life quality (QoL), shortened life expectancy. Little is known about their differences of progression between Young Onset PD (YOPD) and Late Onset PD (LOPD) patients [Chaudhuri K.R.,2014]. Analysis the influence of PD onset age on the spectrum and progression of NMS is needed.

Methods: 798 patients with PD (PwPD) are registered in movement disorders electronic database of the Siberian region. 236 non-demented PwPD were included (mean age: 66.3±5.8 years; PD mean duration: 6.7±5.4 years; H&Y stages 1–4, women:men=109:127) divided into two groups by progression motor manifestation (homogeneous by gender, stage): I–93 individual with PD diagnosed under 45 years (YOPD), II–143 LOPD. Clinical assessments were conducted using the UPDRS, H&Y Scale, MoCA-test, Beck depression inventory II, Hospital anxiety and Depression Scale, Apathy Scale, PD Sleep Scale, Epworth Sleepiness Scale, Questionnaire for Impulsive-Compulsive Disorders(ICDs) in PD–Rating Scale, Bristol stool scale, Scale for Outcomes in PD for Autonomic Symptoms, PDQ-39, Sniffing Stix Test.

Results: YOPD patients had higher frequency of ICDs, anxiety, low energy, sleepiness(p<0.05), LOPD patients had higher frequencies of cognitive impartment, depression, apathy, sleep disorders, perceptual problems/hallucinations, constipation(p<0.05). No significant differences were found in severity of psychotic symptoms (previous suicide attempt/thoughts), olfactory dysfunction, urinary problems, and between YOPD and LOPD patients in the annual severity change of each NMS.

Conclusion: PD onset age may be used as a predictive indicator for the symptomology and PD prognosis allowing selective treatment strategies.

Disclosure: Nothing to disclose

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PR2069

Diabetes mellitus and Parkinson's disease

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Background and aims: To investigate the association of type 2 diabetes mellitus (DM) with markers of Parkinson's pathology in patients with early de novo Parkinson's disease (PD).

Methods: Using the Parkinson's Progression Markers Initiative database, we performed a case-control study comparing PD patients with DM (PD-DM) to those without DM (PD). The two groups were matched for age, gender, disease duration and years of education. Diagnosis of DM was based on clinical history and confirmed by two consecutive measurement of serum glucose levels >126ml/dl. We investigated for associations and differences in motor and non-motor features, in molecular and structural imaging, and in cerebrospinal fluid (CSF) markers of PD pathology. Subsequently, we performed Cox proportional hazards analysis to investigate whether the presence of DM was predictive for PD progression over a 36-months follow-up period. To assist our conclusions, we also performed in parallel similar comparisons between controls with (C-DM) and without DM (HC).

Results: PD-DM patients had higher motor scores (p<0.01), lower striatal dopamine transporter binding (p<0.05), and higher tau CSF levels (p<0.05) compared to PD patients. C-DM also showed lower striatal dopamine transporter binding (p<0.05), and higher tau (p<0.05) and α-synuclein (p<0.05) CSF levels compared to HCs. DM was a predictor for worse motor progression (Hazard Ratio [HR]=4.521, 95% Confidence Interval [C.I.]=1.468–13.926; p<0.01) and worse cognitive decline (HR=9.314, 95% C.I.=1.164–74.519; p<0.05) in PD patients.

Conclusion: DM presence predisposes towards a PD-like pathology and when present in patients with PD is linked to a more aggressive phenotype.

Disclosure: Nothing to disclose

PR2070

Swallowing difficulties and Parkinson's disease

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Background and aims: Swallowing difficulties in Parkinson's disease (PD) have a multifactorial pathogenesis that has not been thoroughly elucidated. We investigated whether swallowing difficulties are associated with presynaptic dopaminergic deficits, distinct clinical phenotypes, CSF biomarkers as well as whether they can predict motor symptom progression and the development of cognitive impairment in early de novo PD patients.

Methods: Using the Parkinson's Progression Markers Initiative database, we included 398 early de novo PD patients in the analysis. Swallowing difficulties were evaluated using the Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale Part-II, Item 2.3 (Chewing and Swallowing). We investigated differences in striatal [123I]FP-CIT single photon emission computed tomography (SPECT) levels, motor and non-motor features and CSF biomarkers in early de novo PD patients with and without swallowing difficulties.

Results: The prevalence of swallowing difficulties in early de novo PD patients was 12.3% (49/398). PD patients with swallowing difficulties had significant lower [123I]FP-CIT uptakes in the striatum (P=0.016), caudate (P=0.008) compared to those without swallowing difficulties. The degree of swallowing impairment (MDS-UPDRS-II, item 2.3) and [123I]FP-CIT uptake in the striatum (rs=−0.157; P=0.002) and caudate (rs=−0.156; P=0.002) were significantly correlated. PD patients with swallowing difficulties have increased non-motor symptoms burden compared to those without swallowing difficulties.

Conclusion: Our findings demonstrate a close relationship between swallowing difficulties and presynaptic dopaminergic function in early de novo PD patients. Such patients, have a significant burden of non-motor symptomatology without prominent motor involvement.

Disclosure: Nothing to disclose

PR2071

Speech difficulties are linked to striatal dopaminergic deficits and cognitive decline in early de novo patients with Parkinson's disease

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Background and aims: The mechanisms underlying speech abnormalities in Parkinson's disease (PD) are still poorly understood and little is known on their prognostic value in PD progression. We investigated whether speech difficulties are associated with striatal dopaminergic deficits and whether are linked to progression of symptoms in early de novo patients with PD.

Methods: We included 353 early de novo PD patients from the Parkinson's Progression Markers Initiative database in the analysis. Speech difficulties were evaluated using the Unified PD Rating Scale Part-III (UPDRS-III), Item 3.1 (Speech) ≥ 1. We investigated differences in striatal [123I] FP-CIT single photon emission computed tomography (SPECT) levels, motor and non-motor features. Cox proportional hazards analysis was carried out to investigate whether speech difficulties were predictive of a faster disease progression and development of cognitive impairment.

Results: The prevalence of speech difficulties in early de novo PD patients was 43.9% (155/353). PD patients with speech difficulties have increased motor and non-motor symptoms burden as well as significant lower [123I]FP-CIT uptakes in the striatum (P<0.001), caudate (P=0.006) and putamen (P<0.001) compared to those without. Cox proportional hazards analysis showed that the presence of speech difficulties in early de novo PD patients predicts the development of cognitive impairment at a three-year follow-up (P=0.008), whereas has no influence on PD motor progression (P>0.10).

Conclusion: Our findings demonstrate that speech difficulties are associated with worse motor symptoms, loss of striatal presynaptic dopaminergic function and may be predictive of a more rapid cognitive decline in early de novo PD patients.

Disclosure: Nothing to disclose

PR2072

Improvement of dystonia management by specific training of family doctors

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Background and aims: Although an under-diagnosed condition, dystonia syndromes (DS) represent the third most common disorders in movement disorders centers. DS is difficult to recognize due to its large phenomenological complexity. We have shown lack of specific training in DS by general neurologists and familiy doctors in the study performed by European network for the Study of DS (A valaldas et all Eur J Neurol 2015).

Aim of present study was to improve diagnosis and treatment of DS by specific training in dystonia.

Methods: A questionnaire was developed and sent to dystonia patients and neighbor part of eastern Slovenia during year 2010. ang 2015. (5 years after specific training of general neurologists and family doctors was introduced in postgraduate medical education).

The questionnaire was composed of 30 questions divided in 3 parts (I General questions, II Specific questions on disease, III Availability of therapy).

Results: Total questionnaires processed: 467 in 2010 and 367 in 2015. All regions of the countries appeared to be well repersented in the respondent sample. In 2010, only 27% said that they obtained a corect diagnosis promptly within one year of first DS symptoms, for 19% of respondents, diagnosis had taken 3-5 years, and in 14% of patinets longer than 10 years. in 2015. (5 years after continuous education) significantly higher number of responders (35%) had obtained diagnosis within one year of first DS while only 7% waithed for over 10 years.

Conclusion: Collaboration in specific training for general neurologist and familiy doctors could represent the basis for improving dystonia management.

Disclosure: Nothing to disclose

PR2073

Evolution of ON-time following one-year open-label opicapone in BIPARK-I study

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Background and aims: ON-time evolution following 1-year, open-label (OL), once-daily (QD) opicapone (OPC) treatment in patients with Parkinson's disease (PD) on levodopa-therapy and with motor fluctuations.

Methods: After completion of the placebo- and active-controlled double-blind (DB) part, 495 (91.3%) patients continued to a 1-year OL-part, in which all subjects were treated with OPC (5, 25 or 50 mg OPC). All subjects began with 25-mg OPC QD for 1-week. Then, the investigator freely adjusted the levodopa therapy and/or OPC based on the dopaminergic response and/or associated adverse events. The primary efficacy variable was the change from baseline in OFF-time, based on patient diaries.

Results: Relative to DB baseline, the OFF-time reduction at OL endpoint was above 2 hours in all DB subgroups, with no significant differences between them. As expected, the inverse pattern was seen for the change in ON-time. The largest mean increase from OL baseline was seen for ON-time without dyskinesia for those subjects who had been treated with placebo or entacapone in the DB part. For DB opicapone subgroups, most of the gain in ON-time was ON-time with non-troublesome dyskinesia or without dyskinesia. Importantly, in the opicapone 50-mg, there was a noticeable shift from ON-time with non-troublesome and with troublesome dyskinesia to ON-time without dyskinesia. By-visit analysis showed that increase in ON-time was observed early, with a relevant increase immediately at first OL visit.

Conclusion: Following 1-year use of OPC, ON-time evolution mirrored the OFF-time pattern for which the largest increase observed was ON-time without dyskinesia.

Disclosure: Nothing to disclose

PR2074

Switch to Opicapone from Entacapone based on experience in BIPARK-I study

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Background and aims: To clarify how easily can entacapone (ENT) be switched to opicapone (OPC), in levodopa-treated patients with Parkinson's disease (PD) and motor-fluctuations.

Methods: Switch data from the double-blind (DB) to the open-label (OL) phase of a Phase-III, multicentre, randomised, placebo- and active-controlled, parallel-group study. In the DB phase, ENT patients took each ENT dose concomitantly with each levodopa daytime dose. OPC patients took each OPC dose as an additional bedtime dose administered at least 1 hour after the last daily dose of levodopa. In the 52-week OL phase, all patients received a bedtime daily-dose of 25mg OPC for the first week and thereafter OPC and levodopa doses were adjusted according to clinical response except on last month when both were to remain stable.

Results: A total of 122 patients were randomized to ENT. On the last visit of the DB phase, ENT patients took each ENT dose concomitantly with each levodopa daytime dose and the OL OPC dose, in the same day, as an additional bedtime dose administered at least 1 hour after the last daily dose of levodopa. On the following days, patients took each levodopa daytime dose alone and the OL OPC dose as the additional bedtime dose. Switch from ENT to OPC was considered safe and well tolerated with an immediate improvement of the OFF-time reduction.

Conclusion: Overnight switch from ENT to OPC was considered safe and well tolerated with an immediate improvement of the OFF-time reduction.

Disclosure: Nothing to disclose

PR2075

Normalization of timed neuropsychological tests with the PATA rate and Nine-Hole Pegboard Tests

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Background and aims: Timed neuropsychological tests do not consider physical impairment during scoring procedures. We developed a new method based on the Pata Rate Task (PRT) and on the Nine-Hole Pegboard Test (9HPT) as a measure of dysarthria and upper limb dysfunction, that normalizes the time spent on verbal and motor effort during timed tests. We tested the method on 24 patients with Friedreich Ataxia (FRDA), a neurological disease with motor and speech impairment

Methods: We defined the time spent on phonation and hand movement during neuropsychological testing as Verbal Effort Fraction (VEF) and Motor Effort Fraction (MEF). We measured both experimentally on 65 healthy controls on following tests: Attentional Matrices (AM), Trail Making Test (TMTA and TMTB), Symbol Digit Modalities Test (SDMT), Phonemic Fluencies (PF), Semantic Fluencies (SF). We developed correction formulas to normalize VEF and MEF considering the patient's PRT/9HPT scores, PRT/9HPT normality limits, and the test timing.

Results: VEF and MEF ranged between 13.5% to 61.7% of total test time. In FRDA patients, the effect of normalization improved all test results (SDMT 8.0%, AM 48.4%, TMT-A 41.8%, TMT-B 35.2%, PF 2.8%, SF 3.0%). At the individual level, the normalization method improved equivalent scores with fewer patients showing impaired scores after correction.

Conclusion: We propose an innovative method, that could be easily integrated in clinical practice, to reduce the impact of neurological disability on timed neuropsychological tests. The method was effective on FRDA patients, and the impact was higher at the single patient level.

Disclosure: Nothing to disclose

PR2076

Cognition in Friedreich Ataxia: A neuropsychological and RS-fMRI study

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Background and aims: Several studies have evaluated cognitive impairment in Friedreich Ataxia (FRDA) reporting a modest and discordant cognitive dysfunction. Previous activation fMRI studies showed low activation patterns during motor and behavioral tasks. To date, no resting-state fMRI (RS-fMRI) analysis has been performed in FRDA.

Methods: We tested FRDA patients and sex, age, and education matched controls with an extensive neuropsychological battery (Table 1). All MRI studies were performed on the same 3 Tesla scanner. For each subject, BOLD signal time course was calculated over different regions chosen because linked to the specific tested cognitive functions. The resulting functional connectivity (FC) maps were entered in a second level analysis to test for differences between the two groups. Differences were considered significant for $P<0.0011$, corrected for multiple comparisons.

Type of test	List of tests	Time (min)
Global Assessment	The Montreal Cognitive Assessment	10
Language	Naming Nouns and Pointing	10
Intelligence	Raven Colored Progressive Matrices	15
Executive Functions	Symbol Digit Modalities Test Attentional Matrices Trail Making Test Brief Stroop Test Weigl's Sorting Test Phonetic and Semantic Fluencies	60
Memory	Digit Span 10/36 Spatial Recall Test Rey Auditory Verbal Learning Test	20
Visuoperception and Visuospatial Functions	Segment Length Discrimination Mental Rotation	30

Table 1. Neuropsychological Battery

Results: We enrolled 24 FRDA patients and healthy controls (HC) (Table 2). Results of neuropsychological tests are shown in Table 3. Nineteen patients and twenty HC underwent the RS-fMRI analysis, with two FRDA patients that were excluded because of motion artifacts. Clusters of significant difference in FC emerged between the two groups for the FRDA>HC contrast at the level of the right and left paracingulate gyri, the right superior frontal gyrus, the right medial frontal gyrus and the left middle temporal gyrus.

Variable	FRDA	Controls	Sig. (p)
Age	31.3±15.0	30.7±15.5	0.331
Education	12.1±2.9	12.5±3.2	0.393
Gender (M/F)	15/9	15/9	1.000
PTR	18.9±4.4	32.2±6.9	**0.001**
9HPT	98.3±85.9	19.3±2.7	**0.001**
GAA1	677.0±282.8	-	-
GAA2	906.3±310.4	-	-
SARA	18.7±7.2	-	-

Table 2. Demographics

Test	FRDA	Controls	Mean difference (95% CI)	Sig. (p)	Effect Size
MOCA	22.3 (3.6)	26.2 (2.3)	-3.83 (-5.59; -2.07)	**0.001**	0.74
Pointing Names	23.9 (0.3)	24 (0.2)	-0.08 (-0.26; 0.09)	0.317	0.20
Naming Nouns	13.9 (1.3)	14.2 (1.2)	-0.25 (-0.98; 0.48)	0.452	0.15
RCPM	29.6 (6.3)	33 (5.4)	-3.33 (-6.61; -0.06)	**0.026**	0.46
Digit Span	7 (4.4)	6.5 (1.1)	0.50 (-1.36; 2.36)	0.621	0.10
1036 immediate	18.5 (6.6)	22.9 (3.8)	-4.68 (-7.52; -1.40)	**0.007**	0.55
1036 recall	6.5 (2.4)	8.2 (1.8)	-1.67 (-2.89; -0.45)	**0.015**	0.50
RAVLT immediate	40.8 (12.6)	47.5 (9.4)	-6.71 (-11.73; -1.68)	**0.015**	0.50
RAVLT recall	9.3 (3.9)	10.5 (3.4)	-1.21 (-2.87; 0.45)	0.083	0.35
SLD	26.9 (2.2)	28.5 (1.7)	-1.63 (-2.74; -0.51)	**0.009**	0.53
Mental Rotation	93.3 (15.9)	105.8 (4.7)	-12.54 (-18.92; -6.16)	**0.001**	0.67
SDMT	35.8 (10)	57.3 (13.6)	-23.92 (-29.52; -18.31)	**0.001**	0.86
Attentional Matrices	50.5 (8.7)	55.5 (3.2)	-17.58 (-22.43; -12.74)	**0.015**	0.50
TMT-A	67 (68.9)	29.8 (8.8)	37.12 (9.08; 65.21)	**0.001**	0.68
TMT-B	127.3 (57.7)	73.2 (24.2)	55.04 (33.11; 76.97)	**0.001**	0.80
Brief Stroop Test	50.1 (20.3)	26.9 (7.4)	-23.13 (14.40; 31.86)	**0.001**	0.81
Weigl's Sorting Test	12.6 (2.2)	13.6 (1.5)	-0.96 (-2.20; 0.28)	0.138	0.30
Semantic Fluency	18.5 (5.8)	23.7 (4.9)	-5.08 (-8.75; -1.42)	**0.001**	0.74
Phonemic Fluency	27.5 (11.7)	41.3 (8.8)	-13.88 (-19.19; -8.56)	**0.001**	0.75

Table 3. Neuropsychological tests in FRDA and controls

Conclusion: FRDA showed a worst than expected and diffuse cognitive impairment with widespread alterations of FC. The paradigm of FRDA patients being cognitively normal should be revised in favor of a non-demented, but diffusely impaired phenotype.

Disclosure: Nothing to disclose

MS and related disorders 3

PR2077

Fampridine improves horizontal eye movements in patients with multiple sclerosis and internuclear ophthalmoplegia: A double-blind, placebo-controlled crossover study

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Background and aims: Internuclear ophthalmoplegia (INO) is a common cause of visual symptoms in patients with multiple sclerosis (MS). It is characterized by slowing eye adduction during horizontal saccades. Recent studies suggest fampridine may improve nerve conduction in MS patients. This was a study in MS patients with INO to determine effects of fampridine on eye movements.

Methods: This was a randomized, doubleblind, placebo-controlled, cross-over study with fampridine in 24 MS patients with INO. Patients received a single dose of 20 mg fampridine or placebo on two separate occasions. We analyzed eye movements recorded by the EyeLink1000 at baseline and at multiple time points post-dose. The primary outcome measure was the Versional Dysconjugacy Index (VDI), peak velocity. Secondary outcome measure was the VDI First-Pass Amplitude (FPA). Higher VDI and FPA values indicate a delay in eye adduction associated with INO. These measures were compared with a mixed model analysis of variance; patients served as their own control-group.

Results: All patients completed the study. A significant change of -17.4% (95% CI: -22.4%, -12.1%; p<0.0001) in VDI and -12.5% (95% CI: -18.9%, -5.5%; p<0.01) in FPA were observed after fampridine administration compared with placebo, indicating significant improvement in eye adduction. The main adverse event reported after administration of fampridine was dizziness (61%).

Conclusion: Fampridine was associated with a significant decrease in VDI, corresponding with an improvement in INO severity. Future studies must determine whether fampridine treatment in MS patients with an INO also leads to clinical improvement of visual symptoms.

Disclosure: Biogen (Boston, USA) funded this study.

PR2078

Effect of early initiation or switch to fingolimod on relapse outcomes in patients with relapsing-remitting multiple sclerosis: Pooled analysis from Phase 3 and Real-World studies

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Background and aims: Early treatment optimisation with high-efficacy therapies may improve short- and long-term disease outcomes in patients with multiple sclerosis (MS). We report the effect of fingolimod (0.5 mg once-daily) on relapse outcomes in treatment-naïve patients and those who switched to fingolimod after receiving one or more disease-modifying treatments (DMTs).

Methods: Data were pooled from phase 3 core and extension and real-world studies. Based on prior treatment, patients (N=6401) were divided into: treatment-naïve (n=1439), 1-DMT (n=3150), 2-DMTs (n=1393) and ≥3-DMTs (n=419). The annualised relapse rate (ARR) was estimated from a negative binomial ARR model on period (on study or pre-study), number of prior DMTs, age, sex, disease duration and period×number of prior DMTs interaction. Relapse-free patients were stratified by disease duration quartiles (Q1 [0–4 years], Q2 [>4–8 years], Q3 [>8–14 years] and Q4 [>14 years]), number of relapses before enrolment (0, 1, 2 and >2) and number of prior DMTs.

Results: In the overall fingolimod population, the ARR after 12 months of treatment was 73.7% lower versus baseline (0.3 vs 1.14). Treatment-naïve patients showed the greatest reduction (82.2%), followed by 1-DMT (78.7%; p<0.02 versus treatment-naïve patients), 2-DMTs and ≥3-DMTs groups (70.2% and 57.4%, respectively; both p<0.0001 versus treatment-naïve patients). A similar trend was observed after 24 months (Figure). Early switch to fingolimod was associated with a higher percentage of on-study relapse-free patients (Table).
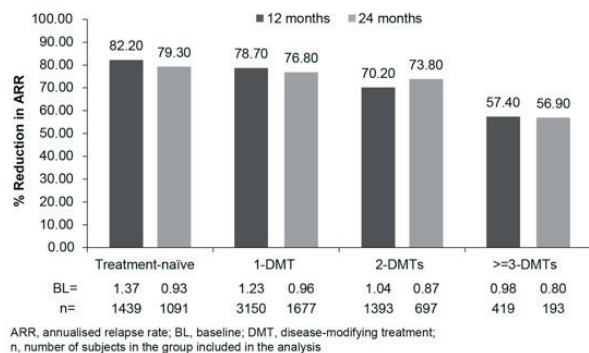
Figure. Percentage reduction in ARR after 12 and 24 months of fingolimod treatment

MS disease duration and number of prior treatments	Relapses in the year prior to enrolment			
	0	1	2	>2
Q1 (0-4 years)				
Treatment-naïve (n=438)	17 (85)	163 (76)	113 (72)	31 (66)
1-DMT (n=378)	46 (77)	115 (67)	59 (63)	27 (51)
2-DMTs (n=87)	18 (82)	25 (78)	8 (42)	6 (43)
>=3-DMTs (n=05)	0	2 (50)	1 (100)	0
Q2 (>4-8 years)				
Treatment-naïve (n=249)	15 (94)	105 (73)	41 (60)	14 (67)
1-DMT (n=451)	68 (82)	161 (75)	74 (64)	21 (55)
2-DMTs (n=193)	48 (91)	57 (72)	27 (64)	9 (47)
>=3-DMTs (n=33)	8 (89)	12 (63)	2 (67)	2 (100)
Q3 (>8-14 years)				
Treatment-naïve (n=172)	9 (60)	79 (78)	30 (75)	14 (88)
1-DMT (n=440)	79 (83)	156 (73)	56 (58)	18 (51)
2-DMTs (n=198)	45 (78)	52 (58)	18 (50)	7 (50)
>=3-DMTs (n=72)	25 (66)	10 (44)	4 (50)	1 (33)
Q4 (>14 years)				
Treatment-naïve (n=199)	19 (91)	95 (77)	26 (67)	8 (50)
1-DMT (n=375)	59 (79)	133 (64)	39 (60)	11 (42)
2-DMTs (n=212)	58 (82)	63 (70)	22 (49)	4 (67)
>=3-DMTs (n=82)	22 (73)	17 (53)	5 (50)	2 (20)

DMT, disease-modifying treatment; MS, multiple sclerosis
n=Number of patients observed for at least 18 months (period Month 0 to Month 24)
Green>=70%, Yellow=51–69%, Orange=<50%
Earlier switch to fingolimod was defined as a sooner start of treatment after disease onset, after fewer relapses and/or fewer DMT cycles

Table. Percentage of relapse-free patients after 24 months of fingolimod treatment: stratified by disease duration, number of relapses before enrolment and number of prior DMTs

Conclusion: Early initiation or early switch to fingolimod was associated with better relapse outcomes after 12- and 24-months of treatment versus switching to fingolimod after multiple DMTs.

Disclosure: This study was funded by Novartis Pharma AG, Basel, Switzerland. Detailed disclosure of each author will be included in the poster.

PR2079

Reduction in progression to disability milestones by ocrelizumab in patients with relapsing multiple sclerosis: An exploratory analysis of pooled OPERA I and OPERA II studies

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Background and aims: Ocrelizumab has been shown to reduce disease activity and disability worsening in patients with relapsing multiple sclerosis (RMS). On the Kurtzke Expanded Disability Status Scale (EDSS), scores of 4.0 (restricted walking) and 6.0 (unilateral aid) represent important benchmarks of multiple sclerosis disability accumulation. The effect of ocrelizumab was compared with interferon beta-1a (IFN beta-1a) on confirmed progression to disability milestones in patients with RMS.

Methods: In this exploratory analysis of the intention-to-treat (ITT) population of pooled OPERA I and OPERA II trials, 829 IFN beta-1a-treated and 827 ocrelizumab-treated patients were evaluable. Kaplan–Meier analyses were used to estimate the risk of 12- and 24-week confirmed progression to EDSS ≥ 4.0 (patients with baseline EDSS ≤ 3.0 [IFN beta-1a, n=544; ocrelizumab, n=538]) and to EDSS ≥ 6.0 (ITT population).

Results: By 96 weeks, a significantly lower percentage of ocrelizumab- vs. IFN beta-1a-treated patients had confirmed 12-week (3.5% vs. 7.2%; hazard ratio [HR]: 0.40; p<0.001) and 24-week (2.6% vs. 5.3%; HR: 0.39; p=0.004) progression to EDSS ≥ 4.0 in patients with baseline EDSS ≤ 3.0. Ocrelizumab also consistently and significantly reduced the risk of confirmed 12- (2.1% vs. 4.6%; HR: 0.40; p=0.002) and 24-week (1.7% vs. 3.9%; HR: 0.41; p=0.005) progression to EDSS ≥ 6.0 versus IFN beta-1a in the ITT population.

Conclusion: The effect of ocrelizumab on reduction of risk of progression to EDSS ≥ 4.0 and ≥ 6.0 was consistent with the benefit of ocrelizumab in reducing overall confirmed disability progression in RMS.

Disclosure: Sponsored by F. Hoffmann-La Roche Ltd.

PR2080

Relation between immunoglobulin levels and JC virus serology on multiple sclerosis patients

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Background: The BIONAT study showed decreasing of immunoglobulins (Ig) G levels under natalizumab. One patient developed PML while being negative for JC virus. There was a false negative result due to hypogammaglobulinemia.
Aims: To evaluate the impact of IgG level on JCV index value.
Methods: We collected biological data from MS patients treated with natalizumab between 2007 and 2015. JCV index values were obtained by GEN-2 test. The Ig quantitative assays, T cell and B cell counts were carried out by the Laboratory of the CHRU of Lille. The evolution of the IgG and M levels and the JC index over time under treatment was studied by multivariate linear regression models.
Results: Analysis involved 1419 JCV index coupled with Ig quantitative assays from 348 patients. There was a significant decrease of IgG during the first 6 months of treatment (p <0.001). During follow-up under natalizumab, 74 patients had an IgG level lower than 6.9 g / L. There was no significant correlation found between JCV serology and IgG level. The lack of correlation between the IgG level and the JCV index value may be related to the low number of patients with abnormal low levels of IgG in our population. However, we suggest appreciating that JCV index with IgG levels especially when the patient is negative for JCV exposition to avoid any false negative.
Conclusion: We did not show any correlation between the JC virus index and the IgG levels, but warn about the potential false negative result due to an hypogammaglobulinemia.
Disclosure: Nothing to disclose

PR2081

Neuronal dysfunction induced by mitochondrial complex IV inhibition is enhanced during experimental multiple sclerosis: Neuroprotection through the nitric oxide/cGMP/PKG pathway

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Background and aims: A close link between inflammation and neurodegeneration has been demonstrated during multiple sclerosis (MS), suggesting that immune mechanisms may promote neuronal degeneration and irreversible disease progression. In this scenario, it has been proposed a pathogenetic role for mitochondrial dysfunction. We then investigated, with electrophysiological recordings, if experimental autoimmune encephalomyelitis (EAE) may increase neuronal vulnerability to mitochondrial dysfunction induced by mitochondrial complexes inhibitors.
Methods: EAE was induced in Biozzi ABH mice by the injection of syngeneic spinal cord homogenate. Extracellular field potential recordings were performed in the striatum during the acute relapsing phase of the disease.
Results: We found in EAE mice, with respect to control mice, a markedly enhanced neuronal toxicity caused by the exposure to complex IV inhibitor sodium-azide (worsening the field potential amplitude loss by 65.7%, n=10, p<0.001). We then investigated which pathogenic mechanism might link inflammation to the enhanced toxicity of sodium-azide, focusing on nitric oxide (NO) and its intracellular pathway (involving soluble guanylyl cyclase and protein kinase G). Interestingly, we found that the inhibition of NO synthesis and of its intracellular pathway, significantly counteracted the enhancing effect of inflammation on sodium-azide neuronal toxicity, exerting neuroprotective effects.
Conclusion: Neuroinflammation accompanying EAE enhanced neuronal dysfunction caused by mitochondrial complex IV inhibition, supporting the hypothesis that mitochondria represent a potential link between inflammation and neurodegeneration. Interestingly, the modulation of NO-activated intracellular pathways counteracted this detrimental effect, with implications for the development of neuroprotective strategies for inflammatory brain disorders.
Disclosure: This study was supported by Fondazione Italiana Sclerosi Multipla (FISM)

PR2082

Evaluation of modified Rio score (MRS) as a predictive score in clinical trial sub-populations of multiple sclerosis (MS) patients treated with subcutaneous interferon beta 1-a

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Background and aims: The MRS stratifies MS patients by early disease activity and may predict long-term therapeutic response. We evaluated whether MRS predicts later disease activity in patients treated with subcutaneous (sc) interferon (IFN) beta-1a 22/44 µg from different clinical trial sub-populations.

Methods: We included 44 µg treatment arms from the REFLEX(ION) (clinically isolated syndrome; n=158) and REGARD studies (relapsing-remitting MS [RRMS; McDonald 2001]; n=203), and 22/44 µg arms from the SPECTRIMS relapsing cohort (secondary progressive MS; n=189) and PRISMS long-term follow-up early treatment cohort (RRMS [Poser criteria]; n=367). Follow-up ranged from 96 weeks (96w; REGARD) to 15 years (Y15; PRISMS). MRS at Y1 of treatment (48w, REGARD) was assessed as a predictor of clinical disease activity-free (CDAF) status or disability progression (Expanded Disability Status Scale).

Results: For REFLEXION, REGARD and SPECTRIMS, >93% patients with CDAF status at Y3 (REGARD 96w) had MRS of 0 at Y1 (REGARD 48w). In PRISMS, among patients with MRS 0 at Y1, >20% were CDAF at Y6 and 6%–10% at Y15. The risk of disability progression in PRISMS over 7–8 years was greater for patients with MRS of 2–3 versus 0 (hazard ratio [HR] 2.15; 95% CI 1.54–2.99) and 1 versus 0 (HR 1.59; 95% CI 1.13–2.25); for SPECTRIMS , these values over 6 years were 1.46 (95% CI 0.94–2.26) and 1.47 (95% CI 1.01–2.15), respectively).

Conclusion: The modified Rio score was a reasonable predictor of future disease activity in patients receiving sc IFN beta-1a, including more contemporary patient populations.

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PR2083

Anti-MOG antibodies associated syndromes: Report of 15 cases

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Background and aims: Anti-myelin oligodendrocyte glycoprotein antibodies (MOG-Abs) have been described in a number of CNS inflammatory conditions. We report clinical, MRI and CSF data of a patient cohort seronegative for anti-aquaporin-4 antibody (AQP4-Abs) and positive for MOG-Abs.

Methods: A commercial kit was used to analyze AQP4-Abs, while a live-cells (HEK293A) immunofluorescence assay was used for the detection of serum MOG-Abs with a cut-off at 1:160.

Results: Among 354 patients tested between March 2014 and December 2016, 15 MOG-Abs positive cases were identified. Seven patients had flu-like or gastrointestinal symptoms in the 4 weeks prior to onset, while serological evidence of a recent infection with HSV1, Borrelia Burgdorferi, and Cytomegalovirus was obtained in 3 cases. Clinical presentations included optic neuritis in 6 cases, myelitis in 6, optic neuritis and myelitis in 2, and cerebellar signs in one. Mean follow-up was 41.4±67 months. Five patients experienced relapses. Spinal cord MRI noted short lesions in 8 patients and a cervical longitudinally extensive lesion in two subjects. Pleocytosis and/or an increased protein level were noted in 5 patients. Three patients retested for MOG-Abs after the index event in absence of relapses, resulted negative.

Conclusion: Serum MOG-Abs are associated with neurological syndromes characterized by involvement of the spinal cord and optic nerve, often preceded or accompanied by an acute infection. It is essential to test MOG-Abs in the acute phase since antibody titer normalizes in non-relapsing patients.

Disclosure: Nothing to disclose

PR2084

Differentiation by MRI between multiple sclerosis and MS-like syndromes with markers of "better explanation" of the diagnosis.

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Background and aims: Multiple sclerosis (MS) white matter lesions are inflammatory-demyelinating (WM-ID) and perivenular whereas white matter lesions of primary small vessel disease migraine and systemic autoimmune diseases with neurological involvement are mainly ischemic and periarteriolar. In MS the "central vein (CV) sign" that can be visualized by T2* MRI sequences, is present in about 75% of the WM-ID lesions. In the other diseases the frequency is lower than 50% (Solomon, 2015; Mistry, 2016; Vuolo, 2016). In this study the CVsign was compared in definite MS and in MS patients with markers of "better explanation" of the diagnosis (MS-like), for evaluating differences in the pathogenic mechanisms.

Methods: Relapsing remitting patients fulfilling the 2011 McDonald diagnostic criteria for MS were included: n= 50 (30 definite MS and 20 MS-like). For detection of the CVsign, the patients underwent to contrast-enhanced MRI scans, including a T2* sequence. The frequency of brain WM lesion with CVsign was assessed in each patient, establishing a treshold frequency of 50% for identifying patients with WM-ID and with WM-I lesions.

Results: The median frequency/ patient of CVsign was higher in definite MS than in the MS-like group: 91% (range 67-100%) vs 17.5% (range 9-83%; p< 0.0001). A CVsign frequency higher than 50% was observed in 30/30 MS patients (100%) and in 5/20 MS-lke patients (25%; p< 0.0001). All the MS-like patients above the 50% treshold had a frequency of the CVsign within the range of definite MS: 70-83% (median 74%).

Conclusion: The CVsign can identify pathogenesis of most the MS–like patients.

Disclosure: Nothing to disclose

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PR2085

Long-term outcomes in patients with early multiple sclerosis treated with teriflunomide: TOPIC extension study

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Background and aims: TOPIC (NCT00622700) evaluated the efficacy and safety of teriflunomide in patients with a first clinical episode suggestive of MS (N=614). Patients completing TOPIC, still on-study at completion, or experiencing relapse determining conversion to clinically definite MS (CDMS; primary endpoint), were eligible to enrol in the extension. Here, we report clinical outcomes from the TOPIC extension through to completion (≤7 years' treatment).

Methods: In the TOPIC extension, teriflunomide-treated patients continued to receive their original dose; the placebo group was re-randomized 1:1 to teriflunomide 7mg or 14mg.

Results: Out of 423 patients entering the extension, 316 (75%) completed it. Cumulative observations through 7 years of follow-up were: (1) lower risk of relapse determining conversion to CDMS in the 14mg/14mg vs the placebo/14mg group (hazard ratio [95% confidence interval] 0.529 [0.317, 0.883], P=0.0149); (2) annualized relapse rate ≤0.163, with ≥61% of patients free from relapse across all treatment groups; and (3) most patients (≥78%) remained free from 12-week disability worsening. On MRI outcomes, the gadolinium-enhancing lesion count was low through to extension completion. The most common reason for discontinuing treatment was patient choice (43/107 discontinuations). The nature and incidence of adverse events were comparable to those in other teriflunomide clinical studies, most being mild to moderate in nature.

Conclusion: Together with data from studies in patients with established relapsing MS (RMS), observations in this population of patients with first symptoms suggestive of MS demonstrate consistent efficacy and safety outcomes with long-term teriflunomide treatment across a range of RMS subtypes.

Disclosure: Study supported by Sanofi Genzyme.

PR2086

Evaluation of No Evidence of Progression or Active Disease (NEPAD) in patients with primary progressive multiple sclerosis in the ORATORIO trial

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Background and aims: Primary progressive multiple sclerosis (PPMS) is characterised by steadily increasing neurologic disability. No evidence of progression or active disease (NEPAD), a novel endpoint that assesses the combined absence of composite disability progression and clinical and MRI disease activity, is investigated here in PPMS patients.

Methods: In a post-hoc exploratory analysis of the ORATORIO trial, 234 placebo- and 465 ocrelizumab-treated patients were evaluated to assess the proportion of patients with NEPAD from baseline to Week 120, defined as having no evidence of progression (NEP; no 12-week confirmed progression of ≥1/≥0.5 points on the Expanded Disability Status Scale if the baseline score was ≤5.5/>5.5 points, respectively; no 12-week confirmed progression of ≥20% on the timed 25-foot walk test and 9-hole peg test), no brain MRI activity (no new/enlarging T2 lesions and no T1 Gd+ lesions) and no protocol-defined relapse. Brain MRI assessments were conducted at baseline and Weeks 24, 48 and 120.

Results: Compared with placebo, ocrelizumab increased the proportion of patients with NEPAD at Week 120 (9.4% vs 29.9%; risk ratio ocrelizumab vs placebo [95% CI]: 3.15 [2.07, 4.79]; p<0.0001). A consistent effect of ocrelizumab was also observed on all three components of NEPAD. Sensitivity analyses will also be presented.

Conclusion: In ORATORIO, the proportion of patients with NEPAD increased approximately 3-fold with ocrelizumab compared with placebo. NEPAD may represent a useful composite outcome to assess the absence of clinical and MRI features of disease progression and activity in patients with PPMS.

Disclosure: Sponsored by F. Hoffmann-La Roche Ltd.

PR2087

Neurofilament light in serum for monitoring multiple sclerosis: A new quantitative tool for measuring disease activity and therapeutic response

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Background and aims: The neurofilament light (NFL) is a biomarker of axonal damage, previously only measurable in cerebrospinal fluid (CSF). However, recently developed ultrasensitive immunoassays can determine NFL in serum. In multiple sclerosis (MS), CSF NFL concentration reflects disease activity and the efficacy of disease-modifying therapies (DMTs). This study determined the effects of disease activity and DMTs on serum NFL and investigated the correlation of serum and CSF NFL in MS.

Methods: NFL concentrations were measured in paired serum and CSF samples (n=521) from 373 subjects: 286 MS, 45 other neurological conditions, and 42 healthy controls (HCs). In 138 MS patients, the serum and CSF samples were obtained pre- and post-treatment with a median interval of 12 months. The NFL concentration was measured using ELISA in CSF and using an in-house ultrasensitive single molecule array assay in serum.

Results: In MS, the correlation between serum and CSF NFL was r=0.723 (p<0.001). Serum concentrations were significantly higher in relapsing-remitting MS patients (26 ng/L) and in progressive MS patients (36.1 ng/L) than in HCs (12.5 ng/L; p=0.019 and p<0.001, respectively). Treatment with DMTs reduced serum NFL levels from 30.3 ng/L to 18.7 ng/L; p<0.001). Patients with relapse or radiological activity had significantly higher serum NFL levels than those in remission (p<0.001) or those without new lesions on MRI (p<0.001).
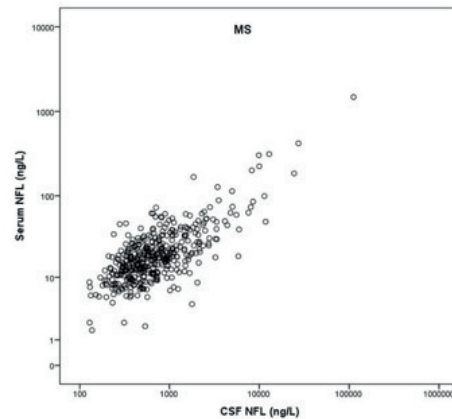
Correlation between serum and CSF NFL in MS patients
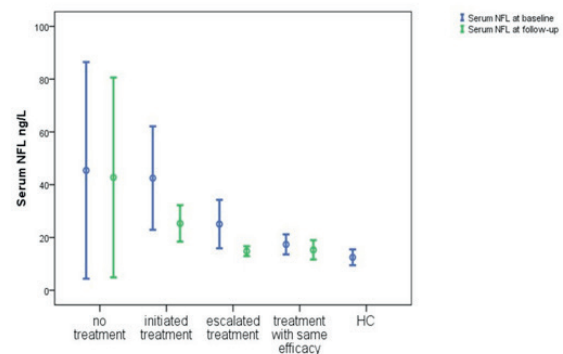
Serum NFL concentrations in MS patients at baseline and at follow-up and in healthy controls
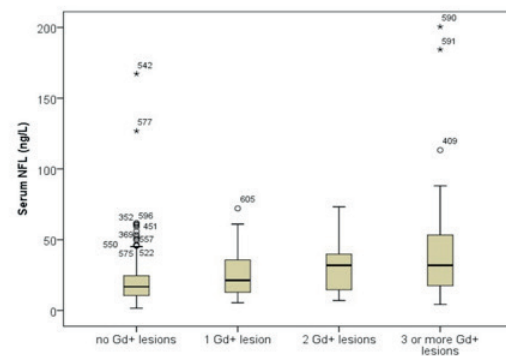
Serum NFL concentrations in MS patients with different numbers of Gd-enhancing lesions

Conclusion: Serum and CSF NFL levels were highly correlated and disease activity and DMTs had similar effects on serum and CSF NFL levels. NFL determination in serum for detecting axonal damage may represent a new era in MS monitoring.

Disclosure: Nothing to disclose

PR2088

Could mindfulness-based intervention (MBI) improve social cognition in multiple sclerosis?

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Background and aims: Social cognition is the individual´s ability to understand others mind and feelings. It is one of the six core functional cognitive domains. Accumulating evidence suggests that patients with multiple sclerosis are impaired in social cognition, including theory of mind (ToM) and emotion recognition. Deficits in social cognition might have a drastic impact on quality of life and in the social relationships.

Objective: To study if a mindfulness-based cognitive therapy could improve the altered social cognition of patients with multiple sclerosis (MS).

Methods: We study patients with multiple sclerosis and altered social cognition. They participated in a Mindfulness-Based Stress Reduction (MBSR) program. The intervention involved 1.5 hour weekly sessions and they were administered during 8 weeks. A spanish validated test for social cognition (Movie Assessment Social Cognition) was performed in the pre-intervention period, at 8 weeks (post-intervention) and at 24 weeks of ending the intervention.

Results: 31 patients with RRMS were studied. The mean age was 43 and 95% were females. The range of the disease duration was between 1 to 25 years. After the mindfulness therapy the number of correct answers in the movie assessment social cognition test were significant higher than at the baseline (z value -2.19, p=0.028).

Conclusion: Mindfulness based therapy can improve the altered social cognition in multiple sclerosis and therefore the quality of life of the patients.

Disclosure: Nothing to disclose

PR2089

Retinal fiber layer thickness as a measure of global and visual impairment in multiple sclerosis

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Background and aims: Several studies demonstrated that RNFL thickness in associated with several MRI measures of brain and spinal cord atrophy and with measures of global and visual disability. Evoked potentials (EPs) are extensively used in MS as a marker of damage along eloquent nervous pathways. The association of Multimodal EPs with RNFL has never been explored.

Methods: 100 patients received a diagnosis of multiple sclerosis at San Raffaele Hospital and underwent brain MRI, multimodal EPs, OCT, high and low-contrast visual acuity (LCVA) and lumbar puncture.

Results: EPs were correlated with RNFL (ρ=-0.297, p=0.003). Similar correlation were observed considering separately VEP (ρ=-0.238, p=0.020) and MEP-SSEP (ρ=-0.248, p=0.015). The latter were associated with global disability (EDSS) (ρ=+0.245, p=0.016), disease duration (ρ=+0.399, p<0.001), and brain MRI lesion load (ρ=+0.398, p<0.001). VEPs were instead correlated with LCVA (ρ=-0.317, p=0.002). The RNFL thickness (considering eyes without previous optic neuritis) analysis demonstrated a correlation with both global (EDSS: ρ=-0.303, p=0.003) and visual disability (LCVA: ρ=+0.248, p=0.018), EPs, and separately VEP and MEP-SSEP. The association was significant also in relation to lesion load and disease duration (respectively, ρ=-0.374, p<0.001 and ρ=-0.237, p=0.02). As markers of CNS inflammation, microvesicle count, gadolinium enhancing lesion at brain MRI scan, and the presence of oligoclonal bands in CSF were significantly correlated to each other but not with the other clinical or OCT/neurophysiological data.

Conclusion: In early MS, RNFL thickness is associated with accumulation of damage within CNS revealed by visual pathway damage (VEP and visual acuity), spinal cord damage (MEP-SSEP and EDSS), and brain lesion load.

Disclosure: Nothing to disclose

PR2090

Brain functional reorganization in MS: Good or Bad

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Background and aims: Experimental data concerning the changes in cerebral grey matter in MS is ambiguous until the present day.

Our aim: To assess a relationship between neurodegeneration and brain functional reorganization in clinical presentation of MS.

Methods: 166 MS patients, 40 healthy control subjects were investigated. Study protocol included neurological assessment, MRI studies and FDG-PET. MRI morphometry was performed by open access software. Regional Cerebral Metabolic Rate of Glucose (RCMRglu) was expressed in percent of mean global CMRglu. RCMRglu levels were ranged from group to group of patients with increasing disease duration.

Results: We revealed 3 main patterns of rCMRglu changes. First pattern reflects decrease functional activity in RRMS with disease duration more than 10 years and SPMS patients. Second pattern reflects compensatory functional activity increase followed by exhaustion in patients with advanced RRMS and SPMS; this pattern corresponds to the generally accepted definition for functional reorganization. Third pattern is "paradoxical" as it demonstrates functional activity increase bilaterally in n.lentiformis in RRMS patients with disease duration more than 2 years and SPMS patients; in Brodmann area (BA) 4 in SPMS patients; in dominant hemisphere BA 10 in RRMS patients with disease duration over 5 years and in SPMS patients.

Conclusion: The pathophysiology for this pattern is interhemisphere disconnection and inhibition alteration due to corpus callosum atrophy. Such functional activity increase may lead to further neurological decline. Thus, increase of functional activity in above mentioned brain structures in patients with severe atrophy can be of a pathological nature and lead to increasing of neurological deficit.

Disclosure: Nothing to disclose

PR2091

The effects of natalizumab and fingolimod on clinical and MRI measures in relapsing remitting multiple sclerosis: A two-year comparative study

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Background and aims: To compare the effects of natalizumab (NAT) and fingolimod (FTY) on clinical and MRI measures in relapsing-remitting multiple sclerosis (RRMS) patients after two years of treatment.

Methods: Fifty-six RRMS patients starting NAT (n=30) or FTY (n=26) underwent 3T brain scans and clinical evaluation (EDSS, relapse rate) at baseline, year 1 (Y1) and 2 (Y2). T2 and T1 lesion volumes (LV), brain, white matter (WM), gray matter (GM), deep GM volumes and their changes were measured. No evidence of disease activity-3 (NEDA-3) was evaluated.

Results: At baseline, the two groups were matched for demographic, clinical and MRI variables. Both drugs significantly reduced relapses at Y2, especially in NAT-patients (0.03 vs 0.23, p=0.03). In NAT-patients, at Y2, fewer new T2 lesions occurred (0.83 vs 6.85, p=0.01), EDSS remained stable, while T2 and T1 LVs decreased (p=0.003 and p=0.0004). In FTY-patients, at Y2, EDSS remained stable, while T2 and T1 LVs increased (p<0.0001 and p=0.01). A higher proportion of NEDA-3 occurred in NAT- vs FTY-patients at Y2 (56.7% vs 26.9%, p=0.02). At Y2, brain (-0.56%, p=0.01 [FTY]; -0.73, p=0.02 [NAT]), WM (-1.56%, p=0.001 [FTY]; -0.65, p=0.05 [NAT]) and deep GM atrophy (-1.40%, p=0.007 [FTY]; -1.12%, p=0.004 [NAT]) progressed in both groups. GM atrophy progressed in NAT-patients (-0.90%, p=0.04). Significantly increased T2 (p<0.0001) and T1 (p=0.0001) LVs were found in FTY- vs NAT-patients comparisons.

Conclusion: NAT and FTY reduce disease activity in RRMS. NAT could have a more significant effect on WM inflammatory lesion accumulation, while both drugs modify atrophy progression.

Disclosure: Nothing to disclose

PR2092

Evaluating effect of teriflunomide on cortical atrophy in a subgroup analysis of patients defined by baseline MRI activity in the Phase 3 TOPIC study

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Background and aims: In TOPIC (NCT00622700), teriflunomide reduced risk of conversion to clinically definite MS (CDMS) vs placebo in patients with a first clinical episode suggestive of MS, and also reduced MRI activity. Effects of teriflunomide on cortical grey matter volume (CGMV) change in TOPIC patients, and in patient subgroups defined by baseline MRI activity, are described.

Methods: Patients were treated with placebo (n=197), teriflunomide 7mg (n=203), or 14mg (n=214) for ≤108 weeks. Post-hoc subgroup analyses were performed according to baseline gadolinium-enhancing (Gd+) lesion status. Percentage change in CGMV was evaluated using SIENAX multi-timepoint analysis. Data from Month (M) 6, 12, 18, and 24, standardized for follow-up duration, were analysed relative to baseline. Treatment group comparisons were made using rank ANCOVA.

Results: In the overall TOPIC population (N=614), teriflunomide 14mg significantly reduced median percentage CGMV loss vs placebo (relative reduction: M6, 119.2%; M12, 61.4%; M18, 66.8%; and M24, 40.2%; P<0.05 at all timepoints). In total, 34.5% of patients had ≥1 Gd+ lesion per MRI scan at baseline, and 65.5% of patients had 0 Gd+ lesions at baseline. The effect of teriflunomide on median percentage CGMV change in each of the subgroups was consistent with the effect observed in the overall TOPIC population and will be presented.

Conclusion: Consistent with the reduced risk of conversion to CDMS, teriflunomide slowed CGMV loss across all timepoints over 2 years in TOPIC, including in subgroups defined by baseline MRI activity. Results indicate teriflunomide may have a favourable impact on the early neurodegenerative component of MS.

Disclosure: Study supported by Sanofi Genzyme.

Muscle and neuromuscular junction disease 2

PR2093

Mechanisms of muscle weakness in facioscapulohumeral muscular dystrophy

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Background and aims: Facioscapulohumeral muscular dystrophy (FSHD) is one of the most common hereditary muscle disorders. Despite increasing knowledge about the molecular pathways underlying this disease, it remains unknown how these changes translate to muscle weakness.
Methods: We included 14 FSHD patients and 12 healthy controls, and measured individual health-related quality of life, functional performance and muscle strength. In all participants, muscle contractile capacity was measured in vivo, using quantitative muscle testing and MRI imaging, and ex vivo, using histopathological evaluation and single fiber studies of tibialis anterior as well as vastus lateralis muscle biopsies.
Results: FSHD disease severity was associated with loss of contractile muscle volume (p<.001), which in turn was associated with functional impairment (p<.001). Muscle volume was reduced in tibialis anterior (p=.001) due to a larger proportion of atrophic type 1 fibers (p<.001). Muscle volume was preserved in vastus lateralis (p=.545) due to concomitant type 2 hypertrophy (p<.001). Quadriceps specific force (force corrected for cross-sectional area) was reduced in all FSHD participants independent of disease severity (p=.007).
Conclusion: FSHD severity is associated with muscle weakness as a result of 1. reduced muscle volume due to fiber atrophy and fatty infiltration, and 2. reduced specific force. Our findings establish that different muscle types may respond differently to FSHD pathology. This may contribute to the specific pattern of muscle involvement in FSHD, and is important to consider in therapeutic trials or when collecting tissue for research.

PR2094

Cardiac troponin T splicing as possible biomarker of cardiac dysfunctions in skeletal muscle from myotonic dystrophy type 1 and type 2 patients

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Background and aims: Myotonic dystrophy type 1 (DM1) and type 2 (DM2) are autosomal dominant neuromuscular disorders characterized also by cardiac dysfunctions. They are caused by expanded CTG or CCTG repeats with aberrant alternative splicing of different genes. Perturbation of splicing and expression of cardiac Troponin T (cTnT) in cardiac tissue is considered one cause of cardiac dysfunctions in DM. In adult life cTnT is expressed in cardiac muscle and in injured skeletal muscle. Recently we observed that cTnT was expressed in adult skeletal muscle from both DM1 and healthy subjects although with a different expression pattern. Our aim was to verify if the expression of cTnT in adult skeletal muscle might be considered a biomarker of heart dysfunctions in patients with DM.
Methods: Muscle biopsies were taken from 6 DM1, 3 DM2 and 6 healthy subjects. RT-PCR analysis with primer flanking cTNT exon 5 was used to study the expression pattern of cTnT. The protein expression was analysed by western blot.
Results: RT-PCR has revealed the presence of adult cTnT isoform excluding-exon 5 in skeletal muscles from healthy subjects while in DM the expression of fetal cTnT isoform including-exon 5 was also present. No cTnT protein expression was evident in skeletal muscles from both healthy and DM subjects.
Conclusion: cTnT is expressed at RNA level in adult skeletal muscle. Moreover, in DM skeletal muscle the alternative splicing of cTnT is altered as in cardiac muscle. These data will be correlated with findings of cardiac dysfunctions and with histopathological features of skeletal muscle.

PR2095

Myotonic dystrophy type 2 – data from the Serbian Registry

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Background and aims: To analyze characteristic features of myotonic dystrophy type 2 (DM2) patients enrolled in the Serbian Registry.

Methods: In December 2016, Registry comprised 75 DM2 patients, but five patients were excluded. DM2 patients were compared with 70 adult-onset DM1 subjects matched for gender and age.

Results: Majority of DM2 patients were women (63%), with mean age at enrollment 51 ± 11 years. Age at onset was later in DM2 (37 ± 11 vs. 33 ± 9 years, $p<0.05$). Diagnostic delay was similar for DM2 and DM1 (12 ± 11 vs. 10 ± 7 years, $p>0.05$). Cranial and distal muscle weakness was less frequent in DM2 ($p<0.01$), while proximal was similar in both diseases ($p>0.05$). Walking assistance was needed in 6% of DM2 vs. 20% of DM1 patients ($p<0.05$). Specific features of DM2 (absent in DM1) were: hand tremor (56%), hyperhidrosis (52%), brisk tendon reflexes (40%) and calf hypertrophy (26%). Cataract was less common in DM2 (76% vs. 95%, $p<0.01$). AV block I was present in 3.2% DM2 vs. 14.3% DM1 subjects ($p<0.01$), and pacemaker in 3% vs. 11% ($p=0.08$). Dyastolic dysfunction of the left ventricle was more common in DM2 (42% vs. 18%, $p<0.01$), as well as diabetes (36% vs. 12%, $p<0.05$). Pulmonary restriction was seen in 5% of DM2 and 62% of DM1 cases ($p<0.01$).

Conclusion: DM2 is characterized by female predominance, later onset, less muscle weakness and infrequent conduction abnormalities compared to DM1. Presence of tremor, hyperhidrosis, brisk reflexes, calf hypertrophy, diastolic dysfunction and diabetes is suggestive of DM2.

Disclosure: Nothing to disclose

PR2096

Pattern and impact of pain in a national survey of genetic muscle disease

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Background and aims: Pain is often overlooked in genetic muscle diseas, despite there being large studies showing that pain may affect over two thirds of such patients - and is often treatable.

We set out to discover how prevalent pain is in New Zealand patients with these conditions and how it affected their quality of life, their particiation in society and their use of public health resources

Methods: In 2015-6 a national study called MD-Prev of the frequency and impact of genetically determined muscle disease was undertaken in New Zealand. 964 patients were asceertained. All participants were offered a chance to answer questionnaires regarding their condition and its impact (see figure 1)
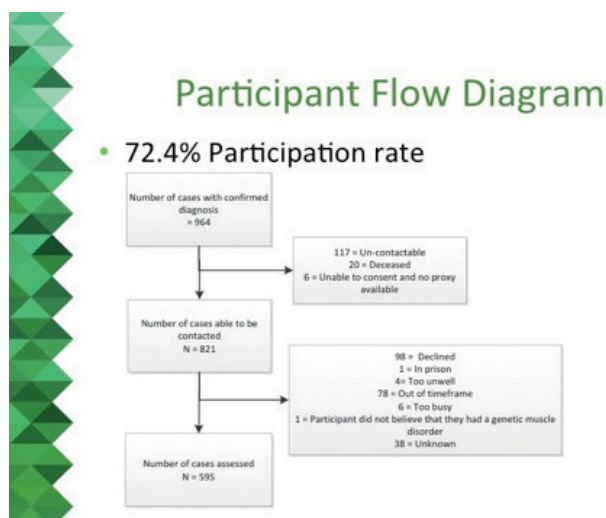
Figure 1. Study design

Results: 598 of the 964 (62%) patients agreed and were able to fill in questionnaires.

Demographics of our patiens are seen in Figure 2. The most common conditions were myotonic dystrophy type 1, dystrophinopathies, facioscapulohumeral dystrophy (FSHD) and limb girdle muscular dystrophies (LGMD)

affecting 35.6%, 19.5%, 12.8% and 9.6% respectively.

Pain was common in our patients affecting 61% over all. It was higher in LGMD 74.0% and FSHD 69% but somewhat lower in dystrophinopathies 62.5% and myotonic dystrophy 58.7% (Figure 3). Pain scores were higher in FSHD and myotonic dystrophy than dystrophinopathies. Higher pain scores were associated with decreased QoL, decreased participation in society and greater use of the health system. (p<0.05 for each.

Figure 2. Participation Demographics
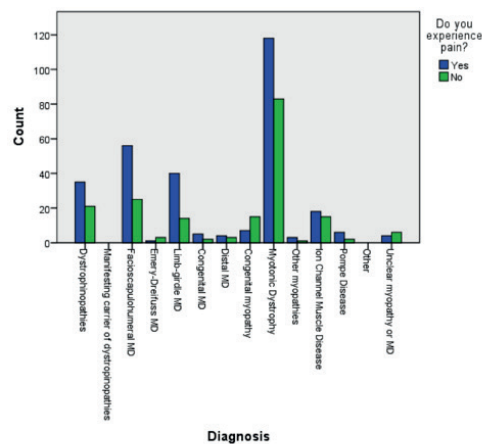
Figure 3. Pain by Diagnosis

Conclusion: Pain is a significant aspect of genetic muscle disease and treating it may lead to substantially better outcomes for patiants

Disclosure: Nothing to disclose

PR2097

Long-term observational study of patients with inclusion body myositis (IBM) receiving intravenous immunoglobulin (IVIG)

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Background and aims: IBM is characterized by a relentlessly progressive muscle weakness. Controlled clinical trials with IVIG for 3 months failed to demonstrate efficacy, but case reports and retrospective series with treatment for several years suggest positive effects. In the present study, we assessed the long-term effects of IVIG in IBM.

Methods: 73 patients fulfilled the ENMC criteria of IBM and 38 of these patients provided sufficient clinical data for a retrospective analysis including MMT6, walk tests, IBM-functional-rating-scale (IBM-FRS), and swallowing-related quality-of-life-scale (SWAL-Qol).

Results: Patients (72% male) were observed for a mean of 6 years. The mean age at disease onset was 59.5 years. 65% suffered from dysphagia, 77% used walking aids and 33% used a wheelchair. 22 had received IVIG for at least 50% of the time and 16 had received no pharmacological treatment. Patients with IVIG treatment displayed a significantly ameliorated decline of the mean MMT6 score per year (mean +/-SD: -1.175+/-0.49 vs. -2.815+/-0.59; p<0.05), depended significantly later on a cane (3.6 years vs. 7.6 years; p<0.05) and had less decline in maximum walking distance compared to untreated patients. No difference of any clinical parameter was noted when comparing presence or absence of cN1A antibodies.

Conclusion: IVIG treatment improved relevant clinical parameters in the long-term course of IBM compared to untreated patients. The data support a treatment attempt with IVIG in selected patients and call for a placebo-controlled clinical trial with IVIG treatment for one year.

Disclosure: JS has received grants, personal fees or other compensations from Bayer, Biogen, BioMarin, Biotest, CSL Behring, Grifols, Novartis, Octapharma, VitalAire.

PR2098

Hearing impairment in patients with myotonic dystrophy type 2

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Background and aims: As we observed several patients with myotonic dystrophy type (DM2) with hearing loss in daily practice, we performed an international cross-sectional study to systematically assess auditory characteristics of patients with DM2.

Methods: Patients with genetically confirmed DM2 were included prospectively. Interviews about DM2 and hearing symptoms were held, and all patients underwent routine otolaryngological examination, pure-tone audiometry (PTA: 0.25, 0.5, 1, 2, 4 and 8kHz), speech audiometry, tympanometry, acoustic middle-ear muscle reflexes, and Brainstem Auditory Evoked Potentials (BAEP).

Results: 31 Dutch and 25 French DM2 patients (61% female) were included with a mean age of 57 years (range 31-78). PTA showed that in 87% of the tested ears at least one of the hearing thresholds was outside the 95th percentile of the general population with the same sex and age (ISO 7029 standard). The median hearing threshold of the DM2 cohort was higher when compared to the general population (P<0.001 for all frequencies). The sensorineural hearing loss could be localized in the cochlea. A significant correlation was found between hearing loss and age, even when corrected for presbycusis.

Conclusion: Cochlear sensorineural hearing loss is indeed a frequent symptom in patients with DM2, resembling early presbycusis. Therefore, we recommend to inquire after and inform about hearing impairment in this population and easily perform a PTA to treat this symptom adequately by prescribing hearing aids when indicated.

Disclosure: Nothing to disclose

PR2099

Correlation of assessments of activities of daily living and muscle strength in refractory myasthenia gravis in the REGAIN study

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Background and aims: REGAIN, a phase 3, multicentre, double-blind, placebo-controlled, randomised study, assessed the safety and efficacy of eculizumab in patients with anti-acetylcholine receptor antibody–positive refractory generalised myasthenia gravis (gMG; N=125). Correlation between subjective and objective measures of MG-related impairment is assessed in patients with refractory gMG from the REGAIN study.

Methods: The Myasthenia Gravis Activities of Daily Living (MG-ADL) assessment tool is a physician-directed, patient-reported measure that evaluates symptom severity of MG-specific ADLs. The Quantitative Myasthenia Gravis (QMG) tool is a clinician-reported assessment tool that evaluates muscle strength. Assessments were performed at regular intervals during the 26-week treatment period, including weekly for the first 4 weeks. Correlation analyses were performed for total score and change from baseline at week 26 by treatment group using Pearson's r.

Results: Change from baseline in MG-ADL and QMG total score over time, using a repeated-measures model, showed rapid and sustained improvement in the eculizumab arm compared with placebo over 26 weeks: MG-ADL, eculizumab -4.2 [95%CI (-5.2, -3.3)], placebo -2.3 [95%CI (-3.2, -1.4)] (P=.0058); QMG, eculizumab -4.6 [95%CI (-5.8, -3.4)], placebo -1.6 [95%CI (-2.8, -0.5)] (P=.0006) (Figure 1). MG-ADL and QMG total scores at week 26 are correlated [r=0.68, 95%CI (0.57, 0.76), P<.0001] (Figure 2), as are total score changes from baseline [r=0.67, 95%CI (0.56, 0.76), P<.0001] (Figure 3).

Change in MG-ADL and QMG Total Score From Baseline to Week 26: Repeated Measures
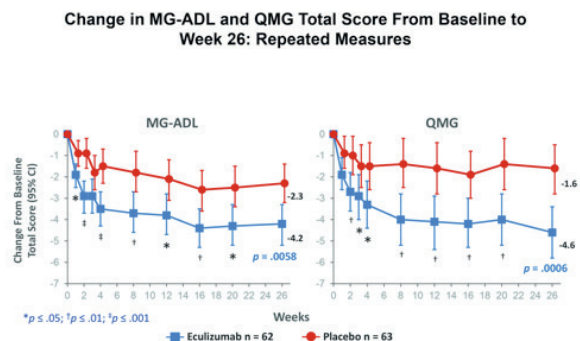
Figure 1. Change from baseline in MG-ADL total score and QMG total score (LS mean and 95% CI) over time from baseline to Week 26: repeated measures. Larger negative change from baseline indicates greater improvement.
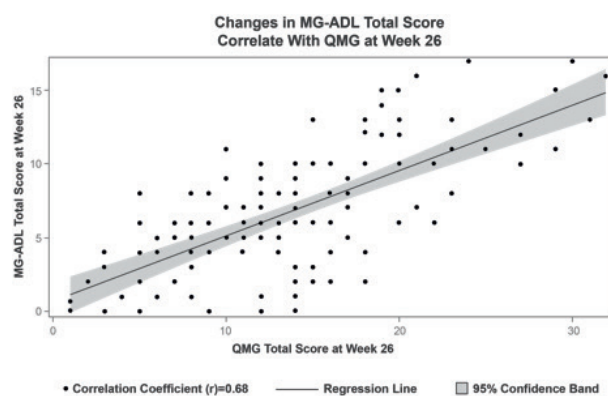
Figure 2. Correlation plot of MG-ADL total score versus QMG total score at week 26.
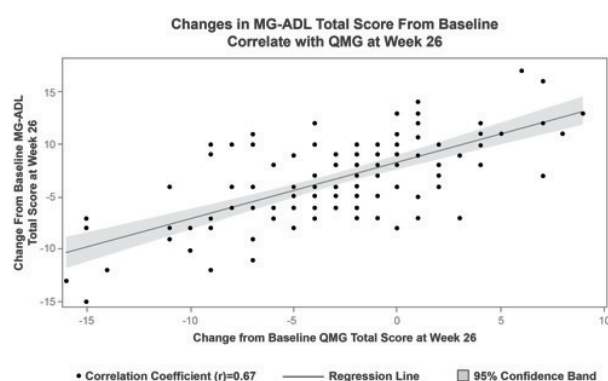
Figure 3. Correlation plot of MG-ADL total score versus QMG total score in change from baseline at week 26.

Conclusion: Patient-reported measurements of ADLs and physician-assessed measurements of muscle strength correlate in this study. As complementary measures but independent disease measures, they provide a more comprehensive picture of the status of patients with refractory gMG.

Disclosure: This study (NCT01997299) was sponsored by Alexion Pharmaceuticals (New Haven, CT, USA).

Neuroepidemiology

PR2100
Cancelled

PR2101
The association of alcohol consumption and smoking with multiple sclerosis prognosis

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Background and aims: The evidence that environmental exposures are important in the development of Multiple Sclerosis (MS) is well-established. This study aimed to evaluate the effect of smoking and alcohol and their possible interaction on the clinical course of MS.

Methods: A sample of MS patients (McDonald criteria) was recruited in the Novara Hospital (Italy) in 2009-2012. Smoking and alcohol history were evaluated with the European Prospective Investigation into Cancer and Nutrition (EPIC) lifestyle questionnaire. Severity of MS was assessed through the Multiple Sclerosis Severity Score (MSSS).

Results: Our sample included 351 consecutively enrolled patients, 190 ever-smokers and 283 ever-drinkers. Sex ratio (M/F) was 0.49 and relapsing-remitting form accounted for 76%. Mean age at onset was 33.0±10.1 years, median time from disease onset to MSSS evaluation was 10.0 (range:1.0-48.0) years with median MSSS of 2.70 (range:0.1-9.9). Age- and gender-adjusted logistic regression models were estimated comparing the upper versus lower tertiles of the MSSS distribution. Ever-smokers were almost 2 times more likely to fall in the upper tertile compared with never-smokers (p=0.024). No dose-dependent associations were found between smoking, alcohol and MS severity. When analyzing smoke-alcohol interaction, the group of ever-smoker/never-drinker patients was 6 times more likely to fall in the upper MSSS tertile compared with the group of never-smoker/never-drinker patients (p=0.013), but this association is strongly mitigated by concomitant alcohol consumption (see plot).

Four sub-groups considering smoking and drinking status

Six sub-groups considering smoking status and lifetime alcohol load

*Odds Ratios (OR) refer to Age- and gender-adjusted logistic regression models comparing the upper versus lower MSSS tertiles
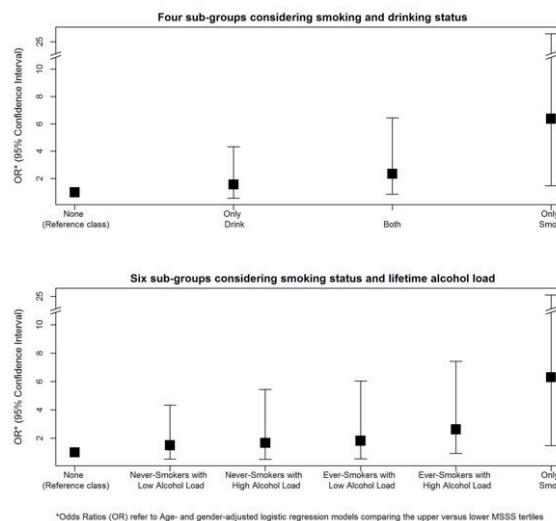
Covariate	Categories	OR*	95% CI	p-value
Smoking habits	*Ever VS Never*	1.893	1.09-3.29	0.024
Smoke Load (Pack/yr)	Low smoke Load	2.388	1.23-4.65	0.010
	High smoke Load	1.451	0.73-2.89	0.289
	Never smokers	1.000		
Drinking habits	*Ever VS Never*	0.901	0.44-1.87	0.779
Alcohol Load (Drinks/yr)	Low Alcohol Load	0.750	0.34-1.66	0.477
	High Alcohol Load	1.078	0.49-2.37	0.852
	Never drinkers	1.000		
* Odds Ratios (OR) refer to Age- and gender-adjusted logistic regression models comparing the upper versus lower MSSS tertiles				

Conclusion: Our study revealed that smoking is associated with more severe disease and provided support to the hypothesis that alcohol consumption may attenuate this association.

Disclosure: Nothing to disclose

PR2102

Striking reduction in stroke incidence over the last decade in Portuguese rural populations

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Background and aims: Stroke incidence has been declining worldwide. Rural populations, however, are traditionally not targeted by population-based campaigns alerting for stroke symptoms/ quick action and surveillance of risk factors (RF). Hospital services on the other hand have been reorganised all over the country with implementation of stroke units and stroke code pathways. Effect of these measures on stroke incidence and short-term outcome was determined using data from two community-based studies undertaken in 1998-2000 and 2009-2011 in populations residing in the same geographical area.

Methods: Both studies used standard diagnostic criteria and multiple overlapping sources of information, including hospital discharge data and family doctor's databases. Short-term outcome was measured by the modified Rankin Scale (mRS) and a disabling stroke defined when the 28-day mRS>prestroke mRS and 28-day mRS>1.

Results: In 1998-2000 period 226 first-ever strokes were registered compared to 193 in 2009-2011, an incidence of 305 and 227/100000 person-years, respectively. Median age of patients increased from 74 to 76 years and approximately 50% were women in both periods. Prevalence of VRF increased (>1 RF: 24 to 30%). Standardized to the 2011 Portuguese population, stroke incidence decreased 39% (incidence rate ratio=0.61, 95%CI 0.50-0.74), a 44% reduction for those over 75 years of age and 48% in women. Incidence of disabling stroke reduced 55% as well as haemorrhagic (48%) and ischaemic stroke (33%).

Conclusion: Risk of stroke, mainly of disabling stroke was substantially reduced eleven years apart. This reduction was complemented by a better short term outcome, suggesting stroke burden has been fought adequately by measures undertaken meanwhile.

Disclosure: Nothing to disclose

PR2103

Last update on genetic epidemiology of hereditary peripheral neuropathies (HPN) in Bulgaria

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Background and aims: This study aims to study the genetic epidemiology of HPN in the Bulgarian population and to establish the prevalence of the different types of neuropathies. Bulgarian population consists of three major ethnicities: Bulgarians, Turks and Roma (Gypsies) characterized by different origin, biological history and cultural anthropology.

Methods: Our cohort consists of 1316 patients with a clinical diagnosis of HPN. 933 affected have been genetically verified, while in 383 the molecular basis remains to be discovered. All the patients have undergone neurological, neurophysiological, and genetic testing.

Results: We diagnosed patients with 17 different types of HPN, caused by mutations in the following genes: PMP22, MPZ, Cx32, YARS, MFN2, NDRG1, CTDP1, HK1, GDAP1, SH3TC2, HINT1, BSCL2, GARS, HSP22, IGHMBP2 and TTR. The distribution of patients with genetically confirmed diagnosis among the different ethnicities is: 639 Bulgarians, 263 Gypsies and 31 Turks. The most frequent form in Bulgarians is CMT1A (37%), followed by TTR-FAP (16%) and dominant intermediate CMT (DI-CMT), caused by mutations in YARS gene (10%). Among Roma the most common HPN are CMT4D (49%), CCFDN (31%) and CMT4G (12%). Mutations in Cx32 gene count for half of the Turks diagnosed with HPN.

Conclusion: There are significant differences in the distribution of HPN in Bulgarians and Roma. In Bulgarians autosomal dominant HPN (88.4%) are much more frequent than autosomal recessive forms, while in Roma predominate autosomal recessive HPN (93.5%). These results contribute to the development of adequate diagnostic algorithm in the different ethnicities in the country.

Disclosure: Nothing to disclose

PR2104

Risk factors of sudden death from subarachnoid hemorrhage

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Background and aims: One in every four subarachnoid hemorrhage (SAH) patients dies suddenly outside hospitals but most SAH risk factor studies focus only on hospitalized patients. We aimed to study the differences in risk factors between hospitalized SAH and sudden death SAH patients.
Methods: The population-based FINRISK study cohort of 65 521 individuals was followed up for 1.52 million person-years. Sudden deaths from SAH were confirmed in autopsy. Cox proportional hazards model calculated hazard ratios (HRs), with all analyses adjusted for known SAH risk factors, marital status, and socio-economical status. Competing risks model analyzed differences in risk factors between hospitalized SAHs and sudden SAH deaths.
Results: We identified 98 sudden death SAHs and 445 hospitalized SAHs. Individuals smoking over 20 cigarettes per day had elevated sudden death SAH risk (HR 5.04 (95%CI 2.22-11.44)) and hospitalized SAH risk (HR 2.93 (95%CI 1.92-4.47)). Per SD (21.4mmHg) increase, hypertension elevated risk for sudden death SAH more (HR 1.34 (95%CI 1.09-1.65)) than risk for hospitalized SAH (HR 1.25 (95%CI 1.12-1.38)) (p=0.05). Participants living alone had elevated risk for sudden death SAH (HR 2.09 (95%CI 1.33-3.28)) but not for hospitalized SAH. No sudden death SAHs occurred in normotensive, never-smokers aged under 50.
Conclusion: Sudden death SAH risk is highest among people with most adverse risk factor profiles and among lone-livers, whereas it is rare among normotensive never-smokers aged under 50. Hospital-based studies underestimate role of risk factors in SAH.
Disclosure: Nothing to disclose

PR2105

Optic neuropathies: A case series study

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Background and aims: Optic neuropathy refers to damage to the optic nerve. The main symptom is vision loss (unilateral or bilateral). The leading causes are anterior ischemic optic neuropathy, either arteritic (AAION) or most likey nonarteritic (NAION), and optic neuritis, due to infectious/post-infectious, autoimmune or most likely demyelinating disorders. Hereditary, metabolic or toxic causes are less frequent.
Methods: Retrospective and descriptive study including all patients admitted in our hospital from 2005 until 2015 with a final diagnosis of optic neuropathy.
Results: We identified 114 cases, of which 62.3% were women, 37.7% were men and 15% were bilateral. Average age was 55.6 years. Autoinmmunity tests were performed on 65% of patients, as well as serologies (81.6%) and neuroimaging techniques (95%, of which 95% were MRIs and 5% were CT scans).
Conclusion: The most frequent etiology found was NAION (52.6%), with 56.6% of women and an average age of 67.4 years. In this particular group we found: hypertension (65% of cases), diabetes (33.3%) and dyslipemia (41.6%) and current smoking (18.3%). Two cases were caused by carotid dissection and one was associated with tadalafil use. The second most common cause was demyelinating optic neuritis (22%), with 84% of women and an average age of 33.4 years. Other etiologies were toxic, such as tobacco-alcohol (3.5%) and drug-induced (2.6%); infectious (3.5%) and AAION (2.6%). 13.2% of patients remain without diagnosis. The visual recovery was good in optic neuritis cases and poor in NAION ones.
Disclosure: Nothing to disclose

PR2106

Prevalence of Huntington's disease in Russia

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Background and aims: To date, only two published systematic reviews on Huntington's Disease (HD) prevalence (by Rawlins et al. and Sajjad Baig et al.) included Russia into analysis. The majority of Russian epidemiological studies were published solely in Russian language, authors included only five small Russian studies into analysis. We aimed to do a retrospective analysis of HD prevalence in Russia.

Methods: We searched for all works which estimated HD prevalence in Russia and which were published in English and/or Russian after 1994. In our search, we used PubMed, eLIBRARY.RU platform, and Russian State Library databases. We applied meta-analysis procedure using Freeman-Tukey transformation under random effect model with REML method.

Results: We found 27 epidemiological studies with estimation of HD prevalence in 18 out of 85 Russian regions. Some studies had missing data. In all studies HD diagnosis was based only on typical clinical presentation, and the majority of HD cases were not genetically confirmed. We estimated HD prevalence across studied Russian regions as 1.91 per 100,000 [95% CI: 1.32; 2.59]. However, results of analyzed studies are heterogeneous: $Q(26)=377.05604412$, p-value<0.00000001; amount of heterogeneity tau^2$=0.00000262$ (SE$=0.00000065$).

Conclusion: To our knowledge, it is the most comprehensive analysis of general HD prevalence in Russia based on published data. Only scattered local epidemiological studies on HD were conducted in Russia with relatively poor methodological approach. This demands to conduct the epidemiological study across the country using a standardized protocol.

Disclosure: Nothing to disclose

PR2107

Is Parkinson's disease more prevalent than previously thought?

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Background and aims: Parkinson's disease (PD) is a common neurodegenerative disorder. The frequency of PD varies depending on the diagnostic criteria, study population, and epidemiologic methods used. Healthcare administrative databases in which medical diagnoses are coded according to the International Classification of Diseases (ICD), are valuable resources for epidemiological studies.

Methods: In Hungary, a country with 10 million inhabitants and a single payer health insurance system we have launched the Neurohun 2004 – 2017 project. In the framework of the Hungarian Brain Research Program we created a database from medical and medication reports submitted for reimbursement purposes to the National Health Insurance Fund from all hospitals and outpatient services and pharmacies throughout the country in a four-year period of time, between 2010–2013. We validated the number of physician administered ICD-10 diagnosis of PD (ICD-10, code G20) by the number of patients with pharmacy refills of dopaminergic medications.

Results: In the 4-year period there were 31,578 patients with newly established G20 diagnoses, all of them had at least 1 refill of dopaminergic medication. This corresponds to an incidence of 79/100,000/year. In the 4-year period 69,629 patients were given at least once a G20 diagnosis, of these 18,507 died. Prevalence of G20 is therefore 511/100,000/year. Of the prevalent cases 48,099 had at least 3 refills, and a further 21,484 had 1 or 2 refills.

Conclusion: Both incidence and prevalence of PD is higher in Hungary than previously estimated. The physician-assigned number of PD diagnoses is confirmed by pharmacy refills of disease specific medications.

Disclosure: Nothing to disclose

PR2108

Residents of the poorer districts of Budapest suffer haemorrhagic stroke 9 years younger than their fellows from the wealthier districts

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Background and aims: Nevertheless the incidence of haemorrhagic stroke is in decline, Hungary is still in the frontline when it concerns stroke mortality. The National Health Insurance System offers universal access to healthcare, but the country shows significant socioeconomic inequalities among its subregions. We aimed to evaluate whether these inequalities have an impact on outcome of intracerebral haemorrhages (ICH) in all the 23 districts of the capital, Budapest.

Methods: In the framework of the National Brain Research Program we created the anonymized NEUROHUN database from medical reports submitted for reimbursement purposes to the National Health Insurance Fund and identified all spontaneous ICH cases from 1 January 2004 to 31 December 2013 among the inhabitants of Budapest. We have followed them up for survival until 30th April, 2014.

Results: Age at onset among the 8941 ICH cases correlated significantly with the mean annual taxable income of the districts: patients of the poorest district suffered ICH at the age of 64±11, while those from the wealthiest at 73±12 years. We have found a similar correlation between age at onset and the rate of residents on social aid: the higher the proportion of inhabitants on social aid, the younger the age at onset of ICH. We haven't found any correlation between income, proportion on social aid, population density and incidence or fatality (acute or long-term).

Conclusion: Patients residing in the poorer districts of the capital suffer haemorrhagic stroke at strikingly younger ages. These correlations identify social groups demanding improvement of stroke prevention.

Disclosure: We have performed the study in the framework of the National Brain Research Program.

Neuroimaging 2

PR2109

Abnormal functional connectivity of thalamic sub-regions contributes to fatigue in MS

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Background and aims: Despite the importance of the thalamus in multiple sclerosis (MS), only limited data on sub-regional thalamic functional connectivity (FC) and its relationship with fatigue are available. We investigated sub-regional thalamic FC abnormalities in MS patients and their correlation with the severity of fatigue.

Methods: Structural and resting-state (RS) fMRI data were acquired from 187 MS patients and 94 healthy controls (HC). Five thalamic sub-regions (frontal, motor, post-central, occipital, and temporal) were identified according with their structural connectivity-based parcellation, and they were used to perform a seed-based RS-FC analysis. Fatigue Severity Scale was assessed in MS patients and correlated to thalamic RS-FC abnormalities.

Results: Compared to HC, MS patients showed increased thalamic RS-FC with sensorimotor cortices and cerebellum, as well as reduced thalamic RS-FC with dorso-lateral prefrontal cortex (DLPFC) and caudate nuclei. Divergently, temporal thalamic sub-region showed increased RS-FC with the precuneus, along with reduced RS-FC with the anterior cingulate cortex (ACC) and cerebellum. Fatigued (F) patients, compared with non-fatigued (NF) patients, showed increased thalamic RS-FC with sensorimotor cortices, and reduced thalamic RS-FC with the DLPFC, caudate nuclei, ACC and cerebellum. In F-MS patients, frontal thalamic sub-region showed increased RS-FC with the precuneus. In F-MS patients, thalamic RS-FC abnormalities correlated with more severe fatigue, for the frontal and temporal thalamic sub-regions.

Conclusion: Thalamic RS-FC abnormalities with sensorimotor and executive areas contribute to the pathogenesis of fatigue in MS. Furthermore, the different behavior of the frontal and temporal thalamic sub-regions highlights their role in the genesis of fatigue in MS.

PR2110

Positron emission tomography (PET) of the brain in the diagnosis of epileptic focus

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Background and aims: In epilepsy PET is often used as part of the pre-surgical preparation of patients for the evaluation of morphological abnormalities and functional disorders and verification of epileptic focus. In numerous clinical and experimental studies it has been shown that a complex interplay of brain structures, which are involved in the generation of epileptic activity, and its suppression (about epilepsy and antiepileptic effects), is formed when the brain epileptization. (Mewasingh L.D., Christiaens F., Aeby A. et al., 2002). The aim of the study is the investigation of the metabolism of fluorodeoxyglucose (FDG) in the brain of a PWE in an interictal period by the method of positron emission tomography (PET).

Methods: We examined 60 patients with drug-resistant epilepsy (DRE) using MRI and FDG PET of the brain.

Results: Hypometabolism of FDG in the brain stem and cerebellum was found in 48 cases (80%). PE and focal hypometabolism of FDG in different lobes of the brain hemisphere were found in 36 (60%) PWE. Identified focus of FDG hypometabolism usually has corresponded with dominant epileptic focus established by EEG-VM. Hypometabolism in the brain stem and cerebellum was revealed among most patients with DRE (48 (80%)) .

Conclusion: Thus, our findings demonstrate FDG hypometabolism in structures of the posterior fossa (brain stem and cerebellum) in patients with DRE, that can be considered as a functional failure and probable cause insufficiency of the brain anti-epileptic system, and are relatively indication to improve the integrative brain control.

PR2111

Changes in effective connectivity in the sensorimotor network after a single dose of Escitalopram evaluated by Dynamic Causal Modelling for fMRI

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Background and aims: Selective serotonin reuptake inhibitors (SSRI) enhance monoaminergic neuro-transmission in the human brain which may enhance sensorimotor learning; however, the mechanisms are not clearly understood. Aim was to evaluate the effect of a single dose of Escitalopram on effective connectivity in the motor network by Dynamic Causal Modeling (DCM).

Methods: We conducted a double-blind placebo-controlled crossover study. Healthy volunteers received either a single dose of 20mg Escitalopram or placebo in an interval of one month. At each time point they performed twice a right hand related activation-task fMRI. Regions of interest (ROI) in the left hemisphere were defined as primary sensorimotor cortex (M1), premotor cortex (PMC) and supplementary motor area (SMA). Bayesian model selection was used to select the best fitting model concerning the two inputs "rest" and "move" on which the coupling parameters were calculated between ROIs using SPM12/DCM12. Mann-Whitney-U-Test was performed for group comparison.

Results: Ten subjects were included (6 males, 4 females; mean age 62; average handedness score 77). 32 out of 40 fMRI examinations were eligible for DCM analysis.

Bayesian model selection revealed the input "rest" on PMC and "move" on SMA regardless of placebo/Escitalopram intake. DCM analysis of this model showed a significant change in connectivity after Escitalopram intake between PMC-M1/M1-PMC and to a lesser extend from SMA-M1/M1-SMA.

Coupling parameters					
	placebo (N=15)		Escitalopram (N=17)		
ROIs	mean (±SD)	variance	mean (±SD)	variance	Mann-Whitney-U-Test
PMC → PMC	-0.23 (±0.03)	0.001	-0.07 (±0.15)	0.021	p = 0.003
M1 → M1	0.13 (±0.08)	0.007	0.01 (±0.16)	0.026	p = 0.030
SMA → SMA	-0.29 (±0.13)	0.016	-0.13 (±0.20)	0.041	p = 0.052
PMC → M1	-0.02 (±0.11)	0.012	0.35 (±0.48)	0.226	p = 0.022
PMC → SMA	0.66 (±0.20)	0.039	0.43 (±0.30)	0.091	p = 0.004
M1 → PMC	-0.39 (±0.08)	0.006	0.06 (±0.47)	0.220	p = 0.022
M1 → SMA	-0.45 (±0.24)	0.060	-0.07 (±0.43)	0.186	p = 0.022
SMA → PMC	0.44 (±0.19)	0.037	0.05 (±0.44)	0.195	p = 0.027
SMA → M1	0.41 (±0.21)	0.043	0.09 (±0.38)	0.144	p = 0.020

Table 1. Estimated coupling parameters by dynamic causal modeling after placebo/Escitalopram intake (ROIs = regions of interest, SD =standard deviation, M1 = primary sensorimotor cortex, PMC = premotor cortex, SMA = supplementary motor area)

Conclusion: DCM revealed a gain of effective connectivity between PMC-M1/M1-PMC after a single dose of Escitalopram. Since PMC is involved in planning hand movements, this increased connection may lead in part to enhanced sensorimotor learning.

Fig.1. Effective connectivity in the left sensori motor network after placebo (A) or Escitalopram (B) intake
Green arrows indicate positive coupling parameters, red arrows indicate negative coupling parameters; (M1 = primary sensorimotor cortex, PMC = premotor cortex, SMA = supplementary motor area)

PR2112

11C-PE2I and 18F-DOPA PET imaging for assessing the severity and rate of progression in Parkinson's disease: The longitudinal study

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Background and aims: 18F-DOPA positron emission tomography (PET) is regarded as the 'gold standard' for evaluating dopaminergic function in Parkinson's disease (PD). Radioligands for the dopamine transporter (DAT) are also used in clinical trials and for confirming PD diagnosis. Currently it is not clear which imaging marker is more reliable for assessing clinical severity and rate of progression. This study was designed to directly compare 18F-DOPA with the highly selective DAT radioligand 11C-PE2I, for the assessment of motor severity and rate of progression in PD.

Methods: Thirty-three mild-moderate PD patients underwent 18F-DOPA and 11C-PE2I PET at baseline (age=55.1±7.0; disease duration=5.9±2.2); twenty-three were followed-up at 19.4±3.3 months.

Results: Standard multiple regression at baseline indicated that 11C-PE2I BPND predicted total UPDRS-III (β=-0.474,p<0.05) and bradykinesia-rigidity scores (β=-0.610,p<0.01), whereas 18F-DOPA Ki did not significantly contribute to either model. Voxel-wise analysis showed negative correlation between 11C-PE2I BPND and motor severity across the whole striatum bilaterally. 18F-DOPA Ki clusters were restricted to most affected putamen and caudate. Longitudinally, negative correlations were found between striatal Δ11C-PE2I BPND, ΔUPDRS-III (rs(21)=-0.43,p=0.040) and Δbradykinesia-rigidity (rs(21)=-0.44,p=0.035). No associations were found between Δ18F-DOPA Ki, ΔUPDRS-III (rs(21)=-0.053,p=0.81) and Δbradykinesia-rigidity (rs(21)=0.026, p=0.91).

Conclusion: This is the first longitudinal study comparing 18F-DOPA and 11C-PE2I rates of decline in PD patients. Results suggest striatal DAT is more closely associated with clinical severity and rate of disease progression than amino-acid-decarboxylase. 11C-PE2I, given its high DAT selectivity may therefore be more effective to objectively evaluate efficacy of neuroprotective treatments in PD.

Disclosure: Nothing to disclose

PR2113

Survival in Parkinson's disease in relation to striatal dopamine transporter binding

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Background and aims: An earlier 6-[18F]fluoro-L-dopa PET study suggested that striatal dopaminergic defect is not associated with survival in Parkinson's disease (PD). The study aimed to investigate whether striatal dopamine transporter binding (DAT), as measured with [I-123]FP-CIT SPECT, can be used to predict mortality in patients with PD.

Methods: A total of 162 patients with PD and abnormal [I-123]FP-CIT SPECT, scanned in years 2007-2012, were followed until October 2016. A Cox regression model was used to investigate survival with independent predictors of age, gender, severity of motor impairment, levodopa-equivalent daily dose of medication, presence of cognitive defects, and putaminal specific binding ratio (SBR) of [I-123]FP-CIT. In addition, associations between striatal and extrastriatal SBRs and survival were investigated using voxel-based analyses.

Results: Higher age (p<0.001), presence of cognitive defects (p=0.001), and more severe motor symptom severity (p=0.002) were significantly associated with increased mortality. No associations were found between putaminal DAT binding (p=0.99) and survival. There were no significant differences in SBRs in any striatal or extrastriatal region between survivors and non-survivors, and no associations were found between SBRs and scan-to-death intervals among non-survivors.

Survival Function for patterns 1 – 3

Survival Function for patterns 1 – 2

Survival Function for patterns 1 – 3
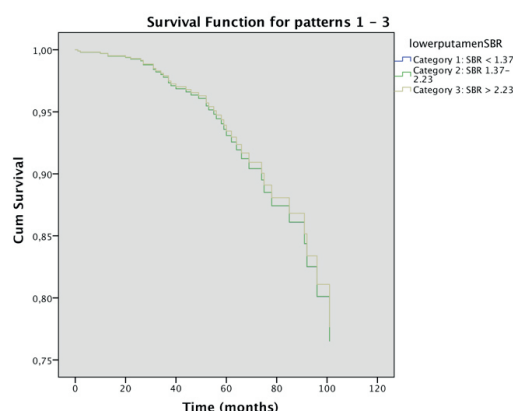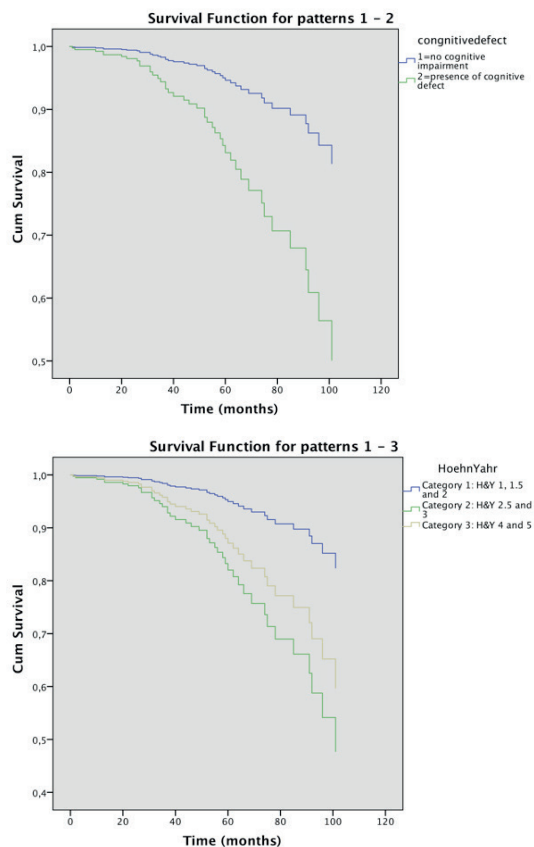
Conclusion: Unlike motor and cognitive symptoms, the degree of striatal DAT loss does not predict mortality in PD. Although presynaptic dopaminergic functional imaging has value as a diagnostic tool, clinical symptom-based characteristics are superior in predicting lifespan. Mortality in PD is not necessarily associated with the nigrostriatal dopaminergic degeneration, or there may be compensatory changes in the nigrostriatal dopamine metabolism, which lessen the value of dopaminergic imaging in predicting survival.

Disclosure: Nothing to disclose

PR2114

In-vivo imaging of α2 adrenoceptors in Parkinson's disease with 11C-yohimbine

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Background and aims: Patients with Parkinson´s diseae (PD) and healthy controls (HC) underwent positron emission tomography (PET) with [11C]yohimbine, an α2 adrenoceptor antagonist, to quantify pathological changes in α2-adrenoceptor expression.

Methods: Patients with PD (N=19) and healthy control subjects (N=13) underwent 90 minutes PET with [11C] yohimbine. The "off" state UPDRS scores were 41 (range 17-55); mean Hoehn and Yahr stage was 2.5 (range 2-3). The kinetic parameters of [11C]yohimbine, including unidirectional clearance (K1), washout rate constant (k2), steady-state volume of distribution (VT) and binding potential (BPND) were determined as described previously using an arteriel blood curve as input function (Nahimi et al., 2015).

Results: [11C]yohimbine K1 values were numerically higher, and the [11C]yohimbine k2 were numerically lower in all brain regions in HC subjects compared to PD patients (see Figure 1). This resulted in a global reduction of [11C] yohimbine VT which reached signifcance in several brain regions (see Figure 2A). [11C]yohimbine BPND estimates in PD revealed a global 11% reduction compared to HC when corpus callosum estimates were used as reference volumes of distribution (Figures 2B and 2C). Parametric images of [11C]yohimbine are shown in figure 3.
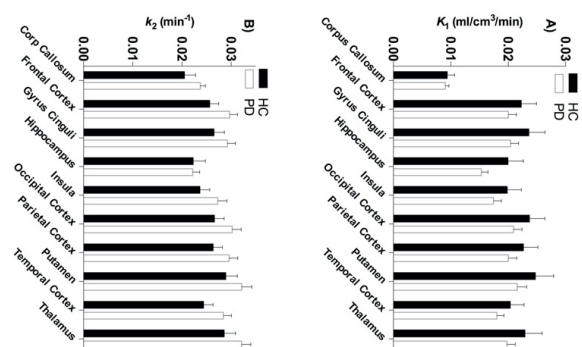
Figure 1A and 1B shows unidirectional uptake clearance and washout rate constant of [11C]yohimbine, respectively, in patients with Parkinson´s disease (PD) and healthy controls (HC).
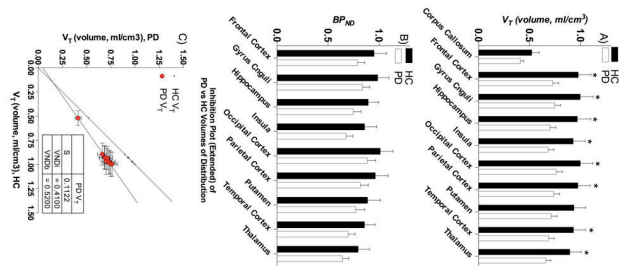
Figure 2A and 2B show [11C]yohimbine VT and BPND. [11C]yohimbine VT was significantly reduced in most regions in PD patients (P<0.05 (*)). Figure 2C shows the 11% reduction in [11C]yohimbine in PD patients, as estimated with the extended inhibition plot, with corpus callosum VT as reference region in PD patients (VNDi) and HC subjects (VNDb).
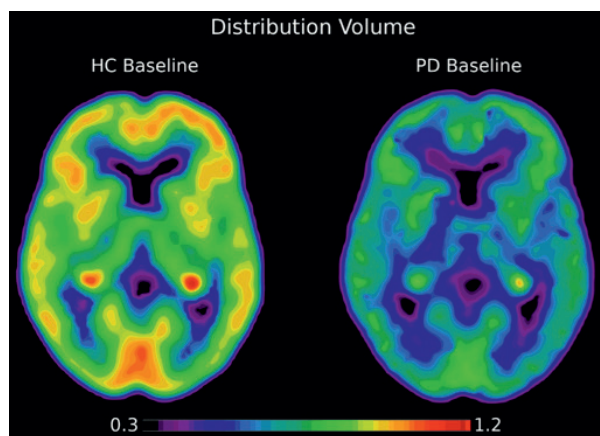
Figure 3 shows summed parametric images of [11C]yohimbine VT in PD patients (N=19) compared to healthy subjects (N=13).

Conclusion: [11C]yohimbine VT and BPND were reduced in brain regions that receive dense noradrenergic innervation. Our findings are in line with a post-mortem study where [3H]clonidine binding was reduced in PD patients. The current finding of a global loss or downregulation of α2-adrenoceptors supports the hypothesis that noradrenergic dysfunction in PD patients is widespread, and that this dysfunction hypothetically can contribute to the development of non-motor symptoms

Neuroimmunology 2

PR2115

CSF NCAM levels are modulated by highly-active DMTs

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Background and aims: Neural cell adhesion molecule (NCAM) expressed by neurons and glial cells has been implicated in neurite outgrowth and synaptic plasticity. CSF NCAM levels improved in acute MS patients treated with steroids. Our aim was to evaluate the effect of DMTs on CSF NCAM levels.

Methods: We measured CSF NCAM levels at baseline and an year later in 69 MS patients (53 RRMS, 16 Progressive MS), and 24 controls using an in-house ELISA. Of this 31 had received natalizumab, 17 mitoxantrone and 21 fingolimod. CSF NCAM levels were related to changes in EDSS and MSSS.

Results: At baseline, mean NCAM were lower in MS patients than controls [268.7 ng/ml (SD 109 ng/ml) Vs 340.6 ng/ml (SD 139 ng/ml), respectively; P=0.019]. In natalizumab and mitoxantrone treated groups, we observed an increase of mean NCAM of + 37.6 ng/mL (SD 17.6-57.6); p=0.01 and + 61.8 ng/mL (SD 12.7-110.8), p=0.01 respectively. However, in the fingolimod treated group mean NCAM decreased by - 60.74 ng/mL; p=0.02. The change in CSF NCAM levels were not predictive of changes in EDSS or MSSS.

Conclusion: Our results confirm that CSF NCAM CSF are lower in MS than controls. In addition, we observed improvement in NCAM levels with natalizumab and mitoxantrone, but not with fingolimod, where the opposite occurred. These changes may represent neuroprotective capacity of highly-active DMTs. Further studies are needed to confirm our results.

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PR2116

Olfactory evoked potentials in patients with limbic encephalitis

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Background and aims: Limbic encephalitis (LE) refers to an inflammatory process localized to structures of the limbic system that produces different neurologic and psychiatric disorders. To our knowledge, this is the first study investigating the olfactory function of patients with paraneoplastic or autoimmune encephalitis.

Methods: 16 LE patients (sex ratio 1:1, mean age 50 years) and 16 age and sex matching healthy control persons were tested. 14 LE patients were tested positive for an autoimmune antibody, 2 patients were seronegative. The Threshold Discrimination Identification test (TDI) was used to test orthonasal olfactory function. Olfactory evoked potentials (OEP) were recorded for objective olfactometry.

Results: 9 LE patients (56%) were hyposmic, 2 patients anosmic (12.5%) and 5 patients normosmic (31.5%). Their mean TDI value + standard deviation was 26.4 + 7.0. All LE patients with olfactory dysfunction (69%) also showed pathological OEP´s. All 16 healthy control persons were normosmic with a mean TDI value of 34.3 + 2.1.

Conclusion: Olfactory dysfunction seems to be a frequent symptom in LE patients. This might be due to structural changes of the limbic system. OEP´s were a suitable method to detect olfactory dysfunction in these patients. Further studies with a larger number of patients and imaging of the olfactory brain and olfactory bulb are needed.

Disclosure: Nothing to disclose

PR2117

B-cell activating factor (BAFF) as a biomarker in the diagnosis of chronic inflammatory demyelinating polyneuropathy (CIDP)

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Background and aims: CIDP is one of the most common forms of autoimmune disease. CIDP diagnosis is based on clinical symptoms, electromyography (EMG) and biopsy.

Methods: Main group (MG) in our study consisted of 59 patients diagnosed with CIDP (mean age:58.2±17.2 years) based on neurological examination and EMG that meets international criteria for diagnosis of CIDP (INCAT, 2001). BAFF was determined in the serum and cerebrospinal fluid (CSF) by using the enzyme immunoassay kits (R&D Systems, Inc.). The control group (CG) included 30 individuals.

Results: BAFF in the CSF was determined in 37 patients in the patient group and in 30 individuals in CG. However, the median level of BAFF in the serum of MG was 465.8 pg / mL [294.9; 596.8], while in CG it was 185.5pg/ml [100.5; 251.2]. The median level of BAFF in the CSF of MG was 68.8 pg/ml [52.4; 85.2], compared to 54.5 pg / ml [39.3; 62.5] in CG. Mann-Whitney test showed a statistically significant difference of BAFF levels in serum (p=0.001) and CSF (p=0.007) of MG compared with the CG. BAFF levels in the serum and CSF in MG did not correlate with one another (R=-0.19; p=0.21). Additionally, our results demonstrated thqt serum levels of BAFF correlate with disease severity as measured by the INCAT disability score.

Conclusion: Determining of the level of BAFF in the serum and CSF may be useful for the diagnosis of CIDP and may show the degree of disease activity.

Disclosure: This research has been granted by institutional support.

PR2118

NMOSD with and without concurrent autoimmune disorders: Comparison of clinical and MRI features

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Background and aims: It is still poorly understood whether the presentation of neuromyelitis optica spectrum disorders (NMOSD) is affected by the presence of concurrent autoimmune diseases (AID).

Methods: We reviewed the clinical and imaging data of 22 NMOSD with IgG anti-aquaporin-4 (anti-AQP4) or anti-myelin oligodendrocyte glycoprotein (anti-MOG) according to the revised diagnostic criteria of 2015. All MRI performed were reviewed by a diagnosis-blind neuroradiologist. The presence of longitudinally extensive transverse myelitis and associated features, spinal cord atrophy, optic nerve involvement and lesions of the dorsal medulla, periependymal areas, diencephalon, corpus callosum, subcortical and deep white matter were assessed, irrespective of disease phase. Patients with and without concurrent AID were compared.

Results: 15 cases with anti-AQP4 and 7 with anti-MOG were identified. Patients' age was 50.90±20.88 years and most were female (n=16). We found 14 AID in 9 patients, the most common being Sjogren syndrome (n=3). Three patients had an overlap syndrome (i.e. more than 3 AID). When comparing NMOSD+AID and NMOSD-only groups, we found no differences between current age, age of onset, first disease manifestation, current EDSS and anti-AQP4/anti-MOG status. The number of treatment options used in patients with NMOSD+AID was higher (p=0.005). Regarding MRI, there was no difference in the frequency of spinal cord changes and optic nerve or brain lesions between NMOSD with and without associated AID.

Conclusion: AIDs are frequent in anti-APQ4 NMOSD (53% of cases) and these patients require more treatments. We failed to find other clinical or imaging differences between groups.

Disclosure: Nothing to disclose

PR2119

Cognitive and FDG-PET/MRI study of patients with persistent cognitive impairment following VGKC-Complex antibodies limbic encephalitis

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Background and aims: VGKC-complex antibodies limbic encephalitis (LE) is considered a monophasic disease with a good response to immunotherapy. Few reports investigated the degree of cognitive impairment after the acute phase. We aim to report the cognitive sequelae and explore the relationship with brain structural and metabolic findings assessed by brain FDG-PET/MRI.

Methods: A series of 7 patients with a previous story of anti-LGI1 (n.5) and anti-CASPR2 (2) treated LE were tested with a neuropsychological battery. Six patients were also studied with brain [(18)F]FDG PET/MRI.

Results: Neuropsychological assessment showed persistent memory impairment, involving verbal (2/6 patients) and visuo-spatial memory (4/6). Executive functions, in particular sustained attention, processing speed and working memory were also affected (5/7 patients). Visual-spatial skills were also impaired in 2/6 patients. On PET/MRI study persistent FLAIR iperintensity of mesial temporal lobes was noted in two patients, whereas mild hippocampal atrophy was present in 5. Two patients with anterograde memory deficit showed increased glucose uptake in the hippocampal region and amygdala; this finding led to re-start immunotherapy with clinical improvement.

Conclusion: Our data show that patients affected by VGKC-complex LE develop persistent cognitive impairment regarding not only memory and executive functions but also visual-spatial abilities and visual-spatial memory. In some cases it's difficult to establish if the deficits are due to persistent inflammatory process, then requiring a further course of immunotherapy. In adjunction with other clinical and paraclinical data combined structural and metabolic information obtained with brain PET/MRI could be useful to address that issue.

Disclosure: Nothing to disclose

Neuro-ophthalmology/ neuro-otology

PR2120

Features of the state of "lid-eye" coordination in patients with Parkinson`s disease and atypical parkinsonism

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Background and aims: Vertical gaze palsy is a pathognomonic symptom of progressive supranuclear palsy (PSP) and often occurs in the advanced stages of Parkinson's disease (PD). There is a variety of the eyelids movements disorders in these diseases such as eyelid retraction, disturbance "lid-eye" coordination and others. At present, the analysis and quantification of these disorders are developed insufficiently.

Aim: To examine the condition of "lid-eye" coordination in patients with PD and atypical parkinsonism with a quantitative assessment of detected violations.

Methods: For simultaneous recording of lids and eyes movements we used videooculography. On the upper eyelid of the patient the round marker was attached, which allowed to measure the coordinates of the pupil and marker simultaneously. The data were processed using a special program, which evaluated the parameters of eyes and lid movements and provided their graphic registration.

The study involved 75 people with PD, 13 - with PSP and 16 with MSA.

Results: Discoordination in "lid-eye" system is best revealed during the investigation of vertical vestibular-ocular reflex. We analyzed the correlation coefficient in the vertical coordinate and evaluated the phase shift between the eyes and lid movements. Two patterns of disturbances were detected: lid movements ahead of eye movements; lid movement lag behind the eye movements. There is a direct correlation between the severity of detected disturbances and the degree of postural instability. "lid-eye" discoordination is more frequent observed in patients with postural disorders.
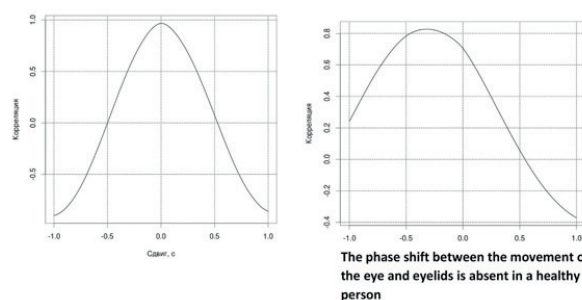
Fig. 2. Cross-correlation function and phase shift of pupil and eyelid position while registration of vertical vestibuloocular reflex

Conclusion: Evaluation of disorders in «lid-eye" system opens new perspectives in the study of the vertical gaze pathology in neurology.

Disclosure: The research is funded by the Ministry of Health of the Republic of Belarus
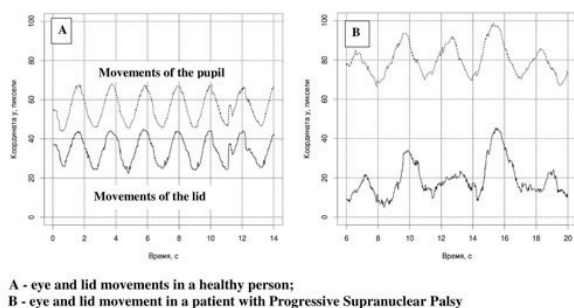
A - eye and lid movements in a healthy person;
B - eye and lid movement in a patient with Progressive Supranuclear Palsy

Fig. 1. Position of pupil and eyelid while registration of vertical vestibuloocular reflex

PR2121

The relationship of retinal atrophy to visual functioning and vision-related quality of life in patients with multiple sclerosis

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Background and aims: Inner retinal layer atrophy in patients with multiple sclerosis (MS) has been validated as a structural imaging biomarker for neurodegeneration, but the impact of retinal atrophy on the patient's visual functioning is unclear. Therefore, the aim of this study was to determine how inner retinal layer thickness relates to low and high contract visual acuity and vision-related quality of life (QoL) and to investigate the effect of previous episodes of MS related optic neuritis (MSON).

Methods: Spectral-domain OCT was performed in 267 patients with MS. Images were segmented for the peripapillary retinal nerve fibre layer (pRNFL) and the macular ganglion cell inner plexiform layer (GCIPL). Ophthalmological evaluations included history on MSON, high (HC) and low (LC) contrast visual acuity (VA) and vision-related QoL.

Results: Independent of MSON, HCVA and LCVA were significantly associated with pRNFL and GCIPL thickness. Vision-related QoL was positively associated with pRNFL (β=0.92, p=0.06) and GCIPL (β=0.93, p=0.02) thickness. This association was independent of MSON. Binocular, but also monocular atrophy of the inner retinal layers was associated with lower vision-related QoL.

Conclusion: This study showed that retinal atrophy has a significant impact on visual functioning in patients with MS. OCT may therefore give useful insight in patients with visual dysfunction and our findings support including OCT and vision-related QoL measures into optic neuritis treatment trials.

Disclosure: The VUMC MS Centre Amsterdam received financial research support for OCT projects from TEVA.

PR2122

Neuro-otological and peripheral nerve involvement in Fabry disease

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Background and aims: Fabry disease (FD) is an X-linked lysosomal storage disease, with multisystemic glycosphingolipids deposits. Neuro-otological involvement leading to hearing loss and vestibular dysfunctions has been described, but there is limited information about the frequency, site of lesion, or the relationship with peripheral neuropathy.

Objktives: To evaluate the presence of auditory and vestibular symptoms, and assess neurophysiological involvement of the VIII cranial nerve, correlating these findings with clinical and neurophysiological features of peripheral neuropathy.

Methods: We studied 36 patients with FD with a complete neurological and neuro-otological evaluation including nerve conduction studies, quantitative sensory testing, vestibular evoked myogenic potentials, videonistagmography, audiometry and brainstem auditory evoked potentials

Results: Neuro-otologic symptoms included hearing loss (22.2%), vertigo (27.8%) or both (25%). An involvement of either cochlear or vestibular function was identified in most patients (75%). In 70% of our patients the involvement of both cochlear and vestibular function could not be explained by a neural or vascular mechanism. Small fiber neuropathy was identified in 77.7%. There were no significant associations between neuro-otological and QST abnormalities.

Conclusion: Neuro-otologic involvement is frequent and most likely under-recognized in patients with FD. It lacks a specific neural or vascular pattern, suggesting multisystemic, end organ damage. Small fiber neuropathy is an earlier manifestation of FD, but there is no correlation between the development of neuropathy and neuro-otological abnormalities.

Disclosure: Nothing to disclose

PR2123

Role of Babinski's asynergy sign in the differential diagnosis of acute vestibular syndrome

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Background and aims: To assess Babinski's flexion asynergy in the differential diagnosis between central and peripheral lesions in acute vestibular syndrome (AVS).

Methods: Medical records of 114 patients with AVS were retrospectively reviewed. All patients underwent a full neurological and otoneurological examination, caloric tests and brain MRI. Babinski's flexion asynergy isconsidered to be positive when the patient cannot sit from a lying position without using his or her arms crossed, but is able to do so with support; if the patient still cannot sit up despite the support, it is considered to be negative (The fact that this difficulty may be the result of lack of strength in abdominal muscles cannot be ruled out).

Results: Of the 114 patients, 72 received a peripheral vestibular lesion diagnosis (vestibular neuritis) and the rest a diagnosis of central lesion (24% in the anterior inferior cerebellar artery -AICA- territory, 76% in the posterior inferior cerebellar artery -PICA- territory.) The sign sensitivity and specificity were 92.9% y 100%, respectively. Sensitivity was 100% in the case of the AICA lesions and 90.6% in the PICA ones. No correlation could be found between the presence of the sign and the age of the patient.

Conclusion: No patient with vestibular neuritis presented the flexion asynergy sign regardless of his/her age, but the sign was present in 92.9% of the patients with central lesion, which makes this sign a useful element when assessing a AVS patient.

Disclosure: Nothing to disclose

PR2124

Multifocal visual evoked potentials in optic neuritis and multiple sclerosis: A review

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Background and aims: The purpose of this review is to present a thorough survey of the results obtained by multifocal visual evoked potential (mf-VEP) in Optic neuritis (ON) and multiple sclerosis (MS) patients including comparisons to other measurements of the visual system. The aim is to evaluate whether mf-VEP can be applied as a valuable method to detect visual pathway involvement in ON and MS and to monitor long term disease course.

Methods: PubMed and EMBASE databases were consulted between 28th of September – 6th of October 2016 . Search terms were "Optic Neuritis AND multifocal visual evoked potential", "Multiple Sclerosis AND multifocal visual evoked potential". Every published study except for reviews of mf-VEP in MS or demyelinating diseases were included in this paper. Furthermore, reference lists of the included papers were searched. Unpublished and ongoing trials were searched for on the https://clinicaltrials.gov/ webpage using the same search terms. In total 38 published studies including mf-VEP measurements were retrieved and results of these are discussed in the following.

Results: Good correlation was shown between mf-VEP and OCT, ff-VEP, MRI(MTR, DTI), 30-2 standard automated perimetry and low-contrast-visual acuity. All but one study showed superior sensitivity and specificity compared to ff-VEP, especially with regards to small, peripheral lesions or lesions of the upper visual field.

Conclusion: In summary, the mf-VEP represents a compelling new method that may be incorporated as a diagnostic and prognostic marker in ON and MS and in monitoring disease course with regards to axonal loss, and de- and remyelination.

Disclosure: Dr. Pihl-Jensen has received support from Biogen Idec for a currently ongoing observational trial of VisionSearch 1 mfVEP measurements in optic neuritis patients. Mr Schmidt reports no disclosures. Dr. Frederiksen has served on scientific advisory boards for and received funding for travel related to these activities and honoraria from Biogen Idec, Merck Serono, Sanofi-Aventis, Teva, Novartis, Genzyme and Almirall. Jette Frederiksen has received speaker honoraria from Biogen Idec, Merck Serono and Teva. She has served as advisor on preclinical development for Takeda.

PR2125

Video head impulse test in patients with cerebellar ataxia

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Background and aims: Video head impulse test (vHIT) is a useful test, and it allows objective and quantitative measurements of vestibulo-ocular reflex (VOR). In this study, we analyzed VOR gains and compensatory saccades in various cerebellar ataxic disorders using vHIT. Also, it was investigated whether clinical factor affect VOR gains in various cerebellar ataxic disorders.

Methods: We consecutively enrolled 32 patients with chronic cerebellar ataxia (men=14, mean age=56) and 42 normal controls who had the VOR data measured by vHIT device (ICS Impulse, GN otometrics, Taastrup, Denmark). The cerebellar ataxia group consisted of 8 spinocerebellar ataxia (SCA), 13 cerebellar type of multiple system atrophy (MSA-C), 1 cerebellitis, and 10 idiopathic cerebellar atrophy. The VOR gains of each canal of cerebellar ataxia were compared with those of control. Normal control subjects defined who showed normal findings on neurologic examination, brain MRI, and vHIT.

Results: In the direct comparison of VOR gains between cerebellar ataxia and normal control, the cerebellar ataxia patients had more decreased VOR gains in AC and PC than normal control (p=0.02, 0.024, respectively). But the VOR gain of the horizontal canal was not different statistically. In the comparison of VOR gains between subgroups, VOR gain of the PC was significantly decreased in SCA patients (p=0.046).

Conclusion: Cerebellar ataxia had lower VOR gain especially in vertical semicircular canal planes. The VOR gains of the PC were different according to the subtypes of the cerebellar ataxic disorders. Analysis of VOR gain with vHIT may be helpful for the differential diagnosis of various cerebellar ataxias.

Disclosure: Nothing to disclose

PR2126

Heterozygous mutations in the AFG3L2 gene are associated with dominant optic atrophy in four Italian families

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Background and aims: Heterozygous OPA1 mutations are the most frequent cause of dominant optic atrophy (DOA), but also OPA3, WFS1 and SPG7 mutations have been reported. Recently, a heterozygous AFG3L2 mutation was reported in a single family with DOA and mild intellectual disability. AFG3L2 mutations have been previously associated with spinocerebellar ataxia 28.

Methods: We investigated four Italian DOA families with neuro-ophthalmological evaluation, brain MRI (3/4 probands), lactic acid at baseline and after standardized exercise (2/4) and audiometry (2/4). Genetic testing included sequence of OPA1 gene and Next-Generation-Sequencing with a panel of 35 genes associated with hereditary optic atrophy.

Results: Optic atrophy presented with a dominant pattern in 3/4 families, whereas one proband was sporadic. Neurological examination was normal in all cases. Ophthalmological evaluation revealed variable degrees of visual loss, impaired color vision and temporal pallor in all cases. Visual field showed central scotoma in 2/4 and a diffuse defect in 2/4. Optical coherence tomography demonstrated diffuse optic atrophy in 3/4 cases and temporal atrophy in 1/4. Audiometry showed sensorineural deafness in 1/2. Lactic acid was normal in 2/2. Brain MRI was unremarkable except for the presence of heterotopic cortical nodule in one case. The sporadic case presented also mental retardation. All cases were negative for OPA1 mutations whereas heterozygous pathogenic mutations were found in the AFG3L2 gene (c. 1385 C>T Family 1 and 2, c. 1220 A>G Family 3, c. 1394 G>A Family 4).

Conclusion: We provide strong evidence that AFG3L2 mutations are causative for DOA in the absence of spinocerebellar ataxia.

Disclosure: Nothing to disclose

Peripheral nerve disorders 2

PR2127

Peripheral nerves impairment in myotonic dystrophy Type 2

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Background and aims: Myotonic dystrophy (DM) is an inherited autosomal-dominant multisystemic disease. Peripheral nerves are frequently involved in petients with DM type 1. Limited data are available concerning peripheral nerves impairment in patients with DM type 2 (DM2). The aim of the study was to access the frequency and type of peripheral neuropathy (PNP) in patients DM2 and identify factors that may be associated with PNP.

Methods: The study comprised 23 patients with DM2, 12 men and 11 women between the ages 20-59 years. The duration of the disease – 2-5 years. Nerve conduction study was performed in median, ulnar, peroneal, tibial and sural nerves of both limbs.

Results: Electrophysiological abnormalities consistent with a diagnosis of PNP were found in 8 patients (34.8%), who were older ($45,9\pm9.5$ vs $37.4\pm7,4$ years) and had a longer duration of DM2 compared to those without PNP (16.4 ± 7.7 vs 10.5 ± 6.1 years). Achilles reflexes were absent in 15 patients with PNP and in 53.3 patients -without. The most common type of PNP in DM2 patients was motor demyelinating (37.5%) axonal motor and sensory polyneuropathy detected in 12.5%.

Conclusion: PNP is common in patients with DM2 and may be one of the multisystemic manifestation of DM2, but is usually subclinical. The most common type is the motor demyelinating PNP. Polyneuropathy is rarely found. Our results suggest the correlation between the presence of MN PNP in DM2 and age of patients ($R=+0.21$; $p<0.05$) and duration of disease ($R=+0.32$; $p<0.05$). No correlations were found between the presence of PNP and gender.

Disclosure: Nothing to disclose

PR2128

Kinetics of nanoparticle albumin-bound and solvent based paclitaxel in the peripheral nervous system: Implications for paclitaxel induced neuropathy

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Background and aims: Peripheral neuropathy is a common side effect of paclitaxel. We studied the access and distribution of different paclitaxel formulations (nanoparticle albumin-bound paclitaxel (nab) and solvent based paclitaxel) with the aim to characterize its uptake, turnover and clearance in the peripheral nervous system (PNS).

Methods: C57/B6 mice were treated with a single dose of the paclitaxel formulations and were sacrificed shortly after injection. By use of a new tracing technique paclitaxel uptake was visualized and quantified in different peripheral nervous system compartments.

Results: Nab-Paclitaxel showed a faster and higher influx and clearance rate compared to solvent based paclitaxel. Statistically significantly more (large diameter) NF200-positive neurons incorporated nab-paclitaxel into their cell body.
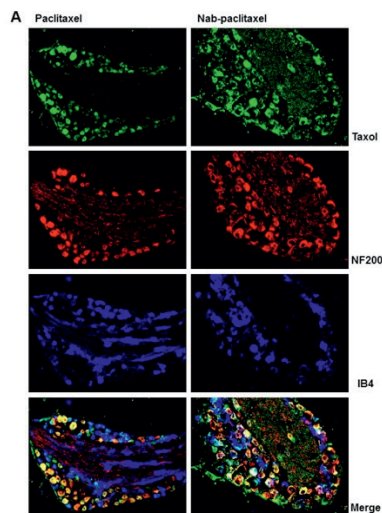
Representative immunohistochemistry staining for taxol (green), neurofilament 160/200 (red) and Isolectin-B4 (blue) in DRG sections 0.5 hours after injection of the concerning drug. Left column represents the paclitaxel treated group. Right column gives insight into the nab-paclitaxel treated group.

Conclusion: This is the first study that characterizes in detail the access of nab-paclitaxel and solvent based paclitaxel into the PNS. Our findings have important implications to understand the mechanism of paclitaxel induced neurotoxicity and to develop neuroprotective strategies by preventing access of paclitaxel to the peripheral nervous system.

Disclosure: Nothing to disclose

PR2129

C1q ablation exacerbates amyloid deposition: A study in a transgenic mouse model of ATTRV30M amyloid neuropathy

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Background and aims: ATTRV30M amyloid neuropathy is caused by deposition of amyloid fibrils composed of aberrant transthyretin (TTR). Complement co-localizes with amyloid . C1q polymorphisms correlate with age of onset in Cypriot patients. We use a double transgenic mouse model of the disease in which C1q is ablated to elucidate modifier role for C1q.

Methods: Animals: mTTR-/-hTTRMet30+/+ mC1q+/+ (V30M) and mTTR-/-hTTRMet30+/+mC1q-/- (V30M C1q KO). Age of animals 3 to 18 months

Amyloid deposition: Thioflavin S staining / hTTR immunohistochemistry (Fig 1A) to quantify stomach amyloid.

Transthyretin levels in the stomach and serum: Western Blot.

Macrophages and biomarkers: WB and/or immuno-cytochemistry: Fas, Caspase-3 (apoptosis), CD68 (macrophages), GRP78 (endoplasmic reticulum stress), C5b-9, Properdin ,C5a (complement) and CD88 (C5a receptor).
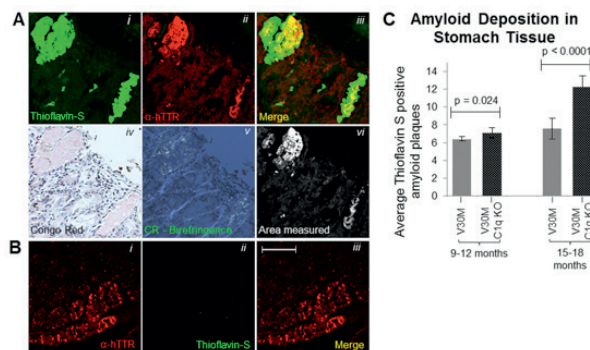
TTR amyloid demonstrated in 15 month (A) but not 5 month old animals (B). C1q ablated animals exhibit more amyloid(C)

Results: Amyloid deposition:

By 15 to 18 months ,the V30M C1q KO mice exhibited 60% more amyloid compared to the control V30M mice (Fig 1C).

Transthyretin levels in the stomach and serum:

A significant decrease in circulating hTTR in serum with age in both strains but more so in V30M C1q KO mice .

Macrophages and biomarkers: All markers were upregulated with age in both strains but significantly more in C1q ablated animals.CD68 was markedly decreased in V30M C1q KO mice (Fig 2A) with fewer macrophages in contact with amyloid deposits(Fig 2B).C5 and CD88 were markedly reduced in C1q ablated animals (Fig 3 A,B)
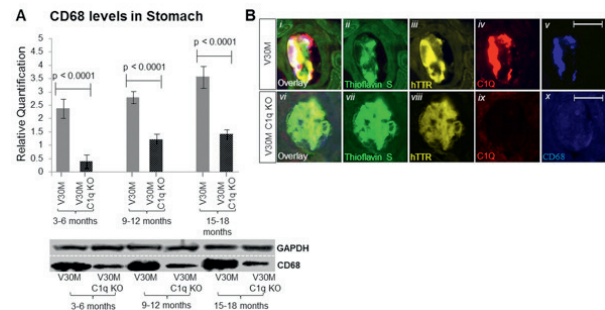
WB demonstrating fewer macrophages (A) and less phagocytosis (B)
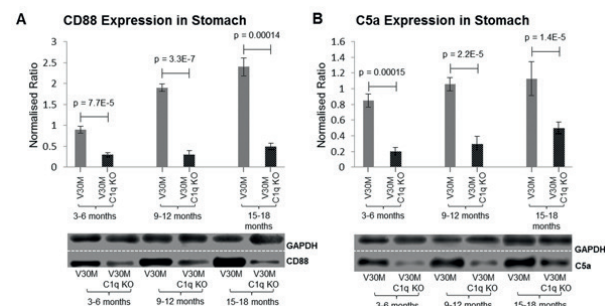
WB demonstrating reduced expression of C5a (A) and its receptor CD88 (B) in C1q ablated animals

Conclusion: The current study supports a modulating role of C1q in TTR amyloidosis. Pharmacological stimulation of macrophages may provide a therapeutic tool in treating amyloidosis.

Disclosure: Nothing to disclose

PR2130

Hemolytic side effects of IVIG: Modeling predicts risk reduction with anti-A/B immunoaffinity chromatography and to a lesser extent with anti-A donor screening

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Background and aims: The risk of hemolytic events (HEs) with intravenous immunoglobulin (IVIG) therapy appears to be linked to isoagglutinins (anti-A and anti-B) in the product.

Methods: Using published anti-A and anti-B titers for seven IVIGs and corresponding HE rates (per 1000kg of IVIG sold) calculated from HEs spontaneously reported to EudraVigilance (Bellac et al. Transfusion 55 Suppl 2, S13-22), we developed a mathematical model to predict the HE risk of IVIGs with given isoagglutinin levels. Applying the prediction model, we calculated the HE risk for an IVIG (Privigen®, CSL Behring) and evaluated risk reduction with two isoagglutinin reduction measures: an anti-A donor screening program eliminating ~5% of donors with high anti-A titers and an anti-A/anti-B specific immunoaffinity chromatography (IAC; Ig IsoLo®) step in the manufacturing process. Isoagglutinin titers in IVIGs from CSL Behring, measured by European Pharmacopoeia direct assay in the context of Official Control Authority Batch Release, were provided by Swissmedic, Bern, Switzerland.

Results: Predicted hemolytic risk was highest for blood group AB, followed by A and B; it was low for O. Anti-A donor screening is expected to reduce hemolytic risk. A greater risk reduction is predicted with IAC isoagglutinin reduction. The combination of both measures is expected to provide little additional benefit (Table).

IVIG production period* / production process	Anti-A (log-2 mean)	Anti-B (log-2 mean)	Predicted hemolytic risk (cases / 1000 kg IVIG used)				
			Blood group A	Blood group B	Blood group AB	Blood group O	Overall population# 42% A, 10% B, 4% AB 44% O
Privigen 2007-2013 chromatographic, no isoagglutinin reduction	5.4	4.21	3.17	1.93	8.45	0.01	1.87
Privigen 2013-2015 Chromatographic, donor screening	4.91	3.85	1.23	1.00	3.87	0.01	0.78
Privigen since Oct 2015 chromatographic, IAC	3.56	2.08	0.20	0.07	0.38	0.01	0.11
Privigen Chromatographic, donor screening + IAC	3.32	1.96	0.17	0.06	0.32	0.01	0.09
Carimune NF / Sandoglobulin Cohn-like	3.09	2.03	0.14	0.07	0.39	0.01	0.09

*Isoagglutinin reduction measures were implemented gradually, depending on regulatory approval in different countries. Donor screening and IAC combined was not implemented. Carimune NF / Sandoglobulin was produced with the Cohn-like process since 1978
#Based on US blood type distribution, similar to Western Europe

Conclusion: IAC isoagglutinin reduction as implemented for Privigen from October 2015 onwards is predicted to produce a meaningful reduction of the hemolytic risk with IVIG. Limitations of the model include reliance on spontaneous HE reports. The results need confirmation with clinical data.

Disclosure: This research was supported by CSL Behring.

PR2131

Charcot-Marie-Tooth 4J with conduction blocks

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Background and aims: The primary demyelinating forms of Charcot-Marie-Tooth (CMT) disease tend to show a diffuse and uniform slowing of nerve conduction velocities, without conduction blocks.

Methods: Clinical case: Male, 36 years old, without family history for neuromuscular disorders. Despite normal infancy, at age 13 he started complaining of frequent falls and paresthesias in the left leg. At age 18, he started noticing distal lower limb weakness, more evident on the left leg, that was slowly progressive proximally and at age of 22 he needed support for long distance. He became wheelchair bound at the age of 32. Weakness in the upper limbs began in the third decade, more pronounced on the right hand and the sensory symptoms worsened recently.

Results: Sural nerve biopsy was remarkable for the demyelinating features. EMG showed a multifocal asymmetric sensorymotor primary demyelinating neuropathy with conduction blocks. The CSF study showed albuminocytologic dissociation. Genetic studies for several hereditary peripheral neuropathies were negative. Considering a possible acquired peripheral neuropathy, oral prednisolone was prescribed with some improvement on the right hand strength but was stopped because of the side effects. IgIV was unsuccessful. NGS testing revealed compound heterozygosity for two mutations in the FIG4 gene: c.122T>C(p.Ile41Thr) and c.500dup(p.Tyr167*). The allelic study showed that each parent had one of the mutations establishing the molecular diagnosis of CMT-4J for this patient.

Conclusion: We report a rare case of CMT-4J with a strikingly asymmetric clinical phenotype and presence of multifocal motor conduction blocks, caused by two novel mutations in the FIG4 gene.

Disclosure: Nothing to disclose

PR2132

Genetic epidemiology analysis of Hungarian Charcot-Marie-Tooth patients

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Background and aims: Charcot- Marie- Tooth neuropathy (CMT) is a genetically and clinically heterogeneous group of rare neurological disorders with an overall prevalence of 1 per 2500. Here we report a genetic epidemiology study and the disease characteristics of Hungarian CMT patients.

Methods: 409 CMT1 and 122 CMT2 patients were enrolled and performed the genetic testing of PMP22, GJB1, MPZ, EGR2 and MFN2 genes routinely. NDRG1 and CTDP1 genes were screened only for founder mutations in Roma patients.

Results: 67.2% of the CMT1 and 33.6% of the CMT2 patients received a genetic diagnosis which indicates a 59.9% success rate in the study population. Considering all the affected individuals, the most frequent gene was the PMP22 (40.5%) which was followed by the GJB1 (9.2%), MPZ (4.5%), MFN2 (2.5%), NDRG1 (1.5%), EGR2 (1%) and CTDP1 (0.8%) pathogenic alterations.

Conclusion: The screening of PMP22, GJB1, MPZ and MFN2 genes resulted in the genetic diagnosis in more than half of the cases and total hit rate was 59.9%. The phenotypic spectrum and the disease severity of the studied patients also varied broadly. Associated features co-occurred more than fifth of the cases in addition to the classical symptoms of CMT, such as central nervous system abnormalities, hearing impairment, cranial nerve involvement or autoimmune disorders.

Disclosure: Nothing to disclose

PR2133

Small peripheral nerve cross-sectional area on ultrasound is a distinguishing feature of CANVAS syndrome

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Background and aims: Patients with Cerebellar Ataxia Neuropathy Vestibular Areflexia Syndrome (CANVAS) have sensory impairment due to dorsal root ganglionopathy. After finding small nerves on ultrasound in two CANVAS patients, we sought to study a larger cohort of CANVAS patients systematically to see if this is a feature of this ganglionopathy

Methods: The ultrasound cross sectional areas of median and ulnar nerves of 14 CANVAS patients were compared with 14 age- and gender-matched healthy controls and 14 age-and gender-matched patients with acquired axonal neuropathy. The individual cross sectional areas of CANVAS and neuropathy patients were also compared with the mean values for our reference population. The ultrasonographer was blinded to the patients' diagnostic status.

Results: The cross-sectional area of CANVAS patients was significantly smaller than tthat of both the controls and the peripheral neuropathy patients at all sites (P<.00001). By contrast, the cross-sectional area of the axonal peripheral neuropathy patients was mildly larger than the healthy controls'at all sites (P<.05). All but one individual measurement of cross-secional area at mid-forearm level in the CANVAS patients fell outside the normal control range and was >2 SDs below a reference mean.

Conclusion: The small nerves in CANVAS probably reflect nerve thinning from axonal loss secondary to ganglion cell loss. This is in contradistinction to the ultrasound abnormality in axonal neuropathy, in which the nerves are mildly enlarged. Our data show a role for ultrasound in the diagnosis of CANVAS ganglionopathy. This may also be applicable to ganglionopathy from other causes.

Disclosure: Nothing to disclose

Sleep disorders 2

PR2134

High anti-streptolysin-O titres and blood-brain barrier damage in narcolepsy type 1 in the first year after symptoms onset

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Background and aims: The chronic neurological disorder type 1 narcolepsy (NT1) is caused by a loss of hypocretin-producing neurons in the hypothalamus. The loss is of possible autoimmune origin. In this study, we measured biological markers of inflammation in the plasma and CSF of NT1 patients at different disease duration.

Methods: One hundred consecutive NT1 patients (57, 18, and 25 with disease duration >3 years (NT1>3y), between 1 and 3 years (NT11-3y), and <1 year respectively (NT1<1y) and 60 subjects with either idiopathic hypersomnia (n=16) or a complaint of subjective sleepiness (n=44) without objective findings were included. Patients underwent blood and cerebrospinal fluid (CSF) samples at diagnostic evaluation, including blood cells count, C-reactive protein (CRP), anti streptolysin-O (ASO) titers, together with oligoclonal band and IgG Index determination. Data were compared across patients' subgroups.

Results: NT1<1y had highest ASO titers, and more frequent (39%) occurrence of altered IgG Index than NT1>3y (14.5%, p=0.016) patients. NT1>3y had higher CRP levels compared to the other NT1 groups. A trend towards higher representation of neutrophils in NT1>3y and of lymphocytes in the NT1 1-3y and in the NT1<1y was observed among the NT1 groups. The other biochemical parameters did not differ significantly among groups.

Conclusion: NT1 close to symptoms onset is associated with evidence of recent streptococcal infection and, possibly, lymphocytosis and mild blood brain barrier damage. Immunological studies on narcolepsy pathophysiology should focus on patients with recent disease onset.

Disclosure: Nothing to disclose

PR2135

Sleep Education in Neurology (SEN): A European survey

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Background and aims: Sleep disorders are often overlooked during neurology residency. For this reason, Young European Sleep Neurologist Association (YESNA) initiated Sleep Education in Neurology (SEN) survey aiming at description of current status and needs of somnological education in Europe.

Methods: A 16-item online questionnaire was distributed to the European neurology residents and recently boarded neurologists. Questions were focused on education experiences and needs in the field of sleep disorders. At the end, we asked 5 simple- or multiple choice questions verifying the responder's knowledge upon sleep disorders.

Results: 432 neurologists replied (55% women, mean age 32.6±8.3 years), from 15 European countries. Most of the participants were residents (68%). Almost all recognised sleep disorder as clinically important issue (94%), however 40% of them didn't have any formal training and another 40% only very limited. 75% agreed that sleep disorders should be part of neurology training. Average number of proper answers to content questions about sleep disorders was 2/5. 83% of participants would like to increase their knowledge in the field of sleep disorders. The most preferred way would be as part of curriculum 76%. The other options would be workshops (41%), video-sessions (34%) and special lectures (33%) during conferences.

Conclusion: Sleep disorders are recognised from residents as important part of neurologicy, however education program is far from optimal. There is a strong need to increase educational effort.

Disclosure: Nothing to disclose

PR2136

Prevalence of sleep disturbances, fatigue, anxiety and depression in multiple sclerosis (MS)

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Background and aims: Sleep disturbances, fatigue, anxiety and depression are major determinants of quality of life in chronic disease. Unsystematic studies with limited numbers of patients provide heterogeneous data on frequency of these conditions in MS.

Methods: German nationwide survey in 26 centers addressing the prevalence sleep disturbances, fatigue, anxiety and depression in MS in a population-based study.

Results: RESULTS: Analysis included 2052 patients (30% males and 70% females) with MS: RRMS>2y, n=1279 (62%); RRMS<2y, n=299 (15%); SPMS, n=356 (17%); PPMS, n=114 (5%). Prevalence of sleep disturbances (Pittsburgh sleep quality questionnaire score [3]5) in MS in general was 73%, in RRMS<2y 60%, RRMS>2y 54%, SPMS 54% and PPMS 58%. Symptoms of fatigue (Modified Fatigue Impact Scale Median-Split[3]34) were reported by 45% of all MS patients, i.e. by 45% with RRMS<2y, 50% with RRMS>2y, 49% with SPMS and 56% with PPMS. Anxiety (Hospital Anxiety and Depression Scale, HADS, anxiety subscale[3]11) was present in 65% of MS patients including 62% of patients with RRMS<2y, 66% with RRMS>2y, 63% with SPMS and 61% with PPMS. Prevalence of depression (HADS depression subscale[3]11) was 60% in MS in general, 62% in RRMS<2y, 61% in RRMS>2y, 58% in SPMS and 55% in PPMS. For comparison, in the German normal population, prevalence of sleep disturbances is at 10%, anxiety at 7% and depression at 18%.

Conclusion: Sleep disturbances, anxiety and depression are highly prevalent in MS independent of disease stage and subtype. Hence, special surveillance of these conditions and psychosocial care at early stages of disease is required.

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PR2137

Replacing the AASM criteria in the maintenance of wakefulness test by scoring short sleep fragments has a significant impact on fitness to drive

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Background and aims: The onset of sleep fragments (SFs) <15 sec while driving can be fatal. However, the American Academy of Sleep Medicine's (AASM) sleep onset criteria does not necessarily take these short SFs into account. We investigated how scoring based on SFs ≥1 second differs from scoring based on AASM criteria (overt sleep, OS) in the maintenance of wakefulness test (MWT).

Methods: The third MWT trial of 66 individuals (44 males, aged 18-81) was scored for SFs (theta dominance on ≥1 occipital EEG channel and eyes closed ≥80%) and compared to the scoring of OS.

Results: As expected, the latency to the first SF was significantly shorter (Mean, M=16.0±9.1) compared to the latency of OS (M=22.9±11.5, p<0.001), and both were positively correlated (r=0.62, p<0.001). Among the different groups determinative of judging fitness to drive (0-20, 20-30, 30-40 min), 5/9 individuals with OS at 40 min switched to 20-30min, 2/9 to <20 min when regarding SFs. In addition, 1/1 individual with OS between 30-40 min switched to 20-30 min, and among individuals with OS at 20-30 min 9/13 switched to <20 min.

Conclusion: In general, SFs appear earlier than OS and also in the absence of OS. In addition, OS might be predicted based on SFs. The method of scoring SFs provides more detailed and accurate information which is currently reduced by the AASM criteria. More importantly, using the definition of SFs leads to relevant changes in the judgement of fitness to drive based on the MWT.

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PR2138

Idiopathic REM sleep behavior disorder – clinical characteristic of 67 patients

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Background and aims: REM sleep behavior disorder is characterized by dream enactment and by REM sleep without muscle atonia. Idiopathic REM sleep behavior disorder (iRBD) is considered as the initial stage of

neurodegeneration with pathological storage of alfa-synuclein. The aim of the study is to describe the cohort of iRBD subjects.

Methods: The diagnosis of iRBD (according to ICSD-3) was set in 62 men and 5 women, average age 66,8 (±SD=7,1) years. The patients were examined clinically including structured interview and MDR-UPDRS, Epworth sleepiness scale (ESS), Montreal Cognitive Assessment (MoCA), night polysomnography and DaTSCAN.

Results: The history of RBD symptoms began at the age of 62.0 (±8.2) years. Other premotor signs of synucleionopathy, constipation, hyposmia and orthostatic hypotension were present in 21%, 33%, and 25% of subjects respectively. 12% were smokers, 46% former smokers, and 42% lifelong non-smokers. The average ESS value was 7.7 (±4.0), and 34% rated ESS ≥10 which is a sign of excessive sleepiness. The average score of MDS-UPDRS III was 6.4 (±5.8). Moderate and severe obstructive sleep apnea (AHI>15) was found in 37%, and periodic limb movements in sleep (>15/ hour of sleep) in 55%. Restless legs syndrome was diagnosed in 34% of subjects. The average value of MoCA was 24.0 (±2.8). DatSCAN displayed abnormality in 26% of the group.

Conclusion: This cross-sectional study in RBD demonstrates frequent occurrence of sleep comorbidities, other premotor symptoms of neurodegeneration, and objective etection of nigrostriatal degeneration in a quarter of the cohort.

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PR2139

Machine learning for feature extraction and classification of narcolepsy from the European Narcolepsy Network (EU-NN) database

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Background and aims: Diagnosis of narcolepsy is challenging because various forms of the disease exist. Using data from the European-Narcolepsy Network (EU-NN) database we aim to build a predictive model with machine learning (ML) approach (stochastic gradient boosting, SGB) and identify the most influential features for the diagnosis of narcolepsy.

Methods: Data from 746 and 702 adult patients were used to build the predictive model of narcolepsy according to current and previous ICSD classification, i.e, narcolepsy with and without cataplexy (NwC-NwoC) and narcolepsy type 1 and type 2 (NT1-NT2), respectively. The predictors included questionnaire, laboratory and biomarkers data (e.g., cataplexy features, multiple sleep latency test (MSLT), hypocretin levels). The patients were randomly split into training and testing sets with a ratio of 0.75/0.25. The optimal model was the one giving the largest area under the receiver operating curves (AUC) in a 10-fold cross-validation scheme during training.

Results: Both classifiers gave high performances in the testing (AUC>0.99, Cohen's kappa=0.98). The cataplexy features were recognized as the most influential predictors indicating high validity of our model. Machine further suggested mean REM latency of MSLT contributed to classify NT1 and NT2, confirmed by logistic regression.

Conclusion: Since numbers of sleep-onset REM periods in MSLT has been criticized as instable and inconclusive parameter for diagnosis, mean REM latency may be a valuable diagnostic marker for differentiating narcolepsies. In summary we provide epidemiological evidence that ML, such as SGB, is valuable in diagnosing narcolepsy, and helps human to extract new features of narcolepsy on machine scale.

Disclosure: Nothing to disclose

Monday, 26 June 2017

Ageing and dementia 3

PR3001

ApoE Status and Alzheimer's disease profile in Tunisian patients

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Background and aims: Till today, ApoE4 is the only well-established genetic risk factor for late onset Alzheimer's disease (LOAD), nevertheless many non genetic factors also contribute to LOAD risk. We aimed to evaluate the association between ApoE status and main environmental, clinical and biological factors associated with this disease.

Methods: We enrolled 97 LOAD patients (diagnostic criteria: DSMIV and NINCDS-ADRDA) and 284 controls. Data concerning clinical and biological parameters, life style and dietary habits were collected via a survey and clinical analysis. ApoE were genotyped using PCR-RFLP. Biostatistical analysis were conducted on SPSS v20.0.

Results: ApoE4 seemed to increase LOAD risk by 4 fold (OR=4.23,p<0.001). ApoE4 allele was more frequent in patients with hypertension (p=0.032) and diabetes (p=0.004). This allele, in the homozygous or heterozygous state, was associated with increased Compliment 3 (p=0.018), total thyroxine T4 (p=0.034), cortisol (0.041) total cholesterol (p=0.021) serum levels and decreased thyroid-stimulating hormone TSH (p=0.044), HDL-c (p=0.012) and potassium (p=0.031) levels. ApoE E4 seems to influence the cognitive profile of our LOAD patients. In one hand, it was associated with low MMSE (0.016), IADL (p=0.001) and verbal fluency (p=0.010) scores and an early age of onset when compared to LOAD ApoE4 non carriers(p=0.015). in the other hand, this alleles didn't significantly affect other treats such as apraxia (p=0.950), apathy (0.508) humour, sleep and personality troubles (p=0.088, p=0.903 and p=0.444, respectively).

Conclusion: Besides its role in AB transport and aggregation ApoE gene seems to be involved in other physiopathological pathways linked to LOAD.

Disclosure: Nothing to disclose

PR3002

Diagnostic utility of FDG-PET in identifying AD dementia with atypical presentation or atypical course

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Background and aims: We performed a systematic review to assess the diagnostic utility of FDG-PET in identifying AD dementia with atypical presentation or course.

Methods: The search was performed on Medline on November 28, 2015. Minimum sample size was set a priori as 5 patients with the target condition. Critical outcomes were sensitivity, specificity and accuracy, or AUC in identifying AD dementias other than typical AD. Proxy outcomes (diagnostic change and increase in diagnostic confidence) were considered. Data were extracted and assessed as to publication bias, heterogeneity, imprecision, risk of bias, indirectness and applicability.

Results: Out of the 15 papers selected, 5 were not appropriate. The remaining 10 studies included a heterogeneous sample of atypical AD dementia patients, including mainly PPA (n=53) and PCA (n=43). These denoted (Figure) high concerns regarding the applicability of the index test (semi-quantitative methods of image analysis are increasingly but not routinely adopted in the clinical context). Critical outcomes were available for only 3 examined papers (n=133, mean AUC=0.87), providing a high level of evidence score. A proxy outcome (diagnostic change in 59.5% of cases) provided a moderate level of evidence.

Figure. Concerns regarding risk of bias and applicability are assessed as "low", "high", or "unclear" for each paper. **Flow and Timing**: interval between the index tests and the reference standard and patient dropouts; **Reference Standard**: the method used to determine the presence or absence of the target condition; **Index test**: the FDG-PET execution and interpretation; **Patient Selection**: methods for subject selection and clinical and demographic features of included patients.
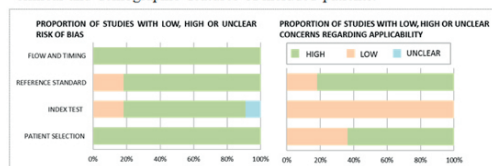
Figure

Conclusion: Data provided high evidence for moderate diagnostic utility of FDG-PET for the differential diagnosis among the main forms of dementia. This evidence is consistent with recommending the clinical use of FDG-PET in patients with atypical presentation or disease course.

Disclosure: This work was supported and funded by the European Academy of Neurology (EAN) and by the European Association of Nuclear Medicine (EANM).

PR3003

Incremental value of automated assessment of FDG-PET compared to visual reading, in the diagnostic work-up of patients with dementing neurodegenerative disorders

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Background and aims: We performed a systematic review to assess whether the automated assessment FDG-PET scans adds sufficient information to visual reading, to be required to optimize differential diagnosis in patients with dementing neurodegenerative disorders.

Methods: Minimum sample size was set a priori at 30 subjects with the target condition. Critical outcomes was the incremental value of automated assessment as compared to visual reading. Proxy outcomes identified a priori were accuracy, sensitivity, specificity of visual and automated FDG-PET assessment in identifying disease-specific hypometabolism.

Results: Out of the 14 papers selected by the referent panelist, 2 were not suitable. SPM and 3D-SSP were the most frequently used tools, followed by ROI analysis and PALZ score. The analyzed subjects suffered from heterogeneous neurodegenerative disorders. Critical outcomes were available in two papers, providing a moderate level of evidence. Both studies found an added value of 3D-SSP for the interpretation of visual images (diagnostic accuracy increased from 71 to 90% (P=0.02); diagnostic confidence increased from 3.3 to 4.0 with 3D-SSP (P=0.048)), the improvement effect being larger for unexperienced readers. Studies with proxy outcomes denoted inconsistent specificity (Table). Risk of bias was due to imprecision, use of only reference standard, and applicability in clinical setting (quantitative methods increasingly but not routinely adopted).

Figure. Concerns regarding risk of bias and applicability are assessed as "low", "high", or "unclear" for each paper. **Flow and Timing**: interval between the index tests and the reference standard and patient dropouts; **Reference Standard**: the method used to determine the presence or absence of the target condition; **Index test**: the FDG-PET execution and interpretation; **Patient Selection**: methods for subject selection and clinical and demographic features of included patients.

Table. Comparison between visual and automatic assessment of FDG-PET images: proxy outcomes findings.

Conclusion: Moderate-to-high evidence for a moderate added diagnostic value of automated assessment of FDG-PET over visual reading is consistent with recommending the use of automated assessment of FDG-PET in the diagnostic work-up of patients with dementing neurodegenerative disorders, mainly with unexperienced readers.

PR3004

Diagnostic utility of FDG-PET in differentiating between Alzheimer's and Lewy Bodies disease

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Background and aims: We performed a systematic review to assess the available evidence of FDG-PET utility in the differential diagnosis between Alzheimer's disease (AD) and dementia with Lewy bodies (DLB).

Methods: The search was performed on Medline, Embase, Cochrane, Google Scholar and Cross Reference (October 2015). Critical outcomes (sensitivity, specificity, accuracy of FDG-PET in distinguishing between AD from DLB patients) were assessed versus gold-(pathology) or reference-standard (biomarker-based diagnosis).

Results: Out of the 31 papers selected, 18 were excluded. The remaining 13 studies included a total of 743 patients (512 AD and 231 DLB). The available critical outcomes provided a moderate evidence score (Table). Semiquantitative and visual assessments led to the same sensitivity, specificity and accuracy. FDG-PET provided a specificity range of 67-100%, sensitivity range of 52-92%, and accuracy of 78% (SD 9.1) in the differential diagnosis between AD and DLB. There was a substantial risk of bias regarding patient selection and reference standard. Strong concerns regarded the applicability of the index test (semiquantitative methods of image analysis increasingly but not routinely adopted in the clinical context). Association studies denote a similar profile of cerebral hypometabolism in AD and DLB, with exception of the marked hypometabolism of the visual cortex in DLB.

Table. FDG-PET utility in the differential diagnosis between DLB/AD.

Conclusion: Low evidence for a moderate diagnostic utility of the FDG-PET for the differential diagnosis of AD and DLB leads to a dubious level of recommendation for the use of FDG-PET to differentiate AD and DLB.

PR3005

A comparison of AT8 immunoreactivity in the locus ceruleus and hippocampus of 154 brains from routine autopsies

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Background and aims: It has been recently suggested that phosphorylated-tau (p-tau) pathologies begin in the locus ceruleus (LC) and not in the transentorhinal region.

Methods: We compared semiquantitatively the AT8 immunoreactivity in the LC and hippocampus of 154 brains from routine autopsies.

Results: The numbers of AT8-positive neurons and the severity of AT8-positive neuropil threads (NTs) in the LC were strongly associated: there were no cases with AT8-positive neurons that lacked NTs and 20 cases had only NTs in the LC. P-tau pathologies in the LC were almost equally on both sides, although some cases showed unilateral predominance. The numbers of AT8-positive neurons in the LC and the numbers of AT8-positive neurons and NTs in the hippocampus were also strongly associated. There were only two cases with AT8-positive neurons in the LC that lacked p-tau pathology in the hippocampus, and 21 cases with p-tau pathology in the hippocampus that lacked AT8-positive neurons in the LC. The numbers of AT8-positive NTs in the LC and AT8-positive neurons and NTs in the hippocampus were also strongly associated. There were 7 cases with AT8-positive NTs in the LC that lacked p-tau pathology in the hippocampus, and five cases with p-tau pathologies in the hippocampus that lacked AT8-positive NTs in the LC.

Conclusion: We could not confirm that p-tau pathologies begin in the LC. We suspect their simultaneous occurrences in both hippocampal regions and in LC.

Disclosure: Nothing to disclose

PR3006

Pharmacogenetics of angiotensin receptor blockers in patients with dementia due to Alzheimer's disease

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Background and aims: The angiotensin-converting enzyme is an amyloid-β-degrading enzyme. Angiotensin receptor blockers have been implicated in the modulation of glucose homeostasis and in the boosted secretion of adipocytokines, thus improving insulin sensitivity and potentially slowing cognitive decline in patients with dementia due to Alzheimer's disease (AD).

Methods: Participants with AD according to National Institute on Aging – Alzheimer's Association criteria who did not use angiotensin-converting enzyme inhibitors were screened with the Mini-Mental State Examination, a 15-item Clock Drawing Test, and the Clinical Dementia Rating Sum-of-Boxes (CDR-SOB), and followed for one year. Genotyping was undertaken with TaqMan® Real-Time PCR technology for APOE (rs7412 and rs429358) and ACE (rs4291 and rs1800764), and with PCR technology for ACE I/D. Presence of each ACE polymorphism was correlated with APOE haplotypes and treatment using angiotensin receptor blockers. Kruskal-Wallis test and two-way ANOVA were employed for statistics, $\rho < 0.05$.

Results: Essentially, 191 consecutive patients were recruited, but 121 were excluded for using angiotensin-converting enzyme inhibitors, while 22 used angiotensin receptor blockers and 48 did not use renin-angiotensin system modulators. Overall, 65 patients (92.9%) used cholinesterase inhibitors, whereas 31 (44.3%) had arterial hypertension. All polymorphisms were in Hardy-Weinberg equilibrium. The 40 APOE-ε4 carriers (57.1%) had cumulatively earlier onset of AD ($\rho < 0.0001$). APOE-ε4 non-carriers who carried rs4291-A had cumulatively slower worsening of CDR-SOB scores ($\rho = 0.007$) regardless of treatment with angiotensin receptor blockers.
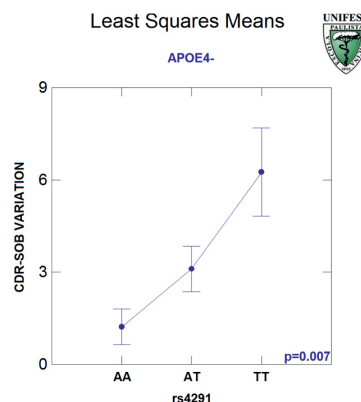
Variations in CDR-SOB scores according to rs4291 genotypes for APOE-ε4 non-carriers.

Conclusion: Angiotensin receptor blockers do not affect cognitive or functional decline in AD, but APOE-ε4 non-carriers who carry rs4291-A have cumulatively slower change of CDR-SOB scores.

PR3007

Cerebral vasomotor reactivity and cognitive impairment

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Background and aims: Cerebral vasomotor reactivity (VMR) represents a hemodynamic parameter that evaluates the capacity of cerebral arterioles to adapt in response to different stimuli in order to maintain a constant cerebral blood flow, its impairment being a consequence of cerebral small vessel dysfunction. The aim of our study is to determine whether cerebral VMR assessed using breath holding index (BHI) is impaired in patients with arterial hypertension and cognitive impairment.

Methods: We included 86 patients with arterial hypertension divided into two groups one with neurocognitive impairment (NCI) ranging from mild to severe aged between 47 and 90 years (70.2±11.4) and the second group without NCI aged between 44 and 86 years (61.8±11.1). We excluded patients with diseases that may impair cerebral VMR. All patients underwent assessment of VMR and neurocognitive functions.

Results: BHI values were significantly lower in the first group (1.01±0.33) compared to the second one (1.27±0.27) and we observed that there was a statistically significant association between BHI values and the presence of NCI (p=0.001). After adjusting for age using logistic regression we found that BHI is an independent predictor for NCI. The percent of patients with impaired cerebral vasomotor reactivity was significantly higher in the group of patients with NCI as compared to the other group (54.35% vs 30%, p=0.02).

Conclusion: According to our study there is significant association between impaired cerebral small vessels functionality and NCI, impaired VMR being also more frequent in patients with NCI. BHI may be considered an independent marker for cognitive impairment.

Disclosure: Nothing to disclose

PR3008

Loss of dorsolateral nigral hyperintensity on 3.0 tesla susceptibility-weighted imaging in dementia with Lewy bodies

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Background and aims: The diagnosis of dementia with Lewy bodies (DLB) may be challenging. Alzheimer's dementia (AD) is the most frequent misdiagnosis. Susceptibility-weighted imaging (SWI) using 3T MRI can detect a dorsolateral hyperintense signal area ("swallow tail" sign) in the substantia nigra (SN) of healthy controls. It corresponds to the nigrosome-1 and lacks in Parkinson's disease. We evaluated its diagnostic utility in DLB patients.

Methods: We recruited 15 DLB patients (8 men, mean age 76.2±7.1), 11 AD patients (4 men, 73.7±7.8) and 10 subjects with subjective memory complaint (SMC) (5 men, 67.2±9.4). All subjects performed MRI study including axial SWI sequences, visually assessed by two blinded neuroradiologists independently. A third rater resolved disagreements. DLB diagnosis required unilateral or bilateral loss of nigral hyperintensity.

Results: Age (p=0.09, Kruskal Wallis Test) and sex (p=0.68, chi2 test) among the groups did not differ. Raters agreed 89% (kappa=0.77, p<0.001). Twelve out of 15 DLB patients lacked nigral hyperintesity unilaterally or bilaterally, unlike the other groups (AD: 4/11; SMC: 1/10; p=0.002, chi2 test). Sensitivity, specificity, PPV, NPV and accuracy of DLB diagnosis by SWI were respectively 80%, 64%, 75%, 70% and 73% vs AD, 80%, and 90%, 92%, 75% and 84% vs SMC.

Conclusion: The assessment of dorsolateral nigral hyperintensity using 3T SWI was able to differentiate DLB from AD and SMC with good diagnostic accuracy. It can be a reliable and noninvasive method to help clinical diagnosis of DLB.

Disclosure: Nothing to disclose

PR3009

Assessing the relationship between CSF β-amyloid and white matter damage in AD

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Background and aims: White Matter (WM) Hyperintensities (WMHs) are common radiological findings in Alzheimer's disease (AD). Their role in AD pathogenesis is still controversial and little is known about their relationship with Cerebrospinal Fluid (CSF) biomarkers amyloid 1-42 (Aβ) and tau. Aim of the study is to assess the relationship between CSF biomarkers and WM damage in patients with AD.

Methods: 42 AD patients with pathological CSF Aβ levels (Aβ+), 23 non-AD demented patients with normal CSF Aβ levels (Aβ-) and 20 non-demented age and sex-matched controls (C) were enrolled. They underwent neurological examination, neuropsychological testing and brain MRI. To quantify WMHs-lesion load (WMHs-LL), FLAIR-hyperintense lesions were outlined using a semi-automated local threshold contouring software (Jim 7.0). To minimize the effect of confounding variables such as vascular comorbidities, we selected only patients with a Hachinski score<3 and without any relevant cardiovascular diseases. We performed non-parametric statistical analyses for between-group comparisons and multiple regression analyses.

Results: We found an increased WMHs-LL in Aβ+ compared with C (p<0.01), and in Aβ+ compared with Aβ- (p<0.05); no significant difference was observed between Aβ- and C with respect to WMHs-LL. The multiple regression analysis showed CSF Aβ concentration to be a predictor of patients' WMHs-LL.

Conclusion: WM damage has a role in AD pathogenesis, independently of vascular risk factors. The correlation between CSF Aβ levels and total WMH volume suggests a direct link between amyloid pathology, WM damage and neurodegeneration.

Disclosure: Nothing to disclose

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PR3010

The occurrence of cerebral infarction in previously diagnosed Hungarian migraineurs

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Background and aims: Migraine has been associated with an increased risk of stroke and other vascular diseases. The one-year prevalence of migraine in Hungary was reported at 9.6% in a previous survey; there are no Hungarian data about the co-occurrence of migraine and stroke. We investigated the prevalence of cerebral infarction and vascular risk factors in patients with earlier diagnosed migraine in Hungary.
Methods: We used the anonymized NEUROHUN database of the Hungarian Brain Research Programme from medical reports submitted to the National Healthcare Fund from all hospital and outpatient neurological services throughout the country for 2004 – 2013. Analyses were performed with the 3-digit codes of the 10th version of the International Classification of Diseases. We analyzed the data of all patients diagnosed with migraine (G43) in 2004 and looked for cerebral infarction (I63) occurring after the diagnosis of migraine. We also collected data about the most important vascular risk factors of migraineurs who had a stroke in this timeframe.
Results: In the year 2004, 6597 patients (5334 women; mean age: 39.2 years, SD: 14.5) were diagnosed with migraine. We found 414 patients (6.3% of migraineurs), who were diagnosed with cerebral infarction after the diagnosis of migraine. Beside migraine, 358 of them had at least one more risk factor (diabetes: 103, hypertension: 339, morbid obesity: 49, hyperlipidemia: 193, hyperuricemia: 24, atrial fibrillation: 37). The median number of risk factors other than migraine was 2.
Conclusion: Migraine was the only risk factor in 56 (13.5%) of 414 cerebral infarctions.
Disclosure: National Brain Research program KTIA-NAP-13-12013-001 from the government of Hungary.

PR3011

Stroke in adults with Down syndrome

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Background and aims: Over the past decades, Down Syndrome (DS) patients had a remarkable increase in their life expectancy, urging the need to improve our knowledge in age-related disorders, such as cerebrovascular diseases. DS patients are at increased risk of stroke when compared with age-matched individuals, however there are only few studies approaching this topic and none focusing on the adult population.
Methods: Retrospective case-series of adult DS stroke patients, admitted to eight Portuguese hospitals, from 2000 to May 2016.
Results: Thirteen adult DS stroke patients were studied, with a mean age of 38.8±13.0 years, 8 (62%) of the female sex. Nine of them had an ischemic stroke, three an intracerebral hemorrhage and one patient had cerebral venous thrombosis. Congenital heart disease accounted for one third of ischemic stroke cases and other third fulfilled the criteria for embolic stroke of undetermined source. Moyamoya Syndrome was the etiology for one intracerebral hemorrhage. Intra-hospital mortality was 31%.
Conclusion: To our knowledge, however small, this is the only case-series of stroke in adult DS patients. Congenital heart disease, a frequent cause of ischemic stroke in DS accounted only for one third of ischemic stroke cases, stressing the need to search for other etiologies in these patients. DS patients with stroke seem to have high intra-hospital mortality. More studies, with a higher number of patients, are needed to understand if cerebrovascular events in DS adult patients have distinctive characteristics.
Disclosure: Nothing to disclose

PR3012

Role of ceramide-rich microdomains in regulating cerebral vasculature post ischemia

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Background and aims: The hydrolysis of sphingomyelin catalyzed by the acid sphingomyelinase (Asm) or the neutral sphingomyelinase (Nsm) is one potential pathway for the generation of ceramide. Accumulation of ceramide promotes apoptosis after ischemia. Asm deficiency improves outcome after ischemic stroke. The role of the sphingomyelinase/ ceramide pathway in remodeling the cerebral vasculature after ischemia/ reperfusion (I/R) injury is poorly understood.

Methods: In-vitro, human brain microvascular endothelial cells (hCMEC/D3) were subjected to oxygen-glucose-deprivation (OGD) with or without subsequent reoxygenation/ recultivation. In vivo, focal cerebral ischemia was induced in male mice using middle cerebral artery occlusion (MCAO).

Results: In-vitro, we showed that Asm activity is attenuated upon OGD in hCMEC/D3. Interestingly, ceramide+ intracellular vesicles were formed in endothelial cells after OGD followed by reoxygenation/ recultivation. The number of vesicles peaked 3h after reoxygenation/ recultivation and declined thereafter. Notably, these ceramide+ vesicles strongly co-localized with the Notch-receptor ligand DLL4, a critical regulator of angiogenesis. Additionally, we found partial co-localization of vesicles with CD63 and Rab7, suggesting that these were late endosomes or multivesicular bodies. To study the source of ceramide+ microvesicles, we measured their number after pharmacological Asm or Nsm deactivation using amitriptyline or GW4869, respectively, demonstrating that both sphingomyelinases contributed to their formation. In-vivo, Asm inhibition by amitriptyline (12 mg/kg b.i.d.) enhanced angiogenesis in per-infarct brain tissue.

Conclusion: The current study suggests a novel role of ceramide signaling after I/R. Accordingly, ceramide+, DLL4+, CD63+ and Rab7+ late endosomes/ multivesicular bodies are formed upon I/R controlling post-stroke angiogenesis.

Disclosure: Nothing to disclose

PR3013

Thrombophilia in a prospective cohort of TIA patients: Incidence and prognosis

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Background and aims: Routine screening for thrombophilias is frequently performed in the diagnostic work-up of patients with cryptogenic cerebral ischemia, although its causative role was not convincingly shown. In this study we focused on the thrombophilic alterations associated with the recurrence of cerebral ischemia after a first transient ischemic attack (TIA).

Methods: We performed a prospective observational cohort study at the S.Orsola-Malpighi University Hospital, Bologna. We evaluated all consecutive patients presenting at the emergency department (ED) from August 2011 to December 2015 with signs and symptoms consistent with TIA. All patients underwent to a full standardized diagnostic workup. In case of cryptogenic TIA we also performed a thrombophilic screening including laboratory and genetic tests. Cerebral ischemia (TIA or ischemic stroke) recurrence was detected in a median follow-up of 21 months.

Results: Out of 610 consecutive TIA patients evaluated, 173 were cryptogenic (28%). We found out thrombophilic alterations in 4.7% of total TIA cohort, and 16.7% of cryptogenic TIA. Patients with thrombophilias presented a considerable recurrence of cerebral ischemia when compared to patients without thrombophilic alterations in the follow-up period. A significantly higher risk of recurrence was found for hyperhomocysteinemia and higher FVIII levels.

Conclusion: A higher recurrence of cerebral ischemia was related with hyperhomocysteinemia and higher FVIII levels, suggesting that this alterations could play a role in stroke risk stratification. However, currently we have no pharmacological strategy for treating the most of thrombophilic alterations, thus an all-inclusive thrombophilic routine screening in all cryptogenic stroke patients, also considering the high cost, is not recommended.

Disclosure: Nothing to disclose

PR3014

BNP levels in the first 24 hours after an acute ischemic stroke as a method for predicting atrial fibrillation development

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Background and aims: To determine whether serum BNP (natriuretic peptide type B) levels available in the emergency department, within the first 24 hours of ischemic stroke can predict the occurrence of atrial fibrillation (AF) in patients suspected of embolism of undetermined source.

Methods: Patients with acute ischemic stroke from suspected embolism without a documented history of AF were enrolled prospectively from January 2015 to July 2015. Clinical, demographic and cardiac imaging data were collected. Blood samples to measure BNP levels were taken within the first 24 hours of symptom onset and patients were followed for 12 months. We excluded patients with heart and renal failure or a well documented etiology for the stroke.

Results: A total of 54 patients were included in the study (mean age 71 years SD +/-12, 50.9% males). 13 patients developed AF during follow-up (24%). 10% of the patients didn t have vascular risk factors. Baseline ECG on the ER was normal in 98%. BNP levels in patients who developed AF was higher tan in those who did not develop atrial fibrillation (median of 273.4pg/ml vs 78.3pg/ml, p <0.001). In bivariate analysis and logistic regression, levels greater than 80pg/ml (p=0.024) and female gender (p=0.005) were associated with an increased risk of developing AF.

Conclusion: Moderate elevations of BNP in the first 24 hours after ischemic stroke may help to predict the development of AF in patients with stroke from suspected cardiac embolism.

Disclosure: Nothing to disclose

PR3015

Cancelled

PR3016

Inhibiting aquaporin 4 water transporter improves the outcome of ischemic stroke and inhibits perivascular flow through the basement membranes

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Background and aims: Brain edema is one of the first physiopathological events that occurs during ischemic stroke, with no dedicated treatment option. Aquaporin 4 (AQP4) is the most important water channel in the nervous system, and its inhibition before ischemia using the TGN-020 antagonist in an animal model of stroke proved to alleviate edema on MRI imaging.

Methods: Here we have utilized for the first time a single, post-ischemic, TGN-020 administration on a rat model of ischemic stroke, and performed the first histopathological analysis of the changes induced by the treatment at 3 and 7 days post stroke.

Results: Our data showed that, TGN-020 significantly reduced edema, glial scar, apoptosis and endogenous albumin diffusion, at both 3 and 7 days. Fractal analysis of the astrocytes in the glial scar of treated animals revealed lower values compared to untreated animals, supporting a less arborized and blunter astrocyte morphology compatible with more water deposition in their cytoplasm. Moreover, we have measured thicker vascular basement membranes colocalising with apparently trapped endogenous albumin, as the first bona fide proof that AQP4 inhibition might also regulate the formation and flow of perivascular fluid in the brain, an essential event in clearing away solutes like soluble Aβ.

Conclusion: These findings support TGN-020 as an effective treatment if administrated after ischemia, with putative applications extending beyond the boundaries of ischemic stroke, due to the newly identified functional mechanisms.

PR3017

Anemia at admission is associated with poor clinical outcome in cerebral venous thrombosis

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Background and aims: Anemia is a predictor of poor outcome in ischemic and hemorrhagic stroke. We examined this relationship in patients with cerebral venous thrombosis (CVT).

Methods: Consecutive adult patients with CVT were included from three academic hospitals between 1987 and 2015. Anemia at admission was scored according to World Health Organization definitions (men <8.1mmol/L, non-pregnant women <7.5mmol/L, pregnant women <6.9mmol/L). Patients with missing baseline hemoglobin were excluded. Poor outcome was defined as a modified Rankin Scale (mRS) score ≥ 3 at last follow-up. We also analyzed mortality separately. We adjusted for age, sex, cancer, oral contraceptive use, and center. In a subgroup analysis we stratified anemia into mild, moderate, and severe.

Results: Out of 548 patients, 484 were eligible. Median age was 42 (IQR 28-54) and 67% were women. Mean hemoglobin was 8.3 ± 1.3 mmol/L and 119 (25%) had anemia at admission. Patients with anemia more often had a history of cancer (20% vs. 7%). Median duration of follow-up was 6 months (IQR 6-7). Overall, 65 patients (14%) had a poor outcome. Patients with anemia had a higher risk of mRS ≥ 3 at follow-up (aOR 2.4, 95% CI 1.3-4.6). We found no association with mortality (aOR 1.8, 95% CI 0.8-4.0). Risk of poor outcome increased with severity of anemia (mild anemia: aOR 2.2, 95% CI 1.0-4.6; moderate anemia aOR 2.8, 95% CI 1.2-6.5; severe anemia aOR 3.0, 95% CI 0.5-17.9).

Conclusion: Anemia at admission is frequent and associated with poor clinical outcome in patients with CVT.

Disclosure: Nothing to disclose

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PR3018

Outcome of thrombectomy at 12 months

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Background and aims: Recent clinical trials have shown a significant reduction of disability and mortality at 3 months after ischemic stroke with large vessel occlusion treated with thrombectomy. The data concerning longer time frame of functional outcome are less known. The aim of the study was to assess the outcome of thrombectomy after 12 months.

Methods: A single comprehensive stroke centre retrospective study analysing data of patients treated with thrombectomy from January 2014 to January 2016. Patients were clinically assessed at admission and after 3 and 12 months. Good functional outcome was defined as modified Rankin Scale 0-2.

Results: 69 patients, 39 (56.6%) men, mean age 69.1 (SD 11.6) years were included. Mean NIHSS on admission was 15.5 (SD 5.5), bridging thrombolysis was given to 43 (62.3%). Good outcome at 12 months occurred in 32 (46.4%). Mortality was 25 (36.2%). Statistically significant differences between patients with good and poor outcome at 12 months were age (62.1vs. 75.1, P<0.001), admission NIHSS (13.6 vs. 17.1, P=0.01). There were no differences in mortality comparing "mothership" (n=51) and "drip-and-ship" (n=17) patients, chance for good outcome was non-significantly higher in "mothership" patients (49.0 vs.35.3%). Procedure time was shorter in patients with good outcome (46.6 vs.56.3minutes, P=0.02). Onset-to-recanalization time was not different (236.5 vs.251.7minutes, P=0.7).

Conclusion: The good outcome of thrombectomy at 12 month is relatively high, depending on age and initial NIHSS. Direct transport to the center, mothership approach was not a significant predictor.

Disclosure: Nothing to disclose

PR3019

Transcranial Doppler ultrasonography in a posterior reversible encephalopathy syndrome cohort: How useful is it?

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Background and aims: Posterior reversible encephalopathy syndrome (PRES) is a disorder characterized by acute blood-brain barrier dysfunction, occurring in patients with predisposing conditions and presenting with seizures, encephalopathy, headache and/or vision changes. MRI usually shows vasogenic bilateral oedema while angiograms may be normal or reveal stenosis. We aimed assessing whether transcranial Doppler ultrasonography (TCD), a non-invasive technique, is useful in predicting PRES complications.

Methods: We performed a retrospective chart review of PRES patients, who were evaluated by TCD. Blood pressure (BP), mean cerebral blood flow (MFV), presence of vasospasm criteria and MRI-confirmed ischemia [diffusion-weighted imaging (DWI) positive] or haemorrhage (ICH) were collected along with other covariates.

Results: We identified 26 patients (2008-2016); 22 had both TCD and MRI evaluations. The mean age was 44 (range: 11-74), and half were female. The median delay to TCD was 6 days (range: 0-22). Thirteen patients had vasospasm criteria. Eight patients had ICH, while 13 were DWI positive. Vasospasm was associated with positive DWI (77% vs 33%, p=0.042), but not with ICH (75% vs 50%, p=0.25). Patients with either ICH or DWI positivity had a trend towards higher MFV in the posterior circulation (154+/-74 vs 88+/-9 cm/s, p=0.56). Mean BP was significantly higher among ICH patients (103 vs 84 mmHg, p=0.0038), but not in those with ischemia (94 vs 90 mmHg, p=0.65).

Conclusion: Our data argue that TCD, together with BP values, will likely be useful predictors of PRES complications. Additional studies in larger cohorts are warranted for validation, cut-off establishment and possible therapeutic implications.

Disclosure: Nothing to disclose

PR3020

Comparison of biochemical biomarkers in ischemic stroke patients with unknown history of atrial fibrillation

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Background and aims: The risk of stroke in paroxysmal and permanent atrial fibrillation (AF) is similar, however paroxysmal AF is frequently unknown in patients presenting with ischaemic stroke. Biochemical biomarkers can be used to assess the indication of prolonged ECG monitoring in patients with embolic stroke of undetermined source. The aim of the study was to compare the association of selected biomarkers with occurrence of AF in stroke patients without known history of AF.

Methods: Retrospective monocentric analysis of consecutive ischemic stroke patients without history of AF admitted to comprehensive stroke centre in 5 months' period. As potential biomarkers, we compared parameters of prothrombotic state (D-dimer, fibrinogen, antithrombin III), cardiac function (NT-proBNP, high-sensitivity troponin I), inflammation (CRP) and renal function (eGFR).

Results: Out of 195 consecutive patients were selected 155 patients (average age 66.0 years, 25-96) without history of AF. The use of admission ECG, bedside ECG monitoring in ICU, telemetry, long-term Holter and event loop monitoring led to AF detection in 23 (14.8%) patients. Significant differences in AF and non-AF patients were found in mean levels of NT-proBNP (1713.6 vs 667.4ng/ml, P< 0.001), D-dimer (1017.4 vs 455.5ng/l; P=0.01) and fibrinogen (2.5 vs 3.1, P=0.01). CRP, troponin I, antithrombin III and eGFR were not different between the AF and non-AF patients.

Conclusion: Elevated levels of NT-proBNP, D-dimer and decreased fibrinogen are associated with AF in stroke patients with negative history of AF. Patients with positive biomarkers can be considered as candidates for prolonged ECG monitoring.

Disclosure: Nothing to disclose

PR3021

Automated cIMT is strongly related to carotid arterial stiffness (PWVβ) for Leukoaraiosis patients: An ultrasound study

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Background and aims: Leukoaraiosis (LA) is characterized by cerebral white matter changes (WMC) associated with cognitive decline and aging. Its pathophysiology is poorly understood and its diagnosis still based on MRI and exclusion of other causes of WMC. Recent studies have linked LA and carotid artery disease (CAD). In order to find a reliable diagnostic marker for LA and better understand the association between CAD and LA, we explore the relationship between automated carotid intima-media thickness (cIMT) and one of previously suggested LA markers, one point pulse wave velocity stiffness index (PWVb), in LA patients.

Methods: PWVb and cIMT of carotid arteries were calculated using ultrasound echo-tracking system and AtheroCloud™ software in 26 LA patients and 24 risk-factor matched controls. Automated cIMT was validated against the manual methods using t-test, Mann Whitney test and Wilcoxon test. The coefficient of correlation (CC) between cIMT and PWVb was computed for LA and control groups.

Results: cIMT and PWVβ were significantly higher in LA patients compared to controls. Accuracy of automated cIMT against the manual methods was of 99.14% (p<0.001) vs. 96.63% (p<0.001). The CC between semi-auto/auto cIMT and PWVb for the LA patients was 0.303(p-value 0.133) and 0.429 (p-value 0.029). CC between cIMT and PWVb was 218% and 373% higher in LA patients compared to controls for automated and semi-automated cIMT methods.

Conclusion: We validated new automated cIMT measurement for Leukoaraiosis. Automated cIMT significantly correlated with carotid stiffness marker PWVβ in Leukoaraiosis patients suggesting new powerful diagnostic marker of Leukoaraiosis.

Disclosure: Nothing to disclose

PR3022

Strong association between quantified hemorrhage volume and functional outcome in aneurysmal subarachnoid hemorrhage

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Background and aims: One of the most significant prognostic markers in patients with aneurysmal subarachnoid hemorrhage (aSAH) is the amount of blood on CT, which is frequently estimated with the modified Fisher scale or the Hijdra sum score. Drawbacks of these scales are that they are coarse, have moderate interobserver agreement and are cumbersome. Quantitative volume measurement assesses hemorrhage volume more precisely, however the clinical value is currently unknown. The aim of this study was to associate quantified hemorrhage volume with functional outcome.

Methods: All consecutive patients with aSAH from the prospective cohort admitted to our institution between December 2011 and January 2016 with non-contrast CT (NCCT) within 24 hours after ictus available were included. Automatic hemorrhage segmentation software was used to determine the hemorrhage volume. Functional outcome was assessed after 6 months on the modified Rankin scale (mRS). Ordinal regression was used to calculate the odds ratio (OR) with 95% confidence interval for a shift in the direction of poor outcome on the mRS per dl increase in hemorrhage volume.

Results: We included 244 patients. Median hemorrhage volume increased significantly with increasing mRS. (Figure 1). The OR of increase in mRS was 1.43 (95%CI 1.30 – 1.58) per dl increase in hemorrhage volume.
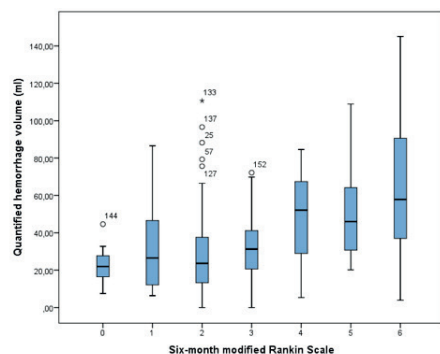
Distribution of hemorrhage volumes across different categories of mRS

Conclusion: This preliminary analysis shows a strong association between quantified hemorrhage volume and functional outcome in aSAH patients.

Disclosure: Nothing to disclose

PR3023

Elevated factor VIII activity increases the risk of cerebral venous thrombosis: A case-control study

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Background and aims: Elevated factor VIII activity (FVIII) is a risk factor for leg-vein thrombosis and pulmonary embolism. We assessed whether elevated FVIII is also associated with cerebral venous thrombosis (CVT).

Methods: We performed a matched case-control study. As cases we assessed patients with CVT admitted between July 2006 and December 2016. Controls were healthy hospital-staff employees matched for age (within 5 years) and sex. FVIII was measured at least 3 months after diagnosis of CVT. Elevated FVIII was defined as FVIII activity >150 IU/dl. A logistic regression analysis was used, adjusting for age and sex.

Results: We included 116 cases and 116 controls. For cases, mean age was 40 (±11) years and for controls 41 (±11) years. In both groups 99/116 (85%) were women. The median time between CVT diagnosis and blood collection was 18 months (interquartile range 7-39 months). Cases more often had elevated FVIII compared to controls (83.6% vs 28.4%, p<0.001). After adjustment, elevated FVIII was associated with a 15-fold increased risk of CVT (adjusted odds ratio [aOR] 15.3; 95% confidence interval [CI] 7.8-30.1). Stratification by sex showed a stronger association in men (aOR 22.8; 95% CI 2.8-184.3) than in women (aOR 14.7; 95% CI 7.2-30.2).

Conclusion: Elevated FVIII is a strong risk factor for CVT.

Disclosure: Nothing to disclose

PR3024

Factors influencing the first hour of the acute ischemic stroke management

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Background and aims: Thrombolysis is an effective treatment in ischemic stroke, but the principal limitation in its application is the time. Previous NINDS indications suggested that the door-to-treatment time should be lesser than 1 hour. In our large geographical area with more than 3 millions of inhabitants, we analysed data of ischemic stroke admissions to evaluate factors influencing the achievement of this temporal target.

Methods: All consecutive patients admitted to 11 Hospitals in Northern Italy for ischemic stroke were enrolled during a 6 months period. Demographical data, time of single steps of stroke pathway and treatment procedures were registered for each patients. Statistical analysis was conducted using t-test and chi-square test for univariate and logistic regression for multivariate analysis.

Results: 1688 patients were recruited (Median age: 76 years). A stroke code during transport was applied in 19.3% of subjects, while we registered an application of this code in 26.7% of patients at triage. Door-to-treatment time was significantly associated with age, clinical severity, the use of EMS and high urgency codes used during the transport and at triage ($p<0.05$). At multivariate analysis, clinical severity (OR: 1.027; 95%CI: 1.002 – 1.054) and high urgency code used at triage (OR: 1.726; 95%CI: 1.134 – 2.629) were predictors of a management time lesser than one hour.

Conclusion: A prompt identification of the disease also at Emergency Department triage with the assignment of a high urgency code could allow to optimize the stroke management, reducing the avoidable time.

Disclosure: Nothing to disclose

PR3025

Cost-effectiveness in Preventive Antibiotics in Stroke Study (PASS)

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Background and aims: The preventive antibiotics in stroke study (PASS) is a multicentre, randomised, open-label trial compared intravenous ceftriaxone at a dose of 2g, given every 24h intravenously for 4 days, in addition to stroke unit care, or standard stroke unit care without preventive antimicrobial therapy in acute stroke patients. Here, we report the cost-effectiveness.

Methods: Economic evaluation was performed from a societal perspective with a time horizon of 3 months. Volumes and unit costs of all direct and indirect medical and non-medical care were assessed. Primary outcome was cost per unit of the modified Rankin scale (mRS) and per quality-adjusted life year (QALY) for cost-effectiveness and cost-utility analysis. Incremental costs-effectiveness analyses were performed to determine extra costs per unit decrease in the mRS and extra costs per additional QALY.

Results: 2538 patients were available for the intention-to-treat-analysis. Prophylactic ceftriaxone prevented infections (clinical diagnosis OR 0.55 [95% CI 0.44–0.70], $p<0\cdot0001$), but was not associated with a shift on the mRS score distribution (adjusted common OR 0.94 [CI 0.82–1.09], p=0.41). After 3 months, there was a significant difference of 0.008 in QALY's (CI 0.003-0.013) in favor of ceftriaxone. The probability of ceftriaxone being cost-effective ranged between 0.67-0.89. A probability of 0.75 was attained at a willing-to-pay-level of €2290 per unit decrease in Rankin score and of €12200 per QALY.

Conclusion: Preventive ceftriaxone did not influence functional outcome but it is a cost-effective therapy. The economic benefit must be weighed against the risk of antibiotic resistance development.

Disclosure: Netherlands Organization for Health Research and Development, Netherlands Heart Foundation, and the European Research Council.

Child neurology/developmental neurology

PR3026

Structure of the intracranial vessels and elastic-viscous properties of erythrocyte membranes in children with connective tissue dysplasia

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Background and aims: To study the structure of intracranial vessels and elastic-viscous properties of erythrocyte membranes in children with connective tissue dysplasia.

Methods: The main group consisted of 60 children with signs of connective tissue dysplasia in age from 10 to 16 years. The comparison group consisted of 40 healthy children. Magnetic resonance angiography was performed on the apparatus with a field strength of 1.5 Tesla. In order to examine the state of the cytoplasmic membrane of erythrocytes were manufactured dry preparations of erythrocytes. Preparations was scanned by atomic-force microscope. Quantification of the elastic membrane was performed by calculating the Young's Modulus.

Results: In patients of group 1 hypoplasia of the right transverse sinus occurred in 5% of cases, arteriovenous malformations - in 5% of cases, hypoplasia of the left transverse sinus - in 10.5% of cases, hypoplasia of the left sigmoid sinus - 5% of cases, hypoplasia of the left internal jugular vein - in 10.5% of cases. In group 2 the development of intracranial venous anomalies have been identified. Patients of group 1 had a Young's modulus equal to 182,68 MPa, in the comparison group - 111,48 MPa.

Conclusion: For children with severe dysplasia of the connective tissue characterized by the presence of intracranial venous malformations. In children with connective tissue dysplasia higher Young's modulus of the membranes of red blood cells than children of the comparison group, indicating a reduced ability of red blood cells to deform when passing through the microvasculature.

Disclosure: Nothing to disclose

PR3027

Parkinsonism in children: Clinical and etiological characterization from a tertiary referral center

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Background and aims: Parkinsonism in children is rarely observed and differs from the classical appearance in adults: bradykinesia and rigidity are the most frequent features, resting tremor is rare and can be episodic. Aim of this study was to evaluate clinical features, causes and disease course of a cohort of pediatric patients with parkinsonism referred to a tertiary referral center for pediatric movement disorders.

Methods: We included in an ad-hoc database patients aged under 18 years presenting with parkinsonism as the cardinal feature at disease onset, or during disease course seen in our Institute between 1990 and 2016. Clinical features, disease course, and investigations were reported and periodically updated.

Results: 85 patients (33F, 52M) were included. Mean age at disease onset was 6.8 years and mean follow-up duration was 8.4 (± 9.4) years; the main or only clinical feature at disease onset was parkinsonism in 16.4% of patients and dystonia in 20%; mean age at onset of parkinsonism was 12.6 (±6.1) years. Tremor was observed in 5/85 cases (5.8%). A definite diagnosis was reached in 71 (83.5%) of patients (Figure 1): 11.2% were affected by acquired conditions and 88.7% by genetic disorders (Table 1), the most frequent ones being Neurodegeneration with Brain Iron Accumulation (28%), neurotransmitter synthesis disorders (10%) and Huntington's disease (7%). Additional pathological findings were frequently observed.

Figure 1. Causes of pediatric parkinsonism in the present series.

Diagnosis	Number of cases	%
GM1 gangliosidosis	3	4,2%
Huntington's disease	5	7,0%
Fragile X-associated tremor/ataxia syndr (FXTAS)	1	1,4%
Wilson's disease	3	4,2%
Juvenile Parkinson's disease (Parkin)	1	1,4%
Rett's syndrome	1	1,4%
Dravet syndrome	2	2,8%
MCT8 deficiency (Allan-Herndon-Dudley syndr.)	1	1,4%
Complicated HSP	1	1,4%
Chediak Higashi disease	1	1,4%
RANBP2	1	1,4%
Ceroidolipofuscinosis CLN3	3	4,2%
Ataxia telangiectasia	1	1,4%
Mitochondrial diseases	3	4,2%
Bilateral Striatal Necrosis	2	2,8%
DYT12/DYT12-like dystonia	3	4,2%
Neurotransmitters synthesis defects	7	9,9%
NBIA	20	28,2%
Progressive myoclonic epilepsy	4	5,6%
Total	63	88,7%

Table 1. Rare genetic diseases causing parkinsonism in the present series. HSP: hereditary spastic paraplegia

Conclusion: Differential diagnosis of pediatric parkinsonism largely differs from adult cases. Rare genetic neurodegenerative diseases underlie most cases, but potentially treatable disorders are not infrequent and need a prompt diagnosis and therapy.
Disclosure: Nothing to disclose

PR3028

Acute flaccid paralysis in an eleven-month old child - a diagnostic and therapeutic challenge

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Background and aims: Acute Flaccid Paralysis (AFP) is characterized by focal poliomyelitis-like spinal cord paralysis with minimal sensory symptoms. Its severity and frequent lack of identification of a pathogen make it a treatment challenge. The number of diagnosis has increased, especially in the USA, since 2012.
Methods: Case-report.
Results: An eleven-month old female with unremarkable background was admitted at our hospital due to 48hour history of a progressive paralysis and respiratory distress needing support ventilation; the neurological examination revealed a hypotonic-arreflexic-tetraplegia, remaining examination was unremarkable.
Neuroaxis-MRI revealed a non-enhancing lesion C1-D9 extending upwards to the tegmental medulla, preferentially involving the gray matter and posterior columns, brain MRI was normal. CSF revealed albumino-cytological dissociation. PCR for adenovirus was positive on respiratory secretions. One month before she had hand-foot-and-mouth disease and the PCR for adenovirus was positive on feces but negative on respiratory secretions excluding enterovirus-D68. Possible etiologies were infectious or immune and she was treated with methylprednisolone, immunoglobulin and cidofovir. PCR for neurotropic virus on CSF, and antiAQP4, anti-MOG and antiNMDA on blood were negative. EEG was normal. Control neuroaxis-MRI (12th day) showed significant improvement of the spinal lesion but revealed a new non-enhancing left fronto-parietal cortical lesion with restricted diffusion compatible with encephalitis. Immunoglobulin was repeated and she started fluoxetine (inhibitor of enterovirus replication). The infant showed clinical improvement with withdrawal from support ventilation and presents an asymmetric tetraparesis.
Conclusion: Our case illustrates the current difficulties in the management of AFP since the literature on how to treat these cases, especially such young patients is scarce.
Disclosure: Nothing to disclose

PR3029

The tonic response to the infant knee jerk as an early sign of cerebral palsy

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Background and aims: Early identification of infants at risk of cerebral palsy (CP) is desirable in order to provide early intervention. We investigated whether the presence of tonic responses (TRs, continuous muscle activity occurring after the typical phasic response), clonus or contralateral responses during infancy is related to the later diagnosis of CP or the presence of cystic periventricular leukomalacia (cPVL).

Methods: We included 34 very high-risk infants (median gestational age 31.9 weeks) who participated in the LEARN2MOVE 0-2 years trial (Hielkema et al. 2010). Brain lesions were documented by neonatal brain imaging; 10 infants had cPVL. Longitudinally, video-recorded EMG knee jerk assessments were performed during infancy (1-4 times). Developmental outcome was assessed in all infants at 21 months corrected age (CA). Binomial generalized estimating equations models with repeated measurements were fitted using predictor variables.

Results: Infants who later were diagnosed with CP (n=18) showed more often than infants who were not diagnosed with CP (n=16) i) TRs – from 4 months CA onwards, ii) clonus - from 13 months CA onwards, and iii) contralateral responses - from 15 months CA onwards. Part of the differences between the children with and without CP could be attributed to the presence of cPVL.

Conclusion: These data partially uncover the pathophysiology of the 'growing into a deficit phenomenon' of children with CP. Especially the assessment of tonic responses may be a valuable add-on to the clinical repertoire to appraise a high risk of CP.

Disclosure: Nothing to disclose

PR3030

Diffusion Kurtosis Imaging in bilirubin encephalopathy of neonates

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Background and aims: To assess microstructural alterations in the cerebrums of bilirubin encephalopathy of neonates in early stage by using Diffusion Kurtosis Imaging (DKI)

Methods: Forty patients with bilirubin encephalopathy and 20 full-term healthy neonates as the control group underwent conventional MRI and DKI scanning on a 3.0T MR imager. The fractional anisotropy (FA),mean diffusion (MD), mean kurtosis (MK),axial kurtosis (Ka) and radial kurtosis (Kr) values were computed in 7 regions of interest (ROIs)-Bilateral globus pallidus,dorsal thalamus,frontal lobe,temporal lobe,auditory radiation, substantia nigra and inferior olivary nucleus — in both controls and bilirubin encephalopathy patients. The correlations between DKI values and jaundice peak values, as well as the TSB (total of serum bilirubin) values on the day of cerebral MRI examination in patient group were investegated.

Results: There were statistically difference in FA Kr value of bilateral globus pallidus and MK, Ka, Kr value in bilateral inferior olivary nucleus between groups (all P<0.05). Correlation analyses revealed strong correlations between jaundice peak values and FA, Ka values of dorsal thalamus (r=-0.3990, .374, both P<0.05). MK value of bilateral globus pallidus had the highest correlation with the TSB values on the day of cerebral MRI examination(r=0.521, P<0.05).

Conclusion: DKI technique can show cerebric microstructural change in bilirubin encephalopathy of neonates. MK value of globus pallidus on the day of MRI might be a sensitive index in evaluating the severity of brain damage, which may contribute to the diagnosis of bilirubin encephalopathy.

PR3031

Pallidal deep brain stimulation for pediatric generalized dystonia

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Background and aims: Pallidal deep brain stimulation (DBS) is an effective treatment for medically intractable generalized dystonia. Most evidence concerns primary dystonia and the role of DBS in acquired disorders with dystonia is debated. Little is known for pediatric patients, although younger patients with shorter disease duration seem to benefit more and faster from DBS surgery.

Methods: Review of pediatric dystonia patients who underwent pallidal DBS surgery at our center.

Results: Since 2003, we implanted 3 pediatric dystonia patients with bilateral pallidal electrodes. Surgery took place at the age of 9 for patients 1 and 2 and 14 for patient 3. Disease duration was 5 and 3 years for 2 primary generalized dystonia patients (DYT1 negative), and 14 years for the third patient with generalized dystonia probably secondary to neonatal complications (1.5T MRI was normal). Patient 1 had to be reimplanted due to hardware infection 2 years after surgery and developed a worrisome status dystonicus. Both him and patient 2 had remarkable benefit from surgery. Patient 3 acquired the capacity to eat by himself and write, improved his dysarthria, and ameliorated his pain. The fixed component of his disease limited his motor benefit. None of them had to be reopperated due to electrode dislocation related to growing up.

Conclusion: In our experience, pediatric dystonia patients have sustained motor and disability benefit from pallidal DBS, specially when performed previously to the development of fixed posturing. Moreover, we report a case of probable secondary dystonia who still experienced great improvement in disability.

Disclosure: Nothing to disclose

Epilepsy 3

PR3032

Morphological changes of cerebellum in epilepsy

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Background and aims: We evaluate cerebellar grey matter volume changes in temporal lobe epilepsy patients using AAL atlas, dividing cerebellum into 18 substructures. We aim to determine which substructures differ in temporal lobe epilepsy patients compared to controls, nature of this difference and whether there is a significant difference in cerebellar grey matter volume in temporal lobe epilepsy patients who underwent temporal lobe resection and are seizure-free compared to those with less favourable outcome.
Methods: Study participants were 36 temporal lobe epilepsy patients and 38 healthy controls. All patients in this study later underwent temporal lobe resection: 27 seizure-free patients and 9 with persistent seizures after the surgery. Subjects were examined using 1,5T MRI. Cerebellar volume was adjusted for total intracranial volume, age and gender and measured by means of voxel based morphometry. Image processing was performed automatically using Matlab and SPM v.12 software. Cerebellar substructures were defined using AAL atlas embodied in SPM software.
Results: Total cerebellar grey matter volume appears non-significantly smaller in epileptics. Analyzed within substructures grey matter volumes of two frontmost and the rearmost structures of cerebellar vermis were of larger volume in epileptics. Total cerebellar grey matter volume is significantly smaller in patients who underwent temporal lobe resection and are non-seizure-free compared to seizure-free ones.
Conclusion: Total cerebellar grey matter volume tends to be non-significantly smaller in temporal lobe epilepsy patients compared to controls, nevertheless some parts of vermis are significantly larger in epileptics. Total cerebellar grey matter volume reduction is associated with worse temporal lobe resection outcome.
Disclosure: Nothing to disclose

PR3033

Analysis of intrafamilial clinical disparity in Lafora disease

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Background and aims: Lafora disease (LD) is an autosomal recessive form of progressive myoclonic epilepsy of adolescent onset characterized by intractable seizures, myoclonus and progressive and fatal neurological deterioration.
Objektives: To study the frequency of clinical disparity, in terms of age of onset, course of disease, and evolution among siblings with LD.
Methods: We identified 16 LD families with at least two affected siblings in our database. We analyzed age of onset, seizures types, and differences in evolution, mainly duration of the disease. We used a grade score (from grade 0=1 year to grade 5≥10 years) to quantify years of discrepancy.
Results: Regarding age of onset, grade 4-5 discrepancy was found in only 2/14 families with available data. In 11 families the discrepancy was grade 0-1 and in one family grade 2. In 9 families there was discrepancy in seizure type at onset (myoclonus, generalized tonic-clonic or focal visual). In terms of duration of the disease, discrepancies were more common: grade 3 or more in half of the families
Conclusion: Among siblings affected with LD there is a small variability regarding age of onset but moderate variability regarding years of duration of the disease. Identifying factors that slow disease progression may help the discovery of new therapies for this deadly disease.
Disclosure: Nothing to disclose

PR3034

The spectrum of fixation-off sensitivity: The Arabic Gulf Experience

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Background and aims: Fixation-off sensitivity (FOS) is a phenomenon induced by elimination of central vision/fixation, and may either mainifest clinically with seizures or only represent an EEG abnormality. FOS is suspected when epileptiform discharges consistently occur for as long as the eyes are closed and disappear when eyes are open. The objective of this presentation is highliting the steps for diagnosis of FOS and demonstrating the different electroclinical types.

Methods: The technique proposed by Panayiotoplous is applied for selected patients whom epileptiform discharges occured whenever their eyes were closed and disappeared when their eyes were open, using underwater goggles covered by semitransparent tape in adequately lit environment to impede central vision and fixation.

Results: From April 2004 to April 2016, 9 of 2,400 patients had had one or more video-EEGs with FOS (Figure 1), yielding an approximate incidence of 0.37%. Seven patients were diagnosed as idiopathic generalized epilepsies phenotypes, one with symptomatic focal epilepsy, and one considered to be within the spectrum of benign childhood seizure susceptibility syndrome. FOS EEG abnormalities were occipital in seven patients and generalized in two patients. In one patient, FOS and inverted fixation-off sensitivity was demonstrated. In two siblings, FOS was associated with electrical status epilepticus and atypical childhood epilepsy with centrotemporal spikes.
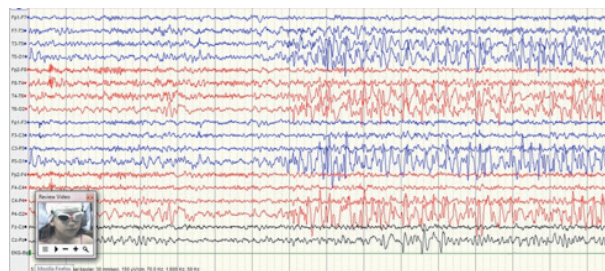
Figure 1: Fixation-off sensitivity. EEG recording with lights on. High-voltage bilateral occipital epileptiform discharges reappeared when the child closed her eyes and persisted as long as her eyes were closed. Low-cut filter, 1.6 Hz; high-cut filter, 70 Hz.

Conclusion: To the author's knowledge, this the first time to demonstrate the FOS phenomenon in the Gulf region. The author's opinion that FOS is not uncommon and proposes that the technique recommended by Panayiotopoulos should be applied to selected patients with occipital or generalized paroxysms during EEG recording.

Disclosure: Nothing to disclose

PR3035

Clustering and cyclicity of spontaneous recurrent seizures in mouse pilocarpine model of chronic epilepsy

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Background and aims: Seizure clustering is common and significant phenomenon in patients with epilepsy. The seizure clusters in some animal models have been reported, but it is not well described in mouse pilocarpine models. This study investigated the detailed characteristics of seizure clustering in mouse pilocarpine model.

Methods: We induced status epilepticus (SE) with intraperitoneal injection pilocarpine in five-week old male C57BL/6 mice, and monitored the following spontaneous recurrent seizures (SRSs) of chronic stage by long-term continuous video-EEG monitoring. A seizure cluster was defined as occurrence of one or more seizures per day for at least three consecutive days and at least five seizures during the cluster period. We analyzed cluster duration, seizure free period, cluster interval, seizure frequencies during and outside of the seizure clusters.

Results: All the 28 mice displayed seizure clusters and 97.6% of the seizures occurred during the cluster periods. The seizure clusters were followed by seizure free periods showing cyclic pattern. The mean duration of seizure clusters were 6.2 ± 2.5 days and the mean interval was 17.4 ± 6.4 days. The mean seizure frequency was 6.7 ± 2.8 per day during the cluster and 2.3 ± 0.7 per day during the total recording periods. The SRS also occurred in clustered within a day.

Conclusion: We demonstrated that seizure occur in clusters in chronic stage of mouse pilocarpine model. These characteristics should be kept in mind when using this animal model for drug discovery studies. This model could be appropriate for studying the unrevealed mechanism of ictogenesis.

Disclosure: Nothing to disclose

PR3036

Neurophysiological differences between patients with drug-resistant epilepsy and patients with controlled epilepsy

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Background and aims: To study the neurophysiological characteristics of drug-resistance epilepsy (DRE) by using spectral analysis (SA) of the EEG.

Methods: We observed 80 patients with DRE and 80 patients with controlled epilepsy (CE) underwent standardized EEG. Additional SA was performed on segments of EEG paroxysmal activity (PA).

Results: PA was registered in all patients with the DRE and in 90.1% - with the CE. There was correlation between the PA localization and drug-resistance ($\chi 2=26,42$; $p<0,01$). Compared to CE group, the DRE demonstrated the higher proportion of PA was in the temporal (25% in the DRE and 7.5% - CE) and the frontal (45% and 8.8%) areas. In DRE group the PA were observed more frequently over the right hemisphere patients (53.8% in the DRE and 30% - CE) and over the left hemisphere in CE (32.5% and 50%). Obtaining spectral power values were normally distributed across registered bands with the absence of fronto-occipital differences. In contrast, in CE group there was growth gradient of spectral power of theta activity from the occipital lobes to the frontal lobes. The increased mean values were found in Fp1 and Fp2 relatively O1 and O2 at 2.02 and 2.07 times, respectively ($p<0,05$).

Conclusion: This study had shown the fronto-occipital specific differences of PA in patients with DRE. We observed similar degree of the involvement of diencephalic and mesencephalic structures in paroxysms generalization in DRE, while only diencephalic regions played a crucial role in CE. These findings have clinical implication in diagnosis and treatment of patients with DRE.

Disclosure: Nothing to disclose

PR3037

A six-month follow-up of persons living with epilepsy, newly diagnosed at the CARAES tertiary neurology reference centre at Ndera, Kigali (Rwanda)

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Background and aims: We retrospectively analysed demographics and outcome of newly diagnosed people living with epilepsy (PWE), presenting for the first time at the CARAES neuropsychiatric hospital (Ndera) during the first six months of 2016.

Methods: In December 2016, data were collected from the medical records using a standardised questionnaire for demographics and six-month outcome data. Missing data were obtained following a telephone survey. In case no follow-up by phone was possible, records were excluded from the analysis.

Results: A total of 238 PWE could be contacted by phone. Age ranged from two months to 78 year with a median age of 13 years and male PWE accounted for 56.3%. 67.6% PWE come from rural areas. The average time between seizure onset and first consultation at the centre was in average 2.1 years. Generalised seizures were most frequently observed with 88.7% followed by non-classified seizures with 5.9%, and simple partial and complex partial seizures with 5.5%. A total of 40% of 175 EEG showed abnormal findings. Sixteen (6.7%) PWE had a family member with epilepsy. At diagnosis, 49.2% of PWE presented monthly up to five seizures, 26.4% between 5-30, 8.4% more than 30 seizures and 16.0% an unknown number. After a six-month period 30.3% of PWE were seizure-free.

Conclusion: The significant percentage of PWE from rural areas and interval between seizure-onset and consultation requires improved epilepsy health intervention strategies, including focused education of the communities and referral systems.

Disclosure: Study support: UCB Pharma CSR supports an epilepsy programme at the CARAES neuropsychiatric hospital.

PR3038

A comparison of the responsiveness of EQ-5D-5L and the QOLIE-31P and mapping of QOLIE-31P to EQ-5D-5L in epilepsy

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Background and aims: To investigate the responsiveness of and correlation between the EQ-5D-5L and the QOLIE-31P in patients with epilepsy. Moreover, the aim was to develop a mapping function to predict EQ-5D-5L values based on the QOLIE-31P for the use in economic evaluations.

Methods: The dataset was derived from two clinical trials, the ZMILE study in the Netherlands and the SMILE study in the UK. In both studies, patients' quality of life using the EQ-5D-5L and QOLIE-31-P was measured at baseline and 12 months follow-up. Spearman's correlations, effect sizes (EF) and standardized response means (SRM) were calculated for both the EQ-5D-5L and QOLIE-31P domains and sub scores. Mapping functions were derived using ordinary least square (OLS) and censored least absolute deviations models.

Results: A total of 510 patients were included in this study. Moderately strong significant correlations were found between both instruments. The EQ-5D-5L showed substantially high ceiling effects and rather small EFs and SRMs whereas the QOLIE-31P did not show ceiling effects and also showed small to moderate EFs and SRMs. Results of the different mapping functions indicate that the highest adjusted R^2 we were able to regress was 0.239 using an OLS model with squared terms, leading to a mean absolute error of 0.103.

Conclusion: Results presented in this study emphasize the importance of the development of condition-specific preference-based instruments which can be used within the QALY framework and hence incorporated as an important supplement in economic evaluations. Development of such instruments may ensure that benefits of health-care interventions are adequately reflected in QALY estimates.

Disclosure: Nothing to disclose

Motor neurone diseases 2

PR3039

MRI of the brainstem and cervical spinal cord as a predictive factor for bulbar and respiratory impairment in amyotrophic lateral sclerosis

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Background and aims: Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease. Mechanisms contributing to the death are mostly swallowing disorders due to bulbar impairment and respiratory insufficiency due to diaphragmatic weakness.
Methods: We enrolled 41 patients non-demented carrying a limb-onset ALS and 21 controls. 27 patients had a second examination at 3 months. The R2*, volumetry, spectroscopy and diffusion tensor imaging (DTI) sequences were analyzed with 3 Teslas brain and cervical spinal cord MRI. All the MRI data were anonymized during the post processing. For each patient, ALS functional rating scale revised (ALSFRS-r) was administrated every three months until the death or the loss of follow-up.
Results: At baseline, diffuse brain atrophy was observed with predominance in brainstem and motor cortex. Mean diffusivity (MD) was increased in left posterior limb of internal capsule and a decreased Naa peak in precentral gyrus was observed. At 3 months, volume was decreased in pons and medulla oblongata, MD was increased in medulla oblongata. At baseline bulbar atrophy correlated with bulbar sub-score of ALSFRS-r at 6 months (r=-0.498), with the shift of bulbar sub-score between 0 and 6 months (r=0.614). The shift of volume in cervical spinal cord between 0 and 3 months correlated with respiratory sub-score of ALSFRS-r at 3 months (r=-0.527) and 6 months (r= -0.648) and with the shift of ALSFRS-r between 0 and 3 months (r=0.569) and between 0 and 6 months (r=0.638).
Conclusion: Bulbar and cervical spinal cord volume could be very promising surrogate biomarkers of prognosis, global handicap, bulbar and respiratory impairment.
Disclosure: Nothing to disclose

PR3040

Rate of Motor Unit Number Index (MUNIX) and ALSFRS-R decline over 21 months period in amyotrophic lateral sclerosis (ALS)

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Background and aims: Motor Unit Number index (MUNIX) is a non-invasive method requiring minimal electrical stimulation. The technique utilizes the surface-recorded compound muscle action potential (CMAP) and electromyographic (EMG) interference pattern to compute the MUNIX. Only few previous studies described the rate of MUNIX decline over time and compared it to that of ALSFRS-R. We aimed to perform longitudinal simultaneous MUNIX and ALSFRS-R recordings in order to evaluate MUNIX as a marker of disease progression in an Irish cohort of ALS patients by determining and comparing the rates of decline in these two disease progression measures.
Methods: We performed simultaneous MUNIX and ALSFRS-R measurements in 6 muscles in a cohort of 43 patients, 3-monthly over 21 months period to determine and to compare rates of decline of MUNIX and ALSFRS-R over time.
Results: Of 43 enrolled patients (M:F ratio: 30:13), 25 were of spinal, 12 of bulbar onset & 6 ALS-FTD. 31 and 25 participants reached month12, and 15 respectively. MUNIX declined earlier, significantly faster than ALS-FRS and at different rates in individual muscles (overall 3.6%/month, range between 2.61%±0.06 and 4.43%±0.07). ALSFRS-R decline rate was 2.5%/month. Subgroups with bulbar, upper, lower limb onset and FTD-MND showed different decline rates of ALSFRS- R while the rate of MUNIX decline was similar in all subgroups. CMAP declined at a rate of 2.9%/month.
Conclusion: We determined and compared the rates of decline of MUNIX and ALSFRS-R longitudinally in ALS subgroups.
Keywords: MUNIX, ALSFRS-R, Longitudinal study
Disclosure: Nothing to disclose

PR3041

Angiogenin in the skin of patients with amyotrophic lateral sclerosis. An immunohistochemical study

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Background and aims: Angiogenin (ANG) is a member of the ribonuclease superfamily which is implicated in angiogenesis. ANG maintains normal vasculature and thereby protects motor neurons from various stress conditions. It is suggested that ANG may play a role in pathomechanism of amyotrophic lateral sclerosis (ALS). However, there have been no studies of ANG in ALS skin.

Methods: We made a quantitative immunohistochemical study of the expression of ANG in the skin from 20 patients with sporadic ALS, 20 patients with other neurologic or muscular disorders (control group A), and 20 patients without neurologic or muscular disorders (control group B).

Results: The nuclei of the epidermal cells showed a weak ANG immunoreactivity in ALS patients. These findings became more marked as ALS progressed. On the other hand, the nuclei in control groups A and B show a strong positive reaction. The optical density for ANG immunoreactivity of the nucleus in the epidermal cells in ALS patients was significantly lower (p<0.001) than in control groups A and B. There was a significant negative relationship (r=-0.82, p<0.001) between the optical density for ANG immunoreactivity of the nucleus and duration of illness in ALS patients.

Conclusion: These data suggest that changes of ANG in ALS skin are related to the disease process and that metabolic alterations of ANG may take place in the skin of ALS patients.

Disclosure: Nothing to disclose

PR3042

MicroRNA in Amyotrophic Lateral Sclerosis: Evidence for different pathophysiology in genetic and sporadic ALS

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Background and aims: MicroRNAs are small non coding RNAs that are associated to stress granules, mitochondria and other subcellular organelles in muscle. Few studies have explored microRNAs role in muscle in ALS.We previously observed that there is a different serum microRNA profile in spinal versus bulbar ALS. We have investigated muscle biopsies in a series of ALS cases both sporadic (sALS) and genetic (SOD, C9ORF72 mutation) since they have different pathogenesis.

Methods: We studied, in EI Escorial proven ALS cases, muscle biopsies obtained for diagnostic reasons both myomicroRNAs (miR-1;miR-206;miR-133a;miR-133b;miR-27a) and angiogenic/inflammatory microRNAs (miR-155;miR-146a;miR-221;miR-149*) by qRT-PCR. ALS cases were divided according to gender and age of onset.

Results: All microRNAs studied were strongly up-regulated in muscle biopsies of ALS patients versus controls with the exception of miR-149*. Significant overexpression of miRNAs was present in genetic versus sALS and in male versus female gender. Morphometric analysis shows a muscle fibre atrophy in ALS patients compared to controls. Two genetic ALS (SOD, C9ORF72) showed up-regulation particular miR-206 and miR-27a both myomiRNA profile and angiogenic/inflammatory miR-155, miR-146a and miR-221 that directly correlates with the degree of atrophy and particularly dysregulated in SOD patient.

Conclusion: These results provide evidence on molecular role of microRNAs in ALS. We observed an increased expression of microRNAs in genetic ALS and dysregulation of inflammatory microRNAs. MiRNAs have been shown to be both protector and deleterious in ALS. MiR-206 expression was found to be elevated in muscle of SOD mutated patient. MiR-206 is thought to be involved in re-inervation.

Disclosure: Nothing to disclose

PR3043

Euro-MOTOR: A multi-centre population-based case-control study of pesticides exposure as risk factor for Amyotrophic Lateral Sclerosis

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Background and aims: Long-term exposure to pesticides has been proposed as a risk factor for neurodegenerative disorders including Amyotrophic Lateral Sclerosis (ALS), however research has been complicated by difficulty in assessing historical exposures.

Methods: Incident ALS cases and matched controls were recruited over 4 years in Ireland, Italy and the Netherlands. Trained investigators carried out structured interviews of participants to gather details of lifetime occupational history. Job-Exposure-Matrices (JEM) were applied to occupational data to characterize risk of exposure to pesticides. Logistic regression models adjusting for age, gender, education and cohort were used to determine the association between pesticide exposure and ALS risk.

Results: 1,557 patients and 2,922 controls were included. We found increased odds ratios (ORs) for ALS with any history of exposure to any pesticides (OR 1.34; 95%CI: 1.09 – 1.63), and to herbicides (OR 1.35; 95% CI: 1.06 – 1.71), insecticides (OR 1.31; 95% CI: 1.07 – 1.62) and fungicides (OR 1.38; 95% CI: 1.11 – 1.70) separately. These findings were robust to sensitivity analyses, and were unchanged after correction for physical activity, smoking and alcohol consumption.

Conclusion: Our findings provide new evidence for an association between pesticide exposure and ALS in European populations. Further work is ongoing to identify any population specific differences and dose-response relationships.

Disclosure: The research leading to these results has received funding from the European Community's Health Seventh Framework Programme (FP7/2007–2013; grant agreements no. 259867).

PR3044

Frequency of neuropsychiatric disorders in first and second degree relatives of patients with Amotrophic Lateral Sclerosis (ALS)

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Background and aims: An increased frequency of schizophrenia, suicide and other neuropsychiatric conditions has been reported in in family members of patients with ALS (Byrne et al, 2013). This finding has been supported by the presence of a polygenic overlap of 14% between ALS and schizophrenia based on combined GWAS analyses (McLaughlin et al, Nat Comm in press).

Methods: The cognitive profile of first degree (FDRs) and second degree relatives (SDRs) was assessed using the Edinburgh Cognitive and Behavioural Amyotrophic Lateral Sclerosis Screen (ECAS). Neuropsychiatric status was determined using UK Biobank Thoughts and Feelings Questionnaire. Additional assessments including the Obsessive-Compulsive Inventory Revised (OCI-R), Barrett Impulsiveness Scale (BIS-11), Dimensional Apathy Scale (DAS), Autism Spectrum Quotient (AQ), Adult ADHD Self-Report Scale (ASRS), Community Assessment of Psychic Experiences (CAPE-15), The Ten Item Personality Inventory (TIPI) were used to further assess individuals as deemed appropriate.

Results: A total of 19 first and 23 second degree relatives have been evaluated from 6 ALS probands. None had clinical evidence of ALS. Of these 31% scored below the normal cut offs for ECAS based on age and educational attainment. Based on traits analysis, 71% had evidence of moderate to severe depression, and 15% demonstrated evidence of obsessive compulsive traits.

Conclusion: First and second degree relatives of ALS probands exhibit higher frequencies of cognitive impairment, and a higher burden of neuropsychiatric pathology. These findings support the presence of a biological overlap between ALS and psychiatric traits.

Disclosure: Nothing to disclose

PR3045

Comorbidities can impact the survival in amyotrophic lateral sclerosis?

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Background and aims: Amyotrophic lateral sclerosis (ALS) is a rapidly fatal neurodegenerative disorder, even if some cases show longer survival. The aim of this study was to evaluate the influence of comorbidities on ALS survival in relation to other clinical and demographic factors.

Methods: We examined newly diagnosed ALS cases from January 2001 to December 2013 in our regional ALS Centre, followed up until December 2015. Each patient was evaluated for: age at onset, sex, lower/upper motor neuron onset, delay from onset of symptoms to diagnosis (ODI), clinical phenotype, time to generalization (TTG), NIV, PEG and presence of comorbidities as diabetes, autoimmune and oncologic diseases. Influence of variables on survival in subgroups was estimated using the Kaplan Meier method and Logrank test.

Results: 394 incident ALS patients were included. 25.13% patients had one comorbidity and 2.23% had two or more comorbidities. Median survival time from symptoms onset and from diagnosis was 46.3 months and 29.44 months respectively. Comorbidities, considered individually or in association, did not influence the survival. Independent predictors of short survival were bulbar phenotype (p= 0.036), lower motor neuron onset (p=0.042), shorter time to generalization (p=0.0002), short ODI (p<0.0001). Favourable factor was a younger age at onset (p<0.0001).

Conclusion: The comorbidities were not associated to short ALS survival whereas bulbar phenotype, TTG, age at onset, lower motor neuron onset and ODI influenced the survival. Larger ALS population are needed to evaluate the influence of comorbidities on ALS risk and clinical course.

Disclosure: Nothing to disclose

PR3046

SIGMAR1 gene novel mutation causes distal hereditary motor neuropathy phenotype

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Background and aims: SIGMAR1 gene encodes a non-opioid endoplasmic reticulum (ER) protein which is involved in a large diversity of cell functions and is expressed ubiquitously in both central and peripheral nervous systems. Alterations of its normal function may contribute to two different phenotypes: juvenile amyotrophic lateral sclerosis (ALS 16) and distal hereditary motor neuropathies (dHMN).

Methods: Case report

Results: We describe a female patient from a non-consanguineous couple, who presented with progressive distal wasting and weakness of the lower limbs at the age of 4. Involvement of the distal upper limbs became noticed at the age of 17 imposing difficulties with fine hand movements. Her neurological deficits remained stable after her early 20's. She functioned independently when examined at the age of 37. Neurological examination revealed symmetric severe muscle wasting and weakness in distal lower and upper extremities, foot drop with equinovarus deformity and hammer toes, generalized areflexia and normal sensation of all modalities. Electrophysiological evaluation was compatible with a pure motor peripheral involvement. Pulmonary function tests were normal. Sequencing analysis detected a heterozygous compound mutation of the SIGMAR1 gene: deletion c.561_576del, on exon 4 and a deletion of all exon 4.

Conclusion: Mutations on SIGMAR1 gene has increasingly been recognized as a cause of some forms of dHMN and ALS. Our patient presented with a novel mutation causing a dHMN phenotype with distal predominance of muscle weakness and wasting, and absence of pyramidal signs.

Disclosure: Nothing to disclose

Movement disorders 7

PR3047

Sensory trick phenomenon in cervical dystonia: A functional MRI study

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Background and aims: The mechanisms underlying the sensory trick (ST) effect in dystonia (DYT) remain to be fully understood. This study investigates the patterns of brain functional MRI (fMRI) during resting-state (RS) with and without ST and during the ST imagination in subjects with cervical DYT.

Methods: We recruited 17 patients with cervical DYT and 15 healthy controls (HC). In 9 patients (DYT-trick), ST almost reversed head rotation to primary position. Subjects underwent RS fMRI, and DYT groups repeated RS fMRI performing ST. DYT patients also performed a functional MRI task in which they were asked to imagine an ipsilateral ST (i.e., slight touch on the cheek/chin).

Results: DYT-notrick subjects showed an increased connectivity of the sensorimotor network relative to HC during RS fMRI without ST. During RS fMRI with ST, DYT trick patients showed a reduced connectivity of the sensorimotor network relative to RS fMRI without ST, while DYT-notrick did not show any ST effect. During the imagination of ST, DYT-trick cases had an increased recruitment of the cerebellum bilaterally compared to DYT-notrick subjects.

Conclusion: This study suggests an hyperconnectivity of the sensorimotor areas during RS in cervical DYT-notrick subjects. In DYT-trick patients, the ST was associated with a "normalization" of such a phenomenon. The increased activation of the cerebellum in DYT-trick patients during the ST imagination suggests a possible role of this area in modulating cortical activity. These findings call for novel therapies for cervical DYT such as electrical stimulation of cerebellum and modulation of proprioception using vibration or electrocutaneous stimulation devices.

Disclosure: Nothing to disclose

PR3048

Brain structural alterations in patients with dopa-responsive dystonia

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Background and aims: Mutations in the GCH1 gene, encoding GTP cyclohydrolase 1, the enzyme critically important for dopamine production in nigrostriatal neurons, are the most common cause of dopa-responsive dystonia (DRD) (DYT5a). It has been suggested that DRD is a neurochemical rather than neurodegenerative disorder. This study aims at investigating grey and white matter (WM) brain structural alterations in DRD subjects.

Methods: This study included a series of 9 genetically confirmed DRD patients and 35 age-matched healthy controls. Participants underwent 3D T1-weighted and diffusion tensor (DT) MRI to study cortical thickness, basal ganglia volume, and WM tract damage.

Results: DRD patients relative to healthy controls showed a cortical thinning of the right precentral gyrus, an increased volume of the putamen bilaterally and a trend toward an increased volume of the right pallidum. Compared to healthy controls, DRD subjects had a widespread pattern of WM damage involving the genu of the corpus callosum and the right cerebral peduncle, corona radiate, WM underneath the primary motor and premotor cortices, external capsule, anterior limb of the internal capsule, temporal and orbitofrontal WM.

Conclusion: DRD patients show a focal pattern of grey matter atrophy in the primary motor cortex against a widespread WM damage, suggesting possible neurodegeneration. A peculiar feature of DRD patients is the increased volume of basal ganglia. It remains to be established whether these changes are causative rather than an effect of the disorder.

Disclosure: Nothing to disclose

PR3049

Unilateral peduncolopontine nucleus stimulation in progressive supranuclear palsy: A randomized trial

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Background and aims: Progressive supranuclear palsy (PSP) is a disabling disorder without effective treatment. Deep brain stimulation (DBS) of the peduncolopontine nucleus (PPN) has been applied to Parkinson's disease and atypical parkinsonism with some improvement in falls, balance and gait. Since PSP presents with disabling gait and balance disorders, we designed a double blind randomized study to assess the efficacy of unilateral PPN-DBS in this disease.

Methods: Patients with Richardson's syndrome underwent PPN implantation at the Toronto Western Hospital. Patients were assessed preoperatively, and at 6 and 12 months postoperatively after 1-week period in either the ON and the OFF stimulation condition, before and after an acute levodopa challenge (if any dopaminergic treatment at baseline). Primary outcomes were the differences in gait, postural stability and fall subitems of the PSP Rating Scale between the stimulation ON and OFF conditions at 6 and 12-month follow-up. Any adverse event was recorded.

Results: In our cohort (eight patients; age at surgery, 68.5±3.5 years; disease duration, 7.1±2.9 years) unilateral PPN-DBS did not significantly change gait, postural stability, and falls at the two time points. Two patients had intraoperative bleeding with recovery, and one patient had a lead fracture during the follow-up.

Conclusion: Unilateral PPN-DBS did not improve axial motor symptoms in our patients. However, our sample is small and does not allow to exclude a clinical effect in larger samples of patients or with bilateral surgery. Moreover, a better response to PPN-DBS at an earlier stage of the disease or in other PSP phenotypes cannot be excluded.

Disclosure: This study was supported by a CurePSP grant.

PR3050

Functional lesional neurosurgery for tremor - a systematic review and meta-analysis

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Background and aims: Incisionless neurosurgery has again created interest in lesional treatments for tremor. This work evaluates safety and efficacy of lesional interventions for tremor due to Parkinson's disease (PD), Essential Tremor (ET) and Multiple Sclerosis (MS) using radiofrequency ablation (RF), focused ultrasound (MRIgFUS) and gamma knife (GK).

Methods: Systematic review of the Medline and Cochrane databases between January 1990 and June 2016. Studies with a minimum of n=5, follow-up ≥ 3 months and validated tremor quantification were selected for random effects meta-analysis.

Results: 1247 publications were screened, 84 included. Best effect on PD tremor is by treating the ventral intermediate nucleus (V.im.) by RF (Hedge`s g: -4.15) over V.im. by GK (-2.2), subthalamic nucleus (STN) by RF (-1.12) and globus pallidus internus (GPi) by RF (-0.88). For ET results were similar for V.im. by MRIgFUS (-2.47) and RF (-2.46) but less efficacious by GK (-2.13). For MS tremor, V.im. ablation by GK (-1.96) was more effective than by RF (-1.63). Rates of persistent side effects after unilateral lesions in PD were 15.9±14.7% (RF V.im.), 14.7±5.0% (RF STN), 8.3±15.1% (RF GPi), 1.6±0.8% (GK V.im.) and 4.9±6.9% (MRIgFUS V.im.). For ET, rates were 6.3±7.1% (RF V.im.), 1.9±2.4% (GK V.im.) and 10.9±11.4% (MRIgFUS V.im.) and 37.7±23.9% for MS (RF V.im.).

Conclusion: This meta-analysis of lesional neurosurgical interventions for tremor proves the validity of the V.im. target but also shows that target and technique effects differ according to etiology.

Disclosure: Nothing to disclose

PR3051

Blink reflex recovery cycle to differentiate progressive supranuclear palsy from corticobasal degeneration: A pilot study

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Background and aims: Progressive Supranuclear Palsy (PSP) and Corticobasal Degeneration (CBD) are rapidly progressive neurodegenerative disorders, clinically featured by parkinsonism and additional debilitating symptoms. The differential diagnosis between PSP and CBD is difficult because of the overlap of clinical features. R2 Blink Reflex Recovery Cycle (BRRC) is a neurophysiological tool used to evaluate brainstem excitability. R2 BRRC is abnormal in several movement disorders as Parkinson's disease and dystonia. We evaluated R2 BRRC in differential diagnosis of PSP and CBD determining sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV).

Methods: Patients affected by PSP and CBD were prospectively enrolled, according to currently accepted diagnostic criteria. Patients underwent clinical (Hoehn&Yahr-stage, UPDRS-ME) and neurophysiological (R2 BRRC) assessments. R2 BRRC was performed at interstimulus intervals (ISIs) of 100-150-200-300-400-500-750 ms.

Results: Thirty subjects were enrolled: 12 PSP and 8 CBD patients and 10 healthy controls. A significantly different amplitude of R2 was observed at ISIs of 100-150-200-300 ms between PSP and CBD patients (p=0.006, p<0.00001, p<0.00001 and p=0.02 respectively) and also between PSP and healthy controls (p<0.00001, p<0.00001, p<0.00001 and p=0.0004 respectively); no significant differences were found between CBD and controls (Fig.1). An early R2 BRRC differentiated PSP from CBD with a sensitivity and a specificity of 87.5% and 91.7% respectively; PPV and NPV were 91.7% and 87.5% respectively.
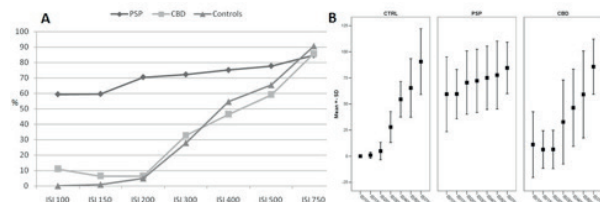
R2 blink reflex recovery cycle graph-curve of PSP, CBD and control groups. X-axis: ISIs in ms. Y-axis: ratio of the conditioned to the unconditioned R2 response in percentage (A). Error bars with mean values +/- S.D. of the R2 blink reflex recovery component at ISIs of 100, 150, 200, 300, 400, 500 and 750 ms among the three study groups (B).

Conclusion: R2 BRRC is a useful tool in differentiating PSP from CBD patients. Predominant brainstem tau-aggregates distribution in PSP, in contrast with involvement of neocortex in CBD, could explain the brainstem disinhibition in PSP patients.

Disclosure: Nothing to disclose

PR3052

Serum cytokines profile in GBA-associated Parkinson's disease

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Background and aims: Parkinson's disease (PD) is the second most common neurodegenerative disorder. Neuroinflammation is obviously involved in PD pathogenesis. In PD, microglial activation suggests a chronic inflammatory process; furthermore, there is evidence of its association with non-motor symptoms. GBA mutations, the most common genetic risk factor of PD, was widely shown to influence on the vast majority of non-motor symptoms, but the pathogenesis of this process remains unknown. Our aim is to compare the serum cytokine profile in sporadic PD (sPD) and PD associated with mutations in the glucocerebrosidase gene(GBA-PD).

Methods: Plasma samples of 18 patients with sPD, 15 patients with GBA-PD (L444P, N370S mutations and E326K, T369M polymorphisms) and 15 healthy age and sex match controls were included. We measured a number of cytokines: interleukin-1-beta (IL-1b), interleukin-6(IL-6),interleukin-10 (IL-10) and interferon-γ (IFN-γ) by ELISA method. Statistical analysis was carried out using SPSS 17.0.

Results: Plasma levels of all analyzed cytokines were significantly higher in GBA-PD compared to sPD and controls. The level of IL-1b, IL-6, and IFN-γ was significantly higher in GBA- PD compared to sPD and controls (Table 1). The level of IL-10 was higher in GBA-PD compared to controls, but did not reach statistical significance compared to sPD. There was no difference in the level of cytokines between sPD and controls.

Table 1. Serum cytokines level

Cytokines	Cytokines level (pg/ml), median (min-max), p*		
	sPD (N=18)	Controls (N=15)	GBA-PD (N=15)
Interleukin-1-beta (IL-1b)	1,1 (0,70-1,45) p<0,0001	0,93 (0,52-1,51) p<0,0001	1,6 (0,94-2,95)
Interleukin-6 (IL-6)	0,92 (1,08-2,88) p=0,015	0,49 (0,01-3,35) p=0,001	1,71 (0,65-5,91)
Interleukin-10 (IL-10)	3,66 (1,46-20,51) p=0,114	2,2 (0,42-10,66) p=0,007	5,69 (2,43-15,39)
Interferon gamma (IFN-γ)	0,15 (0,08-9,03) p<0,0001	0,13 (0,09-9,25) p=0,005	3,9 (1,34-11,77)

*compared to GBA-PD

Conclusion: GBA-PD is characterized by high serum cytokine level. Inflammation process in GBA-PD may be associated with lysosomal and mitochondrial dysfunction

and may lead to the development of non-motor symptoms and earlier disease onset.

Disclosure: The work was supported partially by Russian foundation for basic research (RFBR) №16-04-00764

PR3053

Non-motor symptoms in a cohort of asymptomatic for PD, carriers of the p.A53T alpha-synuclein (SNCA) mutation

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Background and aims: It is now well established that Parkinson's disease (PD) is associated with a broad spectrum of neuropsychiatric, autonomic, sleep and sensory phenomena, collectively termed non-motor symptoms. Even though such symptoms become increasingly prevalent with advancing disease, many of them can also antedate motor signs. Whether this sequence of events, potentially reflecting Braak staging, may occur in genetic forms of PD, and in particular in the prototypical synucleinopathy associated with the p.A53T mutation in the SNCA gene, encoding for a-synuclein, has not been well studied. Accordingly, the objective of this study was to assess non-motor symptoms in a cohort of asymptomatic for PD, carriers of the p.A53T alpha-synuclein (SNCA) mutation.

Methods: Five asymptomatic p.A53T carriers (1 male and 4 female, mean age: 46) underwent UPDRS III, Epworth Sleepiness Scale, REM Behavior Disorder Screening Questionnaire (RBDSQ), UPDRS I, UPDRS Ia, SCOPA-AUT, QUIP, UPSIT, GDS and MOCA. Four of them underwent DaTScan and three out of five Polysomnography (PSG).

Results: None of the carriers had evidence of motor symptoms (UPDRS III=0). DaTScan was normal in all examined subjects. None had evidence of RBD or olfactory dysfunction. Cognition, as assessed by MOCA, was within normal limits. All subjects reported anxiety, and three out of five reported bowel dysfunction, urinary dysfunction and mild depression.

Conclusion: Certain non-motor symptoms may antedate nigrostriatal dopaminergic degeneration in p.A53T SNCA-related Parkinsonism. Further prospective follow-up and expansion of this cohort are needed to validate these findings.

Disclosure: This study was funded by Michael J. Fox Foundation (PPMI study).

PR3054

Predicotrs of cognitive impairment in Parkinson's disease: A prospective longitudinal study

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Background and aims: More than half of Parkinson's disease (PD) patients develop cognitive impairment during the disease course, which significantly affects the quality of life, prognosis and mortality. The aim of this study was to report the rates and predictors of progression to either mild cognitive impairment (MCI) or dementia, in PD patients, using standardized neuropsychological methods.

Methods: In this longitudinal study, a comprehensive neuropsychological battery covering five domains (attention/working memory, executive, verbal, and visual memory, language, and visuospatial) was administered to 132 nondemented PD patients and to 105 healthy matched controls(HC). MCI was diagnosed according to level 2 of the Movement Disorder Society Task Force criteria. Patients were classified as having normal cognition, MCI, or dementia at baseline and followed in yearly intervals for 3 consecutive years. Kaplan-Meier curves and Cox proportional hazard models were used to examine cognitive decline and its predictors.

Results: Patients averaged 66.8 years of age, 66% men, who had PD on average for 6.3 years. The cumulative incidence of cognitive impairment was 12.5% at year 2. 15% of incident MCI cases had progressed to dementia by the last follow up. In a multivariate analysis, predictors of future decline were older age (p<0.001), male sex (p<0.005), higher Unified Parkinson's Disease Rating Scale motor score (p<0.001), presence of freezing (p<0.005), worse global cognitive score (p< 0.001) and REM sleep behavior disorder (p<0.005).

Conclusion: Transition from normal cognition to cognitive impairment, including dementia, occurs frequently in PD. Certain clinical and cognitive variables may be useful in predicting progression to cognitive impairment in PD.

Disclosure: Nothing to disclose

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PR3055

Time-adherence to pharmacotherapy according to single question in patients with Parkinson's disease taking three and more daily doses of dopaminergic medication

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Background and aims: Study was aimed to detect extent of adherence to pharmacotherapy in patients with Parkinson´s disease (PD) who take three and more daily doses of antiparkinsonian drugs according to single question about time-adherence and to identify factors that contribute to the low level of time-adherence.
Methods: Survey covered 124 non-demented patients with idiopathic PD. We used validated Slovak versions of questionnaires and scales: 8-Item Morisky Medication Adherence Scale (for PD and comorbidities), 8-Item Parkinson's disease Quality of Life Questionnaire (PDQ-8), Geriatric Depression Scale (GDS), Non-Motor Symptoms Scale (NMSS), MDS-UPDRS parts III and IV, 9-Item Wearing-off Questionnaire (WOQ-9) and isolated question for time-adherence "Do you take your medication at same time every day (as it has been prescribed)?"
Results: From overall 124 participants, 33.9% had high level of adherence, 29.8% had medium level and 36.3% had low level of adherence. Time-adherence was significantly lower than overall adherence – only 50.8% patients followed timing of prescribed medication. Compared to time-adherent subjects, time-nonadherent patients had significantly lower total adherence to pharmacotherapy for PD and comorbidities (p<0.001), and higher total score in MDS-UPDRS IV (p<0.001), WOQ-9 (p<0.001), PDQ-8 (p=0.009), GDS (p=0.015), and NMSS (p<0.001). Detailed analysis of NMSS domains revealed positive correlations between time-nonadherence and sleep/fatigue and attention/memory subscore (Rho=0.246, p=0.006 and Rho=0.338, p<0.001, respectively).
Conclusion: Time-nonadherence is more frequent phenomenon than overall nonadherence and is associated mostly with motor fluctuations, reduced quality of life and nonmotor symptoms - especially forgetfulness, fatigue and depression.

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PR3056

STN DBS can temporarily improve balance disorders in Parkinson's disease (PD) patients

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Background and aims: Subthalamic nucleus deep brain stimulation (STN DBS) can influence on balance and gait disorders, but there are some conflicting information. Therefore the aim of this study was to evaluate the impact of STN DBS on balance disorders in PD patients.
Methods: DBS-group consisted of 20 PD patients (7F,13M) who underwent bilateral STN DBS. POP(postoperative)-group consisted of 15 PD patients (6F,9M) in median 24 month-time after surgery. Control group (MED -group) consisted of 24 patients (13F,11M) who did not undergo surgical intervention. UPDRS III scale and balance tests (UpAndGo Test, Tandem Walk Test) were measured during 3 visits (V1 –preop for DBS group, V2, V3) in total OFF phase. The mean period between visits was 9±3months.
Results: We have observed the improvement in balance tests (UpAndGo, TWT) in V2/V1 DBS-group period (p<0,05), which was not observed in other (MED, POP) groups. The effect was not observed in V3/V2 DBS-group period. The comparable UPDRS III changes were also observed in V2/V1 (p<0,05) vs V3/V2 (p>0,05) DBS-group periods whereas V3/V2/V1 in MED-group and POP-group UPDRS III OFF scores were statistically changed (p<0,05).
Conclusion: STN DBS can temporarily improve balance disorders in PD patients, with the strongest effect during first 6 postoperative months.

Disclosure: Nothing to disclose

PR3057

UPDRS III and RS latency indicate that STN DBS has therapeutic neuromodulatory effects in PD

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Background and aims: Subthalamic nucleus deep brain stimulation (STN DBS) has been claimed to change the progression in animal models, but there are lacking information about the possible neuromodulatory effects of STN DBS in humans. The aim of study was to evaluate the impact of STN DBS on changes in UPDRS and reflexive saccades (RS) parameters in OFF phase for 3 PD groups: early-DBS STN (DBS-group), late-DBS STN (POP-group) and one with only medication therapy (MED-group).

Methods: DBS-group consisted of 20 PD patients (7F,13M) who underwent bilateral STN DBS. POP-group consisted of 15 post-DBS PD patients (6F,9M) with median 24 month-time after surgery. Control group (MED-group) consisted of 24 patients (13F,11M) who did not underwent surgical intervention. UPDRS III scale and RS parameters (latency, amplitude,duration,peak of velocity) were measured during 3 visits (V1,V2,V3) in total OFF phase. The mean time period between visits was 9±3months.

Results: We have observed the comparable UPDRS III increase in V3/V2/V1 of MED- and POP-groups (p<0,025) but not in V3/V2(p>0,05) vs V2/V1(p<0,05) of DBS-group in DBS and Med OFF situation. There was also interesting relation between RS latency and DBS treatment: the only change in V2/V1 DBS-group vs no change in MED-group and POP-group (p>0,05).

Conclusion: The strongest effect of STN DBS on RS parameters was during first 6 postoperative months whereas the most influential effect of STN DBS treatment on UPDRS III OFF score was observed during 6-12 months after surgery (but not in longer post-DBS periods). Partially supported by grant: NCN Dec-2011/03/B/ST6/03816

Disclosure: Nothing to disclose

PR3058

Impulse control disorder, sleep and non-motor symptoms in an urban Russian Parkinson's disease cohort: A controlled study

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Background and aims: Relationship of impulse control disorder (ICD) with sleep and other non-motor dysfunctions using validated scales in Russian urban Parkinson's disease (PD) population is unclear. The aim was to explore the prevalence and the link of ICD with above variables in a controlled study.

Methods: 226 consecutive PD patients from central area of Moscow were screened for ICD (N=34, mean age 66.2±8.4 years, 20 males) and compared to a control group (N=30, mean age 70.3±6.1 years, 14 males) without ICD. Specifically, sleep (PD sleep scale 2 (PDSS-2)) and non-motor dysfunction (MDS Unified Parkinson's disease Rating Scale (MDS-UPDRS, part 1) were noted.

Results: 15% of the population had ICD (binge eating (29.5%), punding (14.7%), hypersexuality (5.8%), compulsive shopping (2.9%), dopamine dysregulation syndrome (2.9%). Multiple ICDs were prevalent (44.2%). MDS-UPDRS part 1 and PDSS-2 (disturbed sleep subdomain) were significantly worse in PD-ICD versus controls (p=0.012 and p=0.024 respectively) while other domains were non-significant. Rapid eye movement behaviour disorder screening questionnaire, State-Trait Anxiety Inventory and levodopa equivalent doses were not different between PD-ICD and controls. Depression was worse (Geriatric depression scale, p=0.026) in PD-ICD.

Conclusion: This Russian controlled study of ICD reveals an ICD prevalence rate of 15% and is in line with published data. However, the patterns of ICD differ with multiple ICD's and binge eating being common. PD-ICD have worse sleep (PDSS-2, disturbed sleep subdomain), non-motor symptoms (MDS-UPDRS 1) and depression. Further large scale studies to address the non motor burden of ICD is required.

Disclosure: Nothing to disclose

PR3059

Differentiation between Parkinson's disease patients and SWEDDs based on the MDS-UPDRS

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Background and aims: Up to 15% of suspected Parkinson's disease (PD) patients do not show dopaminergic deficits on a SPECT scan (SWEDDs), possibly leading to unnecessary treatment in populations not evaluated by SPECT scan. We aimed to differentiate de novo PD patients (DeNoPD) and SWEDDs using Item Response Theory (IRT) models of individual MDS-UPDRS item scores.

Methods: Differences in IRT parameters between DeNoPD patients and SWEDDs were estimated for each MDS-UPDRS item using baseline data from the Parkinson's Progression Marker Initiative study. Probability of PD was calculated using ratios of individual likelihoods from evaluating both models on each patient's baseline data. Differentiation power of individual MDS-UPDRS items was assessed through 1) an iterative algorithm adding item per item and evaluating sensitivity and specificity, and 2) an individual item contribution to likelihood differences.

Results: Differentiation based on all items was 86.3% sensitive and 62.7% specific to detecting PD. The iterative algorithm selected a subset of 14 items with 94.9% sensitivity and 57.8% specificity (figure 1). When 14 items with the largest individual likelihood contributions were selected (figures 2 & 3), sensitivity and specificity were 90.0% and 42.2%.

Figure 2. Difference in likelihood between those from the DeNoPD model and SWEDD model. A positive value means that the DeNoPD model described the data better than the SWEDD model, and vice-versa. For the upper panel, negative value are desirable, for the lower panel, positive values are desirable. Red dots: median; Blue bars: 95th percentiles.
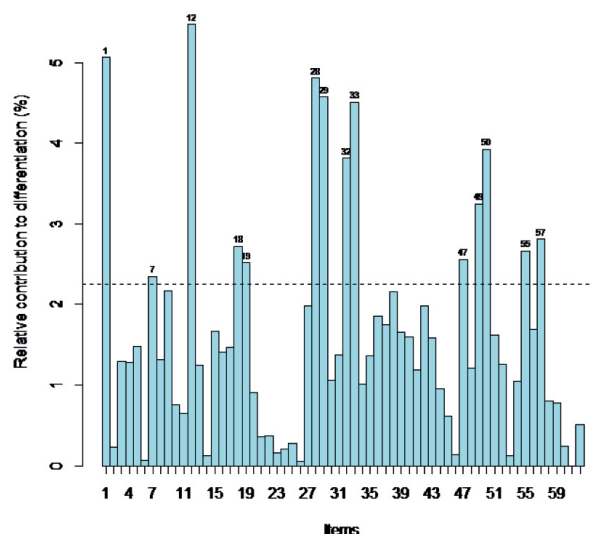
Figure 3. Contribution of individual MDS-UPDRS items to differences between the DeNoPD and SWEDD cohort (see figure 2). The 14 most contributive items (relative contribution above threshold – dashed horizontal line) were selected to be evaluated together to determine their combined differentiation power.

Conclusion: The proposed model allowed differentiation to a higher degree of sensitivity and similar specificity compared to visual clinical examination (Bajaj et al, 2010). A subset of 14 MDS-UPDRS items could differentiate equally well, paving the way to a shortened differentiation questionnaire. Differences between the two item selection algorithms may be due to interaction or information overlap between items, which the iterative algorithm seemed to better take into account.

Disclosure: Data were obtained from the Parkinson's Progression Markers Initiative (PPMI) database (www.ppmi-info.org/data). For up-to-date information on the study, visit www.ppmi-info.org.

Figure 1. Item addition steps taken during the iterative algorithm, with sensitivity and specificity at each step. The path of item selection is shown in green.

PR3060

Treatment for advanced Parkinson's disease: Cross-over and dual treatment with deep brain stimulation and continuous intrajejunal levodopa infusion

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Background and aims: Both deep brain stimulation (DBS) and continuous intrajejunal levodopa infusion (CLI) are efficacious treatments of motor symptoms in advanced Parkinson's disease (PD). They improve quality of life, reduce medication induced motor fluctuations and dyskinesias. Sometimes, the chosen therapy does not have the anticipated or a lasting effect, after which patients receive combined therapy or cross-over. Knowledge about the indications for and effects of combining these therapies are scarce.

Methods: A retrospective study was performed. The records of all patients with PD, who underwent DBS and had CLI treatment started before or after DBS, were assessed. Baseline characteristics, reported symptoms before the second treatment, levodopa equivalent daily dose and motor symptoms (UPDRS) were recorded. Furthermore, the effect of the alternative or additional advanced therapy was evaluated 6 months after initiation.

Results: Eleven patients concurrently or consecutively treated with DBS and CLI between May 2001 and December 2015 were identified. Of these, 7 were initially treated with DBS and 4 had CLI as initial treatment, all but one continued both therapies. Mean age at first advanced treatment was 53 years (range 42-65). In 3 patients response fluctuations were the indication for a second advanced therapy, in 8 both dyskinesias and response fluctuations. No patients experienced worsening after the second advanced therapy. Five experienced no benefit, 4 experienced some and 2 much improvement.

Conclusion: This retrospective study suggests that patients, in whom the effect of the first advanced therapy is suboptimal, may benefit from changing to another advanced therapy or combining treatments.

Disclosure: Dr. Dijk, Dr. de Bie and Mr. van Poppelen are researchers of the INVEST study. This investigator initiated multicentre trial is funded by ZonMw Doelmatigheid, project number 837002509 and by an unconditional grant of Medtronic Netherlands.

PR3061

Comparison of eye movements in patients with Parkinson's disease and patients with essential tremor

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Background and aims: Differences in eye movements may differentiate between Parkinson's disease (PD) and Essential tremor (ET), as in PD and ET different parts of the eye movement networks are pathologically involved. In this pilot study we explore eye movement abnormalities in PD compared to ET and healthy controls (HC).

Methods: Eye movements of 20 PD patients, 20 ET patients and 20 HC were investigated using the double magnetic induction method. The protocol included reflexive and voluntary saccades as well as smooth pursuit eye movements (SPEM). Groups were compared using an unpaired t-test and Mann-Whitney U test.

Results: The mean age in PD patients was 66 years (range 44-84), in ET patients 63 years (range 44-84) and in HC 63 years (range 51-78). We found an increased latency and decreased gain of horizontal and vertical reflexive saccades and voluntary saccades in PD patients, compared to ET patients and HC. ET patients showed a significant hypometric gain of SPEM compared to HC (but not compared to PD patients).

Conclusion: The increased saccadic latency and hypometria in PD patients supports the involvement of the basal ganglia in PD, in contrast to ET patients and HC (who had normal latency and gain). In ET patients SPEM gain was decreased indicating cerebellar involvement. Thus, there are significant differences in eye movements between PD and ET, providing insight in pathological involvement of neural networks in these disease entities which are potentially clinically relevant.

Disclosure: Nothing to disclose

PR3062

Salivary Total and Oligomeric alpha-synuclein in healthy subjects of different ages

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Background and aims: The pathological hallmark of PD is alpha-synuclein (α-syn) aggregation. Oligomers of α-syn (α-synolig) exerts neurotoxic effect in PD. In PD patients we detected lower salivary α-syntotal and higher α-synolig than healthy subjects. Previous studies have shown that α-syn aggregates increase during aging. The aim of this study is to measure α-syntotal and α-synolig concentration in healthy subjects of different ages.

Methods: 70 healthy subjects of different sex and ages (from 20 to 88-year-old) were admitted to the study. Samples of saliva were collected following the protocol of previous study (Vivacqua et al., 2016). ELISA analysis was performed using two specific ELISA kits: SensoLyte 55550 for α-syntotal and MyBioSource MBS043824 for α-synolig. Statistical significance was evaluated by Mann-Whitney U test. Spearmann Rank correlation coefficient was used for correlations.

Results: Concentration of α-synolig doesn't correlate with age in general population, but a trend of correlation was observed in female population. α-synolig were significantly higher in males confronting with females ($p<0,05$) and in smokers confronting with non smokers ($p<0,05$). α-syntotal was significantly lower in subjects older than 70 years old confronting with others ($p<0,05$).

Conclusion: Dicreased salivary concentration of α-syntotal may reflect the reduction of α-syn monomers, leading to the formation of intracellular inclusions during aging process. The increased levels α-synolig in males confronting to females as well as the trend of correlation of α-synolig with age in famale population are both in accordance with the prevalence of PD, supporting salivary α-syn detection as a promising biomarker for PD.

Disclosure: Nothing to disclose

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PR3063

Pain in neurodegenerative diseases

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Background and aims: Pain in neurodegenerative diseases is often underestimated and left untreated. Aim of this study is to investigate characteristics of pain in Parkinson's disease (PD) comparing to other neurodegenerative diseases like atypical Parkinsonism, spinocerebellar ataxia (SCA), motor neuron disease (MND).

Methods: 136 patients with PD, 39 patients with atypical Parkinsonism, 30 patients with SCA and 35 patients with MND who were consecutively referred to Neurology clinic were enrolled. The motor competence was determined by Unified Parkinson's Disease Rating Scale (UPDRS). The Parkinson disease questionnaire (PDQ39), and Hamilton Depression Scale were also applied. Pain characteristics were estimated by using King's PD Pain Scale.

Results: Pain was first symptom of disease in 18 (7,5%) cases, 156 patients (65%) of whole cohort complained of pain comparing with 120 patients or 88.2% of PD patients who suffered pain. Musculoskeletal type of pain is predominant (96 patients, 61.53%), radicular or neuropathic pain 14 patients, 8,97%), pain secondary to dystonia (19 patients, 12.17%), central pain (21 patients, 13.46%). In 19 patients (12.17% of the complete cohort) referred more than one type of pain. Pain is correlated with lower quality of life and depression. 33 patients or 21.15% of patients with pain used analgetics, non-steroid anti-inflammatory drugs in 83% of the cases.

Conclusion: Pain is frequently overlooked and management is not properly done in terms of choice of analgesic therapy. Pain symptoms may not be identified if doctors do not carefully include questions about pain symptoms as part of a complete patient interview.

Disclosure: Nothing to disclose

PR3064

Effect of deep brain stimulation and botulinum toxin on sleep and pain in dystonia patients

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Background and aims: Pain and sleep problems in dystonia patients are often neglected and untreated but affect significantly quality of life.

Our aim was to see the effect of deep brain stimulation (DBS) and botulinum toxin on sleep and pain in dystonia patients.

Methods: We conducted investigation with anamnesis and treatments' data, Pittsburgh Sleep Quality Index (PSQI), Visual Analogue Scale, McGill questionnaire and Hospital Anxiety and Depression Scale (HADS). The study involved randomly selected 90 dystonia patients (20 generalized dystonia, 35 cervical dystonia and 35 facial dystonia: blepharospasm, oromandibular dystonia and hemifacial spasm). We did the basal testing before treatment. 16 of them (15 with generalized dystonia and 1 with cervical dystonia) were treated with DBS and the others with botulinum toxin. For all patients we did another investigation 6 months after the first one. In addition, we try to see factors that were connected with pain and sleep problems.

Results: After 6 months the pain was reduced in group treated with botulinum toxin (from 76% to 20%) but sleep problems were without significant changes. After DBS we observed significant decrease in frequency concerning sleep problems (from 90% to 10% of patients) and pain (from 90% to 20%) (p<0,05). We found that both symptoms were associated with depression.

Conclusion: DBS helps in relieving of the pain and sleep problems and botulinum toxin relieves pain.

Disclosure: Nothing to disclose

PR3065
Cancelled

PR3066
Pain and Parkinson's disease

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Background and aims: Pain is a very common and troublesome non-motor symptom in Parkinson's disease (PD). However, there is no consensus for clinical measures or biomarkers associated with pain in PD. We aimed to explore clinical correlates and risk factors in the development of pain, alongside the relationship between pain and striatal dopaminergic dysfunction in early de novo PD patients.

Methods: Using the Parkinson's Progression Markers Initiative database, we assessed and compared semi-quantified [123I]FP-CIT SPECT as a marker of dopamine transporter (DAT), cerebrospinal fluid (CSF) markers and motor and non-motor features from two groups of early de novo PD patients with pain (n=220) and without pain (n=200). We explored clinical and imaging correlates of pain and the predictive significance of these markers in the development of pain in Parkinson's patients without pain.

Results: Parkinson's patients with pain were more depressed (P=0.002), had reduced quality of life (P<0.001), and increased apathy (P=0.001), sleep disturbances (P<0.001) and fatigue (P<0.001) compared to patients without pain. The severity of pain was associated with depression (r=0.206; P<0.001), UPDRS-I Total (r=0.302; P<0.001), apathy (r=0.192; P<0.001), sleep disturbances (r=0.255; P<0.001), fatigue (r=0.299; P<0.001). Cox multivariate analysis, including all clinical and imaging data, revealed that sleep disturbances (P=0.011) and fatigue (P=0.011) are predictors of the future development of PD pain. In early stages, the presence of pain does not predict motor progression or cognitive decline.

Conclusion: Our findings indicate that pain in early de novo PD is associated with higher non-motor burden scores. Sleep disturbances and fatigue are predictors for pain development.

PR3067
The role of phosphodiesterase 4 in sleep disturbances in Parkinson's disease

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Background and aims: Sleep disturbances are very common in patients with Parkinson's disease (PD). Animal and genome-wide association studies suggested a link between cAMP/PKA signalling, phosphodiesterase 4 (PDE4) expression and daytime sleepiness. We aimed to assess the association between PDE4 expression and sleep disturbances in vivo using combined multimodal MRI and PET molecular imaging with [11C]rolipram in PD.

Methods: 12 PD patients and 5 healthy controls underwent clinical and imaging assessments. Sleep disturbances were assessed with Parkinson's disease sleep scale (PDSS), Epworth Sleepiness Scale (ESS) a measure of excessive daytime sleepiness (EDS), UPDRS-I single items for sleep and fatigue, and non-motor symptom scale (NMSS) domain 2 sleep/fatigue. MIAKATTM was used to generate parametric images of [11C]rolipram volume of distribution (VT) with the Logan plot. FMRIB's diffusion toolbox (FDT) was used to perform probabilistic tractography on each subjects' diffusion data to functionally parcellate the striatum according to cortico-striatal projections generating connectivity maps for limbic, cognitive and sensorimotor subdivisions of the striatum.

Results: Higher ESS scores, indicating greater EDS, correlated with higher PDE4 VT in cortical regions involved in the limbic loop [amygdala (r=0.670), hippocampus (r=0.813), orbitofrontal (r=0.685), cingulate (r=0.663) and temporal cortex (r=0.809)], striatum (0.713), thalamus (r=0.660), hypothalamus (r=0.819) and accumbens (r=0.738). Furthermore, higher EDS was associated with specific increases in PDE4 within limbic portions of the striatum (connectivity based analysis, r=0.788).

Conclusion: Our findings indicate converging evidence for an association between daytime sleepiness and elevated PDE4 in cortical and subcortical limbic regions, implicating PDE4 in the pathophysiology of sleep disturbances in PD.

PR3068

Phosphodiesterases and striatal pathways in Parkinson's disease

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Background and aims: Preliminary human PET studies have demonstrated a loss of PDE10A and PDE4 in patients with movement disorders. We used PDE10A ([11C]IMA107) and PDE4 ([11C]Rolipram) PET molecular imaging combined with DTI based probabilistic tractography to explore the expression of PDE10A and PDE4 in striatal output pathways in healthy controls and patients with Parkinson's disease (PD).

Methods: 24 subjects (12 PD) had [11C]IMA107 and [11C]Rolipram PET, and DTI scans. MIAKATTM was used to generate parametric images of [11C]IMA107 nondisplaceable binding (BPND) and [11C]Rolipram volume of distribution (VT) from the dynamic PET data using the simplified reference tissue model and Logan plot, respectively. FMRIB's diffusion toolbox was used to perform probabilistic tractography to functionally parcellate the striatum according to cortico-striatal, direct sensorimotor striatonigral (substantia nigra/globus pallidus internus) and indirect sensorimotor striatopallidal (globus pallidus externus) projections.

Results: In healthy controls, [11C]IMA107 BPND and [11C]Rolipram VT were more highly expressed in indirect sensorimotor striatopallidal projections compared to direct sensorimotor striatonigral projections ([11C]IMA107 BPND: 18%, p<0.001; [11C]Rolipram VT: 6%, p<0.05). PD patients had higher loss of [11C]IMA107 BPND in direct compared to indirect projections (13%; P<0.01); whereas loss of [11C]Rolipram VT was similar between the direct (24%; P<0.05) and indirect (22% and P<0.05) sensorimotor projections.

Conclusion: Our findings show loss of PDE10A is prominent in the direct striatal pathways; whereas loss of PDE4 expression in both direct and indirect striatal pathways in PD patients; providing new insights in the pathophysiology of PD which may have relevance to the development of targerted treatments.

PR3069

Eye movements in essential tremor patients with concomitant parkinsonian and cerebellar signs

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Background and aims: Some essential tremor (ET) patients display slight parkinsonian or cerebellar signs, which may cause the need for differential diagnosis with Parkinson`s disease (PD) or degenerative ataxias (DA). Eye movement examination, giving some insight into the other movement system, was suggested to help in this diagnosis. The objective of this study was to determine the relationship between the presence of parkinsonian and cerebellar signs and the oculomotor abnormalities in ET patients and compare the pattern of oculomotor abnormalities in ET as compared to PA and DA patients.

Methods: Fifty ET patients, including those with parkinsonian (ET-P) or cerebellar (ET-C) signs, 50 PD patients, 42 DA patients and 42 healthy controls were included to the study. Reflexive, pace-induced and cued saccades were recorded using Saccadometer Advanced. Smooth pursuit and fixation were tested using EOG.

Results: Significant differences of reflexive saccades hypometria were found in ET-P vs. PD (50.0% vs. 66.0%; χ^2=5.8; p=0.016) and of pace-induced saccades hypometria in ET-P vs. PD (0 vs. 70.0%; χ^2=23.2; p=0.000) and in ET-C vs. DA patients (0 vs. 57.1%; χ^2=12.0; p=0.0005). Volitional saccades latency was significantly prolonged in ET-C patients compared to ET patients without concomitant signs (593.5±132.0 vs. 998.4±123.2, p=0.001).

Conclusion: The study showed significant differences between ET with parkinsonian or cerebellar signs and PD and DA patients, but the oculomotor examination has only limited value in differentiation of those patients.

PR3070

Predict cognitive decline with non-clinical markers in Parkinson's disease

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Background and aims: In this study, we investigated whether [123I]FP-CIT SPECT and CSF markers predict Cognitive Impairment (CI) in Parkinson's disease (PD) patients and provide a profile of those most at risk of CI.

Methods: 262 early-stage, de novo PD patients from the Parkinson's Progression Markers Initiative database were stratified into two CI groups: Level 1 diagnosis: all PD patients who had a MoCA score <26; Level 2 diagnosis: PD patients with Level 1 diagnosis, and at least 2 test scores (of HVLT Total Recall, HVLT Recognition Discrimination, Benton Judgement of Line Orientation, Letter Number Sequencing, Semantic Fluency Test and/or Symbol Digit Modalities; irrespective of test domain) greater than 1.5 standard deviation below the mean score in healthy controls. Predictive variables of CI were divided into deciles, providing us with ideal cut-off values for each variable.

Results: At the three-year follow-up, 108/262 (41.2%) PD patients had CI as defined by Level 1, of which 40/108 (37.0%) had CI as defined by Level 2. CSF Aβ42 (Hazard ratio [HR]: 0.996, Wald: 5.035, Confidence Interval [CI]: 0.992-0.999, P=0.025), CSF total tau ([HR]:1.023, Wald: 4.680, [CI]: 1.002-1.044, P=0.031) and caudate [123I] FP-CIT-SPECT uptake ([HR]: 0.332, Wald: 4.146, [CI]: 0.115-0.960, P=0.042) were predictors of cognitive decline. Patients with reduced CSF Aβ42 (<384.6 pg/mL), increased CSF total tau (>45.0pg/mL) and reduced caudate [123I] FP-CIT-SPECT uptake (<1.82) had a 65% risk of developing CI at a 3-year follow-up.

Conclusion: We report that reduced CSF Aβ42, increased CSF total tau and reduced caudate [123I]FP-CIT-SPECT uptake are predictors of cognitive decline in PD.

Disclosure: Nothing to disclose

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PR3071

Smoking prior to multiple sclerosis diagnosis is associated with worse findings in Magnetic Resonance Imaging (MRI)

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Background and aims: Smoking is a modifiable risk factor of multiple sclerosis (MS) and it could be also related to an increased long-term disability progression. In this study, we compared MRI quantitative measures between smoker and non-smoker patients at MS diagnosis.

Methods: MS patients who accepted (99%) to complete a self-administered questionnaire about their exposure to tobacco were randomly selected. By JIM's software, lesion load, black holes (number and volume) and enhancing lesions were quantified and by FMRIB's software library (FSL), normalyzed whole brain, white matter and gray matter volumes were estimated.

Results: 53 MS patients (36 women, 17 men). Mean age 36.02 (18-54) years. Mean duration of disease 3.97 (0-10) years. 59% smokers, 41% never smokers. A significative positive correlation ($p < 0.05$) between number of smoking years and packets-year accumulated at diagnosis and number of T2 lesions was found (table 1). Smoker patients had more T2 lesion load, black holes and enhancing lesions than non smoker patients at diagnosis. A statistically significant difference in T2 lesions number was found between smoker and non smoker patients before diagnosis of the disease (figure 1). A significative negative correlation between the number of smoking years and packets-year accumulated at diagnosis and gray matter volume was found (table 2).

Figure 1. This figure shows that smoker patients had more T2 lesion load, black holes and enhancing lesions than non smoker patients at diagnosis. A statistically significant difference ($p < 0.05$) in T2 lesions number was found between smoker and non smoker patients before diagnosis of the disease.

	nWBV	nGMV	nWMV
NUMBER OF SMOKING YEARS	R= - 0,24	R= - 0,33*	R= 0,05
PACKETS-YEAR	R= - 0,23	R= - 0,24	R= -0,05
* p< 0,05; ** p<0,01.			

Table 2. This table shows the correlations between number of smoking years and packets-year accumulated at diagnosis with nWBV, nWMV and nGMV. A significant negative correlation between the number of smoking years and nGMV was found. nWBV= normalized whole brain volume. nGMV= normalized gray matter volume. nWMV= normalized white matter volume.

Conclusion: MS patients who had smoked before the diagnosis of the disease had higher T2 lesion load and gray matter atrophy. That could be probably associated with a more severe disease course and a faster disability progression rate in smoker patients.

Disclosure: Nothing to disclose

	T2 LESIONS NUMBER	T2 LESIONS VOLUME	BLACK HOLES NUMBER	BLACK HOLES VOLUME	SPINAL CORD LESIONS NUMBER
NUMBER OF SMOKING YEARS	R= 0,27*	R= 0,24	R= 0,21	R= 0,05	R= 0,26
PACKETS-YEAR	R= 0,27*	R= 0,21	R= 0,19	R= -0,05	R= 0,22
* p< 0,05; ** p<0,01.					

Table 1. This table shows results of correlating T2 lesions and black holes (number and volume) and spinal cord lesions number with number of smoking years and packets-years accumulated until MS diagnosis. A significative positive correlation ($p < 0.05$) between number of smoking years and packets-year accumulated and number of T2 lesions was found.

PR3072

Multiple sclerosis and the developing brain: An MRI study of attention system in pediatric patients

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Background and aims: To investigate the impact of multiple sclerosis (MS) on the developing brain by exploring the structural and functional integrity of the sustained attention system, and its effect on cognitive control in pediatric patients.

Methods: We enrolled 57 pediatric MS patients and 14 matched healthy controls (HC). Patients with >3 abnormal tests at neuropsychological evaluation were classified as cognitively impaired (CI). Attention system activity was studied using fMRI during Conners' Continuous Performance Test (CCPT). The structural integrity of network connections was quantified using diffusion tensor (DT) MRI.

Results: Both HC and pediatric MS patients had the age-expected pattern of attention network recruitment. Diffuse network structural abnormalities were found in MS patients compared to HC. During CCPT, with increasing task demand, compared to HC, pediatric MS patients showed increased activation of the left thalamus, anterior insula and anterior cingulate cortex (ACC) and decreased recruitment of the right precuneus. Thirteen patients were classified as CI. Compared to cognitively preserved, CI MS patients had differences in activations/deactivations of brain regions belonging to default mode network (DMN) and salience network and more severe structural damage of their connecting WM tracts.

Conclusion: Our results support the achievement of an age-expected level of functional maturation of the sustained attention system in pediatric MS patients. Abnormalities in the structural integrity of connections between the DMN and salience network (part of the attention system) may result in inefficient regulation of their function and cognitive deficits in these patients.

PR3073

Vitamin D3 supplementation reduces antibody titers against the Epstein-Barr Virus nuclear antigen 1 (EBNA-1) in relapsing remitting multiple sclerosis

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Background and aims: Epstein-Barr virus (EBV) infection and vitamin D insufficiency are risk factors for multiple sclerosis (MS) which may interact. The objectives of this study were to investigate the effect of high-dose vitamin D3 supplementation on antibody levels against the EBV nuclear antigen 1 (EBNA-1) in patients with relapsing remitting (RR-) MS, and to explore the underlying mechanism.

Methods: This study was a randomized controlled trial in RRMS-patients receiving either vitamin D3 (n=30) supplementation (14000 IU/day) or placebo (n=23) during 48 weeks. Circulating levels of 25(OH)D, and anti-EBNA-1, anti-viral capsid antigen (VCA) and anti-cytomegalovirus (CMV) antibodies were measured. EBV-load in leukocytes and EBV-specific cytotoxic T-cell responses were explored, as well as anti-EBNA-1 antibody secretion by in vitro activated B cells.

Results: The median antibody level against EBNA-1, but not VCA and CMV, significantly reduced in the vitamin D3 (526 (368–1683) to 455 (380–1148) U/mL) compared to the placebo arm (432 (351–1280) to 429 (297–1290) U/mL; p=0.023). EBV-load and cytotoxic T-cell responses were unaffected. Anti-EBNA-1 IgG levels remained below detection limits in B-cell cultures.

Conclusion: High-dose vitamin D3 supplementation selectively reduces anti-EBNA-1 IgG levels in RRMS-patients. Our exploratory studies do not reveal a promoted immune response against EBV as the underlying mechanism.

Disclosure: Nothing to disclose

PR3074

Durable improvement in MRI outcomes in treatment-naïve patients with RRMS who discontinued SC IFNB-1a and initiated alemtuzumab: CARE-MS I extension study 4-year follow-up

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Background and aims: Treatment-naïve patients with active relapsing-remitting MS (RRMS), demonstrated improved clinical/MRI outcomes with alemtuzumab versus SC IFNB-1a over 2 years (NCT00530348). Here we examine 4-year MRI outcomes in patients who discontinued SC IFNB-1a after the core study and subsequently initiated treatment with alemtuzumab (NCT00930553).

Methods: Following SC IFNB-1a discontinuation, patients received alemtuzumab 12 mg (2 courses [baseline: 5 days; 12 months later: 3 days]), followed by as-needed alemtuzumab for relapse/MRI activity, or another disease-modifying therapy (DMT) per investigator discretion. Annual MRI assessments: proportion free of MRI disease activity (gadolinium [Gd]-enhancing and new/enlarging T2 lesions), and new T1 hypointense lesions.

Results: 144/187 (77%) SC IFNB-1a-treated patients enrolled to receive alemtuzumab, and 125/144 (87%) remained on study 4 years later. 75% of patients received no additional treatment after 2 alemtuzumab courses. Proportion free of Gd-enhancing lesions after 2 years on SC IFNB-1a increased following 2 years on alemtuzumab (73% versus 92%), and was durable through Year 4 of alemtuzumab (Year 3: 92%, Year 4: 88%, Year 0–4: 78%). A similar pattern was observed for new/enlarging T2 lesions (42% versus 69%, 72%, 67%, Year 0–4: 46%), MRI disease activity (42% versus 69%, 72%, 66%, Year 0–4: 45%) and new T1 lesions (69% versus 88%, 89%, 90%, Year 0–4: 78%).

Conclusion: Alemtuzumab durably improved MRI outcomes in patients who discontinued SC IFNB-1a, consistent with conclusions from a prior controlled study. Based on these findings, alemtuzumab may provide a unique treatment approach with durable efficacy in the absence of continuous treatment.

Disclosure: Sanofi and Bayer HealthCare Pharmaceuticals.

PR3075

Timing of the use of plasma exchange and steroids in progressive multifocal leukoencephalopathy management

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Background and aims: We retrospectively analyzed the effect of plasma exchange (PLEX) and steroids administration timing on the longitudinal clinical course of patients with natalizumab related progressive multifocal leukoencephalopathy (PML) and immune reconstitution inflammatory syndrome (PML-IRIS).

Methods: Clinical and radiological data of 40 Italian patients with PML were analyzed. Patient's data are available until 12 months after PML diagnosis. Longitudinal clinical course (measured by means of EDSS score) and PML-IRIS features (prevalence, days elapsed between natalizumab withdrawal and IRIS manifestation, duration) were compared between patients treated or not to PLEX and between patients taking steroids prophylactically to prevent PML-IRIS (proST) or therapeutically (terST) to treat PML-IRIS.

Results: In patients treated with PLEX, the earlier the patients underwent treatment with PLEX, the earlier they are expected to manifest PML-IRIS (r=0.75, p<0.001). Between group analysis (PLEX yes/no) revealed that PLEX anticipated IRIS (p=0.04) and increased its duration (p=0.03). The prophylactic administration of steroids worsened the longitudinal clinical course and patient's outcome (F[3,99]=3.29, p=0.02).

Conclusion: The current study leads to important exploitable results since it emphasized the need to modify some important clinical procedures when dealing with PML: i) caution on the use of PLEX is recommended as the current data do not support a beneficial effect of PLEX; ii) the use of steroids should be postponed until a well demonstrated PML-IRIS emerged, as their prophylactic use interferes with JC virus elimination, preventing immune reconstitution and in turn worsening the clinical condition.

Disclosure: Nothing to disclose

PR3076

"Multiple sclerosis plus": When auto-immunity builds up

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Background and aims: Multiple sclerosis (MS) is an immune-mediated disease, and its association with autoimmune diseases (AID) has long been debated.

Methods: From a cohort of 635 patients with MS, 66 patients with an history of AID were selected. Controls, matched 1:1, were chosen from the population of patients with MS without AID. Further analysis aimed to compare these groups.

Results: The prevalence of AID was 10.4%. The mean age was 43±13 years; 77% were women. Fifteen different types of AID were identified, the most frequent autoimmune thyroiditis (27%). In 44% of cases the AID was diagnosed before, in 48% it was diagnosed after the diagnosis of MS. The presence of family history of AID was not associated with the risk of developing AID. Our analysis found no association between the presence of AID and disease activity (new lesions, gadolinium enhancement, mean of annual relapse rate, initiation of a second line treatment), either when considering each variable individually or within a composite score. The median EDSS and MSSS was 1.50 (IQR=3.0) and 1.21 (IQR=2.92) respectively in the AID group and 1.50 (IQR=3.0) and 1.65 (IQR=3.0) respectively in the control group. This difference was not statistically significant. The presence of a concomitant AID influenced therapeutic choice in 9 cases, by the initiation of an immunosuppressive agent or suspension of interferon.

Conclusion: The present study underlines the varied range of AID that may coexist with MS. This common ground doesn´t seem to have a negative effect on disease course.

Disclosure: Nothing to disclose

PR3077

Circulating exosomes analysis reveals different microRNA composition in relapsing-remitting multiple sclerosis patients

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Background and aims: Exosomes are a membrane vesicles released from the endocytic compartment of live cells that play an important role in cell-to-cell communication. The major contents of the exosomes are short RNAs that can interfere with the function of the acceptor cells.

Methods: We have isolated exosomes and exosomal RNA from serum of the relapsing remitting multiple sclerosis (RRMS) patients and control subjects. Subsequently we have processed exosomal RNA for the next generation sequencing analysis. The miRNA sequences differentially expressed were validated with qPCR of 96 serum samples from RRMS patients (in relapse and in remission). PBMCs have been isolated from blood of the RRMS patients and from controls and cultured under various TLR stimulations and analyzed with respect to the exosomal miRNA secretion.

Results: Serum exosomes are a reach source of the shortRNA (<300 nt) in MS patients both during relapse and remission. The sequences have been grouped into 14 categories: CDBox, HAcaBox, RefSeq_antisense, lincRNA, lincRNA_antisense, miRNA, other_ncRNA, other_ncRNA_antisense, rRNA, piRNA, rfam, scaRNA, tRNA and tRNA_like. RefSeq_antisense, linc RNA, lincRNA_antisense A significant fractions of exosomal RNA were miRNA that represented 26-31% of the all annotated miRNA sequences.. We have identified four exosomal miRNA that were differentially expressed during relapse in comparison to remission. These miRNA have been also differentially secreted within the exosomes by PBMCs from RRMS patients and from controls.

Conclusion: Our data highlight a differences in serum exosomes miRNA in RRMS patients related to the clinical status of the patients that could lead to a discovery of a new biomarkers of MS.

PR3078

Vitamin D deficiency predicts early conversion of clinically isolated syndrome to clinically definite multiple sclerosis: A preliminary Egyptian study

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Background and aims: It has been suggested that vitamin D influences the immunoregulation and subsequently affects the risk for conversion of clinically isolated syndrome (CIS) to clinically definite multiple sclerosis (MS).Aim of this study: is to detect the early predictors of conversion to clinically definite MS in patients with CIS and to study if deficiency of vitamin D could be a contributor for early conversion

Methods: A longtudinal prospective case control study was conducted on forty-three Egyptian patients diagnosed as CIS according to MacDonald's criteria (2010). Clinical presentation, brain magnetic resonance imaging (MRI) and 25-hydroxyvitamin D levels were evaluated at baseline and after 1 year follow up

Results: Eight patients (18.6%) with CIS were converted to clinically definite MS. Multivariate logistic regression analysis revealed that the CIS patients with initial clinical presentation with optic neuritis (p=0.003), higher MRI brain lesions load (p=0.002) ,lower 25-hydroxyvitamin D level (p<0.001) were associated with early conversion to MS.

Conclusion: The patients with CIS that early presented with optic neuritis, higher MRI brain lesion load and low level of 25-hydroxyvitamin D level are at higher risk for conversion to MS. Early vitamin D supplementation is recommended in patients with CIS in particularly those presented with optic neuritis and higher MRI brain lesion load.

Disclosure: Nothing to disclose

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PR3079

Heterogeneity in individual patterns of microglial activation in multiple sclerosis measured non-invasively with 18F-DPA-714 PET

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Background and aims: Activated microglia, which is thought to play a key role in the pathogenesis of MS, can be measured in-vivo using a positron emission tomography (PET) radiotracer, the 18F-DPA-714. The objective of this study is to investigate individual profiles of microglial activation using 18F-DPA-714 PET in MS.

Methods: Twenty-three patients with relapsing-remitting (RR) or progressive MS (PMS), and healthy controls (HC), underwent a 18F-DPA-714 PET. Maps of differences in tracer binding between patients and HC, were employed to identify voxels with significantly activated microglia. The percent volume of activated microglia (PVAM) over T2-w lesional, perilesional, normal-appearing white-matter (NAWM) and cortical volume, was calculated. Multiple regressions were used to compare the PVAM between patients and HC.

Results: A high heterogeneity in the extent of microglial activation was found across the cohort (Fig.1), with a higher mean PVAM in T2-w lesions (p=0.0001), perilesional WM (p=0.0001), NAWM (p=0.0001), and in the cortex (p=0.001) in patients compared to HC. The regional mapping of microglial activation identified a subset of lesions characterized by a high perilesional inflammation suggestive of smoldering plaques, that was particularly associated with PMS,
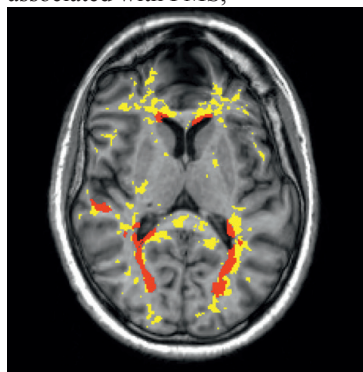
Example of a patient-specific individual map of activated microglia in the normal-appearing tissues (voxels in yellow), generated with 18F-DPA-714 PET, and overlayed onto the corresponding MPRAGE in standard space. Lesional voxels are displayed in red.

Conclusion: 18F-DPA-714 PET allowed to calculate individual profiles of microglial activation, which was consistently greater in patients compared with HC, and to identify possible smoldering lesions, which might represent a PET signature of the progressive form of MS. This technique will enable a large-scale in-vivo exploration of the pathogenic role of microglia in MS, and will allow to clarify whether each disease form is associated with specific microglial signatures.

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PR3080

Effect of extracellular vesicles from CSF of multiple sclerosis patients and healthy controls on astrocytes in culture

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Background and aims: Secretion of extracellular vesicles (EVs), has been described under physiological conditions as well as their ability to modify cells phenotypes. Involvement of EVs in pathological processes like multiple sclerosis (MS), and their capacity of transferring damaging cargoes have also been suggested. We exposed primary cultures of astrocytes to EVs isolated from cerebral spinal fluid (CSF) of MS patients, to study the potential ability of these EVs to induce in receiving cells morphological and functional changes, such as modifications of proliferation rate, apoptosis or cell death

Methods: We collected CSF by patients affected by MS diagnosed according to validated criteria, and by individuals requiring a lumbar puncture for other neurologic diseases. Es obtained by CSF, were separtated by from MVs by differential ultracentrifugation. Pelleted vesicles were suspended with phosphate-buffered saline, pH 7.5 (PBS) and used to treat astrocytes for 24 hours.

Results: MVs from MS patients induced a higher but not significant degree of cell death than those prepared from the CSF of control group (99,35% dead cells vs 89,33; p=0,14). Es from MS patients induced a highly significant degree of cell death effect on astrocytes, compared to Es from controls (94,38% vs 71,21; p=0,0001).

Conclusion: Our study suggests that Es present in the CSF of MS patients, carrie molecules which can be toxic to astrocytes and this is probably the reason why brain cells discard such molecules via different kinds of EVs. Further studies are now necessary to identify the active molecules present in EVs.

Disclosure: Nothing to disclose

PR3081

Integrated motor and cognitive rehabilitation in multiple sclerosis: A controlled study

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Background and aims: Some evidence supports the notion of a cognitive-motor interference phenomenon when motor skills were performed simultaneously to cognitive task. There are no studies examining the effects of "combined rehabilitation" in terms of "cross-modality transfer effects". The aim of our study is to evaluate the effect of a combined integrated motor and cognitive rehabilitation on cognitive and motor performances in patients with multiple sclerosis.

Methods: 60 MS patients (mean EDSS 5.5; 8 relapsing-remitting, 52 progressive) were assigned to integrated-treatment-group (ITG) (33 patients) or to motor-treatment-group (MTG) (27 patients). The IT included a training for executive functions (ERICA) added to exercises tailored on the impaired neuropsychological functions. The cognitive training was performed for 24 consecutive weeks with twice session per week. The MT was done with neuro-motor rehabilitation protocol only. At baseline and at the end of the training all patients underwent a wide range neuropsychological and motor assessment. An ANOVA test was performed to compare the two groups.

Results: the ITG showed improvement not only in selected neuropsychological measures as Stroop test time ($p < 0.032$); phonological Verbal Fluency ($p < 0.006$); Simbol Digit Modality Test ($p < 0.025$); PASAT ($p < 0.018$); Forward verbal span ($p < 0.016$), Spatial Span ($p < 0.005$); Delayed spatial Recall Test 10/36 ($p < 0.020$), but also on motor measures as Tinetti Balance and Gait Scale ($p < 0.05$).

Conclusion: The IT can induce significant improvement of neuropsychological skills particularly in attention and executive function suggesting that could create cognitive strategy and learning of motor control shared common neural pathway.

Disclosure: Nothing to disclose

PR3082

The effects of mechanical focal vibration on walking impairment in multiple sclerosis patients: A randomized, double-blinded vs placebo study

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Background and aims: Multiple sclerosis is a heterogeneous disorders involving in early stage gait and balance. Rehabilitation had a crucial role in improving motor tasks and life quality and specifically Focal Vibrations (FV) could play a role, but they have been used only to reduce muscle tone and fatigue alone or together with botulinum toxin.

Objective: To assess whether FV is effective on walking impairment.

Methods: We performed a single-centre randomized, double-blind, sham-controlled study to investigate efficacy of FV vs sham vibration in 20 RR MS patients. Demographical, clinical and gait instrumental data analysis have been collected for each patient at baseline (T0), after treatment (T1) and after wash out (T2).

Results: Both groups have no clinical and demographic differences. Treated patients showed significant improvements during the first right step ($p=0.007$), average stride lenght ($p=0.012$), double support right ($p=0.016$) and left ($p=0.003$) time. Non-treated patients didn't show any significance for any dynamic variabile. Moreover on posturographic measurements we registered only a trend towards significance in swing area with eyes open ($p=0.087$). Lastly we found a significant inverse correlation in treated group between disease duration and percentage of improvement for DSLT ($r=-0.775$; $p=0.014$) in T1 vs T0 and percentage of improvement of FSS, with an inverse correlation with both disease duration ($r=-0.775$; $p=0.014$) and AGE ($r=-0.733$, $p=0.025$) in T1 vs T0

Conclusion: Our results suggested a beneficial effect of FV on walking impairment in MS patients suffering from spasticity and/or postural instability.

Disclosure: Nothing to disclose

PR3083

GABA and microbiota association in multiple sclerosis and neuro-Behçet's disease

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Background and aims: Gamma-aminobutyric acid (GABA) is not only an inhibitory neurotransmitter but also a potent immunosuppressant. Our aim was to analyze the association between neuroinflammation and intestinal GABA-producing bacteria.

Methods: Fecal GABA concentrations and microbiota were measured in 14 healthy controls (HC), 13 relapsing remitting multiple sclerosis (MS), and 13 neuro-Behçet's disease (NBD) patients from the Istanbul metropolitan area. The microbiota composition was determined by sequencing the V1-V3 region of the rRNA 16S gene.

Results: The mean and standard deviations for the GABA concentrations in HC, MS and NBD were 264.8 ± 221.8, 131.4 ± 59.7, and 371.7 ± 457.0ng/ml. The reduction in MS compared to HC was significant ($p=0.022$) by Mann-Whitney U test. Correlations between GABA concentrations and relative bacteria abundances were calculated by Spearman's method. In HC GABA was correlated with the genera Bacteroides ($r=0.7$, $p=0.010$), Clostridium XIVa ($r=0.6$, $p=0.042$), unclassified Clostridiales ($r=0.6$, $p=0.020$) and unclassified Burkholderiales genus ($r=-0.6$, $p=0.022$). In consistency with previous literature, Prevotella was significantly lower in NBD compared to HC ($p=0.014$). In NBD significant correlations were found for the genus Prevotella ($r=0.6$, $p=0.028$), family Erysipelotrichaceae ($r=0.6$, $p=0.048$), genera Odoribacter, Parabacteroidiales ($r=-0.6$, $p=0.032$ and $r=-0.7$, $p=0.020$) and the order Burkholderiales ($r=-0.6$, $p=0.029$). In MS, GABA levels correlated negatively with the unclassified Ruminococcaceae ($r=-0.7$, $p=0.003$), which is known to use GABA.

Conclusion: Our results suggest a potential link between intestinal GABA and neuroinflammation. Particularly, demonstration of reduced fecal GABA levels and presence of GABA-consuming bacteria in MS patients suggest that GABA deficiency in MS might be induced by the intestinal bacterial content.

Disclosure: Nothing to disclose

PR3084

Gait kinematics correlate with clinical measures of improvement after neurorehabilitation in multiple sclerosis

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Background and aims: Gait impairment is a main disability cause in Multiple Sclerosis (MS). In addition to validated clinical gait measures, kinematics analysis may provide information for treatment customization and assessment. We explored their usefulness in evaluating clinical improvement after rehabilitation in MS.

Methods: Seventeen subjects with progressive MS, male/female, 18-65 years old, Expanded Disability Status Scale (EDSS) 4-6.5, underwent Functional Independence Measure (FIM) scale, six-minute walk test (6MWT) and Berg Balance Scale (BERG) at hospitalization (T1) and after a 4-week neurorehabilitative program (T2). Gait parameters (cadence, velocity, cycle length, symmetry index of gait cycle acceleration) were collected during 10-meter walk test (TMWT) and correlated with clinical measures.

Results: At both time points, cadence correlated with FIM (T1: Pearson's r 0.546, p=0.023; T2: r 0.638, p=0.006), 6MWT (T1: r 0.803, p=0.001; T2: r 0.563, p=0.036), BERG (T1: r 0.675, p=0.003; T2: r 0.518, p=0.033). Velocity correlated with FIM (T1: r 0.590, p=0.013; T2 r 0.673, p=0.003), 6MWT (T1: r 0.773, p=0.002; T2: r 0.641, p=0.014), BERG (T1: r 0.596, p=0.011; T2: r 0.577, p=0.015). FIM improvement correlated with cadence (r +0.501, p=0,040) and velocity (r +0.488, p=0.047) increase. TMWT correlated exclusively with 6MWT (T1 and T2) and BERG (T1).

Conclusion: Cadence and velocity correlated with all clinical measures whereas TMWT showed correlation only with 6MWT (T1 and T2) and BERG (T1), suggesting that quantitative gait kinematics correlate with clinical measures better than TMWT. Cadence and velocity improvement seems to reflect the increase in daily activities-independence (FIM) rather than in walk endurance (6MWT).

Disclosure: Nothing to disclose

PR3085

5 years PANGAEA: Effectiveness of fingolimod in daily clinical practice of RRMS patients in Germany

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Background and aims: Fingolimod (FTY720; Gilenya®, Novartis Pharma AG) is approved for the treatment of relapsing MS. As of August 2016, approximately 160,000 patients have been treated with fingolimod in both clinical trials and the post-marketing setting. PANGAEA (Post-Authorization Non-interventional German sAfety of GilEnyA in RRMS patients) is a non-interventional study, conducted in Germany, to investigate long-term safety, effectiveness and patient reported outcomes in daily practice.

Methods: 4229 patients were enrolled into PANGAEA. By Jan 2017, over 300 patients completed the five year documentation period. Here we present effectiveness data of fingolimod treatment in daily clinical practice for up to five years.

Results: The mean (+/-SD) age of the patients was 39.4(+/-10.0) years. The mean (95%CI) annual relapse rate improved from 1.5+/-0.13 at baseline to 0.42+/-0.08 after 12 months and further improved to 0.29±0.04 after five years. The mean (95%CI) EDSS at baseline was 3.0+/-0.03 and remained stable over five years. In each year of treatment more than 90% of the patients had a stable EDSS, over 70% of the patients were free of relapses and 6-month confirmed disability progression. 45% of the patients neither had a relapse nor disability progression over four years of treatment. Patient reported outcomes evaluated in a sub-study (n=830) confirmed the effectiveness and convenience profile of fingolimod from a patient point of view.

Conclusion: The results of the five year interim analysis of PANGAEA support the positive effectiveness profile of fingolimod, demonstrated in phase III clinical trials with real world evidence data.

Disclosure: This study was supported by the Novartis Pharma GmbH, Nuremberg, Germany.

PR3086

Consistent effects of daclizumab in disease-modifying therapy (DMT)-naïve relapsing-remitting multiple sclerosis (RRMS) patients in DECIDE

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Background and aims: Daclizumab HYP (daclizumab), a structurally distinct form of daclizumab, has demonstrated higher efficacy versus intramuscular (IM) interferon (IFN) beta-1a across several clinically important RRMS patient subgroups, including those with highly active disease or those previously treated with MS DMTs. Here we evaluated daclizumab in DMT-naïve patients with active disease.

Methods: In the multicenter, randomized, double-blind, active-controlled, phase 3 DECIDE study, patients with RRMS (age 18–55 years, baseline Expanded Disability Status Scale score 0–5.0) were randomized (1:1) to receive daclizumab 150mg subcutaneous every 4 weeks or IFN beta-1a 30mcg IM weekly for 96–144 weeks. Efficacy and safety were assessed in patients naïve to IFN beta, glatiramer acetate, and other MS treatments excluding steroids at enrollment.

Results: In each treatment group, 59% of patients were DMT-naïve (daclizumab, n/N=539/919; interferon beta-1a, n/N=546/922). Daclizumab demonstrated greater efficacy over IM IFN beta-1a across several clinical and radiological endpoints, including annualized relapse rate, proportion of patients relapse free, and number of new/newly enlarging T2 hyperintense lesions at week 96 (Table), similar to results demonstrated in the overall intention-to-treat population. Among the DMT-naïve patients, infections were observed in 59% and 53%, cutaneous adverse events in 33% and 17%, and elevations of alanine/aspartate aminotransaminases in 7%/5% and 8%/5% of daclizumab and IM IFN beta-1a treatment groups, respectively. Safety findings were comparable to those observed in other subgroup populations.

Table. Relapse and radiological endpoints in DMT-naïve patients with RRMS in DECIDE

Efficacy endpoint	Daclizumab (95% CI)	IM IFN beta-1a (95% CI)	Treatment difference (daclizumab vs IM IFN beta-1a) (95% CI); P-value
Adjusted ARR (primary endpoint)	0.132 (0.085, 0.205)	0.277 (0.180, 0.425)	% relative reduction: 52.4 (39.9, 62.2) <0.0001
Patients relapse free at 144 weeks, %	74.7	55.2	% relative reduction in risk of relapse: 51.0 (38.0, 61.0) <0.0001
Adjusted mean number new/newly enlarging T2 hyperintense lesions at Week 96*	3.15 (2.21, 4.49)	6.96 (4.87, 9.95)	% relative reduction: 54.8 (45.1, 62.8) <0.0001

*For adjusted mean number of new/newly enlarging T2 hyperintense lesions at Week 96, daclizumab (n=514), IM IFN beta-1a (n=503); ARR: annualized relapse rate; CI: confidence interval; IFN: interferon; IM: intramuscular.

Conclusion: These findings demonstrate the efficacy and safety of daclizumab in DMT treatment-naïve patients and support the overall findings from DECIDE across several clinically relevant RMS patient subgroups.

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Neurogenetics 2

PR3087

An original PGK deficiency phenotype: Case description and physiopathologic hypothesis

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Background and aims: Phosphoglycerate kinase is a key glycolytic enzyme directly involved in cellular generation of ATP. PGK deficiciency (PGKD) classically associates hemolityc anemia, central nervous system involvement (seizures, mental retardation, parkinsonism) and/or myopathy.

Methods: A 39-year-old man, first presenting classically with psychomotor developmental delay and hemolytic anemia, was diagnosed at 3 years with PGK deficiency, and amino-acid substitution 163 Asp/Val.

Results: At age 5, he started experiencing iterative hemiplegias of abrupt onset and short durations, and later on encephalopatic events with disturbed consciousness, cephalalgia and hemiplegia. Parkinsonism appeared at 31 years. Neurologic explorations revealed retinitis pigmentosa and cerebral folate deficiency (MTHF 22nmol/L, N>41). Muscle biopsy and thorough genetic studies found no argument for a mitochondriopathy. Folate substitution resulted in a moderate improvement. To our knowledge, such a clinical phenotype has only been described in patients with PGKD and this specific mutation. The association of encephalopatic episodes, retinitis pigmentosa and parkinsonism, along with cerebral folate deficiency, is highly evocative of a mitochondrial disease. Mitochondrial involvement has been reported in PGKD, and an impaired interaction between oxydative phosphorylation and glycolysis could here be caused by PGK tertiary structure alteration or the imbalance between ATP and ADP induced by PGKD. The hemiplegic episodes could be described as hemiplegic migraine-like events, hence an altered ionic channels functionning, supported by the suggested interaction between PGK and an Na/K pump, could also be evoked.

Conclusion: This work reports a unique PGKD presentation, and tries and describes the potentially underlying physiopathologic mechanisms supporting those originals clinical findings.

Disclosure: Nothing to disclose

PR3088

Loss of PDE10A expression in patients with PDE10A and ADYC5 mutations

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Background and aims: To assess phosphodiesterase 10A (PDE10A) expression in vivo, using [11C]IMA107 PET in patients with PDE10A and adenylate cyclase 5 (ADYC5) mutations.

Methods: We studied two unrelated patients with de novo heterozygous p.Phe300Leu PDE10A mutation (Patient 1, 61F; Patient 2, 23F); one patient with heterozygous p.Ile625Phe PDE10A mutation (Patient 3, 26F); and one patient with heterozygous p.R418W ADYC5 mutation (Patient 4, 38M). Patients 1 and 2 presented in childhood with progressive chorea and Patient 1 developed levodopa-responsive parkinsonism in the fifth decade. Patient 3 presented with childhood onset of paroxysmal kinesigenic dyskinesias. Patient 4 presented with childhood onset of progressive chorea and dystonia. All patients underwent one [11C]IMA107 PET scan and one MRI scan.

Results: Patients 1 and 2 showed >70% decreases in [11C]IMA107 BPND in the striatum (−72% in caudate and −78% in the putamen) and 65% loss of [11C]IMA107 BPND in pallidum compared to a group of healthy controls. Patient 3 showed >20% decreases in [11C]IMA107 BPND in the striatum (−21% in caudate and −31% in the putamen) and 9% loss of [11C]IMA107 BPND in pallidum; and Patient 4 showed >10% decreases in [11C]IMA107 BPND in the striatum (−8% in caudate and −11% in the putamen) and 9% loss of [11C]IMA107 BPND in pallidum compared to a group of healthy controls.

Conclusion: PDE10A expression is decreased in patients with PDE10A and ADYC5 mutations and pharmacological modulation of PDE10A could help restoring physiological levels of cAMP, and therefore alleviate symptoms.

Disclosure: Nothing to disclose

PR3089
Cancelled

PR3091
Cancelled

PR3090

Exome sequencing in patients with impulse control disorders in Parkinson's disease: A pilot study

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Background and aims: ICD is frequently associated with dopamine agonist (DA) therapy in PD. There are growing evidence of a high heritability for ICD in general population and PD. We aimed to identify genetic variants associated with impulse control disorders (ICD) in Parkinson's disease (PD).

Methods: We selected 36 PD patients on DA therapy with (n=18) and without (n=18) ICD, matched for age and gender. Exome sequencing was performed using MedExome SeqScape EZ kit and NexSeq 500 sequencer. Variants with a strong functional impact (Cadd-score$\geq$12.37) and in brain-expressed genes were selected. Allele frequencies, and their distribution in genes and pathways were analyzed respectively with single variant test and Optimized Sequence Kernel Association Test (SKAT-O), and then replicated in the independent Parkinson's Progression Markers Initiative (PPMI) cohort.

Results: We identified five pathways associated with ICD (p<1x10-2) from the analysis of the 6953 variants selected. Association with "adenylate cyclase activating pathway" (p=1.6x10-3) was replicated in PPMI cohort (p=2.0x10-2), resulting in a significant combined p-value of 3.7x10-4 (Fisher's combined test). Among the 10 most associated variants (p<0.001), two were laying on genes (RasGRF2 and PDE2A) implicated in ERK and cAMP signaling pathway, respectively.

Conclusion: Our results suggest that genes implicated in the signaling pathways linked to G protein-coupled receptors participate to genetic susceptibility to ICD in PD. These results are in accordance with the pharmacology of DA, and the importance of ERK and cAMP signaling pathways in the dopamine-dependent plasticity in the striatum. Results from this pilot study need to be replicated in independent cohorts.

Disclosure: Nothing to disclose

Neuroimaging 3

PR3092

Changes over time in striatal DAT availability in Parkinson's disease: Relevance to levodopa-induced dyskinesias

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Background and aims: As Parkinson's disease (PD) progresses, the density of the dopamine transporter (DAT) continues to decline in the striatum while PD patients are at risk for developing levodopa-induced dyskinesias (LIDs). Here, we intend to study the role of DAT-specific imaging as a prognostic marker of dyskinesias.

Methods: We retrospectively selected 42 PD patients who underwent SPECT imaging with 123I-Ioflupane (DAT-specific in vivo marker) five years ago during the diagnosis of PD. 15 patients of the 42 were rescanned with 123I-Ioflupane SPECT 6.3 ± 3.0 years after their first scan. We divided the PD patients according to the presence or absence of dyskinesias as LIDs and non-LIDs. SPECT data were analysed for the putamen by a semi-quantification approach using the occipital cortex as a reference.

Results: 10 PD patients had developed LIDs, while 32 were non-dyskinetic. The putaminal mean 123I-Ioflupane uptake in the LIDs (1.7 ± 0.4) group was not statistically different as compared to the non-LIDs group (1.7 ± 0.5; $p>010$). All 15 PD patients who had a second SPECT scan had significant reductions in the putaminal 123I-Iofluplane uptake ($p<0.001$) as compared to the first scan. Within the group of 15, the LIDs (N=8) had significantly lower DAT uptake (1.1 ± 0.3) as compared to the non-LIDs group (N=7); (1.5 ± 0.5; $p<0.05$).

Conclusion: 123I-Ioflupane SPECT imaging in de novo PD, cannot predict the onset of LIDs within five years from diagnosis. As shown in the subgroup that repeated 123I-Ioflupane SPECT imaging, an onset of LIDs may be linked to a faster decline of putaminal DAT availability.

Disclosure: Nothing to disclose

PR3093

Unraveling essential tremor - manipulation of the sensorimotor loop with a novel quantitative fMRI approach

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Background and aims: Essential tremor (ET) is a high prevalent movement disorder with yet unclear pathophysiology and overlapping clinical features with other tremor disorders. In ET efferent motor activity and afferent sensory activity are intermingled, thereby hampering identification of truly tremor related brain areas (efferent drive) in neuroimaging studies. With a novel fMRI approach, we manipulate both motor and sensory input to gain insight in the sensorimotor closed loop.

Methods: Fifteen ET patients (eleven men; mean age 58.8 yrs$\pm$18) with bilateral postural arm tremor, were studied off medication. Subjects performed a motor task with the right hand using a haptic manipulator during fMRI. Tasks included an active isometric motor task (exerting a static torque to the handle) and a passive movement task (going along with a continuous multi-sinusoidal perturbations). Results were derived from a block-design of the group comparing active motor tasks and passive motor conditions, with the tasks and the movement parameters used as regressors (FWE corrected, $p <0.05$).

Results: The active motor task versus the passive movement in ET was associated with activation in bilateral cerebellum, bilateral basal ganglia, thalamus, SMA and motor cortex. The reversed contrast did not show any activations in motor networks.

Conclusion: Our findings show accurate identification of motor network activity during isometric contraction versus passive movement. By manipulation of the sensorimotor loop we are able to reveal specific motor network activations. This novel quantitative approach is a promising new technique to study pathophysiological mechanisms in hyperkinetic movement disorders, and potentially lead to new diagnostic approaches.

Disclosure: Nothing to disclose

PR3094

Exploring the social brain: Combined structural and effective connectivity

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Background and aims: Non-verbal communication is indispensable for everyday social interaction and critically depends on reading and understanding of body language. Despite this significance, underlying brain networks remain little understood and deficits after brain damage rarely considered and recognized. The aim of the study was to assess the architecture of the social brain network, integrating functional and structural connectivity.

Methods: In healthy participants, we recorded functional MRI (fMRI) and diffusion tensor imaging (DTI) during recognition of emotions (happy, neutral and angry) conveyed by a point-light arm seen knocking on a door. Statistical Parametric Mapping 12 and the FMRIB Software Library were used for data analysis, and a novel procedure was developed to inform dynamic causal modelling (DCM) analysis of effective connectivity with measures of structural connection strength.

Results: As compared to neutral knocking, the right superior temporal sulcus (STS) and caudate nucleus are preferentially activated by happy, and the left inferior insula, perigenual anterior cingulate cortex (ACC) and posterior midcingulate cortex (MCC) by angry body motion. The posterior cerebellar vermis (lobule IX) and right amygdala signal a lack of emotional content. Combined effective and structural connectivity analysis reveals functional network architecture and interactions.

Conclusion: This study for the first time reveals the components, connections and interactions of the social brain network for body language reading. The data contribute to better clinical consideration and understanding of socio-cognitive deficits after brain damage. In addition, the developed connectivity analysis may open new perspectives in assessment of different functional networks in normalcy and neurological disease, also for other functional domains.

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PR3095

Comparison of brain atrophy measures for clinical use in multiple sclerosis

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Background and aims: In this study, we compared two available methods (FSL-SIENAx/SIENA 5.0.1 and Icometrix-MSmetrix 1.3) used for grey matter (GM) and brain atrophy estimation on MR images of multiple sclerosis (MS) patients for their future clinical use.

Methods: The methods were tested on a dataset of 3D-T1 and 3DT2-FLAIR sequences of in-house simulated data, MRI of MS patients acquired at different scanners, field strengths, and longitudinal data. The main steps of each atrophy pipeline were evaluated: the percentage of normalized mutual information (NMI%) was used for image registration, while brain extraction and lesion segmentation were assessed using the Dice similarity coefficient (DSC) against manual segmentation (gold standard). Accuracy and precision between the pipelines in brain and GM volume estimation were assessed (Figures 1-3).
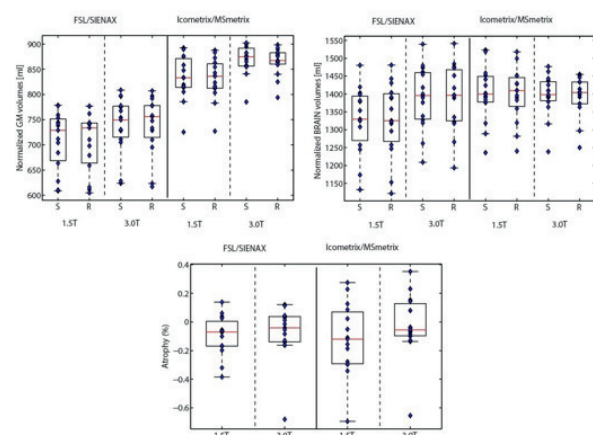
The results of the two cross-sectional pipelines on the dataset of patients acquired on a 1.5T and 3.0T Philips scanners at scan (S) and rescan (R) in the first row. In the bottom graph the results for brain atrophy after the application of the longitudinal pipelines between scan and rescan are shown.
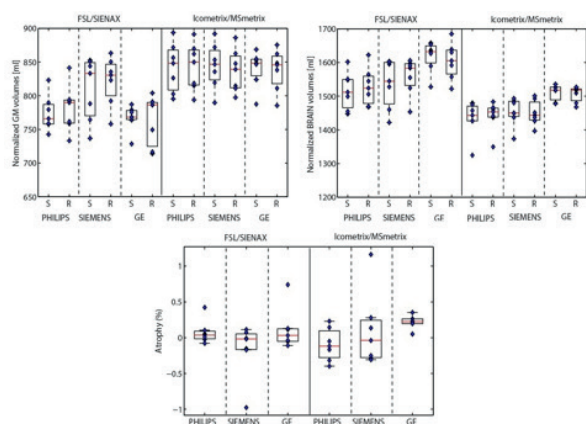
The results of the two cross-sectional pipelines on the dataset of patients acquired on three different 3.0T manufacturers (Philips, SIEMENS and GE) are shown in the graphs of the first row. The results for brain atrophy after the application of the longitudinal pipelines between scan (S) and rescan (R) are represented in the bottom graph.
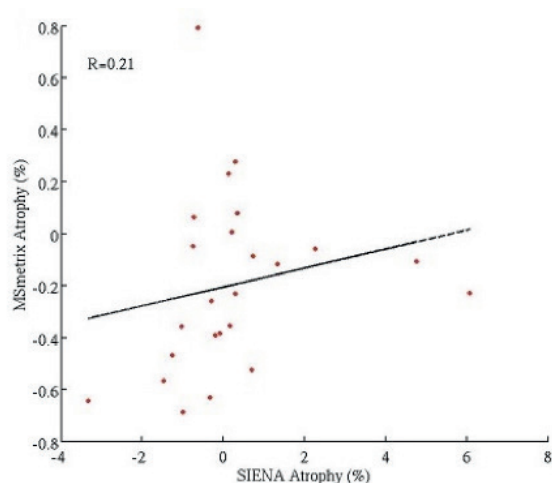
A scatter plot with the correlation coefficient (R) between SIENA and MSmetrix results for brain atrophy assessment of MS patients between baseline and 1 year of follow up is shown (black line represents the linear regression).

Results: Mean NMI% for the image registration performance between the two time-points MRI scans were 71.2% for Icometrix and 59.8% for FSL. The mean DSC for Icometrix lesion segmentation was 0.23 for the longitudinal dataset, while mean DSCs values for brain extraction were respectively 0.96 and 0.93 for Icometrix and FSL. The accuracy for SIENAx was in the range 97.6%÷99.1%, while MSmetrix showed a range of 91.2%÷95.2%.

Conclusion: Both pipelines showed good results with high reliability when run on this dataset. MSmetrix had slightly better image registration and brain extraction performance than SIENAx/SIENA. SIENAx showed a slightly better accuracy for cross-sectional and longitudinal analysis but a higher dependence on image acquisition quality than MSmetrix pipeline.

Disclosure: Nothing to disclose

PR3096

A semi-automatic method to segment multiple sclerosis lesions on FLAIR magnetic resonance images

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Background and aims: Aim of the study was to adapt and evaluate on FLAIR images a recently developed semi-automatic method for segmentation of hyperintense multiple sclerosis (MS) lesions on dual-echo (DE) PD/T2-weighted MRI.

Methods: The method was validated in a cohort of 17 patients with clinically isolated syndrome (CIS) suggestive of MS (mean lesion load=2.5 ±2.3 ml) on FLAIR MRI scans acquired on a 1.5T Philips scanner. Adapting the method to FLAIR sequences, the intensity standardization and the training were avoided. Starting from the lesion seed point (manually identified by an expert physician), the expansion of the segmented region continued to the adjacent pixels until the stop condition was reached combining intensity and edge detection constraints. The algorithm was implemented in Matlab®. Manual segmentations by an expert operator were used as the gold standard (Figure 1). The metrics evaluated were Dice Similarity Coefficient (DSC), Root Mean Squared Error (RMSE) of lesion load, True Positive Fraction (TPF), False Positive Fraction (FPF), and False Negative Fraction (FNF) for each patient.
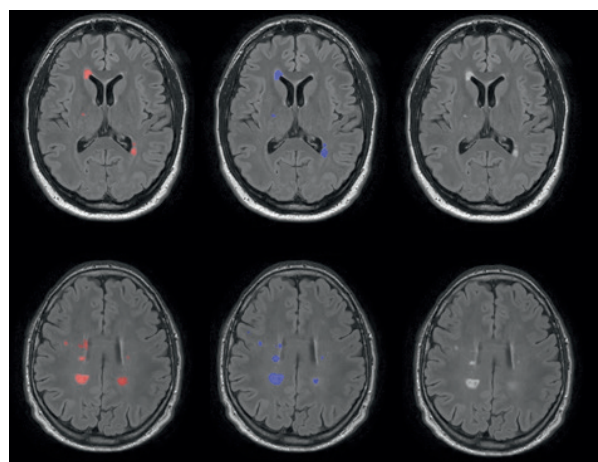
Figure 1. Examples of lesion segmentation for two different patients (in the two rows) performed by the proposed method (in red) compared to the gold standard (manual segmentation) (in blue). The corresponding FLAIR images are shown in the right column.

Results: The validation measures averaged over all patients were obtained: DSC=64% (Figure 2); TPF=0.8; FPF=0.32; FNF=0.19 (Figure 3); RMSE=0.65 ml.
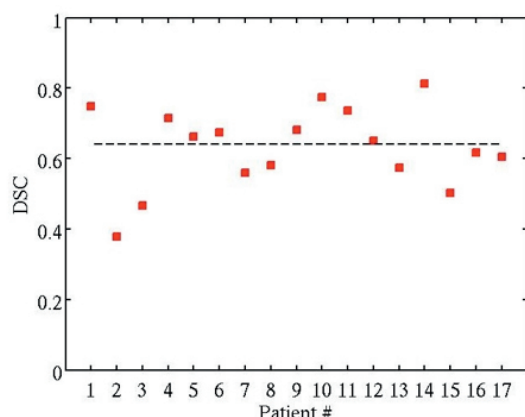
Figure 2. DSC values for all patients are reported in this graph.
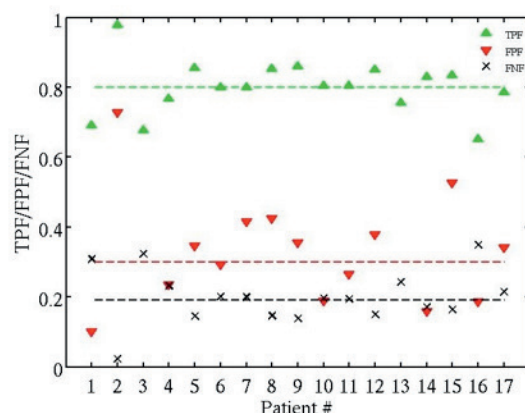
Figure 3. TPF, FPF and FNF values are shown for each patient.

Conclusion: High similarity with the gold standard was found, as well as a low misclassification of lesion voxels and low measurement error. Moreover, the operator time required to extract lesion volumes was importantly reduced. The method did not require training on manual segmentation, making it applicable for research and clinical trials.

Disclosure: Partially supported by Fondazione Italiana Sclerosi Multiple (FISM2013/S/1).

PR3097

Pediatric patients with congenital sensorineural hearing loss: A diffusion Kurtosis imaging study

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Background and aims: Our aim was to assess microstructural alterations in the cerebrums of pediatric patients with congenital sensorineural hearing loss (SNHL) by using diffusion kurtosis imaging (DKI).

Methods: Seventy-two pediatric SNHL patients and 38 age matched healthy volunteers were examined by DKI on a 3.0T MR imager. Fractional anisotropy (FA) and mean kurtosis (MK) values were computed in 12 cerebral regions in both controls and SNHL patients. Subjects were divided into 2 groups − children above 3 years of age (SNHL n=40, control n=20), and children 1 to 3 years of age (SHNL n=32, control n= 18).

Results: As compared with patients below age 3, patients in the older age group were found to have more significant differences in MK than in FA, these appeared in more major areas of the brain. In contrast, 1- to 3-year-old children only had a number of major brain areas showing differences in FA, but no appreciable differences in MK. There were significant decreases in FA or MK values(P<0.05, all) in more areas of the brain in patients with lesions than in patients with normal-appearing brains.

Conclusion: DKI offers sensitive and comprehensive measurements for the quantitative evaluation of age-related microstructural changes in both white and gray matter in SNHL patients. DKI scans in SNHL children showing significant decreases in MK might play an important role in evaluating the severity of the developmental delay of the brain and relate to the prognosis of cochlear implantation.

Neuro-oncology

PR3098
Cancelled

PR3099
The two-week wait pathway for suspected CNS malignancies: Examination and imaging are more important than individual symptoms

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Background and aims: The two-week wait (2WW) urgent referral pathway was implemented to improve waiting times for patients with suspected central nervous system (CNS) malignancies in the United Kingdom (UK). Studies have shown poor diagnostic yield, with only 1-21% of CNS tumours identified via this route. We examined the utility of referral criteria, symptomatology, neurological examination and imaging in detecting CNS tumours.
Methods: We retrospectively studied all adults referred via the 2WW pathway to Whipps Cross Hospital, London, UK between 2007 and 2016. 252 cases were identified. Referral forms and clinical records were analysed for symptomatology, examination findings, investigations and diagnoses. We calculated positive predictive values (PPV) and tested for association with CNS tumours.
Results: Of 252 referred cases, 11% (n=28) resulted in CNS tumour diagnoses. Headaches were the most common symptom prompting referral (54%), followed by visual disturbance (25%), headaches with features suggestive of raised intracranial pressure (24%), nausea and vomiting (22%) and dizziness. No individual symptoms were associated with a positive diagnosis, after correction for multiple comparisons. Factors associated with positive diagnoses included abnormal neurological examination (p=0.002, PPV 12%) and positive findings on prior neuroimaging (p<0.001, PPV 59%). 2 glioblastoma multiforme were identified, which presented with headache and visual disturbance, and progressive motor and sensory deficit, respectively. Neither had imaging prior to referral.
Conclusion: The 2WW pathway has poor diagnostic utility for CNS malignancy. Only abnormal neurological examination and imaging predicted CNS tumours. Recommendations include redefining referral criteria and redistribution of resources to improve early diagnosis.
Disclosure: Nothing to disclose

PR3100
Seizure response to perampanel in drug-resistant epilepsy with gliomas

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Background and aims: Drug-resistant epilepsy occurs commonly in gliomas, possibly due to a shared mechanism of AMPA activation involving epileptic activity and tumor growth. We tested the AMPA-receptor blocker perampanel (PER) in patients with drug-resistant epilepsy (DRE) in low- and high-grade gliomas.
Methods: Seizure response was defined as 50% drop in seizure frequency or seizure-freedom. Cognitive function was examined by CTCS (Computerized Test on Cognitive Speed), which is sensitive to the type of cognitive dysfunction associated with epilepsy and use of anticonvulsants. Treatment policy included reduction of dose or discontinuation of one or more concurrent AEDs, once seizure-free response was observed.
Results: Twelve patients were included patients, median age 41 years, 9 men vs 3 women and 6 months median duration of follow-up. An objective seizure response was observed in 9 (75%) out of 12 patients: 50%-seizure response in three (25%), seizure-freedom in 6 (50%) out of 12 patients, which is plainly more than with other types of DRE. Side-effects occurred in 6 patients. Cognitive function as examined by CTCS improved in six out of eight secondary to lowering of concurrent AEDs. The final median dose of PER was 8 mg (varying 2-12 mg).
Conclusion: Objective seizure response in 9 (75%) out of 12 patients treated by PER in DRE may be interpreted as a surrogate-marker of tumor response often advancing an objective radiological response by 6 months or more in low-grade gliomas. These results warrant further study of PER as anti-tumor agent in gliomas.
Disclosure: Nothing to disclose

PR3101

Late cerebrovascular complications of cerebral radiotherapy

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Background and aims: Radiotherapy is often used in the management of primary brain tumours, and it is a recognized risk factor for the development of cerebrovascular disease in patients with head and neck cancer. However, little is known about late cerebrovascular risks related to cerebral radiotherapy in patients with primary brain cancer.

Methods: We retrospectively collected adults with a supratentorial primary brain tumour and treated with cranial radiotherapy between 1975 and 2006. Seventy-two patients were enrolled. We analysed demographic, radiotherapeutic and radiological features.

Results: Among the 72 patients, 32 were females and 41 males, with a median age at tumour diagnosis of 41. The median follow-up was 14 years, and the most frequently diagnosed tumour was oligodendroglioma (39%), followed by astrocytoma (28%). Twenty-one patients (31%) had a cerebrovascular disease. The median age at stroke was 54 (range:38–72). Ten patients had intracerebral haemorrhage, whereas 11 (15%) had an ischemic stroke, which was symptomatic in 7 cases (64%). Eight and 3 patients respectively presented with lacunar or larger vessel stroke. Patients with tumours near the Willis polygone were more likely to experience stroke after radiotherapy (p=0,0112).

Conclusion: Stroke incidence is increased in patients treated with cranial radiotherapy, which seems to predispose to both ischemic and haemorrhagic stroke. Lacunar stroke is more commonly diagnosed in those patients, suggesting a small rather than large vessel impairment. A larger prospective study has been initiated to further investigate those results.

Disclosure: Nothing to disclose

PR3102

BRAF V600E and TERT promoter mutations and CDKN2A homozygous deletion are frequent in epithelioid gliomas and coexisting lower-grade gliomas

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Background and aims: Epithelioid glioblastomas (E-GBM) are a rare variant of glioblastoma, composed predominantly of monotonous, patternless sheets of round cells with laterally positioned nuclei and eosinophilic cytoplasm. The BRAF V600E mutation has been reported to be found in approximately 50% of E-GBM. Most E-GBM are recognized as primary lesions, although there are a few reports of E-GBM with pre- or coexisting low-grade glioma. Here, we investigated E-GBM with pre- or coexisting lower-grade glioma for genetic associations between their E-GBM components and lower-grade lesions.

Methods: Four E-GBM with a coexisting diffuse astrocytoma-like component, one with a coexisting pleomorphic xanthoastrocytoma (PXA)-like component, one with a coexisting oligoastrocytoma-like component, one with a coexisting anaplastic astrocytoma-like component, and one with a pre-existing PXA-like component, were investigated. Direct DNA sequencing for BRAF, TERT promoter, and IDH1/2 mutations, fluorescence in situ hybridization for ODZ3 deletion, and array comparative genomic hybridization (aCGH) were performed. Each histologically distinct element in each case was separately analyzed.

Results: BRAF V600E, TERT promoter mutations, and CDKN2A homozygous deletion from aCGH results were found in 8 of 8, 6 of 8, and 5 of 5 cases, respectively; exceptionally, one coexisting diffuse astrocytoma-like component in one case lacked these alterations, while its E-GBM component exhibited them. ODZ3 heterozygous deletion was observed only in an E-GBM component in 2 of 8 cases.

Conclusion: The combination of BRAF and TERT promoter mutations and CDKN2A homozygous deletion, which is rare in diffuse gliomas and PXA, may predict the potential of malignant transformation to E-GBM.

Disclosure: Nothing to disclose

PR3103

Sellar atypical teratoid/rhabdoid tumor (AT/RT): A clinicopathologically and genetically distinct variant of AT/RT

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Background and aims: Atypical teratoid/rhabdoid tumors (AT/RT) are rare aggressive tumors of the central nervous system that predominantly affect infants. Although adult AT/RT are rare, accumulated cases have revealed adult-specific AT/RT in the sellar region. Twelve previously reported cases of sellar AT/RT exclusively occurred in adult females, suggesting biological differences from conventional infant AT/RT. We herein investigated a series of six sellar AT/RT to clarify the clinicopathological and genetic outlines of this tumor.

Methods: Six cases of sellar AT/RT were histologically and immunohistochemically assessed. Fluorescence in situ hybridization, direct sequencing, and multiple ligation-dependent probe amplification analyses for the INI1/SMARCB1 gene were performed.

Results: All six cases were adult females, ranging in age from 21-69 years old. Tumors were histologically characterized by a hemangiopericytoma-like stag-horn vasculature within a dense, diffuse proliferation of jumbled cells and a small number of scattered rhabdoid cells. This vascular pattern is not a common finding in AT/RT and appears to be a characteristic histology of sellar AT/RT. Biallelic alterations in the INI1 gene were identified in four out of the five cases analyzed. Three out of the four cases harbored two different mutations, presumably on different alleles (compound heterozygous mutations), and one case of which had a splice-site mutation. Combined with previous findings, the prevalence of compound heterozygous mutations and splice-site mutations was significantly higher in sellar AT/RT than in pediatric AT/RT.

Conclusion: Sellar AT/RT represent a clinicopathologically and possibly genetically distinct variant of AT/RT showing a characteristic demography, different patterns of INI1 alterations, and a histology featured by a unique vasculature.

Disclosure: Nothing to disclose

Neurotoxicology & Neurotraumatology & Spinal cord and root disorders 2

PR3104

Atopic myelitis: A new European case of a probably underestimated disorder.

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Background and aims: Atopic myelitis (AM) is a rare, inflammatory spinal cord disorder which is likely related to either mite antigen-specific IgE positivity and hyperIgEaemia or coexistent atopy (bronchial asthma, atopic dermatitis, food allergy, allergic rhinitis or conjunctivitis). Since its first description by Kira et al. in 1997, AM has mainly been reported in Asian countries. By contrast, only few cases have been documented in Europe.
Methods: A 47-year-old Italian man presented after three days of progressive lower limbs weakness with hypoesthesia/dysesthesia and urinary retention. Spinal cord MRI revealed a longitudinally extensive T2-hyperintense lesion at T10-T12 level, without contrast enhancement. Cerebrospinal fluid examination showed mild hyperproteinorrachia (68 mg/dL) without oligoclonal bands. Common causes of myelopathy were excluded, including multiple sclerosis, neuromyelitis optica spectrum disorder, sarcoidosis, infectious myelitis, cervical spondylotic myelopathy, collagen-vascular diseases, spinal cord tumor and nutritional deficiencies.
Results: Serum IgE level was found extremely high (2367.9 IU/mL) with normal eosinophil count. There was no history of atopy. Measurement of blood antigen-specific IgE showed strong positivity to Dermatophagoides pteronyssinus and Dermatophagoides farinae. The patient was treated with intravenous dexamethasone, human immunoglobulins and plasma exchange with gradual recovery. Isolated, severe proprioceptive deficit persisted after discharge. At one-year follow-up his clinical conditions were slightly improved with persistent gait impairment.
Conclusion: AM is a recently defined, probably underestimated disorder which may cause long-term disability. It should always be considered in diagnostic workup of subacute new-onset myelopathy of unclear etiology. Prompt recognition of the disease is mandatory in order to start adequate therapy and prevent sequelae.
Disclosure: Nothing to disclose

PR3105

Predictors of symptomatic myelopathy in degenerative cervical spinal cord compression

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Background and aims: To update a previously-established list of predictors for neurological cervical cord dysfunction in non-myelopathic degenerative cervical cord compression (NMDCCC).
Methods: A prospective observational follow-up study was performed in a cohort of 112 consecutive NMDCCC subjects (55 women and 57 men; median age 59 years, range 40–79 years), either asymptomatic (40 subjects) or presenting with cervical radiculopathy or cervical pain (72 subjects), who had completed a follow-up of at least two years (median duration 3 years). Development of clinical signs of degenerative cervical myelopathy (DCM) as the main outcome was monitored and correlated with a large number of demographic, clinical, electrophysiological and MRI parameters including diffusion tensor imaging characteristics (DTI) established at entry.
Results: Clinical evidence of the first signs and symptoms of DCM were found in 15 patients (13.4%). Development of DCM was associated with several parameters, including the clinical (radiculopathy, prolonged gait- and run-time), with electrophysiological (SEP, MEP and EMG signs of cervical cord dysfunction), and MRI (anteroposterior diameter of the cervical cord and cervical canal, cross-sectional area, compression ratio, type of compression, T2 hyperintensity). DTI parameters showed no significant predictive power. Multivariate analysis showed that radiculopathy, cross-sectional area (CSA) <70.1 Xmm^2 and compression ratio (CR) <0.4 were the only independent significant predictors for progression into symptomatic myelopathy.
Conclusion: In addition to previously described independent predictors of DCM development (radiculopathy and electrophysiological dysfunction of cervical cord), MRI parameters, namely CSA and CR, should also be considered as significant predictors for development of DCM.
Disclosure: Funded by grant project NT-13449-4 of the Internal Grant Agency of the Ministry of Health of the Czech Republic and by the Ministry of Health of the Czech Republic project for conceptual development in research organizations, ref.65269705 (University Hospital, Brno, Czech Republic)

PR3106

Sortilin gene SNP variant rs12037569 predicts chronic pain 12-14 years after whiplash injury

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Background and aims: Chronic pain is the most commonly encountered symptom after Whiplash (WAD). Seeing WAD in a bio-psycho-social perspective several predisposing psychological factors (e.g. catastrophizing) and social factors (e.g. legal factors) have been associated with the disorder. The biological basis of the disorder has yet to be identified. Intense neck pain upon presentation to the ER after Motor-Vehicle-Collision (MVC) predicts development of chronic WAD. This study investigated whether single nucleotide polymorphism (SNP) variants of pain-related genes were associated with long-term chronic pain after whiplash injury.

Methods: From 835 previously whiplash exposed (12-14 years post-injury), 326 eligible subjects fulfilled an e-questionnaire on current health status, a subgroup of 159 agreed to participate in a genetic sub-study. A candidate gene analysis was performed to investigate the prevalence of 35 pain-related SNP variants. Chronic pain was determined as reported average VAS (neck/and or Headpain11-point) above 5. Associations between chronic pain and SNPs were determined with Pearson's chi square test and applied Bonferroni Correction.

Results: Of 159 tested six were excluded due to low genotyping. Three of 35 SNPs tested were excluded due to failed Hardy-Weinberg Equilibrium. Of the remaining 32 SNP's one SNP of the Sortilin gene was found to be associated with chronic pain (unadjusted $p<0.002$ and Bonferoni-corrected $p< 0.05$, OR=3.3(CI95: 1.5; 7.0))

Conclusion: 12-year post-MVC chronic daily pain was markedly associated with a SNP variant of the sortilin gene(rs12037569). Sortilin has in animal studies been linked to neuropathic and inflammatory pain. This is the first human study to report this association.

Disclosure: Nothing to disclose

PR3107

Genetic polymorphisms of GRIN2A and GRIN2B modify the neurobehavioral effects of low-level lead exposure in children

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Background and aims: Lead (Pb) is neurotoxic and children are highly susceptible to this effect, particularly within the context of continuous low-level Pb exposure. A current major challenge is identification of children who may be uniquely susceptible to Pb toxicity because of genetic predisposition. We examined the hypothesis that polymorphic variants of genes encoding the glutamate receptor, ionotropic, N-methyl-D-aspartate receptor subunits 2A and 2B, GRIN2A and GRIN2B, exacerbate the adverse effects of Pb exposure on these processes in children.

Methods: Participants were subjects who participated as children in the Casa Pia Dental Amalgam Clinical Trial and for whom baseline blood Pb concentrations and annual neurobehavioral test results over the 7 year course of the clinical trial were available. Genotyping was performed for variants of GRIN2A (rs727605 and rs1070503) and GRIN2B (rs7301328 and rs1806201) on biological samples acquired from 330 of the original 507 trial participants. Regression modeling strategies were employed to evaluate the association between allelic status, Pb exposure, and neurobehavioral test outcomes.

Results: Numerous significant adverse interaction effects between variants of GRIN2A, individually and in combination, and Pb exposure were observed among both boys and girls, particularly within the domains of Learning & Memory and Executive Function. In contrast, few interaction effects were observed between variants of GRIN2B and Pb exposure.

Conclusion: These findings suggest potentially distinct roles of GRIN2A and GRIN2B on developmental processes underlying learning and memory as well as other neurological functions in children and demonstrate selective modification of Pb effects on these processes by specific variants of GRIN2A.

PR3108

Atypical transverse myelitis in a patient with newly diagnosed hepatitis C: A case report and review of the literature

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Background and aims: Transverse myelitis (TM) is often the first presentation of inflammatory central nervous system conditions or systemic disease. A cause is not always identified with up to 30% of cases labelled idiopathic.

Methods: Fourteen TM cases have been reported in patients with hepatitis C infection (HCV); often atypical, extensive and recurrent. We present a case and review the literature.

Results: A 60 year old right-handed engineer, previously fit and well, presented with sudden onset leg paraesthesiae and numbness. Few weeks later he developed progressive leg weakness. He had no upper limb, bladder or bowel involvement. Examination showed flaccid paraparesis, brisk reflexes, extensor plantars, and complete T8 sensory level. MRI showed a longitudinally extensive non-enhancing spinal cord lesion (T2-T9). CSF was acelular with elevated protein (0.70); oligoclonal bands were present in both serum and CSF. Vasculitic screen, HIV, cryoglobulins and Aquaporin-4 antibodies were negative. HCV was positive, genotype 1a with moderate viral load. There was no fibrosis on liver ultrasound. He received three days IV methylprednisolone with marked clinical improvement followed by weaning oral steroids. He is awaiting to start AbbVie 3D plus (paritaprevir/ombitasvir/ritonavir plus dasabuvir) with ribavirin.

Conclusion: Isolated TM has been correlated with HCV, particularly in atypical or relapsing presentations. It is uncertain whether the relationship is causal but undertreatment of HCV is linked with relapses. Underlying HCV should be considered as a diagnosis when common causes have been excluded and HCV-positive patients should be considered for treatment.

Disclosure: Nothing to disclose

Peripheral nerve disorders 3

PR3109

Transthyretin-related familial amyloid polyneuropathy: Demographic and phenotypical characterization of a patients' cohort (followed) in a Portuguese Center

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Background and aims: Transthyretin-related familial amyloid polyneuropathy (TTR-FAP), have a high prevalence in Portugal (20.4/100000) with a peculiar geographical distribution in the north of the country where the prevalence raises to 50/100000. Although the phenotypic/genotypic correlation is well known, no phenotypic/geographical region is known in the same mutation.

Methods: Five hundred and eighty seven TTR-FAP (Val30Met) patients from a National Reference Center located in the Center of the country were analysed. A retrospective analysis of demographic and clinical data of patients, originated from different Portugal's regions (North, Center and South) was done. Exclusion criteria were to patients with less than 5 years or more than 7 years of disease duration and those with non-Val30Met mutation.

Results: One hundred and thirteen patients were selected (58 males; 39-year-old median age of onset, IQR [32-55]). 47% of the patients came from the region Center of the country; 37% came from the South and 16% from the North of Portugal. There was no statistical significance regarding gender between the three regions (p=0.308). Although the median age of onset was higher in Southern patients, statistical significance was not achieved (p=0.183). A trend to a higher renal involvement in Southern patients was observed but no statistical significance was achieved (p=0.487). No other statistically differences were observed in the disease phenotype regarding different geographical distribution.

Conclusion: In our study there were no statistical differences regarding demographic or phenotypical features in patients originated from different country regions.

Disclosure: Nothing to disclose

PR3110

Motor nerve conduction studies localize nerve lesion proximal to the actual entrapment site

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Background and aims: Focal neuropathies are primarily diagnosed on the basis of the history and neurologic examination. The diagnosis and localization is also frequently confirmed with an electrodiagnostic examination (EDx), and recently using high resolution ultrasonography (US). In the precise localization of ulnar neuropathy at the elbow (UNE) we have noted some discrepancies between electrodiagnostic (EDx) and ultrasonographic (US) findings. In the present study we aimed to explore the correspondence of the two methods.

Methods: In a group of prospectively recruited patients with idiopathic UNE, four blinded examiners took a history and performed neurologic, EDx and US examinations. The relationship between ulnar nerve cross-sectional area (CSA) and motor nerve conduction velocity (MNCV) was studied in 2cm segments across the elbow.

Results: In 106 patients with UNE at the retrocondylar groove (RTC), the highest CSA and lowest MNCV were noted in the same short segment, usually at or just proximal to medial epicondyle (ME) of the elbow. In 54 patients with UNE at the humeroulnar aponeurosis (HUA) 2 or 3cm distal to ME, the highest CSA and lowest MNCV were noted proximal to the HUA. About half of these patients had a clear constriction of the ulnar nerve at the level of entrapment.

Conclusion: MNCV and CSA were highly correlated in UNE. Ulnar nerve slowing proximal to the entrapment at the HUA was surprising, but consistent with previous studies done on carpal tunnel syndrome showing sensory slowing in the carpal tunnel, and motor proximal to it.

PR3111

Long-term outcomes of patients with ulnar neuropathy at the elbow treated according to etiology of the nerve lesion

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Background and aims: We believe that idiopathic ulnar neuropathy at the elbow (UNE) mainly consists of two conditions: entrapment under the humeroulnar aponeurosis (HUA) and extrinsic compression in the retrocondylar (RTC) groove. Both conditions need different treatments: surgical HUA release and avoidance of inappropriate arm positioning, respectively. We treated our UNE patients accordingly, and studied their long term outcomes.
Methods: We invited our cohort of UNE patients to follow-up examination that consisted of history, neurologic, electrodiagnostic (EDx) and ultrasonographic (US) examinations performed by four blinded investigators.
Results: At mean follow-up period of 881 days history was obtained from 155 (94%) patients with established precise UNE localization: HUA entrapment in 52 and RTC compression in 103. Complete or marked improvement reported 60% and 63%, and partial 22% and 20% patients, respectively. In 107 (65%) patients complete follow-up evaluation was performed: 41 HUA and 66 RTC, with increase of mean compound muscle action potential (CMAP) amplitude $2.1 \rightarrow 4.0$ mV and $7.7 \rightarrow 8.7$ mV (normal>6.5mV), minimal motor nerve conduction velocity increase $11 \rightarrow 20$ m/s and $21 \rightarrow 29$ m/s (normal>31 m/s), and maximal ulnar nerve cross sectional area (CSA) decrease $19 \rightarrow 17$ mm^2 and $11 \rightarrow 10$ mm^2 (normal<10mm^2).
Conclusion: Our study demonstrated significant clinical improvement in $>80\%$ of UNE patients after 2.5 years follow-up. Subjective reports were also supported by EDx and US findings. We think that these results support our clinical approach to UNE that takes into account presumed etiology of the ulnar nerve lesion.
Disclosure: Authors were supported by the Republic of Slovenia Research Agency, Grant No. P3-0338.

PR3112

Bortezomib-associated polyradiculoneuritis in patients treated for multiple myeloma

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Background and aims: Bortezomib in a proteasome inhibitor frequently used as treatment for multiple myeloma and mantle cell lymphoma. Peripheral neuropathy is a common adverse effect of bortezomib-based chemotherapy, presenting as a progressive, small fiber and painful, axonal, sensory distal neuropathy, usually reversible after its dose reduction or discontinuation. However, rare evidence has shown that bortezomib is associate with polyradiculoneuropathy.
Methods: We retrospectively identified using the database of OncoNeuroTox (center for patients with neurological complications of oncologic treatments) and the database of the Department of Clinical Neurophysiology, 5 patients treated with bortezomib for a multiple myeloma, presenting polyradiculoneuropathy.Clinical records were screened for epidemiologic data, polyradiculoneuritis caracterisation, treatment and evolution.
Results: all patients had a sub acute clinical presentation suitable with polyradiculoneuritis whithin 6 months after bortezomib's introduction. Among the five patient, aged 60 to 76 years old, 3 women, 2 men, four presented motor impairment, and every one of them had paresthesia, hypopalesthesia and areflexia. Three patients had demyelinating signs on nerve conduction study (NCS). All patients had albuminocytologic dissociation in CSF. All patients had intra-veinous immunoglobulin treatment as they kept worsening after bortezomib discontinuation. Stabilization or improvement emerged after IgIV administration in all patients.
Conclusion: Bortezomib can induce a rare severe subacute polyradiculoneuritis with sensory and motor defect which does not respond to treatment's discontinuation. CSF shows albuminocytologic dissociation but NCS does not always display demyelinating signs. This important side-effect should promote systematic close clinical follow-up, as early-warning signs have to be searched for and immuno-modulator treatement might be required.
Disclosure: Nothing to disclose

PR3113

Chemotherapy-related peripheral neuropathy: Clinical and electrophysiological features in 22 patients

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Background and aims: Cancer treatment related neurotoxicity represents the second serious adverse effect after the hematological toxicity. Peripheral neuropathies constitute the majority of the chemotherapy-induced neurological impairment. We describe herein a series of patients addressed to the neurophysiology unit to assess peripheral neurological symptoms occuring after chemotherapy. We report the electrophysiological features, response to treatment and quality of life impairment.
Methods: A series of consecutive patients referred to our department for peripheral neurological disorders were included. All patients had neurological examination, electromyography with nerve conduction study (NCS) and quality of life assessment (McGILL QoL questionnaire). We also evaluated the response to neuropathic pain medication.
Results: Twenty-two patients were included (sex ratio=0.8; mean age=62.6 years). Presenting symptoms were neuropathic pain (86%), paresthesia (63%) and muscle weakness (27%). Average delay between chemotherapy and symptoms was 10.6 months. Mean QoL questionnaire was 74 (50-112). NCS showed axonal sensory neuropathy in 11 patients (50%), axonal sensory and motor neuropathy in five patients (22%), mononeuropathy multiplex in two patients (9%) and demyelinating sensory neuropathy in one patient (4%).There was no statistically significant association between the underlying cancer or chemotherapy and the NCS results. Neuropathic pain medication was administered in all patients, including tricyclic antidepressants, pregabalin, gabapentin and carbamazepin. Only 18% of patients were satisfied with treatment despite the association of two or more molecules.
Conclusion: Our study highlights the impact of chemotherapy-induced neuropathy on the quality of life of cancer patients. Early neuropathic pain treatment could be required in order to improve the status of these patients.
Disclosure: Nothing to disclose

PR3114

Relevance and frequency of different types of Charcot-Marie-Tooth neuropathy in a large population of patients studied at a single clinical site

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Background and aims: The aim of this study is to describe our large population of CMT patients, and, within this, highlight specific phenotypes.
Methods: The patients were routinely tested for common genes (PMP22, GJB1, MPZ, MFN2), while in specific cases we followed the candidate gene approach, testing single genes based on the genotype-phenotype correlation. The NGS techniques were used when routine genetic testing was negative and a clear genotype-phenotype correlation could not be identified.
Results: 679 cases are present to date in our database of CMT patients. In 185 (27.2%) patients, in spite of a clinical diagnosis of CMT, a genetic diagnosis is still lacking; 175 (25.7%) patients had alternative diagnosis (i.e hereditary spastic paraparesis). In 319 patients (46.9%) a defined genetic diagnosis was reached, 56.4% females and 43.5% males. Among these, we frequently observed patients affected by CMT1B and CMT2F. We observed 21 (6.5%) patients with CMT1B and 8 patients (2.5%) affected by CMT2F. At the first visit, the CMT1B phenotype was clearly length-dependent: 71.4% patients showed impairment of the lower limbs and saving of the upper limbs; the mean CMTNS was 11.9 and the mean age was 48.8 years. 75% of patients affected by CMT2F, present with the same phenotype; the mean CMTNS was 8.1 and the mean age was 63.1 years.
Conclusion: In conclusion, we describe our large population of CMT patients and a specific phenotype in CMT1B and 2F patients, which may help in addressing the diagnostic algorithm.
Disclosure: Nothing to disclose

PR3115

Association between Helicobacter pylori infection and Guillain-Barré Syndrome: Meta-analysis

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Background and aims: Helicobacter pylori (H.pylori) is a Gram negative bacterium, considered to trigger autoimmune gastrointestinal disorders. This pathogen has also been linked to the autoimmune sequelae in extra-gastrointestinal diseases and peripheral neuropathies. Guillain-Barré Syndrome (GBS) is a demyelinating polyneuropathy, usually with post-infectious onset. Growing evidence suggests the possible effect of H. pylori infection in the development of GBS. The aim of the present study is to estimate the prevalence of H.pylori antibodies in GBS.

Methods: A search of the literature was performed, using PUBMED database, until January 2017. Data were extracted from six case-control studies and a stratification analysis was conducted according to cerebrospinal fluid (CSF) or serum detection material. The control cohort in these studies did not include only healthy subjects.

Results: Six studies were considered eligible for meta-analysis. In the CSF subgroup, 105 participants were involved (40 GBS patients and 65 controls), while the serum subgroup included 325 participants (152 GBS and 173 controls). Due to low heterogeneity (I2<57%, P>0.07), the fixed-effect model was used. The prevalence of anti-H. pylori IgG was significantly associated with GBS compared to controls, in both CSF (95% CI: 9.66-186.56, OR: 42.45, Pz<0.00001) and serum (95% CI: 1.30-4.11, OR: 2.31, Pz: 0.004) subgroups.

Conclusion: This meta-analysis revealed that there is a strong association between H. pylori antibodies and the development of GBS, especially in the CSF subgroup. H.pylori infection may have an important role in the pathophysiology of GBS.

Disclosure: Nothing to disclose

Peripheral nerve disorders 4

PR3116

Corneal confocal microscopy as surrogate marker in inflammatory neuropathies

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Background and aims: There is an unmet need for better diagnostic tools to further delineate clinical subsets of heterogeneous chronic inflammatory demyelinating polyradiculoneuritis (CIDP) to facilitate treatment decisions. Corneal confocal microscopy (CCM) is a non-invasive and reproducible imaging technique. This study aims to establish CCM as new method reflecting peripheral nerve damage and ongoing inflammatory activity.

Methods: In a prospective approach patients before and during therapy and healthy controls were studied using CCM to quantify corneal nerve damage and immune cell infiltration.

Results: Patients with CIDP revealed a reduction in corneal nerve fiber (CNF) measures and an enlargement in corneal immune cell infiltrates, CNF parameters decreased with longer disease duration. The number of dendritic cells in proximity to corneal nerve fibers was increased in patients with early disease and correlated with the degree of motor affection. In painful neuropathies a further reduction in CNF parameters and an increase in non-dendritic cells became apparent. The longitudinal approach reflected therapeutic effects. CCM was able to detect inflammatory activity in CIDP patients, in comparison with diabetic neuropathy controls.

Conclusion: Our findings suggest a considerable potential of CCM as a surrogate marker for CIDP. Corneal nerve fiber loss may reflect severity of neuropathy and quantification of distinct cells around the CNF plexus may help in stratifying CIDP subtypes, clinical course and disease activity.

Disclosure: Nothing to disclose

PR3117

Evaluation of age related changes in superficial peroneal nerve conduction studies of patients with suspected peripheral nerve diseases

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Background and aims: This study evaluates if superficial peroneal sensory nerve conduction studies (SP NCS) are affected by age, and compares common parameters from sensory NCS amongst different age subgroups. SP NCS often distinguish neuropathy from L5 radiculopathy, and the rate of detecting neuropathy with SP NCS has been reported to be significantly higher compared to other sensory nerves. While neuropathy is common amongst the elderly, its unclear if age affects sensory NCS and confound NCS results.

Methods: We performed NCS with SP in 150 patients with leg weakness, paresthesias, and pain. Those with pedal edema were excluded. Amplitude, latency, and conduction velocities in age-differentiated samples were analyzed. The proportion of patients for which NCS was not obtainable (non-responders) was also analyzed. Age subgroups included age ≤39y.o (n= 44), 40-59 (n= 56), and ≥60y.o (n= 50).

Results: Chi-square test showed a significantly higher proportion of non-responders in the group ≥60y.o (n= 50) (NR=21) in comparison to (NR=8) (NR=3) in age groups 40-59, and ≤39, respectively. Anova test showed significant decrease in amplitude between age groups with F=5.83 and P=0.004. There was no evidence to suggest that latency or conduction velocities changed with age.

Conclusion: This study clearly establishes that SP SNAPS are more difficult to obtain in patients over the age of 60 with concurrent reduction of amplitude in elderly. For patients over 60 with peripheral nerve diseases, we suggest age related changes in the superficial peroneal NCS should be considered prior to establishing a diagnosis.

Disclosure: Nothing to disclose

PR3118

Lysophosphatidic acid induces Schwann cell dedifferentiation associated with peripheral nerve injury

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Background and aims: Lysophosphatidic acid (LPA) is a pleiotropic signaling lipid that acts as ligand for at least six specific G protein coupled receptors. Schwann cells (SC) are known to mainly express the LPA1 receptor subtype. An emerging body of in vivo evidence has linked LPA with injury induced peripheral nerve demyelination as well as neuropathic pain. However, the molecular mechanism underlying its demyelinating effect has remained largely unclear.

Methods: Myelinated dorsal root ganglia (DRG) cultures were treated either with LPA, LPA + AM095 (LPA1 antagonist) or vehicle. We assessed myelin basic protein, tumor necrosis factor alpha (TNF-α) as well as the SC differentiation marker Sox10 by immunocytochemistry. Additionally, myelin was investigated by sudan black staining. To study the relevance of LPA on demyelination in vivo, we performed sciatic nerve crush in C57BL/6 mice treated with AM095 at 10mg/kg.

Results: LPA caused a significant reduction of myelin as demonstrated by sudan black staining and immunocytochemical analysis of myelin basic protein. Demyelination was paralled by a downregulation of Sox10 as well as an upregulation of TNF-α. LPA mediated effects were found to be blocked by addition of the LPA1 receptor antagonist AM095. In C57BL/6 mice, AM095 treatment prior to crush injury increased Sox10 expression in SCs in the distal nerve stump.

Conclusion: These data indicate that LPA may be a critical factor to shift SCs towards an injury-associated phenotype and contribute to the onset of Wallerian degeneration.

Disclosure: Nothing to disclose

PR3119

Expanded B-cell receptor clones are present in peripheral blood samples in patients with chronic demyelinating inflammatory neuropathy

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Background and aims: Following reports that pathogenic antibodies are present in a minority of patients with chronic demyelinating inflammatory neuropathy (CIDP), we here study whether oligoclonal expansions of B-cell clones are present in patients with this disease.

Methods: B-cell receptor (BCR) repertoire was analyzed use next generation sequencing on RNA extracted from blood samples in 30 patients with CIDP: 10 patients with active disease and starting treatment (group 1), 10 patients with stable disease using intravenous immunoglobulin (IVIg) treatment in which treatment withdrawal was attempted (group 2), and 10 patients in remission (i.e. no treatment in the last 12 months, group 3). Samples were acquired at baseline (group 1, 2 and 3) and 6 months after start or stop treatment (group 1 and 2).

Results: Most CIDP patients had highly expanded BCR clones, regardless of disease activity and response to treatment. In group 1, the most expanded B-cell clones at baseline showed no overlap with the expanded BCR clones after improvement.

Conclusion: Based on these preliminary data expanded BCR clones are observed in the peripheral blood of most CIDP patients, regardless of disease activity (active, stable disease or remission/cure). Functional characterization of these expanded clones remains to be performed.

Disclosure: This research is funded by the Prinses Beatrix Spierfonds.

PR3120

Polyneuropathy: Working beyond the guidelines

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Background and aims: Polyneuropathy (PNP) is a most common disease in neurology. The diagnostic workup in patients with a PNP in guidelines seems to be insufficient. We determined the prevalence of different diagnoses of PNP in a Dutch hospital, and evaluated the diagnostic workup of PNP patients according to guidelines. (1,2)

Methods: A retrospective cross-sectional dossier study of patients with symptoms of PNP who visited the neurology department of a general hospital in 2014 and 2015.

Results: Included were 324 patients, in 121 patients (37.3%) no cause was found, and 88 patients (27.2%) had diabetes mellitus. Other causes were vitamin deficiency or overdose in 48 patients (14.8%), medication in 33 patients (10.2%), CIPN in 26 patients (8.0%), alcohol in 22 patients (6.8%), immune-mediated in 17 patients (5.2%), renal insufficiency in 15 patients (4.6%), and other in 33 patients (10.2%). Performing additional investigations not according to the guidelines, was done in 173 patients (53.4%), and resulted in finding a cause in 37 patients (11.4%).

Conclusion: Current guidelines concerning the diagnostic workup in patients with PNP need to be adjusted, and an extensive diagnostic workup should be considered in patients with PNP.

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Disclosure: Nothing to disclose

PR3121

Diabetic polyneuropathy: Additional investigation is recommended

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Background and aims: Diabetes mellitus is an important cause of polyneuropathy (PNP), accounting for 32% to 53% of all cases.1 In current guidelines no additional diagnostic workup is recommended in patients with PNP and diabetes mellitus. (1,2) However, studies suggest that up to 50% of patients with diabetes may have an additional cause of the PNP. (3,4) We evaluated the diagnostic workup of patients with diabetic PNP.

Methods: A retrospective cross-sectional dossier study of patients with diabetic PNP who visited the neurology department of a Dutch hospital in 2014 and 2015.

Results: A total of 88 patients were diagnosed with diabetic PNP. In 29 patients (33.0%) an additional cause was found; in 22 patients one additional cause, in 6 patients two additional causes, and in 1 patient three additional causes were found. With history taking, an additional cause was found in 26 DPN patients, and with laboratory analysis in 13 patients.

Conclusion: Current guidelines concerning the diagnostic workup in patients with diabetic PNP need to be adjusted, and an extensive diagnostic workup should be considered in patients with diabetic PNP.

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Disclosure: Nothing to disclose

PR3122

The role of autoimmunity in chronic idiopathic axonal polyneuropathy

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Background and aims: Chronic idiopathic axonal polyneuropathy (CIAP) is a term used to describe neuropathies with insidious onset and slow progression over at least 6 months with no aetiology being identified despite appropriate investigations and where neurophysiology reveals axonal damage. Up to 30% of patients with chronic axonal neuropathies will have CIAP. We aimed to assess the role of autoimmunity in this group.

Methods: Patients already assessed by a Neurologist in a tertiary neurology unit and labeled as having CIAP were recruited for this study.

Results: Between January 2016 and December 2016, 59 patients were examined (66.1% males, mean age 71.5±8.6 years). After obtaining a detailed medical history and requesting further neuropathy investigations as clinically indicated, only 39 (66.1%) were found to have CIAP (61.5% males, mean age 72.2±10.0 years); 3 patients had diabetes, 4 reported excessive alcohol consumption, 4 have been exposed in neurotoxic agents, 2 had cancer, 4 were gluten sensitive, 1 had rheumatoid arthritis and 2 monocloncal gammopathy of unknown significance (MGUS).

From the 39 patients with true CIAP, 27 (69.2%) had some evidence of abnormal autoimmune tests suggestive of an autoimmune predisposition (i.e. positive one or more of ANA, ANCA, TPO, TG and RF or presence of another autoimmune disorder).

Conclusion: In 1 out of 3 patients considered as having CIAP the diagnostic work-up may be incomplete. The vast majority of truly CIAP patients show indirect evidence of autoimmunity, suggesting that an autoimmune mechanism could be responsible for the neuropathy.

Disclosure: Nothing to disclose

Posters on Display

Posters on Display

POD001

Corpus callosum agenesis associated with multiple sclerosis

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POD002

Central nervous system cryptococcosis in patients with different immunological status – Cerebrospinal fluid and imaging findings

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POD003

Bruns syndrome caused by intraventricular neurocysticercosis

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POD004

Congenital myasthenic syndromes in a population with Myasthenia gravis

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POD005

Biogenic amine metabolites in CSF of severely head - injured patients

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POD006

Cancelled

POD007

Sign Language aphasia: Anatomy of language in deaf signers

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POD008

Papilledema as a rare initial presentation of Neuro-Brucellosis: Case report and literature review

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POD009

Effect of serum 25-hydroxycholecalciferol level on the severity and prognosis in acute ischaemic stroke patients

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POD010

Seizures with a presumed autoimmune basis

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POD011

Evaluating eslicarbazepine acetate impact on mood in people with epilepsy

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POD012

A rare case of Weston-Hurst syndrome

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POD013

European survey on Parkinson's disease patients: Results from the feasibility evaluation of SYNAPSES (StudY to observe SafiNAmide in clinical Practice during the firSt post-commErcialization phaSe) study

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POD014

The occurence of demyelination in a patient with connective tissue disorders, is it a coincidence or is there a relation?

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POD015

Cancelled

POD016

Cancelled

POD017

Isolated Sixth Cranial Nerve Palsy in Preeclampsia: A Case Report

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POD018

Efficacy of mycophenolate in primary progressive active multiple sclerosis: A case series report

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POD019

A case of limbic encephalitis in a patient with common variable immunodeficiency

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POD020

Optimization of antidepressive therapy in elderly patients with depression

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POD021

Ebola virus or Zika virus: What are neurologists afraid of more?

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POD022

Clinical manifestations of pain syndromes with various forms of parkinsonism

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POD023

Delusion of parasitosis in a patient with progressive-relapsing multiple sclerosis: A coincidence, or something else?

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POD024

Clinical features and outcome of amyotrophic lateral sclerosis-like disorders

Z. Brahem, I. Bedoui, A. Riahi, H. Derbali,
M. Messelmani, M. Mansour, J. Zaouali, R. Mrissa
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POD025

A curious case of myotonia-A novel gene mutation

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POD026

The association between clinical parameters and retinal nerve fiber layer thickness in patients with multiple sclerosis

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POD027

Intranuclear inclusions in skin sample from patient with fragile X-associated tremor/ataxia syndrome

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POD028

Edaravone attenuates intracerebroventricular streptozotocin-induced dementia of Alzheimer's type by modulating inflammatory cytokines, expression of choline acetyltransferase and rho-kinase-II

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POD029

Non-epileptic paroxysmal states in epilepsy

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POD030

Video head impulse test can detect brainstem dysfunction in multiple sclerosis

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POD031

Magnetic resonance imaging in pseudotumour cerebri

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POD032

Investigation of multiple sclerosis mimicking lesions with tract based spatial statistics and voxel based morphometry

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POD033

Observational cohort study on safety and efficacy of copamer (a new brand-generic Glatiramer acetate) 40mg in Iranian patients with RRMS

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POD034

Neuroimaging indicators of post-stroke dementia

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POD035

Investigation of the risk factors for ischemic stroke and stroke subtypes in patients with chronic kidney disease

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POD036

Values of vanillylmandelic acid and homovanillic acid in the urine as potential prognostic biomarkers in ischemic stroke patients

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POD037

Hashimato's encephalopaty with partial response to steroid therapy

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POD038

Multiple Sclerosis-Care Optimisation Tool (MS-COT): A clinical application prototype to predict future disease activity

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POD039

The influence of CAT-262 polymorphism on catalase activity in patients with ischemic stroke

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POD040

Effect of cladribine tablets on relapse rates and the proportions qualified relapse-free in patients with multiple sclerosis: analysis of the CLARITY and CLARITY Extension studies

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POD041

Cancelled

POD042

A review of clinical and epidemiological characteristics of HaNDL syndrome patients in a tertiary hospital.

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POD043

Human leukocyte antigen (HLA) typing in Iraqi patients with multiple sclerosis (MS)

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POD044

Lymphocyte-to-monocyte ratio at 7-days is associated with 3-month outcome in acute ischemic stroke

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POD045

Decompressive craniotomy in cerebral venous thrombosis, tertiary center experience in UAE

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POD046

Dopamine receptor genetic variants are not associated with response to risperidone in autistic children

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POD047

Salbutamol therapy in congenital myasthenia: A case report.

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POD048

Evoked potentials in the diagnosis of combined craniofacial trauma

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POD049

Respiratory function in Parkinson's disease

P. Nigro, N. Tambasco, N. Murgia, S. Simoni,
M. Romoli, F. Ripandelli, E. Brahimi, F. Paolini Paoletti,
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POD050

Serum lactate as a biomarker of malignancy in gliomas

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POD051

The fast VOR under dimenhydrinate, diazepam and cinnarizine in healthy adults

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POD052

The use of acupuncture and physical exercise in the complex treatment of patients with chronic non-specific lower back pain

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POD053

The value of somatosensory evoked potentials in the rehabilitation of patients with traumatic neuropathy

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POD054

SMART-Stroke like migraine attacks after radiation therapy

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POD055

Cancelled

POD056

The risk of mortality from cerebrovascular diseases and meteorological conditions

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POD057

Orbitofrontal epileptogenic network evidenced by invasive exploration with cerebral depth electrodes

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POD058

Introduction of a patient leaflet for cerebral venous thrombosis in the UK

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POD059

Brain diffusion kurtosis imaging in rats with acute alcohol intoxication accompanied by diffuse axonal injury

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POD060

Diffusion kurtosis imaging detects microstructural changes in the brain after acute carbon monoxide intoxication in rats

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POD061

Clincial and immunological comparison in patients with post-operative hypothyroidism and autoimmune thyroiditis

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POD062

Cancelled

POD063

Rationale and design of the REALITY trial of the effects of alemtuzumab on multiple sclerosis-related fatigue, and patient- and caregiver-reported outcomes: An observational real-life study

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POD064

PLENO study design: An open-label, randomised, 24-week safety and tolerability study in Portuguese patients with relapsing-remitting multiple sclerosis transitioning from subcutaneous interferon-beta to peginterferon Beta-1a

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POD065

Quality of life over 36 months in patients with relapsing-remitting multiple sclerosis treated with alemtuzumab in routine clinical practice: LEMQoL study design

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POD066

Quality of life in self-sufficient patients after stroke

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POD067

Cancelled

POD068

Is month of birth associated with a risk of Guillain-Barré syndrome?

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POD069

RAPD and low grade glioma

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POD070

Duodopa frequent side effects in Colentina Clinical Hospital

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POD071

Patterns of cerebral atrophy in brain small vessel disease

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POD072

Cancelled

POD073

Epidemiology of Wilson's disease in Ukraine

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POD074

Cancelled

POD075

The activity of the kynurenine pathway of tryptophan metabolism in brain areas in rats with symptoms of Parkinson's disease

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POD076

Abnormal gravity and pressure sensations in migraine patients

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POD077

3D image overlay assist patients with Parkinson's disease

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POD078

Late components of cervical vestibular evoked myogenic potentials

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POD079

NEDA-3 status 12 months after switching from natalizumab to fingolimod in patients with relapsing-remitting multiple sclerosis

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POD080

Risk factors and clinico-neuroimaging status in patients with symptomatic intracranial atherosclerosis

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POD081

Relation of serum levels of homocysteine, vitamin B12 and folate to cognitive functions in Egyptian multiple sclerosis patients

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POD082

Cancelled

POD083

Carotid artery changes in patients with ischemic stroke and metabolic syndrome

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POD084

Forehead Tremor: A clinical presentation of ocular myasthenia gravis?

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POD085

Spontaneous intracranial hypotension-from orthostatic headache to coma

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POD086

Retrospective diagnosis from post-mortem of a Sudden Unexplained Death in Epilepsy (SUDEP) case

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POD087

Non-motor symptoms and their influence on the quality of life in Parkinson's disease patients

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POD088

Development and utilization of a custom analysis pipeline in application to the integrated analysis of independent multiple sclerosis datasets

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POD089

Cancelled

POD090

Fatigue and myasthenia gravis

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POD091

Successful treatment of normal tension glaucoma with medicinal herbs

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POD092

Cancelled

POD093

Cancelled

POD094

Cancelled

POD095

Two cases of paralytic ileus related to neuromyelitis optica spectrum disorders (NMOSD)

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POD096

Cancelled

POD097

Isolated central hypoglossal nerve palsy due to lacunar stroke: A case report

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POD098

Cancelled

POD099

Sonolysis in Prevention of Brain Infarctions during Internal Carotid Endarterectomy (SONOBIRDIE) Trial - an ongoing randomized controlled trial

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POD100

Acute porphyric polyneuropathy in a pregnant woman with systemic lupus erythematosus

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POD101

Benign reversible influenza-associated leuko-encephalopathy

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POD102

Cerebral amyloid angiopathy-related inflamation: the answer or the tip of the iceberg?

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POD103

Varicella zoster virus meningitis under ustekinumab because of plaque psoriasis

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POD104

Myasthenia gravis triggering Takotsubo syndrome

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POD105

Magnetic resonance spectroscopy in the diagnosis of symptomatic epilepsy in children

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POD106

The genetic characteristics of epileptic encephalopathy in children

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POD107

Cancelled

POD108

Cancelled

POD109

Intravenous immunoglobulin treatment for Guillain-Barré syndrome: A Colentina Hospital center experience

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POD110

Analysis of the prevalence of the etiological forms of epilepsy, types of epileptic seizures in the Kharkiv region of Ukraine according to the developed depersonalized electronic register

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POD111

Cognitive impairments in patients with severe intoxication with carbon monoxide

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POD112

Modulation of Na+/K+ ATPase activity of rat brain synaptosome by Norepinepherine and Serotonin

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POD113

Cancelled

POD114

Bilateral spontaneous internal carotid artery dissection - a patient oriented approach

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POD115

Reduction of melatonin secretion as one of the potential mechanisms of the geomagnetic disturbances influence in multiple sclerosis

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POD116

Diagnosis and management of auto-immune encephalitis

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POD117

Symptomatic viral infection during acute ischemic strokes: Its structure and correlation with neurological recovery

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POD118

Electrophysiologic evaluation of spontaneus swallowing and yawning in patients with multiple sclerosis

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POD119

Multiple ring enhancing lesions - ADEM in an elderly patient

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POD120

Long-term difference in the incidence of motor complications between ergoline and non-ergoline derived dopamine agonists

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POD121

Recurrent limb-shaking Transient Ischaemic Attacks – successfully treated with carotid endarterectomy of the asymptomatic side

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POD122

Lymphocyte subsets in the peripheral blood of fingolimod-treated Japanese patients with multiple sclerosis

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POD123

Headache as first symptom of multiple sclerosis: Frequency and evolution

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POD124

PHACE Syndrome – a polymorphic diagnosis, case series

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POD125

Sturge-Weber syndrome: A case report in Ouagadougou, Burkina Faso, West Africa

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POD126

Endothelial dysfunction in patients with multiple sclerosis and autoimmune thyroid disease

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POD127

Cancelled

POD128

Ischemic hallucinations

A. Mendez[1], P. Pire[1], M. Roson[1], A. Perez[1], M. Villa[1], A.J. Castellano Vicente[1], E. Martínez López[2], M.E. Novillo[1]
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POD129

Riluzole-induced recurrent pancreatitis

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POD130

Age and negative hormone receptor status but not the proliferative marker ki67 correlate with brain metastases in breast cancer patients (a retrospective observational descriptive study)

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POD131

Post-malaria neurological syndrome: A rare complication following an uncomplicated plasmodium falciparum infection

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POD132

Botulinum toxin injections in abdominal wall can prevent early relapse after giant abdominal wall hernia surgery

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POD133

Serum ferritin and uric acid levels and association with the disease progression in Parkinson's diasease

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POD134

Noncirrhotic portal vein thrombosis presenting with hepatic encephalopathy due to polycythemia vera and MRI findings

T. Yoldas, B. Gökçe Çokal, S. Keskin Güler, M. Kekilli, F. Pirinccioğlu, H.N. Günes
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POD135

Severe, early MS rebound after cessation of Fingolimod due to West Nile meningitis

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POD136

Abnormalities in blood components can help determine stroke type and severity

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Menoufiya school of medicine, Neurology, Shebin elkom, Egypt

POD137

Cancelled

POD138

Massive cerebral air embolism in a patient with pulmonary aspergillosis

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Busan, Korea, Republic of

POD139

Cancelled

POD140

Cancelled

POD141

Cancelled

POD142

The possible role of apelin in migraine pathogenesis

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POD143

Role and significance of urodynamic recordings in detection of first signs of multiple sclerosis

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POD144

Cancelled

POD145

Somatogic disorders in post-stroke patients

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POD146

The impact of psychosocial stress on the frequency of TTH episodes among secondary schools students

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POD147

Epidemiological variables and shunt necessity of intracranial hypertension patients

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POD148

Cancelled

POD149

In and outside the box decisions in acute ischemic stroke

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POD150

Nocebo in motor neuron disease: Meta-analysis of placebo-controlled clinical trials.

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POD151

Clinical features of depression in patients with Parkinson's disease aacompanied by mixxed sleep apnea syndrome

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POD152

Pneumocephalus caused by spontaneous cerebrospinal fluid leak

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POD153

Acute stroke during the course of herpes simplex encephalitis in an HIV-positive individual

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POD154

Thrombosis of the deep cerebral venous system presenting as acute-onset amnestic syndrome in a factor V Leiden heterozygous patient: A case report

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POD155

Real-life safety and tolerability of teriflunomide in relapsing-remitting multiple sclerosis

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POD156

Tetrabenazine and management of tardive dyskinesias: A case report

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POD157

Cancelled

POD158

Cluster-like headache caused by spontaneous intraorbital haematoma

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POD159

Diagnostic difficulties of Huntington's disease

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POD160

Differences in pupillary light reflex between hereditary optic neuropathy and ethambutol induced optic neuropathy

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POD161

Cancelled

POD162

A comparison of characteristics between young stroke patients with and without symptomatic stenotic lesion in the intracranial artery

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POD163

Early onset Friedreich Ataxia without cardiomyopathy

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POD164

Safety of acupuncture for patients taking warfarin or antiplatelet medications

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POD165

Nature of neurological damages to fighters who are fighting in Donbas

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POD166

A case of radiologically isolated syndrome suggestive of demyelinating disease in Klippel-Trenaunay syndrome

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POD167

Limbic encephalitis associated with acute metabolic imbalance

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POD168

Myopathy related to vitamin D deficiency in the elderly: A rare but often forgotten treatable condition. Two case reports

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POD169

Evaluating early topiramate-induced cognitive impairment in migraine and epilepsy treated patients

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POD170

Chronic abdominal migraine with medication overuse

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POD171

Cancelled

POD172

On the different etiologies causing cavernous sinus syndrome

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POD173

Stroke awareness in Northern Cyprus

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POD174

The relationship of blood pressure variability and cognitive function in the patients with arterial hypertension

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POD175

Lateralization and localization of bilateral mesial frontal lobe epilepsy with sEEG: A case report

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POD176

Obstacles in diagnosis and treatment of myasthenia gravis in Nepal

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POD177

Spontaneous cervical carotid dissection: Functional prognosis

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POD178

Bilateral abducens and incomplete oculomotor paresis as initial symptoms in recurrent lymphoblastic T-cell leukemia: A case report.

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POD179

A rare case of nivolumab-induced myasthenic crisis

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POD180

Cancelled

POD181

Cancelled

POD182

Sexual disorders in women with epilepsy in fertail age

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POD183

Anti-GQ1b antibody syndrome presenting as acute, fluctuating ophthalmoparesis, gait ataxia, and dysautonomia without areflexia

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POD184

Cancelled

POD185

Visual evoked potentials and retinal optical coherence tomography in optic neuropathy and age-related macular degeneration

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POD186

Benfotiamine in neurorehabilitation ischemic stroke diabetes mellitus

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POD187

Cancelled

POD188

Serum heavy neurofilaments and retinal nerve fibre layer thickness assessment in patients with multiple sclerosis on treatment with fingolimod

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POD189

Immune-mediated necrotizing myopathies: presentation of 4 new cases

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POD190

Neurological findings in children with optic disc drusen

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POD191

ALS-Like Syndrome as first clinical presentation of HIV infection. Case Report.

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POD192

Amyotrophic Lateral Sclerosis in the Republic of Bashkortostan (Russia).

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POD193

The activity of proteins of apoptosis in children with neuromuscular disease and cerebral palsy

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POD194

Chronic progressive external ophthalmoplegia-like syndrome in a HIV infected patient after long term highly active antiretroviral therapy (HAART) exposure.

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POD195

Cancelled

POD196

In-hospital stroke of cardiosurgery department patients

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POD197

Cancelled

POD198

Cancelled

POD199

Historical model on benefits and costs in natural and treated Multiple Sclerosis course: an attempt to cost comparison

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POD200

Lentiform Fork Sign: An early distinct MR imaging feature of irreversible dystonia/ myoclonus appearance in acute renal failure.

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POD201

Migraine with comorbid panic disorder: the search of optimal therapeutic strategies (prospective study)

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POD202

Fatigue in multiple sclerosis and other comorbidities

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POD203

Design of a Clinical Trial Evaluating the Efficacy and Safety of IGIV-C in Patients with Myasthenia Gravis Exacerbations

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POD204

Cancelled

POD205

Anti-NMDA receptor encephalitis in a patient with paranoid schizophrenia: a diagnostic challenge

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POD206

Caspr2 antibody encephalitis in a patient with prostate cancer

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POD207

Neurofibromatosis Type I – a Multidisciplinary Approach of a Rare Condition

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POD208

Multiple cranial mononeuropathies and brain stem demyelination associated with human immunodeficiency virus-1 infection and viral suppression

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POD209

A case of motor neurone disease presenting with isolated acute dysarthria

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POD210

Brainstem TIA upon infusion of autologous hemtopoietic stem cells cryopreserved with dimethylsulfoxide - a case report

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POD211

Congenital myasthenic syndrome secondary to MUSK gene mutation

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POD212

Ischemic sciatic neuropathy in a patient with liposarcoma

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POD213

Acute carotid thrombosis after carotid stenting in a patient with essential thrombocythemia

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POD214

Safety and tolerability of dimethyl fumarate in a real-world relapsing-remitting multiple sclerosis population

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POD215

Cancelled

POD216

Musculoskeletal Discomfort, Psychosocial Burden and Associated Factors among Foreign and Native Nursing Attendants in Taiwan

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POD217

Anxiety and depression assessment in multiple sclerosis patients

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POD218

Two interesting cases of Herpes Zoster opthalmicus with neurological presentation

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POD219

Cancelled

POD220

Neurologic Symptoms as Display of Aggressiveness of Vertebral Hemangiomas

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POD221

Cancelled

POD222

Utilization of videomotion analysis for assessment of balance in the patients with DBS for Parkinson's disease

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POD223

Characteristics of headache in patients with nontraumatic subarachnoid hemorrhage and brain arteriovenous malformation

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POD224

A rare co-existence of anti-GABA B and anti-SOX1 receptors in patient with limbic encephalitis as a paraneoplastic disorder, resulting in lung cancer diagnosis.

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POD225

Progressive multifocal leukoencephalopathy (PML) and immune reconstitution inflammatory response syndrom (IRIS) in a psoriasis patient treated with dimethyl fumarate.

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POD226

Cannabis Abuse: from Tako-tsubo cardiomyopathy to cerebral vascular infarcts and cognitive disorders.

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POD227

Cancelled

POD228

Clinical features and disease onset in multiple sclerosis patients

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POD229

Neurophysiological states of the CNS in the acute period combined craniofacial trauma

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POD230

Late-onset rupture of spontaneously occluded superior cerebellar artery dissection, case-report

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POD231

Special features of vestibular dysfunction of patients with migraine

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POD232

Lightening may pose a danger to patients with deep brain stimulation

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POD233

Cancelled

POD234

Quality of life in multiple sclerosis patients

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POD235

Ischemic stroke and myocardial infarction in winter. Comparison of the onset and outcome of diseases by atmospheric parameter

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POD236

Chocolate consumption and the Hungarian Nobel Laureates

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POD237

Cancelled

POD238

Fulminant Marburg-like course of initially relapsing-remitting multiple sclerosis

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POD239

Changes in retinal oxygen saturation in multiple sclerosis patients with optic neuritis

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POD240

Biliary dysfunction-associated headaches: a clinical point of view

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POD241

Cancelled

POD242

Concomitant ischemic stroke and convexity subarachnoid hemorrhage: four cases in one year.

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POD243

Positive persistent visual disturbance - Visual Snow Syndrome. Case Report.

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POD244

Cancelled

POD245

THREE CASES OF JAW-OPENING DYSTONIA WITH RATING OF OROMANDIBULAR DYSTONIA QUESTIONNAIRE – 25 AND MODIFIED GLASGOW BENEFIT INVENTORY FOR BOTULINUM NEUROTOXIN (BoNT)

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POD246

Thirty-year follow-up of patients with multiple sclerosis: analysis of a Portuguese hospital-based cohort

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POD247

Clinicoepidemiological study of patients with Duchenne Becker muscular dystrophy in Saint Petersburg and Leningrad region

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POD248

A Rare Etiology in Differential Diagnosis of Totally External Ophthalmoplegia; Paraneoplastic Neurological Syndrome

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POD249

Transient abducens nerve palsy after cervical traction: case analysis and review of literatures

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POD250

Cancelled

POD251

Obesity-hypoventilation syndrome presenting with cerebral oedema and 'pseudosubarachnoid haemorrhage'

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POD252

A peculiar case of Thomsen disease with myofibrillar muscle alterations

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POD253

The survival of patient in postanoxic coma with myoclonus: Clinical and electrophysiological correlates

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POD254

Multicenter study of a Personalized, digital Coaching Program after Stroke: design & rationale

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POD255

Comorbidity conditions in migraine: Clinic based study in Kyrgyz Republic

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POD256

Cancelled

POD257

Clinical outcome following decompressive hemicraniectomy in severe stroke and poor-grade aneurysmal haemorrhage

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POD258

Neuroimaging findings facilitated the recognition of an under-diagnosed rare muscular disease: Orbital myositis; Need for treatment guidelines.

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POD259

Non-paraneoplastic Limbic Encephalitis and refractory Status Epilepticus in a 20-year-old female: Case Report

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POD260

Reduction of cholesterol levels during Natalizumab treatment

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POD261

Focal seizures in Autoimmune Limbic encephalitis (ALE) associated with positive anti Leucine-rich Glioma-Inactivated 1(LGI1): A diagnostic challenge.

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POD262

A challenging diagnostic work-up in the case of a pregnant woman with acute confusion

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POD263

Management of ischemic optic neuropathy

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POD264

Cancelled

POD265

The role of optical coherence tomography in the evaluation of neuroprotective effects of autologous mesenchymal stem cells transplantation in relapsing-remitting multiple sclerosis

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POD266

Neurophysiological and radiological (MRI) features of epilepsy in elderly.

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POD267

EEG appearance before and after VNS implantation in children with refractory epilepsy – initial report/preliminary study

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POD268

Cancelled

POD269

Intracranial Vessel Wall MRI Contribution to Cryptogenic Stroke Diagnosis

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POD270

The Relationship Between Hand Functions, Postural Stability and Mobility in Patients with Multiple Sclerosis

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POD271

An HIV positive patient with Varicella Zoster-associated aneurysmal cerebral vasculopathy: diagnostic challenges and the utility of 3-Tesla MRI vessel wall imaging.

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POD272

Hemiathetosis and dystonia as a manifestation of non-ketotic hyperglycaemia

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POD273

Effect of Motor And Cognitive Tasks on Balance in Patients with Multiple Sclerosis

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POD274

Primary Angiitis of the Central Nervous System: broad clinical spectrum

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POD275

Clinical features of stroke in young women

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POD276

T-CELL CENTRAL NERVOUS SYSTEM LYMPHOMA MIMICKING GLIOMATOSIS CEREBRI : case report

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POD277

A case of supratentorial extra-axial ependymoma : a very rare entity

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POD278

Glycine receptor antibody mediated Progressive Encephalomyelitis with Rigidity and Myoclonus (PERM): a diagnostic challenge

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POD279

Pseudohypoparathyroidism type 1b presenting with seizures and brain calcification in adulthood

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POD280

Guillain-Barre variants with hyperacute progression

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POD281

Cancelled

POD282

Headache and multiple cranial neuropathy: an unusual presentation of acute motor axonal neuropathy (AMAN)

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POD283

PARK7, HSPA4, SUMO1, NONO, SOD1, RBBP4 and PIAS2 as differentially expressed genes in peripheral blood mononuclear cells of interferon treated, NAB (+) multiple sclerosis patients: the potential role of acetylation and ubiquitin conjugation.

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POD284

Lumbar puncture in the aetiological investigation of ischaemic stroke of undetermined aetiology

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POD285

Erythroblastemia in relapsing remitting multiple sclerosis patients treated with Natalizumab.

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POD286

Syndrome of transient headache and neurologic deficits with cerebrospinal fluid lymphocitosis (HaNDL): atypical presentation

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POD287

If you hear hoofbeats: Streptococcus equi subsp. equi meningoencephalitis complicated by cerebral vasculitis and dural arteriovenous fistula

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POD288

Paraneopalstic anti-NMDAR encephalitis. Case report.

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POD289

Computed tomography permeability to predict hemorrhagic transformation in ischemic stroke

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POD290

Association between gut microbiota and olfactory dysfunction in Parkinson's disease

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POD291

Magnetic Resonance Spectroscopy in the evaluation of mesial temporal sclerosis (case report)

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POD292

Short-term effectiveness of high-intensity laser therapy and electrical stimulation in the treatment of double crush syndrome

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POD293

Non-dominant primary motor cortex repetitive transcranial magnetic stimulation for chronic pain caused by diabetic polyneuropathy: report of a small cross-over pilot study.

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POD294

Cancelled

POD295

Myasthenia Gravis: An unusual cause of foot drop

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POD296

Two sisters with anti-MuSK-positive myasthenia gravis

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POD297

Study of motor cortical areas reorganization and intracortical interaction dynamics after motor imagery training sessions enhanced by brain computer interface: preliminary results.

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POD298

Teriflunomide as a therapeutic strategy in multiple sclerosis patients with concomitant arthritis

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POD299

Cerebral blood flow and heart rate variability in patients with arterial hypertension and coronary artery disease receiving ivabradine in combination with perindopril

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POD300

Cancelled

POD301

Fetal akinesia deformation sequence and recessive central core disease: a rare presentation of mutations in RYR1 gene.

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POD302

Virtualized laboratories for neuroimaging data federation: the GAAIN and NeuGRID collaboration.

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POD303

Vasculitis of central nervous system and renal neoplasia: a case report.

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POD304

Inflammatory biochemical markers and vascular wall stiffness parameters as risk factors of cerebrovascular complications in hypertensive patients with abdominal obesity

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POD305

Levodopa-Carbidopa Intestinal gel infusion therapy in advanced Parkinson's disease: a rare case associated with duodeno-jejunal inflammatory pathology

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POD306

Impact of single and repeated autologous mesenchymal stem cells transplantation on disease progression in relapse-remitting multiple sclerosis patients

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POD307

Cerebrospinal fluid markers to differentiate idiopathic normal pressure hydrocephalus from vascular dementia and Alzheimer's disease

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POD308

Age-related peculiarities of neuromyelitis optica

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POD309

Cerebral involvement in a patient with common variable immunodeficiency: challenge in diagnosis

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POD310

Lymphomatosis cerebri: MRI aspect and clinical course

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POD311

Subacute sclerosing panenchepalitis presenting as rapidly progressive dementia in a young patient

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POD312

Cancelled

POD313

Cerebellar aging in the context of predictive motor timing

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POD314

Congenital variant of Rett syndrome: identification of FOXG1 mutation in a boy

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POD315

Fluctuating neurological deficit in a patient with spinal hematoma

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POD316

The use of botulinum toxin in the treatment of severe bruxism in a patient with epilepsy: a case report

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POD317

The correlation between epileptic seizures and cerebral MRI abnormalities in women with epilepsy

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POD318

Use of alemtuzumab in real world

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POD319

Carotid Artery Dissection Caused by Elongated Styloid Process (Eagle Syndrome)

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POD320

Large Vessel Arteritis and Renal Cell Carcinoma: Coincidence or Consequence?

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POD321

Rapidly Progressive Dementia and Parkinsonism due to Dural Arteriovenous Fistula – A Case Report and Systematic Review

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POD322

Molecular-genetic features of progressive muscular dystrophy Duchenne / Becker in Uzbekistan.

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POD323

Recurrent Optic Neuritis In A Patient With Anti-Myelin Oligodendrocyte Glycoprotein (Mog) Antibodies

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POD324

Challenges in Translating the Disability Assessment for Dementia (DAD) into 63 languages

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POD325

Semantic variant of primary progressive aphasia with early pathological gambling disorder: a case report

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POD326

Recanalization of cerebral venous sinus thrombosis: Can we avoid long-term complications? A descriptive study.

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POD327

To immune response at Parkinson disease.

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POD328

Enteroviral infection in a rituximab-treated patient presenting as a progressive multifocal leucoencephalopathy: A case report.

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POD329

Efficacy and portability in postoperative mortality using intraoperative local chemotherapy by temodeks medication

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POD330

Association between neuromyelitis optica, antiphospholipid antibody syndrome and genetic thrombophilia complicated with pulmonary embolism – case report

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POD331

The role of sex hormones in epilepsy in women of fertile age

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POD332

Orgasmic aura in a patient with posttraumatic epilepsy

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POD333

Functional outcomes of cortical and subcortical recurrent cerebral hemispheric ischemic stroke

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POD334

Meningoencefalitis-like Syndrome as a Presentation of Neuromyelitis Optica Spectrum Disorder

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POD335

Clinical presentation, outcome and negative prognostic factors in NeuroAIDS patients in moldovan tertiary neurological center during a 2011-2016 period

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POD336

Signature tremor as presenting complaint of Vascular Parkinsonism

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POD337

White matter tract damage in Parkinson's disease patients with dementia

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POD338

Double intra and extracranial dissection of blood vessels

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POD339

Clinical outcome in patients with stroke and non valvular AF, older than 70 years

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POD340

Cancelled

POD341

Neurology and The Stone of Madness

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POD342

Unexpected neuroborreliose, case report and literature review

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POD343

Effects of OnabotulinumtoxinA Treatment on Disability and Quality of Life in Patients with Chronic Migraine with Baseline Headache Every Day or Allodynia: A COMPEL Subanalysis

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POD344

Paraneoplastic polyneuropathy as early complication of the small-cell lung carcinoma - a case report

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POD345

Epidermolysis Bullosa Simplex with Muscular Dystrophy: a case report

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POD346

Deep Brain Stimulation in Tremor and Dystonia secondary to Structural Brain Lesions

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POD347

Can Coenzyme Q10 and Creatine slow the progress of Parkinson's disease?

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POD348

LRRK2 p.Ala2010Thr mutation in a patient with Juvenile Parkinson Disease

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POD349

Cancelled

POD350

Spinal neuropathy in Lyme neuroborreliosis- diagnostic difficulties

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POD351

Reversible Hepatocerebral Degeneration-Like Sydrome due to Portovenous Shunts.

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POD352

SMART Syndrome- diagnognostic difficulties and not always fully reversible

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POD353

Cerebral vasomotor reactivity in Fibromyalgia patients and relationship with central neuropathic pain.

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POD354

Platelet and Neutrophil lymphocyte ratios at admission influence the clinical outcome of ischemic strokes

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POD355

Different clinical spectrums of HTLV-I myelopathy

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POD356

Central nervous system manifestations of ulcerative colitis: a case report mini-series

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POD357

Dysphagia and multiple sclerosis –impact in quality of life

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POD358

Epileptic seizures and panic attacks - a close diagnosis

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POD359

Is there mutual dependence between carotid strain and carotid resistance

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POD360

Vogt-Koyanagi-Harada disease presenting with bilateral papillitis

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POD361

Pseudobulbar Affect in Turkish Ms Population: Under-Recognized And Forgotten in Multiple Sclerosis

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POD362

Recurrent embolic stroke: a late diagnosis of silent infective endocarditis

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POD363

Headache in immigrants living in Italy: differences between various ethnic groups.

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POD364

Neuroimaging in the evaluation of headache in a neurology outpatient clinic

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POD365

Tilted disc syndrome mimicking chiasmal compression.

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POD366

Epidemiology, classification and etiology of strokes in patients under 45 years in Clinical hospital center Rijeka

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POD367

Clinical and optical coherence tomography outcome in secondary progressive multiple sclerosis patients after autologous mesenchymal stem cells intrathecal transplantation.

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POD368

Nosocomlal infections in neurocritical care

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POD369

ACE D/D genotype as a possible risk factor for occurence of stroke in children

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POD370

Arterial Spin Labelling (ASL) in Familial Hemiplegic Migraine (FMH) type 2

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POD371

Lithium as a protective factor against dementia in bipolar patients - a retrospective cohort study

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POD372

sICOS levels are increased in sera of multiple sclerosis patients.

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POD373

Coital headache presenting as Linear epicrania fugax on left side

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POD374

Tooth decay after continuous apomorphine infusion treatment in late Parkinson's disease

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POD375

Reversible Carotid and Vertebral Artery Occlusion as a Rare Complication of Giant Cell Arteritis

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POD376

Cancelled

POD377

Hereditary diffuse leukoencephalopathy with spheroids: a rare cause of dementia

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POD378

Normal Pressure Hydrocephalus in Patient with Multiple System Atrophy: Innocent Bystander or Guilty Party

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POD379

Cancelled

POD380

Post-radiation myokymia or "fish moving under the skin"

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POD381

Variants in Human Prostacyclin Receptor Gene in Migraine Patients

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POD382

A case of peduncular hallucinosis due to a right medullo - pontine stroke: Case report and review of literature

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POD383

Transient global amnesia in a young patient without any risk factors

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POD384

Vestibular evoked myogenic potential: An easy neurophysiological tool for evaluating brainstem involvement in multiple sclerosis

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POD385

A Case of Progressive Multifocal Leukoencephalopathy with Immune Reconstitution Inflammatory Syndrome (PML-IRIS) after Liver Transplant with Long Term Survival

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POD386

Cancelled

POD387

Cancelled

POD388

Cancelled

POD389

ACE, MME, IDE and ECE Variants and Alzheimer's Disease Risk in a Tunisian Population

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POD390

Cancelled

POD391

Sporadic Creutzfeldt-Jakob Disease: An atypical case with a motor onset

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POD392

Isolated Vertıcal Ophtalmoplegıa and Mydrıasıs due to Bılateral Mıdbraın Infarctıon

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POD393

Familial cerebral small vessel disease in Filipino immigrant

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POD394

Cancelled

POD395

Severe ophthalmoplegia in Miller Fisher syndrome

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POD396

A kindred of late onset Huntington's disease patients

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POD397

Myasthenia Gravis and Chronic Inflammatory Demyelinating Polineuropathy: Association or Coincidence?

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POD398

Cognitive dysfunction during follow-up of patients with anti-NMDA receptor encephalitis

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POD399

Elevated liver enzymes and vitamin D3 supplementation in multiple sclerosis

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POD400

Cancelled

POD401

Cord Blood in Ischemic Stroke Treatment

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POD402

An unusual form of x-linked adrenoleukodystrophy, case report

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POD403

Cancelled

POD404

Cancelled

POD405

The importance of hair testing for benzodiazepines in a suspected case of idiopathic recurrent study

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POD406

Cancelled

POD407

Cancelled

POD408

Vitamin D Deficiency in Parkinsons Disease Patients: New Therapeautic Target?

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POD409

Assessment of psychopathological state of patients with complicated forms of migraine, depending on the nature of headaches

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POD410

Apomorphine in 'on' freezing and akathisia in a case of Parkinson's disease.

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POD411

Breast cancer as stroke mimic in a male patient

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POD412

A case of thalamomesencephalon infarct presenting as transient global amnesia: Do we overlook the diagnosis?

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POD413

Sudden onset choreoathetosis in a patient with cardiovascular risk factors

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POD414

Cancelled

POD415

Cancelled

POD416

"Late onset friedreich ataxia presented with spastic paraparesis"

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POD417

Cancelled

POD418

Cancelled

POD419

Cancelled

POD420

Tourette Syndrome: a case of refractory motor and vocal tics successfully managed with cognitive-behavioural therapy

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POD421

Spatial orientation in PD and MS patients

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POD422

Cancelled

POD423

Neuropathic pain in multiple sclerosis: prevalence and risk factors

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POD424

Cancelled

POD425

Type 2 Diabetes and Cognitive Impairment: The Double Burden in a Developing Country

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POD426

Standardized psychiatric evaluation in refractory chronic migraine: preliminary results in 13 patients

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POD427

Spectral analyses of spontaneous electroencephalographic activity in migraine: preliminary results in a serie of 29 patients

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POD428

Olfactory dysfunction as a diagnostic marker among the patients with mild cognitive impairment (MCI) and vascular cognitive impairment (VCI)

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POD429

Clinical characteristics of patients with spondylodiscitis and epiduritis in Latvian population

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POD430

Description of early clinical characteristics of patients with relapsing-remitting multiple sclerosis with and without CSF IgM oligoclonal bands

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POD431

Use of oral treatments in patients with multiple sclerosis in real world

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POD432

Emphasizing the importance of evaluation of the risk factors in vascular dementia is an important step in the treatment strategy

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POD433

Cancelled

POD434

Headache, decreased visual acuity and abducens nerve palsy as a clinical presentation of Superior Ophthalmic Vein Thrombosis in patient with V Leiden factor thrombophilia: a case report.

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POD435

Prolonged encephalopathy after lithium overdose

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POD436

Spontaneous intracranial hypotension: A challenging diagnosis for the physicians of the emergency department-A case report

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POD437

Readiness to adopt new technology among people with dementia

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POD438

Cancelled

POD439

Contrast-Induced Neurotoxicity following Angiography

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POD440

Cancelled

POD441

Clinical and Magnetic Resonance Imaging Features of Multiple Sclerosis in the North African Mediterranean region

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POD442

Tumefactive demyelinating lesions, an uncommon fingolimod-related neurotoxic effect?

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POD443

Polysomnographic changes in patients with migraine

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POD444

Lipid storage myopathy with a late onset presentation mimicking an inflammatory myopathy.

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POD445

Cancelled

POD446

Sporadic cerebral cavernous malformation- a case report

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POD447

Carotid Bypass: a safe solution for patients with severe bilateral carotid stenosis.

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POD448

Cancelled

POD449

Influence of meteorological conditions on the incidence and mortality from cerebral stroke in the industrial center

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POD450

Reversible Cerebral Vasoconstriction Syndrome - RSVS and it's correlation with TIA

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POD451

Usefulness of automated EEG analysis to detect epileptic activity in diagnostic EEG recordings

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POD452

A NOVEL ARG191PRO VCP GENE MUTATION in a TURKISH FAMILY with ALS/FTD

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POD453

Wernicke-Korsakoff syndrome in a pregnant woman with hyperemesis gravidarum-a case report

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POD454

The effect of bilateral anodal tDCS stimulation on balance outcomes in patient with Parkinson's disease

M. Al-Jarrah[1], H. Haddoush[2], H. Khalil[2], A. Shorman[2], S. Bani Hani[3]
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POD455

Subarachnoid hemorrhage, Terson's syndrome,spasm of blood vessels

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Special hospital for cerebrovascular diseases Sveti Sava, Belgrade, Serbia

POD456

Ocular myasthenic syndrome, adverse reaction to Omalizumab?

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POD457
Cancelled

POD458

THE SMELL IDENTIFICATION TEST™ VS. THE ODOR MEMORY TEST™ FOR RUSSIAN POPULATION (HEALTHY PEOPLES AND PARKINSON'S DISEASE PEOPLES) (results of 2016)

D. Pokhabov[1], V.G. Abramov[1], E. Zubritskaia[1], Y. Balazeva[1], T. Bozhenkina[1], D. Pokhabov[2]
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POD459
Cancelled

POD460

Does vagus nerve stimulation therapy contribute to neuroplasticity?

P. Myrianthopoulou, Y. Christou, S. Papacostas
Nicosia, Cyprus

POD461
Cancelled

POD462
Cancelled

POD463
Cancelled

POD464

Validation of the Italian version of the Aphasia Rapid Test: an NIHSS-like aphasia test for acute ischemic stroke

A. Pavone[1], S. Napolitano[1], P. Perrone[2], A. Léger[3], Y. samson[3], C. Zavanone[3], M. Panebianco[2]
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POD465

Is interictal EEG activity linked to psychiatric disorders in temporal lobe epilepsy ?

S. Mrabet[1], A. Gargouri[2], I. Kacem[3], I. Abdelkefi[1], N. Kessentini[1], A. Nasri[3], Y. Sidhom[1], M. Ben Djebara[2], R. Gouider[1]
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POD466

Neurological and visual manifestations of hypothyroid Hashimoto's patient

L. Gimoyan, S. Asatryan, G. Silvanyan
Yerevan, Armenia

POD467

Acute coronary syndrome in stroke – diagnostic and therapeutic challenge

B. Petek[1], S. Mofardin[2], V. Svigelj[1]
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POD468

Epilepsy, pregnancy and encephalitis – bad start, happy ending

A. Grigore, E. Terecoasa, V. Tiu, C. Tiu
Bucharest, Romania

POD469

The radiologically isolated syndrome

D.N. Jepsen, G. Pihl-Jensen, J.L. Frederiksen
Glostrup, Denmark

POD470

Cancelled

POD471

Peculiarities of acute period of atherothrombotic and cardioembolic ischemic stroke subtypes

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Bogomolets national medical university, neurology, Kiev, Ukraine

POD472

Uncommon bilateral Internal Carotid Artery (ICA) dissection following a whiplash injury as a cause of ischemic stroke in a young woman

J. Barycki, K. Prus, J. Wojczal, J. Jaworski, S. Stachowicz, P. Luchowski, K. Rejdak
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POD473

Neurosyphilis: a forgotten entity in the 21st century?

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POD474

Cancelled

POD475

A challenging case of Autoimmune Cerebellar Ataxia

E. Barca[1], C. Barcellona[1], F. Granata[2], A. Graceffa[1], C. Terranova[1], A. Ciranni[1], M. Aguennouz[1], C. Rodolico[1], A. Toscano[1], O. Musumeci[1]
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POD476

Cancelled

POD477

Cancelled

POD478

Significantly worse patient-based outcome measures of the impact of disease in Vitamin D deficient MS patients

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Bucharest, Romania

POD479

Is clear the association between sarcoidosis and cerebral venous thrombosis?: A Case report.

M. Palao Rico[1], J.Á. Motos García[2], N. García Lax[2], I. Pellicer Espinosa[3], A. Sanz Monllor[2], I. Sanchez Ortuño[2], J. Marín Marín[3], J.M. Rodríguez García[3], M.L. Martínez Navarro[3]
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POD480

A septic stroke

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POD481

Takotsubo cardiomyopathy leading to new diagnosis of late-onset multiple sclerosis

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POD482

Clinical riddles in hereditary periphereal neuropathies- genetic testing as a clue

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POD483

A case of bilateral thalamic glioma with hydrocephalus

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POD484

Trends in administration of medications in patients with stroke in Ukraine (2007, 2015)

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Danylo Halytsky Lviv National Medical University, Neurology and Neurosurgery, Lviv, Ukraine

POD485

Effectiveness of Georgian MoCA for cognitive screening in Multiple Sclerosis

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POD486

Cancelled

POD487

The Brownell-Oppenheimer variant of sporadic Creutzfeldt-Jakob disease – a very rare cause of rapidly progressive cerebellar syndrome. A study of two cases with neuropathological confirmation

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POD488

Individual evolution of vertebral artery stenting in a case series of male patients with hyperuricemia

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POD489

Safety issues in multiple sclerosis patients treated with alemtuzumab

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POD490

Cyclophosphamide in the treatment of multiple sclerosis: experience of the neurological department of Casablanca-Morocco

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POD491

Neurological illness as a first manifestation of the advanced HIV infection

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POD492

Correction of autonomic nervous system indicators due to the effect of geomagnetic perturbations in patients with remote after effects of closed traumatic brain injury

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POD493

Superficial Cortical vein Thrombosis- Vein of Labbe and Trolard; a mistaken but treatable entity

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POD494

Anti-MOG (Myelin Oligodendrocyte Glycoprotein)-Positive Severe Bilateral Optic Neuritis with Optic Disc Swelling

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POD495

Cancelled

POD496

Familial MuSK Positive Myasthenia gravis and its treatment response- How does it differ from the sporadic type?

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POD497

Cancelled

POD498

Cerebral sinus vein thrombosis during bevacizumab therapy for ovarian cancer

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POD499

Juvenile form of huntington disease in an albanian patient

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POD500

Four-year follow-up of 2 patients with severe cervical dystonia treated with globus pallidus internus deep brain stimulation.

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POD501

Recurrent Acute Aseptic Meningitis due to Neurocysticercosis

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POD502

One and a half vertical syndrome during neuro-Behçet's disease: a rare entity

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POD503

Superficial haemosiderosis of the nevrax complicating a surgical procedure: about a case

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POD504

An unusual case of acute rhombencephalitis.

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POD505

Acute, progressive aquaporin-4 antibodies encephalopathy mimicking herpes simplex encephalitis

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POD506

Patient adherence to subcutaneous interferon beta-1a injections using the RebiSmart® injection device: A retrospective real-world study among Dutch and German patients with multiple sclerosis

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POD507

Sleep studies in fronto-temporal dementia, a long-term EEG and video-EEG monitoring study

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POD508

Association of polymorphisms in MTHFR and APOE genes with the vascular dementia in ischemic stroke patients

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POD509

Title: Neuropsychiatric manifestations of systemic lupus erythematosus (SLE)

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POD510

Recurrent encephalopathy associated with positive Tropheryma whipplei in blood polymerase chain reaction analysis

J. Durães, J. Tomás, A. Gouveia, M.D.C. Macário
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POD511

Impact of invasive EEG monitoring and resective neurosurgical treatment on the quality of life in patients with pharmacoresistant epilepsy through the application of the QOLIE-31 scale

D. Mijatovic[1], Z. Petelin Gadze[2], F. Derke[3], G. Mrak[4], R. Petrovic[5], S. Hajnsek[2]
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POD512

Cerebellar ataxia associated to CV-2 antibodies?

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POD513

Assessment of Demetia education impact – our experience in Zagreb

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POD514

Muscular involvement in sarcoidosis : clinical and pathologic study of four cases and review of the literature

A. Rim[1], A. Bennis[1], S. Marsli[2], H. El Otmani[1], M.A. Rafai[1], I. Slassi[1], B. El Moutawakil[1]
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POD515

Cerebrovascular complications in essential thrombocythemia

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POD516

Autosomal recessive cerebellar ataxia and hypogonadotropic hypogonadism – a diagnostic challenge

P. Salgado[1], R. Carvalho[2], A.F. Brandão[3], P. Jorge[4], I. Alonso[5], M. Magalhães[1]
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POD517

Neurinoma in atypical location

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POD518

Acute myelopathy secondary to cervical intramedullary cavernoma

L. Leitão, S. Cruz, M. Santos, C. Marecos, E.P. Parreira, A.N. Pinto
Amadora, Portugal

POD519

Discontinuation of natalizumab in clinical practice.

J. Perez Lucas[1], J. Álvarez Fraga[2], S. Pastor Yvorra[2],
M. Sastre Real[2], M. Fernandez-Fournier Ferna[1],
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POD520

Cancelled

POD521

Carotid cavernous fistulas: characterization of a population from a tertiary hospital center.

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POD522

The burden of physical and cognitive fatigue in Multiple Sclerosis

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I. Marques[3], M.D.C. Macário[1], L. Sousa[1], I. Santana[1],
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Focused Workshop

Saturday, 24 June 2017

Focused Workshop 1
Management of rare genetic
neurological diseases in the ICU

FW01_1

Diagnosis and management of genetic metabolic disorders in the ICU

J.M. Burgunder
Berne, Switzerland

Genetic errors of metabolism may present with acute or subacute neuropsychiatric symptoms and signs. Most of them are diagnosed during childhood but onset may be seen in adulthood. Acute first presentation is particularly challenging in differential diagnosis and management. A precise anamnesis, including search for triggers, targeted neurological and internal examination will help recognizing them in the acute situation. Acute and recurrent states of confusion, disturbed vigilance along with movement disorder, focal neurological signs, occurring with atypical signs for other acute neurological disorders, suggests a metabolic disorder. Occurrence of an acute exacerbation in the context of a know history of unclear neurological, cognitive and behavioural changes should also raise attention to this possibility. Typical disorders occurring with symptom-free intervals include urea cycle defects and porphyrias. Chronic disorders with acute exacerbation include homocystinuria, Wilson Disease, adrenoleukodystrophy, cerebrotendinous xanthomatosis and some lysosomal disorders. Mitochondrial disorders may occur in both situations. However, the number of such disorders is quite large, most of them being rare entities, sometimes even not yet characterized at the molecular level. Some of these disorders are important to be recognised early in the course, since appropriate management may allow avoiding complications and chronic deterioration. Management in the acute situation follows general guidelines. In some disorders, specific treatments in the acute situation are available, other beeing deleterious, making their recognition all the most important. The presentation will explore general guidance to recognise and manage genetic metabolic disorders in the ICU and provide some specific examples.
Disclosure: Nothing to disclose

FW01_2

Management of genetically based epilepsies in Intensive Care

J.P. Leach
Glasgow, United Kingdom

Management of status epilepticus in ITU aims to stop seizure activity and decrease mortality. By the time of admission to ITU, the risk of mortality in the first year is considerable, especially if this is a first episode of seizure for which the patient hs been treated. This short presentation aims to look at the pitfalls of management in those patients admitted with Status Epilepticus complicating genetic generalised epilepsies. The main focus however will be on the causes of this clinical scenario, hopefully leading to suggestions about investigation and treatment.
Disclosure: UCB Funding a 3-year post for a research fellow carrying out a retrospective study of Status epilepticus in Glasgow from 1995-Present day.

FW01_3

Management of genetic neuromuscular disorders in the ICU

M.S. Damian
FNCS Cambridge University Hospitals, Cambridge, United Kingdom

Patients with inherited neuromuscular diseases who previously would have been refused admission, are increasingly seen in the intensive care Unit (ICU) when the chronic condition decompensates, or with intercurrent infections, respiratory failure or cardiac problems. Infrequently, new presentations of a previously unrecognised condition are admitted as emergencies. Neurologists need to provide detailed and accurate advice to intensivists, who are seldom familiar with management of these conditions. On the other hand, the most urgent questions regarding respiratory weaning, prediction of achievable outcomes, and complications of treatment are different from those encountered in normal neurological practice. Neurologists need to guide management in a multidisciplinary team in the ICU that relies on their expertise, while working under specific constraints of capacity and time. Step down and early specialist rehabilitation are crucial for the patient to achieve the previous quality of life, and use of specialist weaning facilities and respiratory support units is key. This lecture is intended to provide a guide to effective assessment and management of rare neuromuscular conditions. It provides an overview of the way neuromuscular conditions may present clinically in the ICU. A pathway to diagnostic assessment will be provided, including muscle biopsy and use of advanced genetics; management pitfalls will be discussed. Presentation in the session Focused Workshop on Management of rare genetic neurological diseases in the ICU.

Focused Workshop 2
Overarching Theme - Outcome measures in neuromuscular disorders

FW02_3

Quantitative muscle MRI, a powerful surrogate marker in muscular dystrophies

U. Bonati
Basel, Switzerland

In neuromuscular disorders muscle MRI is used for diagnosis and to identify target muscles for biopsy. With the development of new therapies quantitative muscle MRI techniques were evaluated with regard to their potential use as a surrogate outcome measure in neuromuscular disorders. In myopathies MRI-measured fat fraction (MFF) in the skeletal muscles showed excellent correlation with most of the validated functional scores such as the Six Minute Walk Test, the Motor Function Measure or the North Star Ambulatory Assessment and myometric measures. Furthermore, MFF was shown to be able to predict loss of free ambulation in patients with Duchenne muscular dystrophy. MFF was more sensitive to disease progression compared with validated functional scores in Duchenne muscular dystrophy, Charcot-Marie-Tooth disease 1A and inclusion body myositis. Thus, MRI fat quantification techniques may be used as a sensitive surrogate outcome assessment in therapeutic trials in myopathies.

FW02_4

In search of responsive outcome measures in Charcot-Marie-Tooth disease

D. Pareyson
Milan, Italy

Recent clinical trials confirm that assessment of therapeutic efficacy in the slowly progressive Charcot-Marie-Tooth disease (CMT) is a challenge. Research advances in the field will be reviewed. The composite CMT Neuropathy Score (CMTNSv1), used as primary outcome measure (OM), was poorly responsive. Its original version was modified into CMTNSv2 to improve responsiveness and its score was adapted according to Rasch analysis (CMTNS-Rasch) to obtain linear scores; longitudinal data are being collected. Myometry of handgrip and foot dorsiflexion strength was the most responsive among secondary OMs. The CMT Pediatric Scale (CMTPedS) is a reliable and valid measure of disability/impairment for children; it follows the Rasch methodology and is normalized for age. CMTPedS adaptation to adults is under study. The 6-min walking test and Activity Monitors appear promising OMs; besides, CMT-specific disability and HR-QoL scales are under study. Quantitative Magnetic Resonance Imaging (MRI) of lower limb muscles reliably measured fat substitution secondary to denervation in 20 CMT1A patients, with high responsiveness over a 12-month interval. In our hands, gait analysis parameters proved responsive OMs for research as well as for clinical applications. We obtained higher responsiveness by subgrouping CMT patients according to disease severity, which suggests that appropriate selection of patient population and OMs is crucial for clinical trials' design. Skin biopsy provides easy and repeatable access to myelinated fibres and is currently used in the search for adequate biomarkers. The expression of PMP22 at mRNA level did not prove suitable in CMT1A, but other biomarkers are promising.

Disclosure: Nothing to disclose

Focused Workshop 3
Challenges in new clinical trials

FW03_1

Appropriate trial design in the development of orphan drugs

C. Cornu, P. Nony, F. Gueyffier, G. Grenet, B. Kassaï
Lyon, France

Developing orphan drugs is challenging because they tempt to treat serious diseases in a limited number of patients and are therefore assessed by inadequately powered randomized trials (RCTs). We present various strategies to tailor RCTs to rare diseases in order to avoid unnecessary studies and perform adequately designed randomized trials for an unbiased and precise estimate of the treatment benefit, before the marketing authorization.

Objectives: To develop a framework for identifying the best design or design combinations for a precise estimate of the treatment effect using various approaches including mathematical modeling.

Methods: We identified in the literature all possible randomized experimental designs, and built a decisional support tool. We also combined and improved some designs using enrichment strategies. We developed in silico disease and pharmacological models to simulate trials with different designs. In a first step we constructed a realistic virtual population of patients using epidemiological data. We used those data to compute a mathematical model of the disease then combined with pharmacokinetic-pharmacodynamics models for tree rare disease and tree drugs. Then we simulated in silico RCTs with different designs, and compared their performances as measured by the precision of treatment effect estimate, the duration of the trials for sponsors, and for patients.

Conclusion: There is a need to maximize the process of orphan drug development by increasing the precision in estimating the treatment effect. There are many perspectives offered by modeling for selecting the best design of randomized clinical trial for rare diseases.

Disclosure: Funded by the European eranet PRIOMEDCHILD and by the French ministry of health

FW03_2

Clinical trials, health outcomes, and use of administrative data in patients with rare neurological diseases

S. Aymé
Paris, France

Science offers now many opportunities to develop therapies for diseases. Despite that, patient needs are far from being covered partly because the attrition rate of products is higher for Orphan Medicinal Products (OMP) than for other products. Among the determinants are the great phenotypic heterogeneity of most RD, the insufficient knowledge on the natural history, the inaccessibility of already collected data and the absence of interoperability between databases. The RD community is expecting that no opportunity is missed through collaboration between stakeholders, and through database and knowledge accessibility and interoperability. Coordinated efforts are needed to develop the usability of dispersed and diverse resources. The dream of ideal single disease databases filled in by every professional and open to all stakeholders is unrealistic. The reality is that there are currently hundreds of disease registries, mostly national ones, poorly funded and not able to upgrade their system. There are also electronic patient records, but collecting a minimum dataset, not helpful for research, and patient files in natural language in diverse languages. The way forward is at convincing the community to adopt the necessary standards to ensure a minimum semantic interoperability: the Human Phenome Ontology (HPO) for signs and symptoms, and the Orphanet Rare Disease Ontology (ORDO) for clinical entities. The registry community should accept the principle that data should be accessible to third parties and managed by all stakeholders. Recommendations on how to move forward will be presented through examples of initiatives taken in Europe recently.

Disclosure: Nothing to disclose.

FW03_3

Clinical practice guidelines in rare diseases

M. Leone

S. Giovanni Rotondo, Italy

Several neurological conditions meet the definition of 'rare disease' (RD), which are defined based on prevalence (<1/2,000 pop.). Up to 8,000 rare diseases are estimated, affecting over 30 million individuals in Europe. Knowledge of RDs is poorer and treatments opportunities are fewer than for other diseases. RDs are frequently life-threatening or seriously debilitating conditions, which can cause significant morbidity and mortality, can gravely affect quality of life, and can confer a social and economic burden on families and communities. These conditions are, by their nature, encountered very infrequently by clinicians; thus, clinical practice guidelines are potentially very helpful in supporting clinical decisions, health policy and resource allocation. Notwithstanding these difficulties, the EAN considers the production of neurological guidelines a primary tool to improve clinical practice in Neurology and has adopted the GRADE system (Grading of Recommendations, Assessment, Development and Evaluation) as its standard. However, using GRADE in creating guidelines for RDs is challenging and has not yet been explored systematically and in detail. Applying the strategy commonly known as "PICO" (patient, intervention, comparator, outcome) is not always possible. Difficulties are related to identifying groups of patients (often unclear diagnostic criteria), defining relevant outcomes (few studies on patient reported outcomes, frequent use of surrogate outcomes, time-length of some outcomes), and the paucity of randomized controlled trials. Thus, most of the evidence comes from observational studies with many limitations or even case studies or case series. All these difficulties lead to a paucity of RD guidelines of high quality.

Disclosure: Nothing to disclose

Focused Workshop 4
Update on treatable, autoantibody-mediated CNS disorders in children, adolescents and adults: Diagnoses you don't want to miss!

FW04_1

MOG-antibody mediated disorders across the lifespan: Characteristics of a new disease entity

D. Pohl
Ottawa, Canada

In the past decades, autoantibody-associated CNS disorders have increasingly been recognized, often informing treatment decisions. More recently, antibodies against myelin-oligodendrocyte glycoprotein (MOG) have been detected in patients with acute inflammatory CNS disorders. MOG is a component of the outer surface membrane of the myelin sheath, exclusively expressed in the CNS. It has been discussed as a target for CNS autoimmunity since more than 30 years. However, only advanced technology, enabling the detection of MOG in its native conformation, has paved the way to the recognition of anti-MOG as being disease-associated. Initial research focussed on children with acute demyelinating disorders, but it soon became clear that also adults can be affected. Anti-MOG can be detected in children presenting with acute disseminated encephalomyelitis (ADEM) and predicts a non-MS course in children with aquired demyelinating syndromes. Across all ages, anti-MOG is associated with neuromyelitis optica (NMO) phenotypes, as well as with suspected limited forms of NMO, including optic neuritis (ON), chronic relapsing inflammatory optic neuropathy (CRION), longitudinally extensive transverse myelitis (LETM), and recurrent LETM. An initial presentation of ADEM and subsequent development of bouts of ON (ADEM-ON), as well as multiphasic ADEM (MDEM) have also been described to be associated with MOG antibodies. In summary, MOG-antibody associated disorders are distinct from multiple sclerosis (MS) and anti-aquaporin-4 positive NMO. Early distinction between those disease entities is paramount, as outcomes and therapeutic pathways differ. Future research will hopefully elucidate the pathomechanisms of anti-MOG associated disorders, as well as optimal treatment approaches for anti-MOG positive patients.

Disclosure: Nothing to disclose

Over the past decade, autoantibody-associated CNS disorders have increasingly been recognized, often informing treatment decisions. Psychiatric and neurologic manifestations, including epilepsy, have been linked to autoimmunity. Initially, many of those disorders were described as paraneoplastic, occurring mainly in adults. However, we now know that even young children can be affected by autoantibody-mediated CNS disease, sometimes triggered by infections, but often without identifiable causes. This workshop will provide up-to-date, clinically relevant information regarding three entities of autoantibody-mediated CNS disorders: Anti-myelin-oligodendrocyte glycoprotein (MOG) associated disease, anti-N-Methyl-D-Aspartate-receptor (NMDAR) encephalitis, and the spectrum of autoimmune epilepsies, secondary to diverse auto-antibodies or still elusive immune mechanisms. There is increasing evidence that timely and targeted treatment of immune-mediated CNS disorders may improve outcome, and prevent potentially devastating neurological deficits. Therefore, early recognition of those disorders is paramount. We hope that this workshop will help to increase awareness and knowledge regarding this highly relevant, treatable disease entity.

FW04_2

Update on NMDA-receptor antibody mediated disorders

M.J. Titulaer
Rotterdam, The Netherlands

It has been a decade since the discovery of antibodies against the N-Methyl-D-Aspartate receptor (NMDAR), identifying anti-NMDAR encephalitis. It is the most frequent form of autoimmune encephalitis. The patients are frequently young, and ovarian teratomas are present in about one-third of the patients. MRI is often unrevealing. Most important is the detection of anti-NMDAR antibodies in the cerebrospinal fluid, which is more sensitive and specific than serum. The disease is caused by IgG-type antibodies, and not IgA or IgM antibodies. IgG NMDAR antibodies can cause disease in mice and to newborns (passive transfer), and have direct effects in vitro, thereby proofing pathogenicity. There is controversy about the role of IgA and IgM antibodies, but for now their role is limited to research purposes. Patients are frequently refractory to initial immunotherapy (steroids, immunoglobulins or plasma exchange), and second-line immunotherapy (rituximab or cyclophosphamide) can be of additional value. Ultimately, most patients respond to immunotherapy, and recovery can be remarkably well compared to the severity of the illness in the acute phase. Besides ovarian teratomas, anti-NMDAR encephalitis can be triggered by herpes simplex encephalitis (HSVE). It has been shown that up till a quarter of the HSVE patients develop anti-NMDAR encephalitis during their recovery, and immunotherapy is useful in these patients. Some patients also develop a secondary autoimmune demyelination with AQP4 or MOG antibodies. This disease is important to recognize as the symptoms and complications can be fatal when not treated in time, whereas with immunotherapy many patients recover considerably or completely.

Disclosure: Dr. Titulaer received research funds for serving on a scientific advisory board of MedImmune LLC., Guidepoint Global LLC, and a travel grant for lecturing in India from Sun Pharma, India.

FW04_3

Autoimmune epilepsies

C. Bien

Bielefeld, Germany

One of the key challenges in scientific and clinical epileptology is the elucidation of the causes of seizure disorders: in a general sense and on the individual patient level. This has been acknowledged by the International League against Epilepsy by introducing an etiological "level" in its most recent epilepsy classification. "Immune" is now one of six categories (Scheffer IE et al., Epilepsia 2017;58:512). Two main groups of disorders can be subsumed under this category: the autoantibody-defined autoimmune encephalitides (anti-NMDA-receptor encephalitis, anti-LGI1-encephalitis and so on) with a predominantly epileptic phenotype, and Rasmussen encephalitis (RE). Rarer examples of epilepsies resulting from immunological conditions are neurosarcoidosis or lupus erythematosus. Immune-mediated epilepsies are a fine example why etiology is of prime importance in epileptology: Elucidating an immunological cause of a seizure disorder may explain the underlying pathophysiology and informs the clinician about the appropriate therapy and the prognosis.

Disclosure: Nothing to disclose.

Focused Workshop 5
"Cervical Vertigo" - Reality or Fiction?

FW05_2

Cervical vertigo: Head motion-induced dizzy spells in acute neck pain

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Munich, Germany

Head motion-induced dizzy spells in acute neck pain syndrome. The clinical picture of cervical vertigo, triggered solely by a disorder of the neck afferents, is still controversial, although the important contribution of these receptors to spatial orientation, postural control, and head-trunk coordination is well acknowledged. Patients with an acute cervical pain syndrome causing stiffness of neck muscles and mainly unilateral constraints of head rotations often report on head movement-induced spells of dizziness and postural imbalance. About 20% of 350 physicians attending an otoneurological symposium indicated that they have had this experience themselves at least once in their life. In thus afflicted patients spells of dizziness or vertigo perceived as apparent surround motion or as short body perturbations last for a fraction of a second or a second; they are evoked only by rapid head rotations, not by slow head movements, and occur during locomotion, when standing, sitting or bending over. The attacks spontaneously remit with recovery from cervical pain and neck muscle stiffness. These attacks represent a new variant of "cervical vertigo" (A new type of cervical vertigo: head motion-induced spells in acute neck pain. Brandt and Huppert, Neurology 2016) based on head motion-induced misalignment of sensorimotor integration. If the head movement is smaller than intended due to stiffness of neck muscles, the reafference signal is inappropriately smaller and the rapid head movements may be erroneously perceived as external perturbations causing a distressing spell of postural imbalance.

Disclosure: Nothing to disclose

FW05_3

Rotational vertebral artery occlusion: A clinical entity or various syndromes?

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Lübeck, Germany

The rotatory vertebral artery occlusion: a clinical entity or various syndromes? The rotational vertebral artery occlusion syndrome (Bow-Hunter syndrome) is the only form of cervical vertigo with clear pathophysiological evidence. It is extremely rare because it requires several pathophysiological factors to occur: One functional insufficient vertebral artery (occlusion, hypoplasia, terminating in PICA) and a head-movement-related mechanical compression of the contralateral vertebral artery, e.g., by osteophytes or bands. Sustained head deviation (e.g. in the head position of bow hunters) elicits vertebral artery compression either of the dominant or hypoplastic vertebral artery resulting in transient ischemia either of the ipsilateral or contralateral labyrinth or the medullary brainstem. Thus, different syndromes may result from the same pathophysiological principle. Moreover, transient ischemia may elicit paroxysmal excitation or inhibition with different nystagmus directions. Without returning to the straight ahead head position the syndrome leads to syncope or irreversible ischemia. The compression site (C1-C2 vs. subaxial) determines whether vertigo is elicited by contra- or ipsilateral horizontal head movements. Transient nystagmus is usually causes by unilateral vestibular failure, its direction is determined by ischemia either in the labyrinth or in the vestibular nuclei. Clinical examination (of nystagmus) allows dissociating both forms. Surgical removal of the hypomochlion cures the syndrome. Otherwise, natural course usually does not stop rotational vertebral artery occlusion syndrome.

Disclosure: Nothing to disclose

Focused Workshop 6
Rare brain tumors: Advances in management and new drugs

FW06_1
Primary Central Nervous System Lymphomas

P. Roth
Zurich, Switzerland

Despite some progress, primary central nervous system lymphoma (PCNSL) represents a particular challenge in clinical neurooncology. In contrast to the majority of other malignant brain tumors, PCNSL is a curable disease at least in younger patients. Radiotherapy has been a standard treatment which results in high response rates but hardly any durable responses. After the introduction of high-dose methotrexate (HD-MTX), this has been the therapeutic backbone for more than 2 decades. However, it has remained a matter of discussion which drugs should be added to HD-MTX in order to gain additional therapeutic benefit. Response rates can be increased by the addition of agents such as ifosfamide or cytarabine, however, their impact on overall survival is less clear. Similarly, the use of anti-CD20 antibodies like rituximab has remained a controversial issue because data from randomized trials are still lacking. The combination of HD-MTX and radiation therapy does not prolong overall survival and is associated with significant neurotoxicity. Consolidation therapy with high-dose chemotherapy followed by stem cell support is currently being explored in clinical trials. The prognosis of patients who do not qualify for HD-MTX-based chemotherapy is poor. Here, radiation therapy or treatment with alkylating agents such as temozolomide might be used which, however, only rarely results in long remissions. Furthermore, treatment at recurrence is only poorly defined as data from large trials are lacking. Because of the numerous open questions, PCNSL patients should be treated within a clinical trial whenever possible to allow for the development of improved therapeutic regimens.

Disclosure: Nothing to disclose

FW06_2
Rare brain tumours: advances in management and new drugs

U. Herrlinger
Division of Clinical Neurooncology, University of Bonn Medical School

Frequently occuring brain tumors such as high-grade gliomas used to be the mainstay of clinical research in adult neurooncology. With the detection of drugable molecular targets and the availability of suitable targeted agents rare brain tumors have come into the focus as tumors that might be more amenable to targeted therapy than high-grade gliomas. BRAF inhibitors are explored for therapy of pleomorphic xanthoastrocytoma and anaplastic ganglioglioma. The new classification of medulloblastoma is based on molecular findings such as alterations of the WNT or SHH pathways for which already targeted agents are explored in the clinical setting. In some tumors such as meningiomas or chordomas, experimental drug therapy has to be considered after multiple relapses and the impossibility to treat with surgical or readiotherapeutic methods any further. The PDGFR inhibitor imatinib may then be applied to patients with chordoma. Patients with multiple relapses of meningioma may explore the effects antiangiogenic therapy either with the anti-VEGF-A antibody bevacizumab or the multikinase inhibitor sunitinib. NF2-associated schwannoma appears to respond to bevacizumab therapy. Overall, the published data for the efficacy of such drug therapy is scarce and mainly based on small non-randomized case series.

FW06_3

Glioneuronal tumors

R. Soffietti

Turin, Italy

Glioneuronal tumors include according to WHO Classification ganglioglioma, dysembryoplastic neuroepithelial tumor (DNET), desmoplastic infantile astrocytoma and ganglioglioma, papillary glioneuronal tumor, and rosette-forming glioneuronal tumor of the fourth ventricle. Ganglioglioma and DNET are the most frequent variants, prevail in children and young adults and are characterized by pharmacoresistant seizures. They have more commonly an indolent course with long survival following total/near total surgical resection. Radiotherapy and chemotherapy are reserved for recurrent and/or aggressive forms. New molecular alterations have been recently recognized either as prognostic factors or targets of therapy. The most characteristic molecular alteration is represented by the BRAF V 600 E mutation (the same found in melanomas), which is present in 18-58% of cases of gangliogliomas, and can be targeted by specific inhibitors (dabrafenib, vemurafenib, etc). Some trials are ongoing to determine the impact of these new drugs on glioneuronal tumors.

Disclosure: Nothing to disclose

Focused Workshop 7
Vascular contribution to dementia

FW07_1

The concept of vascular cognitive impairment

R. Schmidt
Graz, Austria

Diagnostic criteria separating vascular dementia from other dementias, particularly Alzheimer's disease neglect the real world in which most Alzheimer cases present with at least some vascular brain lesions. Most importantly,vascular lesions, even if subtle, exert significant effects on the patients' cognitive functioning if they coexist with AD pathology. The term vascular cognitive impairment (VCI) accounts for the paradigmatic change in the concept of vascular dementia and encompasses all cognitive disorders associated with cerebrovascular disease, from frank dementia to mild cognitive deficits. Simply put, VCI is a syndrome with evidence of clinical stroke or subclinical vascular brain injury and cognitive impairment affecting at least one cognitive domain. The most severe form of VCI is VaD. Despite these late terminological changes the key issue in VCI, namely what is the spectrum of vascular lesions in the brain that actually contributes to the cognitive-behavioral phenotype of a given patient. There are four ways of approaching this pivotal question. (1) Neuropathology in subjects with pre-mortem clinical assessment, (2) Longitudinal Clinical-Imaging Assessment, (3) the study of microstruture, and (4) voxel-based lesion symptom mapping. The last decade determined microstructural tissue abnormalities as one of the most important factors for cognitive dysfunction in patients with overt vascular lesions. Location-based approaches which will allow to assess lesion burden in strategic tracts very likely represent the next step to further improve our understanding of VCI

Disclosure: Nothing to disclose

FW07_2

Which vascular lesions contribute to dementia: New insight from 7T MRI

G. Biessels
Utrecht, The Netherlands

Autopsy studies identify vascular pathology in the majority of patients with dementia, also in those with a clinical diagnosis of Alzheimer's disease. Detection of this vascular pathology during life mainly relies on MRI. Markers of small vessel disease (SVD) on MRI, including white matter hyperintensities, lacunes, microbleeds and enlarged perivascular spaces, are generally considered to be the prototypical MRI manifestations of the vascular burden in dementia. These lesions are very common in older individuals and their presence and severity is clearly associated with dementia risk. As such, these MR lesions have almost become our conceptual equivalent of SVD. Yet, we should keep realizing ourselves that these lesions represent the consequences of SVD in the parenchyma rather than abnormalities in the small vessels themselves. As such, that they represent an end-stage of SVD. These parenchymal lesions are not sufficiently specific to understand disease processes and SVD lesion-burden alone often relates poorly to cognition in individual patients. There is therefore a need for novel approaches to zoom in on the actual vascular abnormalities in SVD and for measures that better reflect the functional burden of SVDs, also in individual patients. In my presentation I will show how we are using high field 7T MRI to assess the function and structure of the cerebral small vessels and I will review models that may better reflect the functional burden of SVDs. These approaches may help to better understand aetiology, contribute to development of treatment and help to make a more accurate diagnosis.

Disclosure: Nothing to disclose

FW07_3

Management of VCI. Prevention and treatment

L. Pantoni
Florence, Italy

Vascular cognitive impairment (VCI) is a term describing the contribution of vascular factors (including risk factors, vascular events, neuroimaging features, genetic determinants) to cognitive impairment. In this sense, the term VCI covers the almost pure or at least prevalently vascular conditions that cause cognitive decline but also refers to the contribution of vascular factors to neurodegenerative processes. Some of the cornerstones of the topic prevention and treatment of VCI are: 1) the role of the treatment of vascular risk factors in preventing VCI and dementia in general; 2) the role of the treatment of more specific vascular conditions such as small vessel disease that are strongly associated with VCI; 3) the symptomatic treatment of patients with VCI; 4) the role of the presence of certain vascular neuroimaging findings (such as white matter lesions and microbleeds) in predicting the risk of drug treatment complications in some specific situations such as thrombolysis and anticoagulation. Of interest, the American Heart Association/American Stroke Association has recently released a Scientific Statement for Healthcare Professionals for the Prevention of Stroke in Patients With Silent Cerebrovascular Disease. This document represents one the first attempts to provide guidelines in this field.

Disclosure: Nothing to disclose

Sunday, 25 June 2017

Focused Workshop 8
The role of exosomes in mechanisms
of multiple sclerosis

FW08_1

Microvesicles provide a new mechanism of cell communication within CNS and in immune system

R. Furlan
Milan, Italy

Extracellular vesicles (EVs) play a major role in cell-to-cell communication in physiological and pathological conditions. Microglia, the phagocytes of the brain, modulates neighboring cells also through the release of EVs. During the progression of neuroinflammatory diseases such as multiple sclerosis, the activation of immune cells (monocytes, macrophages, microglia, B and T cells), oligodendrocytes and brain endothelial cells, induces the release of microparticles that can be measured in the cerebrospinal fluid (CSF) and peripheral blood of MS patients (Scolding et al., 1989; Minagar et al., 2001; Jy et al., 2004; Verderio et al., 2012). Also in the mouse model of MS, namely experimental autoimmune encephalomyelitis (EAE), increased levels of myeloid-derived EVs have been documented as well as a good correlation between their number and the disease progression. This evidence, along with many other reports, lead to the proposal to use circulating EVs as a diagnostic tool or prognostic biomarkers for monitoring the progression of many different pathologies (Skog et al., 2008; Kosaka et al., 2010; D'Souza-Schorey and Clancy, 2012; Dear et al., 2013; Saenz-Cuesta et al., 2014). Interestingly, the injection of microglia-derived EVs but not that of liposomes of similar composition in the brain of EAE mice, leads to the recruitment of inflammatory cells in the site of injection: this suggests that microvesicles of myeloid origin may be not only a general sign of cell activation but also active players in the context of this disease (Verderio et al., 2012).
Disclosure: Nothing to disclose

FW08_3

Exosomes contribute to the spread of neuroinflammation in multiple sclerosis

K. Selmaj
Lodz, Poland

Mechanisms relevant to the pathogenesis of MS have not been fully elucidated. For example, it is not known how reactivity against CNS components is generated within the peripheral immune system. We propose that a significant contribution to immunoregulatory events may derive from a cell-to-cell communication system involving the secretion of exosomes. It is known that exosomes can cross the blood-brain barrier and thus may contribute to the spread of brain antigens to the periphery. We found that serum exosomes expressed three major myelin proteins, MBP, PLP and MOG. Exosomal content of MOG strongly correlated with disease activity. Serum-derived exosomes induced proliferation of MOG-T cell receptor transgenic T cells confirming that serum exosomes maintained MOG immunogenicity. Among exosomal cargo microRNAs (miRNAs) represent a prominent component and in addition showed unexpectedly remarkable stability. Exosomal RNA Next Gereneration Sequencing (NGS) revealed that circulating exosomes have a distinct miRNA profile in RRMS and 4 circulating exosomal sequences within the miRNA category were significantly down-regulated in RRMS patients vs HC: hsa-miR-122-5p, hsa-miR-196b-5p, hsa-miR-301a-3p and hsa-miR-532-5p. In vitro secretion of these miRNA by peripheral blood mononuclear cells was also significantly impaired in RRMS. Decreased transport of miRNAs significantly extends exosome biological relevance since they can influence changes in the genetic program of the target cell. Importantly, putative targets for all these miRNA include STAT 3 and AHR suggesting their profound involvement in spreading of autoimmune reactions. Further understanding of exosome-dependent mechanisms in MS should provide a novel angle to the analysis of the pathogenesis of this disease.

Focused Workshop 10
Neurobiological and clinical aspects of memory consolidation

FW10_1

How does memory consolidate during sleep – behavioural, EEG, and neuropharmacological evidence

J. Born
Tübingen, Germany

Whereas memories are encoded and retrieved optimally when the brain is awake, the consolidation of memory requires an offline mode of processing as optimally established during sleep. Recent studies have elucidated some of the mechanims underlying memory consolidation during sleep, especially in the hippocampus-dependent declarative memory system. This system is capable of rapidly forming an initial representation for an episode upon its one-time occurrence, i.e., an episodic memory which is, thus, at the basis of the formation of any long-term memory. Consolidation of hippocampus-dependent memories represents an active systems consolidation process that takes place mainly during slow wave sleep (SWS) rather than REM sleep. The neurochemical milieu during SWS, such as minimum cholinergic activity, allows for spontaneous neural reactivations of newly encoded memory representations that originate from hippocampal circuitry and stimulates the gradual redistribution of the representations towards extra-hippocampal, mainly neocortical networks serving as long-term store. The redistribution process goes along with a qualitative transformation of the representation ending up in the formation and storage of abstracted schema-like memories stored in the neocortex. The memory reactivations are synchronized to the <1Hz EEG slow oscillations that dominate SWS and are generated in neocortical networks, partly as a function of the prior use of these networks for encoding of information. By synchronizing hippocampocal memory reactivations with specific activity from other brain areas, including thalamo-cortical spindles, slow oscillations enable persisting plastic changes underlying the long-term storage of memories in the neocortex.
Disclosure: Nothing to disclose.

FW10_2

Brain mechanisms of memory consolidation during sleep – evidence from functional brain imaging

P. Maquet
Liege, Belgium

Memories are thought to be consolidated during sleep by two distinct processes: (1) reinforcement of memory-specific cortical interactions and (2) homeostatic reduction in synaptic efficiency. Using fMRI, we assessed whether episodic memories are processed during sleep by either or both mechanisms, by comparing recollection before and after sleep. We probed whether LTP influences these processes by contrasting two groups of individuals prospectively recruited based on BDNF rs6265 (Val66Met) polymorphism. Between immediate retrieval and delayed testing scheduled after sleep, responses to recollection increased significantly more in Val/Val individuals than in Met carriers in parietal and occipital areas not previously engaged in retrieval, consistent with 'systems-level consolidation'. Responses also increased differentially between allelic groups in regions already activated before sleep but only in proportion to slow oscillation power, in keeping with 'synaptic downscaling'. Episodic memories seem processed at both synaptic and systemic levels during sleep by mechanisms involving LTP.

FW10_3

The hippocampus in aging and disease

T. Bartsch
Kiel, Germany

The hippocampus has a pivotal role in learning and in the formation and consolidation of memory and is critically involved in the regulation of emotion, fear, anxiety, and stress. Studies of the hippocampus have been central to the study of memory in humans and in recent years, the regional specialization and organization of hippocampal functions have been elucidated in experimental models and in human neurological and psychiatric diseases. The hippocampus has long been considered a classic model for the study of neuroplasticity as many examples of synaptic plasticity such as long-term potentiation and -depression have been identified and demonstrated in hippocampal circuits. Neuroplasticity is the ability to adapt and reorganize the structure or function to internal or external stimuli and occurs at the cellular, population, network or behavioral level and is reflected in the cytological and network architecture as well as in intrinsic properties of hippocampal neurones and circuits. The high degree of hippocampal neuroplasticity might, however, be also negatively reflected in the pronounced vulnerability of the hippocampus to deleterious conditions such as ischemia, epilepsy, chronic stress, neurodegeneration and aging targeting hippocampal structure and function and leading to cognitive deficits. Considering this framework of plasticity and vulnerability, basic principles of hippocampal anatomy and neuroplasticity on various levels as well as recent findings regarding the functional organization of the hippocampus in light of the regional vulnerability in Alzheimer's disease, ischemia, epilepsy, neuroinflammation, sleep and aging are reviewed.
Disclosure: T.B. has been supported by the German research Foundation SFB 654, FOR 2093, the German Cluster of Excellence Inflammation-at-Interfaces (ExC 306) and by the Faculty of Medicine, University of Kiel, Germany.

FW10_4

Chairman's concluding remarks

S.F. Cappa
Milan, Italy

The assessment of memory function is a crucial component of clinical evaluation in neurology. In the case, for example, of Alzheimer's disease, the presence of objective impairment of memory is required by all the diagnostic criteria. The adoption of a translational perspective, which takes advantage of the enormous advancement in the neurobiology of memory to inform clinical assessment is thus a highly desirable outcome. The presentations in this workshop represent a contribution to this important aim.
Disclosure: Nothing to disclose

Focused Workshop 11
Assembly and maintenance of the node of ranvier complex in health and disease

FW11_1

Cell adhesion molecules at the nodal complex as targets in disease

J. Devaux
Marseilles, France

Cell adhesion molecules play an important function in the organization of myelinated axons and of the nodes of Ranvier. The complex gliomedin/NrCAM/neurofascin-186 is crucial for the initial aggregation of Nav channels at hemi-nodes. In addition, the complex Caspr1/contactin-1/neurofascin-155 dictates the formation of the paranodal axo-glial complex and participates to the formation of the nodes. In a recent study, we demonstrated that the node of Ranvier is the primary site of the immune attack in patients with Guillain-Barré syndrome (GBS) or chronic inflammatory demyelinating polyneuropathy (CIDP). We found that a subset of CIDP patients with specific clinical features present antibodies directed against contactin-1 or neurofascin-155. Of interest these antibodies are mostly of the IgG4 isotype, a subclass that is believed to be anti-inflammatory. Using animal models, we demonstrated that the passive transfer of IgG4 against contactin-1 induced a chronic progressive pathology associated with conduction loss. These animals did not show signs of immune infiltration, demyelination, or axonal degeneration. Rather, the passive transfer of the IgG4 mediated a selective alteration of the paranodal Caspr1/contactin-1/neurofascin-155 complex predominantly in small motor axons. Using intraneural injections, we further showed that anti-contactin-1 IgG4 have the potency to penetrate the paranodal segments which normally form a barrier to the lateral diffusion of particles. These results pinpoint that IgG4 to paranodal proteins can dismantle the paranodal complex and lead to conduction defects. Cell adhesion molecules thus play important function in myelin physiology and are reliable biomarkers in human inflammatory neuropathies.

Disclosure: Nothing to disclose

FW11_2

Glycolipids at PNS nodes in autoimmmune neuropathies

H.J. Willison
Glasgow, United Kingdom

Autoimmune neuropathies including Guillain-Barré syndrome (GBS) are in part mediated by anti-GM1 ganglioside antibodies induced by preceding infections. Anti-GM1 antibodies target plasma membrane GM1 that is extensively distributed in both glial and axonal membranes, particularly at the node of Ranvier. Antibodies deposited at this site in models of GBS are associated with complement deposition, conduction block, structural disruption of ion channels and macrophage infiltration. In this presentation, data will be shown that investigates the pathological processes underlying nodal injury induced by a range of anti-glycolipid antibodies. These data indicate the high vulnerability of axonal membranes to acute injury and highlight the importance of developing specific axonal projection strategies. Targeting the nodal axolemmal or glial membranes in appropriate animal models allows us to study associated nodal pathology, and determine the downstream consequences on function and axon fate, currently a major area in GBS clinical research.

Disclosure: Nothing to disclose.

FW11_3

Imaging nodes of Ranvier in skin biopsies as an investigative and diagnostic tool in human disease

<u>C. Sommer</u>, K. Doppler
Würzburg, Germany

Increasing numbers of patients with inflammatory neuropathies and autoantibodies to paranodal proteins are being described. Most of these patients have an acute-onset CIDP, a severe motor more than sensory impairment, and some have characteristic symptoms like prominent tremor or severe pain. In our cohort of patients diagnosed as CIDP and GBS, we discovered antibodies to the paranodal proteins neurofascin 155, contactin 1, and caspr. A binding assay to teased mouse nerve fibers is a suitable screening test for these autoantibodies. ELISA, western blot, and proof of binding to HEK293 cells transfected with the antigen in question may be needed to show the antibody specificity. Skin biopsies from several patients revealed that the antibodies not only bind to the Ranvier nodes, but also destroy their architecture. The nodal gap is increased and caspr and neurofascin-immunoreactivity may be lost at the paranodes and nodes. Whether this nodal disruption is complement dependent, and whether the changes are reversible after treatment, is still unknown. Changes of the nodal architecture, however, are not specific for neuropathies with paranodal autoantibodies. We found similar but milder changes in cohorts of mixed neuropathies and of diabetic neuropathy. The significance of these nodal alterations will be discussed.

Focused Workshop 12
End-of-Life issues in neurology

FW12_1

The EAN / EAPC consensus on neurological palliative care – preparation before and at the end of life

D. Oliver
Rochester, United Kingdom

Palliative care aims to provide a holistic approach to the person, and their family/carers, considering the various aspects of care – physical, psychological/emotional, social and spiritual. The European Academy of Neurology has collaborated with European Association for Palliative Care in the production of a Consensus document on palliative care in chronic and progressive neurological disease. This has stressed the importance of the consideration of palliative care early in disease progression and there is increasing evidence that this may improve symptom management, family satisfaction, length of survival and costs.The Consensus has identified particular areas where the palliative care approach earlier in the disease progression may help: Multidisciplinary team care – for assessment and management Communication is key allowing: Goal setting Advance care planning Symptoms should be assessed and diagnosed carefully and managed appropriately and effectively Carers require support - before and after death Discussion about end of life care throughout the disease progression is helpful, particularly if there may be loss of communication and/or cognitive abilities later in the disease. Training and education of all professionals is essential to allow this approach to be available to all patients and families. As a person with a neurological disease progresses and deteriorates it is important to plan ahead and prepare for the end of life. Thus the palliative care approach throughout the disease progression will enable patients and families to have an improved quality of life and quality of dying.

Disclosure: Nothing to disclose

FW12_2

The development of evidence in the effectiveness and use of palliative care in neurological disease – the effectiveness of end of life care

S. Veronese
Turin, Italy

Palliative and end of life care have been recognized as important and necessary in the trajectory of neurological diseases and there is an increasing amount of evidence that there are unmet palliative care needs of both patients and their carers. Services are increasingly providing assistance mainly in neurodegenerative progressive disorders such as amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), Parkinson's disease (PD) and related disorders. Palliative care for cancer patients has shown to have a positive impact on specific outcomes including individual quality of life (IQoL) of the patients, physical symptom control, psycho-social and spiritual issues and reduced caregiver burden of care. This evidence has been used to advocate for the establishment of specific palliative care pathways in neurological conditions and recently an international consensus recommended palliative care in neurology. Over the last ten years a number of randomized and controlled studies have focused on these aims. In the UK severely affected MS patients, were shown to benefit on some individual outcomes. A pilot study involving ALS, MS and PD patients showed a significant improvement in IQoL and physical symptoms of the patients. Recently there have been studies in the UK for people with progressive disease and in Italy for severe MS. Overall the trend of these studies shows positive effects of the diverse palliative care services on neurological patients. Future studies are required to establish the best palliative care provision for the different conditions in terms of timing, setting, interaction with neurological services and modality provision.

Disclosure: Nothing to disclose

FW12_3

Ethical aspects of care at the end of life – with-holding and withdrawing treatment

C. Faull

Leicester, United Kingdom

Patients and families may have a diversity of views on what constitutes quality of life and suffering and they approach decisions about acceptance or continuance of medical treatments in the context of a range of influencing factors. Health care professionals also hold a range of differing views and personal perspectives which may impact on their care and support for patients and emotional resilience. Professional bodies for health professionals and the law of the country provide the legal and ethical contexts for withholding and withdrawing treatments and whilst this provides clarity it can also create significant tensions in delivery of care and the patient's autonomy. This session will explore these issues with particular reference to research in the UK related to withdrawal of assisted ventilation and on resuscitation decision making in advanced disease.

Monday, 26 June 2017

Focused Workshop 13
MDS-ES/EAN: Translational
Movement Disorders including
novelties and neuroscience

FW13_3

**New therapeutic strategies in
Huntington's disease**

J.J. Coutinho Ferreira
Lisbon, Portugal

Drug development in Huntington's disease (HD), like in other neurodegenerative diseases, is challenging with a large compound attrition rate at earlier phases of development and a very high trial failure rate at later stages. The only drugs currently approved by the US Food and Drug Administration (FDA) are the dopamine-depleting agents tetrabenazine and deutetrabenazine, for the treatment of chorea in HD. There are no pharmacological interventions proved to be effective as a disease-modifying therapy. New compounds and other therapeutic strategies are now entering the clinical-development stage exploring new putative mechanisms of interventions. These include new therapeutic strategies targeting immunomodulation or lowering levels of the mutated huntingtin protein (mHTT) (gene therapy, inhibition of synthesis of mHTT, modulation of HTT homeostasis). In a recent review of the international clinical trials databases there were 31 trials for HD being conducted testing 23 different interventions. Interventions currently at a clinical trials stage that explore this new paradigm include inhibition aggregation of mutant huntingtin (PBT2), selective SirT1 inhibitors (selisistat), PDE10A inhibition, RNA interference anti-sense oligonucleotides (ASO), anti-inflammation (laquinimod).
Disclosure: Nothing to disclose

Focused Workshop 14
Seizure detection systems

FW14_1

ECG-based seizure detection

P.A. Boon
Ghent, Belgium

Various neurostimulation modalities have emerged in the field of epilepsy and neurostimulation has become an established therapeutic option with a promising efficacy and adverse effects profile. In "responsive" neurostimulation the strategy is to interfere as early as possible with the accumulation of seizure activity to prematurely abort or even prevent an upcoming seizure. The design of technology required for responsive stimulation is more challenging compared to devices for open-loop neurostimulation, being dependent on adequate sensing and stimulation algorithms and a fast coupling between both. Closed-loop or responsive neurostimulation is a novel approach in the treatment of epilepsy, delivering current upon detection of seizure activity in an attempt to abort or prevent seizure activity. Two devices for responsive neurostimulation are currently available for the treatment of refractory epilepsy: the Responsive NeuroStimulation (RNS) System and Vagus Nerve Stimulation with automated cardiac-based seizure detection (AspireSR). Vagus nerve stimulation has been used widely since its FDA clearance in 1997. Manual activation of the pulse generator with a handheld magnet allows on-demand stimulation when an aura or seizure occurs, but due to reasons such as cognitive impairment, sleep, lack of an aura or the disabling effects of the seizure itself, this may be hard to achieve in practice. A novel type of VNS device, the AspireSR, provides closed-loop VNS stimulation based on the detection of ictal tachycardia that often occurs as a result of ictal activity, on top of the conventional treatments. Two prospective trials, both in the EU and USA hve shown AspireSR to be reliable and safe, while a pivotal trial showing effective and long-term seizure reduction still needs to be performed. Efforts should be made to further identify functional biomarkers, other than ictal tachycardia, that relate to the dynamic aspects of the epileptic brain and its susceptibility to a specific type of neuromodulation. A better tailoring of treatment to the individual patient will further increase therapeutic success.

Disclosure: Not received

FW14_2

EEG-based seizure detection

C. Baumgartner
Vienna, Austria

Objectives of EEG-based seizure detection in the epilepsy monitoring unit include more efficient data analysis, automatic injection of isotopes for ictal SPECT scans, automatic neuropsychological testing as well as seizure alerts and warning to improve patient safety. In the outpatient setting automatic seizure detection could facilitate seizure documentation and counting (‚recognizing the unobserved') as well as warning devices for SUDEP prevention. Requirement for the clinical application of automatic seizure detection devices include high sensitivity and high specificity (low false alarm rates), on-line calculation and short detection latency. Algorithms should be easy and ready to use in a clinical setting without complicated parameter adjustments, a-priori knowledge about individual seizure characteristics and adjustments for individual patients. Problems of EEG-based seizure detection include inter-individual differences in seizure patterns depending on the seizure onset zone, intra-individual differences in seizure patterns depending on conditions at seizure onset, speed and route of seizure propagation, high sensitivity, but low specificity (i.e. high false alarm rates), and artifacts and recurrent rhythmic and high amplitude EEG patterns (e.g. FIRDA, TIRDA, sleep activity) mimicking EEG seizure patterns. Currently available EEG-based seizure detection methods provide a sensitivity of 80-90% and a false alarm rate of 0.2-0.3 per hour. In general performance is better in temporal as compared to extratemporal seizures. In conclusion there exist still limitations for automatic EEG-based seizure detection methods in everyday clinical practice. These algorithms can support, but cannot replace a well-trained epilepsy monitoring team.

Disclosure: Not received

FW14_3

Multimodal seizure detection systems

S. Beniczky
Dianalund, Denmark

Epileptic seizures can occur at any time. Seizures can cause traumatic injuries and ultimately SUDEP. Anxiety for occurrence of seizures affects the quality of life of patients with epilepsy and can result in social isolation. Portable seizure detection systems that could trigger an alarm and call for help would be a valuable help for patients with epilepsy. Recordings in Epilepsy Monitoring Units (EMU) have demonstrated that signals specific for seizures can be derived also from polygraphic channels. Since these modalities are easily implemented in portable devices, this presentation will focus on non-EEG based modalities: surface electromyography (EMG), accelerometry, ECG – Heart Rate Variability (HRV), near infrared spectroscopy (NIRS), and their combination. Prospective, controlled, large-scale multi-center studies provided compelling evidence for the accuracy of EMG and accelerometry-based devices for detecting generalized tonic-clonic seizures. There are promising results on HRV for detecting focal seizures.

Disclosure: Nothing to disclose

Focused Workshop 15
How to improve outcome in acute stroke

FW15_1

Intravenous thrombolysis: Current status and challenges

P.A. Sandercock
Edinburgh, United Kingdom

For many patients with acute ischaemic stroke who reach hospital, can be assessed clinically and radiologically and then start treatment within 4.5 hours of symptom onset, intravenous thrombolysis is of net benefit. This requires a highly organised system of care. The treatment carries a 1-4% chance of fatal intracrnial bleeding within the first week and the risk varies chiefly with the severity of the stroke and whether the patient is receiving antithrombotic medication (chiefly anticoagulants). However, despite that risk, on average, on long-term follow-up, treated patients will have a reduced level of disability and an improved quality of life. The remaining questions are: what imaging is needed, CT, CTA, MR, perfusion; what to do about wake-up strokes and late-presenting patients: what to do with patients on anticoagulants who have a stroke; is it OK sometimes to lower the dose of tpa; how to deliver treatment in settings where resources for health care are limited? The presentation will review the evidence to date and discuss the key controversies.

Disclosure: I was the Chief Investigator of the IST-3 trial of thrombolysis for stroke

FW15_2

Dichotomous versus ordinal regression analysis of the modified Rankin Scale score in Stroke patients

Y. Roos
Academic Medical Center Amsterdam, The Netherlands

In 2015 the Dutch Mr Clean trial group demonstrated for the first time that endovascular treatment for patients with an ischemic stroke of the anterior circulation not only was safe but also improved clinical outcome. By selecting patients on CT-angiography with a thrombus suitable for endovascular removal, clinical outcome could be increased from a good outcome in 1 out of 5 patients to 1 out of 3 patients. After the publication in the NEJM in only 4 following months these results were replicated and confirmed in three other studies. This has transformed the way stroke patients are being treated all over the world dramatically. As usual, clinical trials answer burning clinical questions, but do also provoke new questions to be solved. Questions like – how to select patients as effectively as possible and how to improve logistics so that patients are being treated as fast as possible – time is brain – for sure it is!

Now, just 2 months ago the 2 year follow-up results of the trial were published, showing that the effect of treatment is sustainable on the long term. All these results will be discussed during the presentation. Moreover, results of a cost-effectiveness study on this new treatment will be presented.

FW15_3

Targeting reperfusion injury

G. Stoll

Würzburg, Germany

Rapid restoration of blood flow by pharmacological thrombolysis and/or mechanical thrombectomy is the mainstay of acute stroke treatment, but does not guarantee a favorable outcome. Reperfusion injury denotes the acute, paradoxically harmful aspect of blood flow return in the ischemic brain which involves platelet activation and, surprisingly, immune cell recruitment. In experimental stroke, glycoprotein (GP) Ibα facilitated tethering of platelets to the postischemic brain endothelium by binding to von Willebrand factor (VWF), while firm adhesion and platelet activation was mediated by GPVI signaling. Accordingly, blocking of platelet GPIbα or GPVI, as well as reducing circulating VWF dramatically improved stroke outcome by protecting the microvasculature during reperfusion and in addition accelerated recanalization during thrombolysis. In contrast, blocking platelet aggregation via GPIIb/IIIa had no therapeutic effect, but led to devastating bleeding complications. In the future it will be essential to further dissect platelet functions involved in reperfusion injury from those indispensable as gatekeepers of hemostasis in the stroke-injured brain in order to improve outcome in acute ischemic stroke.

Focused Workshop 16
Handedness, space and cerebral dominance

FW16_1

What determines handedness?

T. Landis
Lausanne, Switzerland

About 90% of humans are right-handed, irrespective of race, culture, writing/reading direction. Predominant right-handedness is unique for humans. Genetics plays some role in the development of handedness. However, single gene theories (Annett, McManus) have recently been refuted by genome wide association studies. "Anatomical laterality" is under genetic control in animals and humans, but humans with situs inversus are predominantly right-handed. Around the 12th week of gestation 80% of the human foetuses are sucking the right thumb, before the motor cortex is functionally linked to the spinal cord. Ocklenburg et al. (2017) found spinal gene expression asymmetries as a possible molecular basis of handedness. 96% of righthanders have left hemisphere language dominance, but only 27% of lefthanders have right hemisphere or mixed language dominance. It is thus of interest to search for tasks which are truly opposite for left- and right-handers. Animals turn towards the side with less cerebral dopamine. Mohr et al. (2003) found right-handers to turn left and left-handers to turn right, which suggests a link between handedness and dopamine. Dieterich et al. (2003) found in a PET study opposite vestibular dominances in left– and right-handers which suggests a link between handedness and the vestibular system. Handedness, the dopamine and the vestibular system all develop in the first trimester of gestation and dopamine plays an important role for the central processing of vestibular information (Jansen et al.2014). We thus postulate that the level on which handedness is determined resides in an asymmetric development of the vestibular dopamine system.

Disclosure: Nothing to disclose

FW16_2

Cortical vestibular dominance in the non-dominant hemisphere

M. Dieterich
Munich, Germany

All sensory modalities are represented in both hemispheres. The functional characteristics of the vestibular system, however, are distinct from other sensory systems in humans. The bilateral central vestibular system is influenced by three factors that cause a lateralisation of functional weight (dominance): (1) the input of the ipsilateral ear, (2) the input of the right ear that is stronger than that of the contralateral and left ears; (3) a hemispheric dominance in the right hemisphere in right-handed and in the left hemisphere in left-handed humans. This has been determined with caloric irrigation in PET as well as galvanic and auditory evoked vestibular otolith stimulation in fMRI. This lateralisation of vestibular function seems to be also the key to understanding some of the cortical mechanisms of spatial hemineglect and pusher syndrome both of which can be interpreted as disorders of 'higher vestibular function' due to their hemispherical dominance in right-handers. These disorders occur with acute unilateral hemispheric or thalamic lesions predominantly of the right hemisphere, which affect the vestibular cortical network. The dominance is reflected in, for example, a temporary improvement of neglect symptoms during caloric vestibular stimulation or the frequency of pushing behaviour, which is significantly higher in strokes of the right hemisphere than of the left hemisphere. Thus, vestibular dominance and handedness are reciprocally located in the two hemispheres. The question of whether handedness is determined by the lateralization of the vestibular system or vice versa may be related to the ontogenetic evolution of these functions early in life.

Disclosure: Nothing to disclose

FW16_3

Right-hemispheric dominance within frontal cortex for voluntary control of spatial attention

F. Duecker

Maastricht, The Netherlands

Unilateral spatial neglect is more common and severe after right hemisphere damage. It has therefore been theorized that the right hemisphere is dominant in attentional control. Yet, the concept of hemispheric dominance remains rather vague and lacks explanatory power, unless it can be linked to the functional organization of attention networks. Over the last two decades, non-invasive brain stimulation techniques (such as transcranial magnetic stimulation) have been used to temporarily induce attention deficits in healthy volunteers. These studies have revealed distinct hemispheric asymmetries in frontal and parietal cortices that inform us on the nature and extent of right-hemispheric dominance. Importantly, these insights have recently been translated into brain stimulation-based interventions aiming to alleviate attention deficits in (stroke) patients.

Disclosure: Nothing to disclose

Focused Workshop 17
Early diagnostics for outcome prediction after traumatic brain injury

FW17_1

Predictive factors for outcome after mild traumatic brain injury - a multifactorial approach (results from the UPFRONT study)

J. van der Naalt
Groningen, The Netherlands

Mild traumatic brain injury (mTBI) accounts for the majority of TBI and a substantial part of patients shows incomplete recovery. Outcome studies with a multifactorial approach are lacking. The UPFRONT-study is a prospective observational cohort study of patients with mTBI, defined with Glasgow Coma Scale of 13-15, admitted to the Emergency Departments of three Dutch level-1 trauma centres. The aim of the UPFRONT-study is to create a prognostic model for six-month functional outcome combining demographic, injury and psychosocial factors to identify patients at risk for incomplete recovery.

Methods: Information on several injury related and demographic factors was obtained at the ED. Two weeks after injury several questionnaires were used to assess mood (Hospital Anxiety and Depression Scale), emotional distress (Impact of Event Scale), coping (Utrecht Coping List) and posttraumatic complaints. Outcome was assessed six months post-injury with the Glasgow Outcome Scale Extended.

Results: From 2013-2015 in total 1151 patients were included with mean age of 46.5 (SD19.2, range 16-92 years). Almost half of patients (44%) did not achieve full recovery six months after injury. Psychological factors, i.e. early post-injury emotional distress and maladaptive coping in combination with pre-injury mental health, education and age were found to be decisive for outcome in logistic regression analyses (AUC = .80) compared to ED predictors alone (AUC = .72). The presentation will focus on the value of the predictors for six-month outcome, comparing factors that already can be discerned at the ED to information obtained in the postacute phase after injury.

Disclosure: Nothing to disclose.

FW17_2

The role of early biomarkers and metabolites for outcome prediction after TBI

O. Tenovuo
Turku, Finland

TBI as our most complex disease poses a great challenge for reliable biomarker diagnostics, reflected by almost total lack of clinical applications. On the other hand, it is difficult to see how the pathophysiological complexity of TBI could be comprehensively assessed by any other means. Special problems for blood-based biomarkers are the blood-brain-barrier and glymphatic system, whose functions are still insufficiently known and which may have a great influence on the blood levels of brain-derived substances. Biomarkers can be used for diagnostics, treatment monitoring, or prediction – with significant overlaps between these indications. Several attempts have been made to find a 'troponin of the brain', which could show if a TBI has occurred. From a clinical viewpoint, it is relatively unimportant to know if a patient has a minimal rapidly resolving TBI, but it would be extremely important to know the true nature and severity of the TBI. This need is highlighted because of the unreliability and poor specificity of our clinical tools, and insensitivity of current imaging. The outcome is often determined by the extent of diffuse damage, which is poorly measurable with current diagnostic methodologies. Existing research has focused on protein biomarkers, with lots of hope and frequent disappointments. Many of the protein biomarkers studied have shown their ability to predict outcome, but it still remains unproven that they have clinically meaningful predictive value beyond clinical and imaging predictors. Blood metabolites, microRNAs, and exosomes may prove to be better alternatives, but with still limited amount of research.

Disclosure: Nothing to disclose

FW17_3

Early MRI Imaging for assessment of axonal injury in moderate and severe TBI

T. Skandsen

Trondheim, Norway

The primary lesions in traumatic brain injury (TBI) comprise focal/multifocal injury and diffuse injury (axonal as well as neuronal and vascular). In parallel, a cascade of cellular processes take place within the brain parenchyma. Traumatic axonal injury (TAI) typically occurs after traffic accidents and sports injuries with high energy, exposing he brain to acceleration–deceleration- or rotational forces; resulting in mechanical stretching and membrane damage of the axons. TAI is more extensive in severe TBI, but occurs across the whole spectrum of TBI, including mild TBI. Clinical MRI, performed during the first four weeks, depicted TAI in 56% of the patients with moderate and 90% of patients with severe TBI in our studies. Moreover, TAI was typically seen together with other primary types of lesions. TAI lesions that can be informative of prognosis were especially those seen in the corpus callosum and brain stem, but these tend to attenuate over time and may be missed if MRI is performed late. The lesion load in these locations was also associated with outcome in the Trondheim TBI studies as well as in other studies. Findings of our own and other recent studies will be presented as will also recommendations regarding MRI protocol for head injury. Clinical MRI was performed in 200 patients within 72 hours in the Trondheim mild TBI study, depicting intracranial lesions in 12%, which will be discussed. Finally, the value of DTI in research and diagnostic of mild TBI will be briefly reviewed.

Focused Workshop 18
Risks and risk management of immune therapies in neurology

FW18_2
MRI in the diagnosis of opportunistic CNS infections

M.P. Wattjes
Amsterdam, The Netherlands

MRI in the diagnosis of opportunistic CNS infections. In addition to the clinical presentation and paraclinical tests such as cerebrospinal fluid analysis, magnetic resonance imaging (MRI) of plays a crucial role in the detection of opportunistic infections. In the context of multiple sclerosis pharmacovigilance, MRI has become an established screening tools for the early detection of adverse events, preferably at an asymptomatic stage. Opportunistic infections represent broad spectrum of diseases. In the context of immunosuppressive treatment, in particular in MS pharmacovigilance, it has become obvious that progressive multifocal leukoencephalopathy (PML) is the most frequent opportunistic infection. The early detection of PML is associated with a better functional outcome. Recent expert opinion guidelines stressed the importance of MRI screening to detect PML at a very early stage. However, the MRI findings can be subtle and difficult to interpret. This includes in particular the lesion differentiation in terms of clinical relevant differential diagnosis such as MS pathology, vascular pathology and other opportunistic infections. Therefore, the detection of opportunistic infections, in particular for pharmacovigilance purposes, requires a high level of neuroradiological expertise and a good and close collaboration with the treating neurologists.

Disclosure: MPW received speaker and consultancy fees from Biogen, Novartis, Roche, Genzyme and IXICO.

Special Session

Saturday, 24 June 2017

Special Session 7
Parkinson's disease and its genetic connotations in the Mediterranean area

SPS07_2

The clinical genetics of Parkinson's disease

E. Tolosa
Barcelona, Spain

There is convincing evidence that the neurodegenerative process in Parkinson disease (PD) begins many years before the onset of the classical motor symptoms. During this prodromal phase symptoms like REM sleep behaviour disorder, hyposmia or constipation may occur. Important efforts have been applied to define the prodromal phase of LRRK2 associated PD, the most common genetic form of PD. Prodromic diagnostic and disease progression markers would provide crucial information on the onset of the neurodegenerative process in this form of PD and information for the design of disease modification trials to delay or prevent the development of motor PD. Studies in our cohort of LRRK2 non manifesting carriers suggest that the prodromal phase in this condition, unlike the prodromal phase of idiopahtic PD, is clinically quite silent. On the other hand our studies as well as those by others suggest that substantia nigra hyerechogenicity on transcraneal sonography may be an early marker of LRRK2-PD. Also, reduced striatal uptake on DAT SPECT and new NMR imaging may reliably detect changes reflecting ongoing nigral disease. Prospective longitudinal studies to define the usefulness of these markers in predicting phenoconversion to PD in these asymptomatic mutation carriers are in progress.

Disclosure: Nothing to disclose.

SPS07_4

Genetics of Parkinson's disease in North Africa

A. Brice
Paris, France

During the recent years, several genes have been implicated in monogenic Parkinson's disease (PD), such as SNCA, VPS35 and LRRK2 in dominant, Parkin, PINK1, DJ1, FBXO7, PLA2G6, ATP13A2, DNAJC6, SYNJ1 in autosomal recessive and Rab39B in X-linked forms. Other genes have been reported but not confirmed yet. In addition, about 30 other risk factors have been identified. In the Mediterranean area, North Africa encompasses several countries that share the same genetic particularities regarding PD. The first is the very high frequency of the dominant G2019S mutation in the LRRK2 gene which accounts for over 1/3 PD cases whether they are sporadic of familial and associated with a wide range of age at onset. Interestingly, homozygous patients are not more severely or earlier affected than heterozygotes. The mutation found is North African results from a single founder effect. Since many patients do not have a family history of PD, penetrance must be reduced (as low as 15% at 80 years in one of the family studies). A recent study suggests that DNM3 is a modifier of the age at onset. The second characteristic is the high rate of consanguinity that explains the large number of cases due to autosomal recessive genes. Among them Parkin is the most prevalent one followed by PINK1 with a particular nonsense mutation (Q456X) found at a high rate. North Africa represents a region in which the frequency of LRRK2 could contribute to testing future disease modifying treatments and the genetic basis of autosomal recessive PD elucidated.

Disclosure: Nothing to disclose

Sunday, 25 June 2017

Special Session 2
EAN Resident and Research Fellow Section round table: Meet the experts and learn about clinical work and research (clinical and laboratory) around Europe

SPS02_1

Round table discussion on laboratory research

S. Beniczky
Dianalund, Denmark

This presentation will summarize how training in neurology is organized in the Nordic countries. Additionally, the training in sub-specialties (like clinical neurophysiology) will be presented, as well as various possibilities for continuing medical education. There is a broad spectrum of graduate and postgraduate programs in neuroscience in Northern Europe.
Disclosure: Nothing to disclose

SPS02_3

Round table discussion on clinical research

K.R. Chaudhuri
London, United Kingdom

Research spans the exciting crossroad of bench to bedside, the latter reflecting a tangible impact of translation of laboratory data to human lives. As such research should underpin all clinical activities although often this is not the case. Increasingly in the modern world, isolated single investigator led research is becoming difficult to be funded, to be developed or indeed to be published. Collaborations are a key and reflect the ability of researchers also to be able to work outside old fashioned silos and be real team players and team workers. Such work also developed leadership qualities for the future. Many such initiatives exist within Europe, for instance in the Parkinson's field. Empowering younger trainees both in the post-doc as well as undergraduate stage is key to success in clinical work and translational research in the long-term.
Disclosure: Nothing to disclose.

SPS02_4

Round table discussion on laboratory research

M. Filippi
Milan, Italy

This presentation will summarize how training in neurology is organized in Italy and which are the challenges and opportunities for researchers in neuroscience. Research experience is not a requirement for a clinical neurologist, but it can enhance his/her preparation for a career in neurology. Participating in research can enrich understanding of what has been learnt in residency coursework. Understanding more about the process of posing questions and investigating them can enhance neurologist learning experience, and help him/her develop skills that will be of benefit in the work as a physician. On the other side, being a Physician-Scientist in Italy is a busy, challenging but rewarding career that offers opportunities to do well for many people by advancing knowledge, developing new treatments for diseases and pushing back the boundaries of the unknown. Many PhD and Post-Doc programs look for a very specific commitment to translational research, the process of converting knowledge to practical applications at the patient's bedside.
Disclosure: Nothing to disclose.

SPS02_5

Round table discussion on clinical research

A. Siva
Istanbul - Cerrahpasa, Turkey

In this Resident and Research Fellow Section Round Table Coffee that will focus on the clinical work and clinical and laboratory research around Europe, I will try to provide some information regarding neurological training in the medical schools in Turkey, the neurology residency programs and finally on postgraduate neurology educational activities. Since The Turkish Neurological Society is a strong society and represents majority of neurologists in the country, though briefly, I will mention mainly about its educational policies and its role in supporting young neurologists in training and in research. Then, I will end up with an update on the hot topic regarding the wish of many young neurologists & neuroscientist who wish to do research. This issue, unfortunately is dominated currently more by limitations rather than options and possibilities. However, despite research grants are few and limited in amount, for a persistent researcher there are a number of options that could be looked for. These are institutional, central-national grants and a few private enterprise donations. The conclusion will be how our expectations start and how real life ends.

Special Session 3
ILAE-CEA/EAN: Epilepsy

SPS03_1

Differential diagnosis

H. Stefan
Erlangen, Germany

Introduction: A wrong diagnosis of epilepsy is made in 20% of patients. Depending on the patient selection criteria even up to 70% are wronly diagnosed.

Methods: Difficult to diagnose non-epileptic and epileptic seizures are demonstrated using video-EEG documentations, MRI, polygraphic and MEG recordings.

Results: The analysis of these cases indictae that several facts fascilitate diagnostic errors like missing informations by eye witness using wrong red flags as warning with regard to misdisagnosis, insufficient knowledge concerning seizure type and incomplete recognition of ictal signs. Clinical criteria for diagnostic strategies are shown.

Conclusion: In cases with doubts with regard to giagnosis of epileptic seizures home video documentation or video-polygraphic recording should be performed.

Disclosure: Nothing to disclose.

SPS03_3

SUDEP

L. Sander
UCL Institute of Neurology, London,, United Kingdom

People with epilepsy particularly those whose seizure are uncontrolled by treatment are much more likely to die prematurely than those without. SMRs of in those with epilepsy is between 2 and 3. In the UK, the commonest epilepsy-related is due to the so called Sudden Unexpected Death in Epilepsy (SUDEP) which accounts for up to one fifth of deaths in some series. SUDEP is more common in those with drug-resistant epilepsy, the annual incidence being as high as one in 100/patient years. Most SUDEP cases are unwitnessed: the commonest circumstance is people found dead in bed or by the bed. Convulsive seizures are the most important risk factor particularly if frequent and nocturnal. Causes are unknown but the most commonly suggested mechanisms for SUDEP are cardiac arrhythmias, respiratory depression and "cerebral shutdown". Full clarification of risk factors and establishment of the mechanisms of SUDEP are important so that preventative measures are put in place to decrease the burden of SUDEP.

Disclosure: LS is based at UCLH/UCL Biomedical Research Centre, which receives a proportion of funding from the UK Department of Health's NIHR Research Centres funding scheme. He receives support from the Dr Marvin Weil Epilepsy Research Fund and the UK Epilepsy Society endows his current position. He has received research grants and honoraria from UCB, Eisai, Teva, Lundbeck and GSK which are involved in the manufacturing of antiepileptic drugs.

SPS03_4

Timing of epilepsy treatment

P.A. Boon
Ghent, Belgium

The goal of medical treatment for epilepsy is to render the patient seizure-free without inducing intolerable side effects. The standard first-line treatment is chronic administration of anti-epileptic drugs (AEDs), typically after a second seizure or even after a first one when the likelyhood of a second one occurring is high. These drugs mainly target the disturbed excitation/inhibition equilibrium by blockage of voltage-gated ion channels, stimulation of the inhibitory GABA-ergic system or inhibition of the excitatory glutamatergic system. Depending on seizure type, epilepsy syndrome, medical history and age of the patient, monotherapy with a specific AED is started. When no optimal response can be achieved, a second monotherapy is commenced. If this too is unsuccessful, a combination therapy of AEDs is administered, although the exact way of substitution or combination is still controversial. Around 60% of the patients respond to monotherapy, but only 5% are aided with subsequent regimens if the second AED fails. A leading cause for therapy failure are the adverse effects associated with AEDs, which can have a considerable negative impact on a patient's life. New AEDs are reported to have a more favorable tolerability and toxicity profile compared to the old ones. However, more than 30% of the patients with epilepsy today remain refractory, even with more than fifteen AEDs available on the market. Refractoriness is defined when 'adequate trials of two tolerated, appropriately chosen and used AED schedules, whether as monotherapy or in combination, fail to achieve sustained seizure freedom. For patients with drug-refractory epilepsy other treatment options can be considered such as epilepsy surgery, neurostimulation, dietary treatments and immune-based therapies.

Special Session 4
Rare neurological diseases

SPS04_1

Dementia not only Alzheimer's diseases: From bed to bench and contrary

A. Federico
Sienna, Italy

The concept of Dementia is usually linked to Alzheimer's disease and related disorders not considering that many other conditions may cause memory loss and dementia mimicking a presenile or juvenile onset Alzheimer's diseases (AD). These conditions may be associated to neuroimaging abnormalities mainly involving cortex (cortical atrophy) or white matter (leukoencephalopathy) or basal nuclei or cerebellum and may be related to lysosomal, peroxysomal, mitochondrial, and other cell organelles dysfunctions. We will report the clinical, neuropathologic, biochemical and molecular genetic data of these syndromes. For some disorders, like Niemann Pick type C disease, we will report the neuropathologic similarities with Alzheimer's disease, consisting in brain tau and neurofibrillary tangles accumulation, indicating that NPC gene may interact with these protein leading similar changes to AD. Finally we will report several clinical criteria and diagnostic algorythms helping in the diagnostic suspicions, that may be confirmed by further biochemical and molecular results. For many of the diseases, early diagnosis may help in the therapeutic possibility and since the majority of the disorders has a genetic origin, it may lead to genetic counselling and prevention

Disclosure: Nothing to disclose.

SPS04_2

Rare causes of stroke

M. Dichgans
Munich, Germany

In up to 30% of patients with acute ischemic stroke the underlying mechanisms remains unknown. Less frequent causes of stroke that may easily be overlooked include arterial dissection, atheroma of the aortic arch, hereditary conditions (e.g. CADASIL, CARASIL, COL4A1/A2-related angiopathies, Fabry Disease), vasculitis, reversible cerebral vasoconstriction syndrome, thrombopilia (e.g. antiphospholipid antibodies; Sneddon syndrome), hematological disorders, and some cardiac disorders. The presentation will provide clinical guidance how to approach these conditions in clinical practice.

Disclosure: HORIZON 2020 | EU FP7 |DFG/DLR | BMBF | DZNE | Fondation Leducq | Vascular Dementia Research Foundation | Wellcome Trust | Corona Foundation | Friedrich-Baur Foundation | Josef-Hackl-Foundation | Intramural funds LMU | Alzheimer Forschung Initiative e.V. (AFI)

Monday, 26 June 2017

Special Session 5
New Neurological Guidelines

SPS05_2

ESO-EAN Guideline on cerebral venous thrombosis

J.M.M.C. Ferro
Lisbon, Portugal

Introduction: We followed the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system, formulating relevant diagnostic and treatment questions, performing systematic reviews of all available evidence and writing recommendations and deciding on their strength on an explicit and transparent manner, based on the quality of available scientific evidence. The guideline addresses both diagnostic and therapeutic topics.
Results: We suggest using MR or CT angiography for confirming the diagnosis of CVT and not screening patients with CVT routinely for thrombophilia or cancer. We recommend parenteral anticoagulation in acute CVT and decompressive surgery to prevent death due to brain herniation. We suggest to use preferentially low molecular weight heparin in the acute phase and not using direct oral anticoagulants. We suggest not using steroids and acetazolamide to reduce death or dependency. We suggest using antiepileptics in patients with an early seizure and supratentorial lesions to prevent further early seizures. We could not make recommendations due to very poor quality of evidence concerning duration of anticoagulation after the acute phase, thrombolysis and/or thrombectomy, therapeutic lumbar puncture, and prevention of remote seizures with antiepileptic drugs. We suggest that in women who suffered a previous CVT, contraceptives containing oestrogens should be avoided. We suggest that subsequent pregnancies are safe, but use of prophylactic low molecular weight heparin should be considered throughout pregnancy and puerperium.
Conclusions: Multicentre observational and experimental studies are needed to increase the level of evidence supporting recommendations on the diagnosis and management of CVT
Disclosure: Nothing to disclose.

SPS05_3

Trigeminal Neuralgia

L. Bendtsen
Copenhagen, Denmark

Trigeminal neuralgia (TN) is an extremely painful disorder, which can be difficult to diagnose and treat. There is therefore a great need for comprehensive guidelines for management of TN. The existing EFNS guideline is excellent. However, since 2008 the diagnostic criteria for TN from the International Headache Society have been changed and important new knowledge has emerged regarding diagnosis, clinical characteristics and imaging and new drugs are emerging. Moreover the recommendations for preparation of guidelines have been updated, in particular has the GRADE system been adopted. The guideline for TN management therefore needs revision. A task force of experts from seven different countries in Europe has been established. The revision is planned to be finalized in 2018. This lecture will present the process and difficulties of the guideline production and the parts of the guideline that are most in need of an update, with updating of new scientific evidence after 2008.
Disclosure: Not received

SPS05_4

Clinical use of F-fluorodeoxyglucose Positron Emission Tomografy (FD-PET) in dementia

M. Boccardi
Brescia, Italy

Introduction: Recommendations for use of FDG-PET to diagnose dementing neurodegenerative disorders are lacking.
Methods: We defined 21 PICO questions on diagnostic issues and for recommending semiautomated analysis to assist visual reading, performed literature reviews and assessed evidence based on study design, gold/reference standard, effect size, risk of bias, results inconsistency, imprecision, and indirectness. Critical outcomes were sensitivity, specificity, accuracy, positive/negative predictive value, area under the curve (AUC), and positive/negative likelihood ratio of FDG-PET in detecting the target conditions. Based on such evidence and expertise, a Delphi panel of experts defined consensual recommendations.
Results: Gold standard (pathology/biomarker confirmation) for assessing FDG-PET-based diagnosis was available in 38.1% of searches, the others providing clinical follow-up (28.6%) or only clinical diagnosis (28.6%). Accuracy versus gold-/reference-standard was available for the comparator term (clinical diagnosis) in only two PICOs. The Delphi panel agreed on recommending the use of FDG-PET for 15 PICOs (diagnosing MCI due to AD, FTLD or DLB, atypical AD, and pseudodementia; differential diagnosis between AD and DLB, FTLD, or VaD, between DLB and FTLD, and between PD and PSP; discriminate pathophysiological

process in CBS; discriminate clinical and molecular features of PPA; detecting PD- and ALS-related cognitive decline; recommending semiautomated assessment to assist visual reading). PICOs relating to preclinical diagnosis led to lack of recommendations.

Conclusions: Despite large use, FDG-PET maturity as a biomarker still suffers from limited quantitative formal evidence. Recommendations are based partly on evidence and partly as good practice points derived from Consensus, with issues needing further research.

Disclosure: Nothing to disclose.

Special Session 6
EFNA/EAN: Eliciting patient's preferences for effective shared decision-making

SPS06_1
Information: How to support patients to take evidence-based decisions

C. Heesen
Hamburg, Germany

Patient information is a prerequisite of patient involvement in decision making founded in the bioethical right of patient autonomy. It is therefore at the core of patient centred medicine which is increasingly developing as a paradigm in medicine. In clinical guidelines but also legal advices patients gain more right but also duties to be informed. While a plethora of medical information exist very few follow rigorous development guidelines. Evidence-based patient information (EBPI) is probably the most elaborate approach in this area which means including patients in the development process and communicating study findings in numbers and graphical formats at best based on systematic reviews. At best EBPI is tested in clinical studies from phase 1-3 comparable to drug developments with the ultimate goal to improve disease adjustment. EBPI is especially relevant in chronic conditions with ambiguous management options. Clinical Neurology includes therefore many scenarios in which this approach can be regarded as the ideal management concept. Examples include decision making on prophylaxis in migraine, decision making on antiepileptic treatment, choice of anticoagulation after cardioembolic stroke, decision making on L-Dopa or apomorphin pump or brain stimulation in Parkinson's disease and immunotherapy in multiple sclerosis. However, as reasoning and decision making might be substantially impaired in neurological conditions neurology imposes considerable challenges f.e. in decisions on treatments in dementia or palliative care. However, fueled by research from oncology and psychiatry evidence is increasing that even here substantial patient involvement is possible. While medical information traditionally has been given via physicians especially the internet has revolutionized patient information, not always at the sake of patients. But as well physicians receive a wealth of information but often from pharmaceutical companies which is often biased. This underlines the need of information based on transparent development guidelines. But EBPI includes other challenges, a major one is communication of medical data which are often difficult to understand even for physicians. Another one is updating which needs considerable ressources. Web-based information modules such as lectures, podcast, educative videos offer many opportunities. Combining web-based at best individually tailored information with face-to-face information in structured decision making processes might be perspective. But in general the developments are slowly and even more so in neurology. In most areas in neurology EBPI virtually do not exist. Some efforts have been made in multiple sclerosis.

Disclosure: Nothing to disclose.

SPS06_3
The impact of carer 'shared (disease management) responsibility' on 'shared decision making' for older persons managing multimorbidity.

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Introduction: For older persons with multimorbidity (PwMs), self-management is a complex process that involves integration of knowledge and tasks for multiple, and often interacting, chronic diseases (1). Shared decision making (SDM) refers to clinicians working together with patients and/or their caregivers to decide which care plan best fits individual patients and their lives, when there is more than one reasonable option (2). The current study aimed to understand the role of caregiver support related to SDM for older PwMs (aged over 65). The data presented were collected as part of an extensive requirements gathering exercise to inform the design of ProACT, a digital health ecosystem that aims to support self-management and improve integration of care for older PwMs.

Methods: Semi-structured qualitative interviews and focus groups were conducted with 38 older PwMs, 17 informal carers and 22 formal care workers across the Irish and Belgian health systems. Interviews and focus groups were transcribed and analysed using thematic analysis.

Results: PwMs in Belgium availed of higher levels of carer support and 'shared responsibility' for disease management with their carers. This was reported as having a potentially positive impact on SDM.

Conclusion: Increased support from caregivers to PwMs may have a positive impact on improving SDM, due to the enhanced 'shared responsibility' between PwMs and carers to disease management.

1. Bayliss, E. A., Ellis, J. L., & Steiner, J. F. (2007). Barriers to self-management and quality-of-life outcomes in seniors with multimorbidities. Annals of Family Medicine, 5(5), 395–402.
2. Van der Flier, W.M., Kunnemann, M., Bouwman, F.H., Petersen, R.C., Smeets, E.M.A. (2017). Diagnostic dilemmas in Alzeimher's disease: Room for shared decision making. Alzeimher's and Dementia: Translational Research and Clinical Interventions, 3(3), 301-304.

Tournament Sessions

Sunday, 25 June 2017

Tournament Basic

TBAS01

TOMM40 polymorphism is associated with cognitive and CSF pathology in patients with dementia

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Background and aims: In this study, we investigated whether variable-length poly-T sequence polymorphism (rs10524523) in the gene encoding translocase of the outer mitochondrial membrane 40 homolog (TOMM40) may contribute to mild cognitive impairment (MCI) and Alzheimer's disease (AD) pathology, and whether it poses as a risk factor for disease progression.
Methods: We enrolled 267 MCI patients and 141 AD patients from the Alzheimer's Disease Neuroimaging Initiative database. Participants were homozygous for APOE ɛ3 and stratified according to poly-T length into homozygous for short (S/S, n=46), homozygous for long (L/L, n=51), homozygous for very long (VL/VL, n=44) and heterozygous (S/L, n=82; S/VL, n=100; L/VL, n=85) groups. We compared clinical symptoms, cerebrospinal fluid (CSF) biomarkers and magnetic resonance (MR) imaging variables amongst these groups and carried out a Cox proportional hazard regression analysis to determine the predictive value of TOMM40 rs10524523 poly-T length in cognitive decline.
Results: Patients with S/L, L/L and L/VL genotypes exhibited worse cognitive performance (ADAS-Cog11: $P<0.05$; ADAS-Cog13: $P<0.05$), and exhibited higher CSF total tau, phospho-tau and decreased CSF Aβ42 levels ($P<0.05$) in comparison to other groups. 309 subjects (75.7%) had an annual decline of 2 or more points on MMSE and 176 subjects (43.1%) had an annual increase of 5.5 points on ADAS-Cog11. L/L genotype (MMSE: [HR]= 2.218, Confidence Interval [CI]= 1.325-3.715, P=0.002; ADAS-Cog11: [HR]= 2.094, [CI]= 1.120-3.917, P=0.021) was a predictor of cognitive decline.
Conclusion: Our results demonstrate a pathogenic role of the L TOMM40 rs10524523 variant in MCI and AD patients and its value in predicting cognitive decline.
Disclosure: Nothing to disclose

TBAS02

Structural organization of the brain connectome in patients with amyotrophic and primary lateral sclerosis

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Background and aims: Consistent motor and extramotor brain pathology supports the notion of motor neuron disease as a system failure. Graph theory is a tool capable of capturing interconnected brain activity/structure at system levels. This study investigated structural and functional neural pathways organization in amyotrophic (ALS) and primary lateral sclerosis (PLS).
Methods: 61 patients with ALS, 29 patients with PLS and 40 healthy controls underwent Diffusion Tensor (DT) and resting state functional MRI. Graph analysis and connectomics assessed global and local topological network properties and intra- and inter-hemispheric between-lobe connectivity.
Results: Both patient groups showed reduced mean structural and increased mean functional local efficiency of the sensorimotor network relative to controls. Moreover, PLS patients showed a reduced functional path-length of the frontal/parietal networks relative to ALS. At the regional-network level, compared to controls: ALS and PLS patients showed structural alterations within the sensorimotor networks; and PLS patients had increased functional connectivity within sensorimotor/basal ganglia networks. ALS and PLS patients showed reduced inter- and intra-hemispheric between-lobe structural and functional connectivity, involving sensorimotor/basal ganglia and frontal regions, while an enhanced interhemispheric connectivity was observed between parietal and basal ganglia nodes. The involvement of frontal connections was greater in ALS relative to PLS. In ALS patients, there was a strong positive correlation between differences in functional and structural connectivity between patients and controls.
Conclusion: This study showed widespread motor/extra-motor network degeneration in ALS and PLS, suggesting that graph analysis and connectomics might represent a powerful approach to detect upper motor neuron

degeneration, extra-motor brain changes and network reorganization.

Disclosure: Italian Ministry of Health (#RF-2011-02351193).

TBAS03

Identification of Usp8 as a toxicity modifying Deubiquitinase for α-synuclein

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[1]University of Oxford, Oxford, United Kingdom, [2]Harvard University, Boston, USA

Background and aims: In Parkinson's disease, misfolded α-synuclein accumulates, often ubiquitinated, in neuronal inclusions termed Lewy bodies. It is unknown whether ubiquitin conjugation in Lewy bodies is due to a defect in enzymes that regulate α-synuclein degradation. Identification and pharmacological modulation of such enzymes could be targeted for therapies.

Methods: Comparative immunohistochemistry and immunoblotting between three brain regions was used to determine the type and abundance of ubiquitin conjugates and relevant interacting proteins in Lewy bodies. iPSc-derived neurons, cultured cells and purified proteins were used to investigate the functional interaction between the two proteins, includeing transient overexpression and shRNA-mediated knockdown. Drosophila genetics were used to study the effect of Usp8 and other deubiquitinases against α-synuclein toxicity in vivo.

Results: We found that ubiquitin immunoreactivity in Lewy bodies is largely due to K63-linked ubiquitin chains, is markedly reduced in the substantia nigra compared to the neocortex and inversely correlates with the content and pathological localization of the deubiquitinase Usp8. Usp8 interacted and partly co-localized with α-synuclein in endosomal membranes and both in cells and after purification, it deubiquitinated K63-linked chains on α-synuclein. Knockdown of Usp8 in the Drosophila eye reduced α-synuclein-induced eye toxicity and reduced α-synuclein levels both in Drosophila and in human cells. In Drosophila dopaminergic neurons, unlike knockdown of other deubiquitinases, Usp8 protected from α-synuclein-induced locomotor deficits and cell loss.

Conclusion: Our findings suggest that removal of K63-linked ubiquitin chains on α-synuclein by Usp8 is a critical mechanism in slowing α-synuclein degradation in dopaminergic neurons that may contribute to α-synuclein accumulation in Parkinson's disease.

Disclosure: Nothing to disclose

TBAS04

Promising and highly diagnostic fMRI paradigms for classifying the level of consciousness of patients with severe chronic disorders of consciousness

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Background and aims: Diagnosis and prognosis of patients with severe chronic disorders of consciousness (scDOC) is still a problem and up to know there are no reliable diagnostic tools. Hence a rate of 43% of misdiagnosis was described. Neuroimaging methods, especially fMRI, seem to give additional information of the state of consciousness but specific and reliable paradigms have to be developed and tested.

Methods: Patients with scDOC undergo fMRI in our clinic. We test different paradigms starting from simple ones like vibration over language understanding to imagination. Patients who cannot or do not want to lie still for the duration of the scanning are anaesthetised using Sevoflurane and Fentanyl. FMRI is performed with a clinical routine 3-Tesla MR.

Results: First results of the vibration paradigm show a correlation between the results and remission of the patient (see figure 1). The vibration paradigm can also be performed under anaesthesia i.e. reasonable results were found. Moreover a study including 27 scDOC patients showed that language paradigms are essential and led to the change of diagnosis in 16 patients (see figure 2 for some examples). Most frequent language activity could be seen within the occipital lobes whereas rare activity was detected within the inFiguferior frontal region.
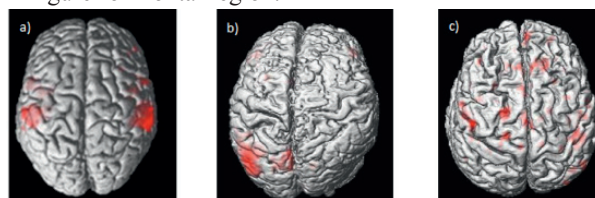
Figure 1: a) Group analysis of n=8 subjects, vibration on the right index finger b) Patient 1: vibration on left thumb and index finger; recovered quickly c) Patient 2: vibration on left thumb and index finger; has not shown any remission up to now
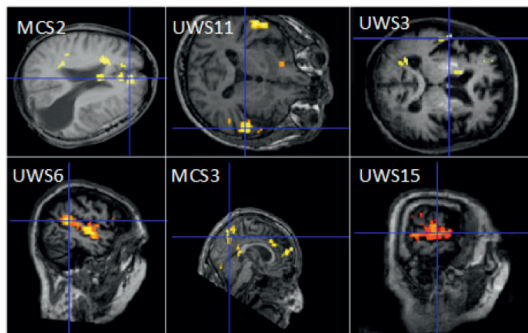
Figure 2: Minimally Consious State (MCS) 2: own name > unfamiliar name; Unresponsive Wakefulness Syndrome (UWS) 11: own name > rest; UWS 3: meaningful sentence > rest; UWS 6: meaningful sentence > meaningless sentence; MCS 3: own name > rest; UWS 15: meaningful sentence > rest

Conclusion: In order to avoid misdiagnosis in scDOC patients we propose a special diagnostic battery of fMRI paradigms which at least should contain language paradigms to minimize diagnostic errors. Moreover we also recommend to include different imagination paradigms as well as testing the proprioceptive nervous system e.g. by vibration.

Disclosure: Nothing to disclose

TBAS05

Sensory attenuation phenomena: Is it the neurophysiological mechanism underlying modulation of beta oscillations?

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Background and aims: Several studies suggest that pathological high amplitude of beta oscillations may cause bradykinesia and other motor symptoms in Parkinson's disease (PD). Recently, it has been showed that PD patients have abnormality in a neurophysiological phenomenon labelled sensory attenuation. Here, we tested the hypothesis that the abnormality in this mechanism has a causal link with the typical abnormality in beta oscillations in PD.

Methods: Eighteen right-handed patients with idiopathic PD and 24 age-matched healthy participants were studied. Somatosensory evoked potentials were elicited after electrical stimulation of the median nerve at the wrist. Electrical activity was recorded at the scalp using a 128 channels EEG. Somatosensory evoked potentials were recorded in 2 conditions: at rest and at the onset of movement (a self-paced abduction movement of the right thumb).

Results: Healthy participants showed attenuation of the N20-P25 amplitude at movement onset (2.13 ± 1.87) compared to rest condition (4.8 ± 2.84) ($P<0.05$). PD patients OFF medication showed mild attenuation of the N20-P25 component at movement onset (3.99 ± 2.31) compared to rest condition (5.03 ± 3.29) ($P<0.05$), whereas they did show greater attenuation of the N20-P25 component at the onset of movement (2.59 ± 1.79) compared to the rest condition (5.02 ± 2.94) when ON medication ($P<0.05$). Preliminary analysis demonstrated a significant relationship between the amplitude of sensorimotor beta power prior to the median nerve stimulation and the amplitude of the SEP.

Conclusion: These results confirmed a significant link between dopaminergic modulation and sensory attenuation.

Disclosure: Medical Research Council

TBAS06

Neurofilament light chain and phosphotau/tau ratio as CSF biomarkers in frontotemporal dementia

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Background and aims: Neurofilament light chain (NfL) in cerebrospinal fluid (CSF) is elevated and the phosphotau/tau ratio (p/t-tau) decreased in frontotemporal dementia (FTD). Additionally, p/t-tau may discriminate FTD with TDP43 inclusions (FTLD-TDP) from tau pathology (FTLD-tau). We examined the diagnostic potential of these individual biomarkers in a large FTD cohort.

Methods: CSF NfL and p/t-tau levels were compared between 45 cognitively healthy controls, 181 behavioral variant FTD (bvFTD), 16 FTD with motor-neuron disease (FTD-MND), 36 semantic dementia (SD), 19 progressive non-fluent aphasia (PNFA), 42 corticobasal syndrome (CBS), and 64 progressive supranuclear palsy (PSP) patients. 50 FTLD-TDP and 23 FTLD-tau patients were included.

Results: CSF NfL was higher in all patient groups than controls ($p < 0.001$, sensitivity 79%, specificity 89%), higher in FTD-MND patients than all other patients, and equally elevated in bvFTD, SD, PNFA, CBS, and PSP. p/t-tau was lower in all patients than controls ($p < 0.001$, sensitivity 73%, specificity 93%), and the lowest in FTD-MND patients. NfL did not discriminate FTLD-TDP from FTLD-tau patients ($p = 0.08$), whereas the p/t-tau ratio did (specificity 81%, sensitivity 65%). In all patients combined, high NfL and low p/t-tau levels were associated with a high CDR-SB (NfL: rs=0.38, $p = 0.005$; p/t-tau: rs=-0.29) and with poor survival (estimated hazard ratio on tertiles NfL: 1.7, p/t-tau: 0.7).

Conclusion: CSF NfL and the p/t-tau ratio were associated with disease severity and prognosis in FTD and therefore interesting surrogate endpoints in clinical trials. Both biomarkers discriminated FTD from controls, but not the individual subtypes, apart from FTD-MND. The p/t-tau ratio discriminated FTLD-TDP from FTLD-tau.

Disclosure: Nothing to disclose

Monday, 26 June 2017

Tournament Clinical

TCLIN01

Neurological complications of acute virus E infection (NeuroCAVE): An observational, prospective Swiss study

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Background and aims: In 2014 an association between acute hepatitis E and neuralgic amyotrophy was described. We prospectively followed-up 52 cases of acute HEV in Ticino (Southern Switzerland) to study the neurological complications associated with HEV infection.
Methods: All adults (18-90 y.o.) consecutively diagnosed (IgM+ and IgG+ ; HEV RNA+/-) since January 2015 underwent neurological examination and, when indicated, further exams (lumbar puncture, EMG, brachial plexus and cervical MRI, cervical root high-resolution ultrasound). Patients were followed up for 6 months.
Results: The majority of patients accessed to the Emergency Department with acute neurological symptoms and were hospitalized. HEV RNA was positive in 15/52 cases, in whom genotype 3 was identified. Overall, we diagnosed 14 neuralgic amyotrophy cases, 19 patients with myalgia and one case of transverse myelitis. Neuralgic amyotrophy was bilateral (although asymmetric) in 9 cases and more common in males, whereas myalgia (with or without CK increase) occurred more frequently in females. Eight cases of neuralgic amyotrophy were confirmed with EMG, showing involvement of the upper trunk of the brachial plexus. Eight NA patients were treated with immunoglobuline, 3 with oral prednisone. Patients with myalgia were not treated and recovered within one month. The common findings of cerebrospinal fluid analysis, MRI and ultrasound in neuralgic amyotrophy patients will be presented.
Conclusion: This is the first prospective study on neurological complications in hepatitis E. Neurological complications of acute HEV genotype 3 infection are frequent among patients, even in cases with mild hepatitis, and consist mainly in neuralgic amyotrophy and myalgia.
Disclosure: Nothing to disclose

TCLIN02

When to stop antiepileptic drugs? A new tool for individual prediction of seizure outcomes.

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Background and aims: When faced with a seizure free person with epilepsy, the question may rise whether antiepileptic drug (AED) treatment is still necessary. Stopping AEDs carries the risk of seizure recurrence, and although many publications studied predictors of seizure outcome it is difficult to apply this knowledge to the individual patient. We created an individualised prediction model for seizure recurrence and long-term seizure outcome, through an Individual Participant Data meta-analysis.
Methods: Systematic review of literature identified all candidate predictors and eligible publications, of which authors were contacted to provide individual participant data. Through regression analysis the strongest predictors were selected. Internal-external cross-validation was performed to ensure generalizability. Ultimately, nomograms were created to visually represent computed prediction models.
Results: Ten cohorts with 1771 patients were gathered, with both children and adults, of which 812 (46%) experienced seizure recurrence and 9% had seizures in the last year of follow-up (median 5.3 years, range 0-23 years). Prediction models for seizure recurrence (c-statistic: 0.65; 95%CI 0.65-0.66) and chance of long-term seizure freedom (c-statistic: 0.71; 95%CI 0.70-0.71) were created with good calibration and stable validation across all ten populations.
Conclusion: It is now possible to compute combined risks of seizure recurrence and the chance of long-term seizure freedom after AED withdrawal. The nomograms are based on a large cohort, validated in both children and adults, and will aid consultation of seizure free people with epilepsy. The nomograms may therefore guide the physician as well as the patient in person-tailored choices.
Disclosure: Nothing to disclose

TCLIN03

Sustained disease remission in aggressive multiple sclerosis after autologous haematopoietic stem cell transplantation

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Background and aims: Despite the advent of new highly-active therapies for multiple sclerosis (MS), long-term disease remission remains elusive and only a small percentage of patients achieves the-so-called no evidence of disease activity (NEDA) status. Against this scenario, autologous haematopoietic stem cell transplantation (AHSCT) has recently demonstrated the potential to maintain disease remission in aggressive MS patients. Our aim was to investigate the long-term efficacy and safety of AHSCT in a multicentre cohort of aggressive MS patients.

Methods: We analyzed data from 35 consecutive patients with aggressive MS (77% relapsing-remitting MS, 23% active secondary progressive MS) treated with AHSCT at Neurologic Departments of Genoa and Turin between 1998 and 2015. All patients underwent the same transplant protocol made of cyclophosphamide followed by carmustine-cytarabine-etoposide-melphalan (BEAM) plus anti-thymocyte globulin. NEDA status (a composite of absence of relapses, no sustained disability progression, and no new T2 or T1 gadolinium-enhancing lesions on MRI), disability scores and reports of adverse events were collected.

Results: NEDA status was achieved by 33 of 35 patients (94%) at 1 year, 21/25 (84%) at 3 years and 11/14 (79%) at 5 years. Improvement was noted in neurologic disability from a median pre-transplant disability score of 6,5 to 6 at 5 years. Adverse events were consistent with expected toxic effects associated with AHSCT and no treatment related mortality was reported.

Conclusion: Our data demonstrate that AHSCT is extremely effective for inducing long-term disease remission in aggressive RRMS patients and it is associated with improvements in neurologic functions.

Disclosure: Nothing to disclose

TCLIN04

Predictive Swallowing Score (PRESS): A prognostic model to predict the need for enteral tube feeding after ischemic stroke.

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Background and aims: Predicting the duration of dysphagia after stroke is important to guide early therapeutic decisions. Guidelines recommend nasogastric tube feeding if dysphagia persists for ≥7 days and PEG placement if dysphagia does not recover within 30 days. We developed and validated a prognostic instrument to predict dysphagia recovery.

Methods: Predictive Swallowing Score (PRESS) was developed in 153 consecutive ischemic stroke patients with initially severe dysphagia. Swallowing was evaluated at four standardised time points and time to dysphagia recovery was analysed using Cox proportional hazards models. We prospectively validated this model in 99 subjects and determined its performance with the area under the receiver operating characteristic curve (AUC) and calibration plots.

Results: The final prognostic model included five variables: age, stroke severity, lesion location, initial dysphagia severity, and initial risk of aspiration. PRESS scores range from 0 to 10 points and were a significant predictor of time to dysphagia recovery (p<0.001). Risk prediction estimates (see Figure) range from 4% to 93% for the need for nasogastric tube feeding and from 0% to 78% for PEG feeding, covering the entire spectrum from rapid to prolonged dysphagia recovery. Model performance in the validation cohort showed an AUC of 0.78 adjusted for overoptimism (p<0.001). Calibration plots indicated high agreement between predicted and observed outcomes. PRESS performed equally well in both hemispheric and brainstem stroke.

Prediction estimates of dysphagia recovery according to Predictive Swallowing Score (PRESS) values.

Conclusion: We have developed and successfully validated an easily applicable prognostic score that can be used to predict the need for nasogastric tube feeding or PEG placement after ischemic stroke.

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TCLIN05

Seizures are locked to multidien rhythms in epilepsy

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Background and aims: Epilepsy is defined by the seemingly random occurrence of seizures. However, recent quantitative analyses revealed circadian[1] and cluster organization[2], suggesting that brain activity is regulated over long timescales. A central but unresolved question concerns the relationship of seizure timing to Interictal Epileptiform Activity (IEA). We analyzed chronic recordings from 37 patients implanted with the Responsive NeuroStimulation system[1] for months to years.

Methods: We formatted IEA hourly counts into continuous time-series and applied wavelet decomposition to resolve component rhythms into periodograms and to estimate instantaneous phase of peak periodicity. We used circular statistics (mean resultant vector length, Omnibus test) to accommodate for varying patient-specific periodicities and study phase locking of seizures in a subset of 14 patients who had reliable seizure detection.
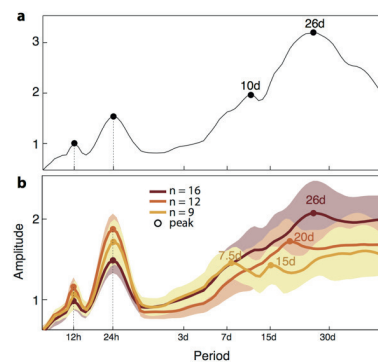
Figure 2. Periodograms of IEA counts from the same subject as in Figure 1 (a) and from all 37 subjects clustered in three groups for better visualization revealed ultradian, circadian, and multidien peaks.
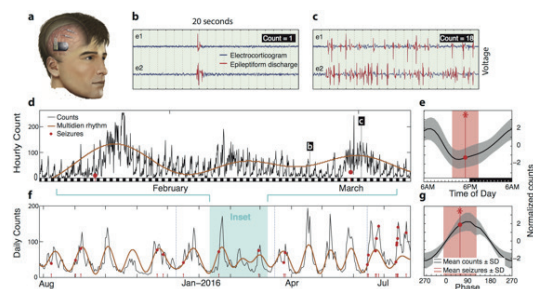
Figure 1. Representative subject showing the implant (a), the detections (b and c) and demonstrating circadian (d) and multidien rhythms in IEA (f). Average normalized amplitude of the circadian and multidien rhythms show phase-locking of seizures at the trough and peak, respectively (e and g, *p < 0.01, Omnibus test).
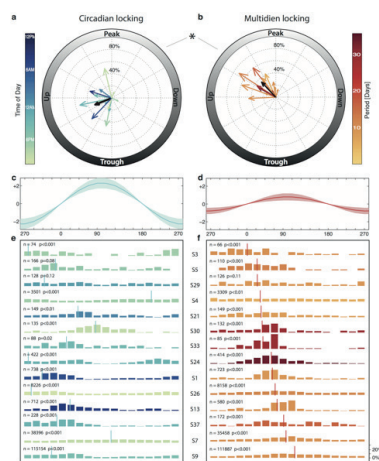
Figure 3. Phase analysis of seizures (N=14 subjects) in relation to underlying circadian (a,c,e) and multidien (b,d,f) IEA rhythm revealed phase locking to rising phase that was more consistent for multidien as compared to circadian rhythm (*p=0.002, Kuiper two-sample test).

Results: We confirmed a circadian distribution of IEA, but more importantly, unraveled superimposed multidien (multiple days) rhythms of IEA that were specific to each subject (Figure 1) and independent of gender or seizure localization. Within subjects, these long periodicities were robust and stable for up to 10 years (Figure 2). Seizures were phase-locked to the underlying multidien rhythm, occurring preferentially during the days-long upslope of IEA (p<0.05 for 13 out of 14 subjects, Figure 3).

Conclusion: Our findings indicate that seizures are not random events and that multidien rhythms of IEA are a critical biomarker for seizure prediction and potentially preventative treatment strategies on the scale of weeks.

References

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TCLIN06

Mechanisms of apathy in REM sleep behaviour disorder

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Background and aims: Apathy is a common and debilitating feature of Parkinson's disease (PD). Our recent studies suggest that blunting of sensitivity to rewards, indexed by pupil dilatation, might be an important underlying mechanism. Whilst PD patients commonly report apathy prior to motor symptoms, it has not been formally evaluated in prodromal cohorts. Patients with idiopathic Rapid Eye Movement Sleep Behaviour Disorder (RBD) have a high probability of developing PD. Here we assess the prevalence of apathy in RBD and investigate whether apathetic RBD individuals show similar blunted reward sensitivity. We explore the relationship between these measures and dopaminergic neuroimaging deficits.

Methods: Apathy was quantified in 65 subjects with idiopathic RBD, 65 age-matched PD patients and 33 healthy controls using the Lille Apathy Rating Scale. RBD subjects also rated subjective symptoms of apathy. Measures of cognition and depression were assessed and the Epworth Scale was used to control for sleepiness in RBD subjects. A subgroup of patients underwent dopaminergic SPECT imaging and testing of reward sensitivity using pupillary and saccadic responses.

Results: Apathy was present in 51% of RBD subjects, 31% of PD patients and 3% of controls. Only 41% of apathetic RBD patients reported symptoms of apathy. SPECT imaging and ocular measures could be used to compare the underlying mechanisms of apathy in RBD and PD.

Conclusion: Apathy is common and under-recognised in RBD and may be a sign of early dopaminergic neurodegeneration. Longitudinal follow-up will reveal the value of clinical and ocular markers of apathy as predictors of future Parkinson's.

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