The Korsakoff Syndrome: Clinical Aspects, Psychology and Treatment

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Abstract — Aims: The Korsakoff syndrome is a preventable memory disorder that usually emerges (although not always) in the aftermath of an episode of Wernicke's encephalopathy. The present paper reviews the clinical and scientific literature on this disorder. **Methods:** A systematic review of the clinical and scientific literature on Wernicke's encephalopathy and the alcoholic Korsakoff syndrome. **Results:** The Korsakoff syndrome is most commonly associated with chronic alcohol misuse, and some heavy drinkers may have a genetic predisposition to developing the syndrome. The characteristic neuropathology includes neuronal loss, micro-haemorrhages and gliosis in the paraventricular and peri-aqueductal grey matter. Lesions in the mammillary bodies, the mammillo-thalamic tract and the anterior thalamus may be more important to memory dysfunction than lesions in the medial dorsal nucleus of the thalamus. Episodic memory is severely affected in the Korsakoff syndrome, and the learning of new semantic memories is variably affected. 'Implicit' aspects of memory are preserved. These patients are often first encountered in general hospital settings where they can occupy acute medical beds for lengthy periods. Abstinence is the cornerstone of any rehabilitation programme. Korsakoff patients are capable of new learning, particularly if they live in a calm and well-structured environment and if new information is cued. There are few long-term follow-up studies, but these patients are reported to have a normal life expectancy if they remain abstinent from alcohol. **Conclusions:** Although we now have substantial knowledge about the nature of this disorder, scientific questions (e.g. regarding the underlying genetics) remain. More particularly, there is a dearth of appropriate long-term care facilities for these patients, given that empirical research has shown that good practice has beneficial effects.

INTRODUCTION

A recent report commissioned by the Alzheimer's Society, and carried out by academics at the London School of Economics and the Institute of Psychiatry at King's College London, estimated that there are now almost 700,000 people with dementia in the United Kingdom, representing 1.1% of the entire population and a cost of £17 billion per year (Alzheimer's Society, 2007). The report focused on three main dementia subtypes: Alzheimer's disease (AD) accounting for two-thirds of all cases; and vascular dementia and mixed dementia, together accounting for nearly one-third of cases. Alcohol-related brain damage or dementia, which may contribute to between 10% and 24% of all cases of dementia, was not considered separately (Smith and Kiloh, 1981; Smith and Atkinson, 1995; Gupta and Warner, 2008).

The mechanisms underlying alcohol-related brain damage or dementia are many and varied and include the direct neurotoxic effects of alcohol and its metabolite, acetaldehyde, thiamine depletion, metabolic factors resulting from intoxication and withdrawal syndromes, cerebrovascular disease, hepatic encephalopathy, alcohol-related physical complications and head injury. Per capita alcohol consumption in England increased by 60% between 1970 and 2006 and this has led to a rapid rise in alcohol harms (DH, 2008). Alcohol contributes to 4.4% of the global burden of disease expressed in disability-adjusted life years lost (DALYS); neuropsychiatric disorders constitute the category with the highest alcohol-attributable burden (WHO, 2007). It is therefore likely that prevalence rates of alcohol-related brain damage are currently underestimated and may rise in future (heavier drinking) generations.

In this paper, we consider one category of alcohol-related brain damage, the Wernicke–Korsakoff syndrome, and detail its clinical characteristics, neurochemistry and genetics, neuropathology and neuropsychology, assessment and management. Because it is a preventable disorder, we also discuss prophylaxis in some detail.

WERNICKE'S ENCEPHALOPATHY

Wernicke's encephalopathy is an acute neuropsychiatric reaction to thiamine deficiency, characterized by confusion, ataxia, nystagmus and ophthalmoplegia (Wernicke, 1881). It is diagnosed more commonly in alcoholics at post-mortem than it is in life (Torvik *et al*., 1982; Harper, 1983, 2006, 2007). Even in hospitals, only 20% of patients with Wernicke's encephalopathy are identified prior to death. This implies that many cases are being missed. Reported prevalence rates at post-mortem are between 1 and 2% in the general population and 12 and 14% in the alcohol misusing population (Harper *et al*., 1986, 1989).

Wernicke's encephalopathy is a medical emergency. Untreated, it leads to death in up to 20% of cases (Harper *et al*., 1986) or to the Korsakoff syndrome in 85% of survivors (Day *et al*., 2008). Up to 25% of the Korsakoff group will require long-term institutionalization (Victor *et al*., 1989).

When Wernicke's encephalopathy is suspected, treatment with high-dose parenteral thiamine should be given promptly to offset the risk of death or the development of the Korsakoff syndrome. Parenteral thiamine is itself associated with a small risk of anaphylactic reactions and should only be given where appropriate resuscitation facilities are available. Ocular abnormalities usually recover quite quickly (days–weeks) and the ataxia usually responds within the first week but takes about 1–2 months or much longer to resolve (Lishman, 1998). Some patients are left with a residual nystagmus and ataxia. Improvements in acute confusion/delirium usually occur within 1–2 days. Global confusion begins to improve after 2–3 weeks

but may take 1–3 months to clear. As the confusion improves, so the memory deficits become more obvious (Day *et al*., 2008).

THE KORSAKOFF SYNDROME: CLINICAL CHARACTERISTICS AND PREVALENCE

Korsakoff (1887, 1889a, 1889b) described a syndrome of characteristic memory disturbance, which he had witnessed in 'not less than 30' cases of chronic alcohol abuse, as well as 16 patients in whom alcohol had not played a role. The latter cases included instances in which the syndrome had developed following persistent vomiting (eight patients), post-partum (sepsis, macerated foetus), acute or chronic infection, toxic poisoning (carbon monoxide, lead, arsenic) or other chronic disease (neoplasm lymphadenoma, diabetes). Although he did not make reference to Wernicke's syndrome, which had been described in 1881, Korsakoff did mention that prodromal confusion and agitation commonly preceded the appearance of the memory disorder, sometimes associated with ophthalmoplegia, nystagmus, ataxia and 'like manifestations'.

Korsakoff characterized the memory disorder as occurring in a setting of clear consciousness, such that the patient gave the impression in conversation that he or she was entirely in possession of his or her faculties but showed a severe impairment of current and recent memory, asking the same questions over and over again, reading the same page for hours on end, and not being able to recognize people whom he/she had met many times since the onset of the illness. Current and recent memory was affected more than remote memory, but the impairment could involve memories from up to 30 years earlier. Sometimes, the disorder was associated with patients inventing 'fictions' (confabulations) in their discourse, and these false recollections often represented real memories jumbled up and recalled out of temporal sequence.

The Korsakoff syndrome does not always manifest itself following a clear-cut Wernicke episode. Some patients are initially comatose or semi-conscious, when the disorder may be complicated by a recent head injury or concurrent chest infection. In such situations it is only when the acute disorder has resolved that the attending doctors may realize that the patient has an underlying Korsakoff syndrome, resulting in delayed or inadequate treatment. Other patients have a more insidious onset (Cutting, 1978), and such cases are more likely to come to the attention of psychiatrists or clinical neuropsychologists. In such cases, there may have been either no known history or only a transient period of Wernicke features. As mentioned above, other cases may not be diagnosed in life but only at autopsy; these cases presumably had suffered from a memory disorder that had not been identified by clinicians during their lifetime (Torvik *et al*., 1982; Harper, 1983, 2006, 2007).

In recent years, the incidence of the Korsakoff syndrome has been reported to be rising in the Netherlands and in Scotland (Kok, 1991; Ramayya and Jauhar, 1997). Suggested reasons for this increase include increased per capita consumption of alcohol, decreased prescribing of prophylactic parenteral vitamins to alcohol-dependent individuals undergoing detoxification in general medical and psychiatric settings, and poorer diet (Smith and Hillman, 1999). Prevalence rates are likely to be higher in areas of socio-economic deprivation and in the 50- to 60-year age group (MacRae and Cox, 2003; Cox *et al*., 2004). In a recent study of 14 patients identified in a general hospital, 7 were under the age of 50 years (Wong *et al*., 2007).

NEUROCHEMISTRY AND GENETICS

The Korsakoff syndrome is relatively unusual among memory disorders in that there is a distinct neurochemical pathology with important implications for treatment. Since animal investigations in the 1930s and 1940s and the important observations of de Wardener and Lennox (1947) in malnourished prisoners-of-war, it has been known that thiamine depletion is the mechanism giving rise to the acute Wernicke episode, followed by Korsakoff's syndrome. Consequently, modifying Victor *et al*. (1971), the Korsakoff syndrome can be defined as

> An abnormal mental state in which memory and learning are affected out of all proportion to other cognitive functions in an otherwise alert and responsive patient resulting from nutritional depletion, i.e. thiamine deficiency.

The genetic factor that predisposes a minority of heavy drinkers to develop this syndrome, rather than hepatic, gastro-intestinal or any other complications of alcohol misuse, remains unclear. Transketolase is the enzyme that requires thiamine pyrophosphate (TPP) as a co-factor, and thiamine depletion affects six neurotransmitter systems, including acetylcholine and GABA. Direct genomic PCR sequences of a high-affinity thiamine transporter gene (SLC19A2) have identified three genetic variants in the Wernicke–Korsakoff syndrome (Guerrini *et al*., 2005).

NEUROPATHOLOGY

The characteristic neuropathology involves neuronal loss, micro-haemorrhages and gliosis in the paraventricular and peri-aqueductal grey matter (Victor *et al*., 1971). There has been debate as to which particular lesions are critical for the manifestation of the prolonged and severe memory disorder, i.e. the Korsakoff syndrome, rather than the Wernicke features. Victor *et al*. (1971) argued that all 24 of their cases in whom the medial dorsal nucleus of the thalamus was affected had a clinical history of persistent memory impairment, whereas five cases in whom this nucleus was not affected showed Wernicke features only. The mammillary bodies were implicated in all the Wernicke cases, whether or not there was subsequent memory impairment. Consequently, Victor *et al*. (1971) argued that damage to the medial dorsal nucleus was critical in giving rise to the memory deficit. However, Mair *et al*. (1979) and Mayes *et al*. (1988) provided careful pathological and neuropsychological descriptions of four patients with a Korsakoff syndrome, whose autopsies showed lesions in the mammillary bodies, the midline and the anterior portion of the thalamus but not in the medial dorsal nuclei. These observations were consistent with some of the findings in patients with thalamic infarction, which have also implicated the anterior thalamic nuclei. More recently, Harding *et al*. (2000) reported that pathology within the anterior principal thalamic nuclei was the critical difference between eight patients, who suffered a persistent Korsakoff syndrome, and five others, who experienced only a transient Wernicke episode. These various observations suggest that the mammillary bodies, the mammillo-thalamic tract and the

anterior thalamus may be more important to memory dysfunction than the medial dorsal nucleus of the thalamus.

However, it is also the case that CT and MRI investigations, as well as autopsy studies, show a variable degree of general cortical atrophy, and that the frontal lobes can be particularly implicated (Shimamura *et al.*, 1988; Jacobson *et al.* 1990). Thalamic, mammillary body and frontal lobe reductions in regional brain volume have now been demonstrated on quantified MRI (Sullivan *et al.*, 2000; Colchester *et al.*, 2001; Kopelman *et al.* 2001). PET investigations show more variable findings, but Reed *et al.* (2003) reported thalamic, orbito-medial frontal, and retrosplenial reductions in glucose uptake using 18-fluoro-deoxy-glucose as a ligand.

NEUROPSYCHOLOGY

A distinction is usually drawn between so-called working memory (or 'primary memory'), which holds information for brief periods (a matter of several seconds) while allocating resources, and secondary memory, which holds different types of information on a permanent or semi-permanent basis. Secondary memory can, in turn, be divided into an episodic or 'explicit' component, semantic memory and implicit memory. Episodic memory refers to incidents or events from a person's past, such that he/she can 'travel back mentally in time', and this is characteristically severely affected in the Korsakoff syndrome. Semantic memory refers to knowledge of facts, concepts and language, and the learning of new semantic memories is variably affected in the Korsakoff syndrome. 'Implicit' aspects of memory, including the response to priming and perceptuo-motor (procedural) memory, are preserved in the Korsakoff syndrome (Fama *et al.*, 2006; d'Ydewalle and Van Damme, 2007).

Some theories have proposed that there is a deficit in the psychological processes involved in the initial 'encoding' of information. For example, it was argued that, whilst Korsakoff patients are able to encode direct, sensory impressions, they have difficulty in 'processing' more meaningful (semantic) material (Butters and Cermak, 1980). Others proposed that there is an impairment in the physiological processes assumed to underlie the storage (consolidation) of information in a more permanent form (e.g. Meudell *et al.*, 1979; Moscovitch, 1982). These processes were traditionally thought to involve the 'transfer' of information from primary to secondary memory, operating during a time period of something less than a minute. Consistent with this hypothesis was the fact that span test scores and other measures of primary or working memory were characteristically intact in Korsakoff patients (Baddeley and Warrington, 1970). Others suggested that there was a specific deficit in the storage of contextual information, such that Korsakoff patients manifested a disproportionate impairment in recalling the spatial or temporal aspects of learned material (Huppert and Piercy, 1978; Postma *et al.*, 2006). A development of this theory is that Korsakoff patients show a deficit in binding complex associations or the relations between items (Cohen *et al.*, 1997; Mayes and Downes, 1997); and from this, it can be argued that there may be dissociations between recall memory (based on recollection) and recognition memory (based on familiarity judgements), depending on which medial temporal-thalamic

connections are damaged (Huppert and Piercy, 1978; Aggleton and Saunders, 1997; Aggleton and Brown, 1999). A further theory was that Korsakoff patients show a retrieval deficit, such that they are unable to suppress inappropriate responses during memory tasks (Warrington and Weiskrantz, 1968, 1970). On the other hand, similar features are often shown by healthy subjects, when they remember something poorly at long delays (Mayes and Meudell, 1981), and retrieval deficits are often a consequence of poor initial encoding.

The retrograde component in the Korsakoff syndrome often extends back 20–30 years (Kopelman, 1989). There is generally a 'temporal gradient' such that earlier memories are recalled better than more recent ones. However, there is considerable controversy concerning the basis of this extensive retrograde memory loss. One theory of retrograde amnesia and of the temporal gradient is that, as memories are 'consolidated' through time, they become independent of thalamic/medial temporal lobe structures and are, thereby, relatively protected against brain pathology within these structures (Squire, 2006). A second theory is that, through time, episodic memories adopt a less vivid, more 'semantic' form, and this protects earlier memories from the effects of brain pathology (Cermak, 1984). A third theory suggests that the hippocampal/thalamic circuitry is always involved in the retrieval and reactivation of memories, and that every time a memory is retrieved, a new trace is laid down, resulting in 'multiple traces' protecting earlier memories against the effects of brain pathology (Moscovitch *et al.*, 2006). These three theories make somewhat differing predictions and, at present, the underlying basis of retrograde amnesia remains highly controversial.

CONFABULATION

Confabulation is sometimes divided into 'spontaneous' confabulation, in which there is a persistent, unprovoked outpouring of erroneous memories, and secondly, 'momentary' or 'provoked' confabulation, in which fleeting intrusion errors or distortions are seen in response to a challenge to memory, such as a memory test (Berlyne, 1972; Kopelman, 1987). Although momentary confabulation is commonly seen in the chronic Korsakoff syndrome, spontaneous confabulation is relatively rare beyond the acute Wernicke confusional phase. Where spontaneous confabulation persists, there is usually concomitant damage to the frontal lobes, particularly the ventro-medial and/or orbito-frontal regions (Gilboa *et al.*, 2006). As with respect to the anterograde and retrograde memory deficits, there are conflicting theories about the underlying basis of spontaneous confabulation (Schnider, 2003; Gilboa *et al.*, 2006; Fotopoulou *et al.*, 2007).

CLINICAL ASSESSMENT OF THE KORSAKOFF SYNDROME

Once the acute confusional state has resolved, careful clinical examination should be carried out to ascertain the core deficits, including a physical examination to elicit Wernicke features. The Mini-Mental State Examination (MMSE) can help to screen for global confusion in a Korsakoff patient on
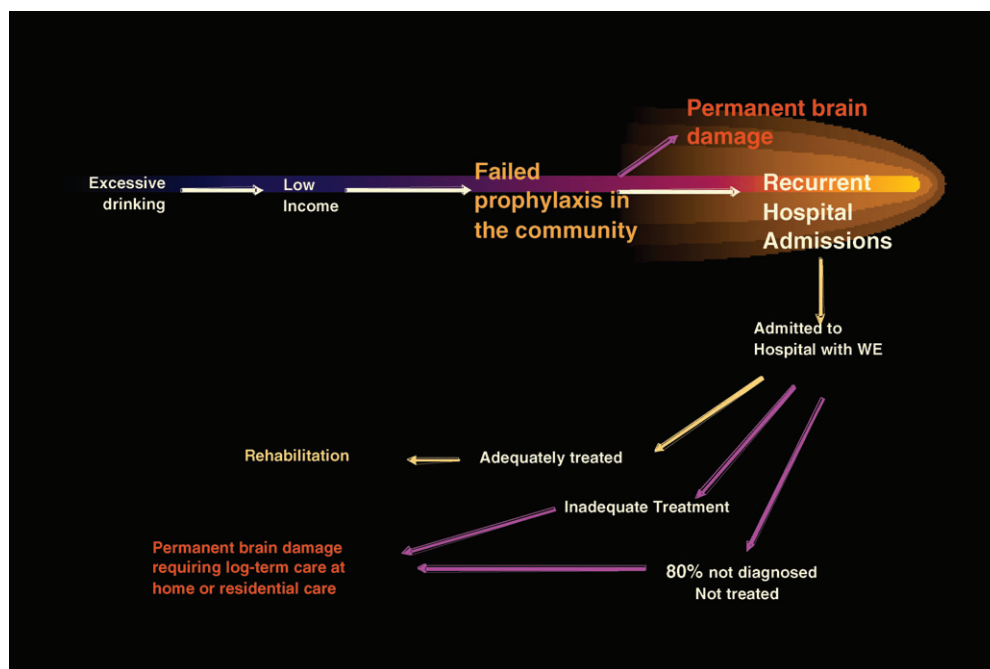
Fig. 1. Opportunities for intervention.

a busy medical ward, but, as it is a very inadequate assessment of memory function, supplementary memory questions should be asked, e.g. about recent news, sporting, family or personal events. A collateral history will elucidate whether the onset was sudden or insidious. A more detailed neuropsychiatric and neuropsychological evaluation is desirable whenever possible.

TREATMENT, PROPHYLAXIS, AND MANAGEMENT OF THE WERNICKE–KORSAKOFF SYNDROME WITHIN THE ALCOHOL-MISUSING POPULATION

Treatment of the Wernicke–Korsakoff syndrome should be instigated as soon as possible with high doses of parenteral B vitamins. As described above, the Wernicke features respond well to high-dose vitamins, and such treatment can prevent the occurrence of a severe chronic Korsakoff state. The small risk of anaphylaxis is outweighed by the high risk of severe brain damage (and of litigation) if such treatment is not administered.

Victor *et al*. (1971) reported that 25% of patients with the alcoholic Korsakoff syndrome recovered, 50% showed improvement through time and 25% remained unchanged. Whilst it is unlikely that any established patient shows complete recovery, the experience of the present authors is that improvement does occur over a matter of years if the patient remains abstinent in, approximately 75% of these patients. On the other hand, it is probably also true that 25% show no change, even following treatment. The impairments in memory and learning improve much more slowly than the acute features of Wernicke's encephalopathy (Day *et al*., 2008).

Recurrent subclinical and more overtly clinical Wernicke episodes are often missed in the alcohol-misusing population, because patients present with non-specific symptoms and signs,

which may be masked by symptoms of alcohol intoxication or withdrawal, or physical illness such as intercurrent infection or head injury, or are not recognized by the inexperienced clinician. In a recent publication, suggestions have been made for identifying patients at risk of developing Wernicke's encephalopathy so that they can be offered prophylactic treatment (Thomson *et al*., 2008). As shown in Fig. 1, there are often repeated opportunities for intervention. In the community, these patients usually present to their local alcohol service or primary healthcare team where prophylactic thiamine may prevent the development of the Wernicke–Korsakoff syndrome (WKS). However, in one study, only a small proportion of GPs and specialist community alcohol services surveyed routinely offered parenteral thiamine (Naik *et al*., 2000). A further opportunity for prophylaxis or early treatment occurs when patients attend Accident and Emergency Departments or are admitted to general medical or psychiatric wards. However, rates of parenteral B vitamin administration in Accident and Emergency Departments are low (Hope *et al*., 1999; NHS Quality Improvement Scotland, 2008). Any patient with alcohol misuse who presents with confusion, nausea and vomiting, fatigue, weakness or apathy should be considered at high risk of Wernicke's encephalopathy and treated appropriately. Unexplained hypotension or hypothermia should also heighten suspicion.

Following diagnosis, these patients often occupy acute medical beds for lengthy periods of time while appropriate placement is being organized. There is a lack of available services for younger people with brain damage and there are no standardized care pathways. Because they are younger than the typical patient presenting to dementia services, and are initially confused and/or have concomitant frontal lobe pathology, they are physically more active and prone to agitation, disinhibition, delusional experiences and aggression (Ferran *et al*., 1996). They are unable to live alone and are usually too difficult to

be cared for in a family setting. They are often passed between services and lack access to expert care (Jacques and Stevenson, 2000). Dementia services generally do not have the skills or capacity to cater for these patients.

A multi-disciplinary service tailored to the needs of these patients would facilitate abstinence from alcohol and include access to detoxification facilities, and expert assessment and re-assessment of memory and intellectual impairment in the intermediate term, e.g. over a 2-year period. Flexible services ranging from specialized residential home care to domiciliary support should be available. Occupational therapy assessments of daily living and neuropsychological assessments of current cognitive function can help to determine whether the patient can go home and, if so, the nature and degree of help and supervision needed. The cornerstone of any rehabilitation programme is abstinence. There is little point discharging a patient home if this means that he/she will continue to drink and pose an increasing burden on their carers. Those with a milder form of the syndrome are more likely to drink again, with potentially disastrous consequences. Korsakoff patients have a reduced tolerance to alcohol and are at high risk of developing alcohol-related injuries and further Wernicke–Korsakoff episodes.

In the UK, the Mental Capacity Act and, on occasion, the Mental Health Act may have to be considered in these patients in the early stages of the syndrome. At a later stage, it may be necessary to invoke a guardianship order. Other legal measures may be required to manage finances and debts.

The Royal College of Psychiatrists have considered the paucity of services for younger people with AD and other dementias (Royal College of Psychiatrists, 2006) and, in particular, recommended close collaboration between substance misuse and dementia services, and the organization of community services to provide flexible and individualized care plans.

IMPROVING BRAIN FUNCTION IN PATIENTS WITH KORSAKOFF SYNDROME

The optimal treatment strategy for patients with an established Korsakoff syndrome is not clear. Discussions have focused mainly on the relative merits of parenteral versus oral thiamine. These patients are at increased risk of developing other psychiatric disorders such as anxiety, depression and psychosis, the severity of which is exacerbated by sensory deprivation. As previously mentioned, it is important that they remain abstinent. Patients in residential care may benefit from frequent family visits. However, in some cases, this may cause distress, for instance if they are continually reminded that a loved one has died, or that they are, in fact, divorced. For those living at home, a weekly outing to a restaurant with a friend for lunch may be the highlight of the week, and afford respite to the carer. Carers may benefit from a support group.

Korsakoff patients are capable of new learning, particularly if the information is cued and of a certain type. It has been shown that they are better able to recall new information over a longer period of time if they are not allowed to guess (Baddeley and Wilson, 1994). That 'errorless learning' is superior to 'errorful' learning has profound implications for styles of nursing and caring. New learning is facilitated if patients live in a calm and well-structured environment and have the support of a psychologist. Memory aids can help, for instance

the use of an alarm that can go off if they stray too far away from the ward (Baddeley *et al.*, 2002). The living environment is important and should be designed to facilitate orientation. Ground floor units, large windows and the use of arrows can all help with orientation and maximize the quality of life.

The nutrition of these patients should be considered. This is often inadequate and not designed to optimize brain function. Could micronutrients improve memory, confusion and cognitive impairment in Korsakoff patients? Repair and replacement of brain cell components is dependent upon 100,000 reactions occurring in the body every hour as a result of DNA being copied: in the vast majority of cases, the copied sequence is surprisingly accurate. This metabolic whirlwind must be fuelled by an adequate supply of nutrients or it will fail, or be sub-optimal. The brain is especially sensitive to damage by free radicals. Lack of a vitamin such as thiamine and related nutrients such as magnesium (also deficient in individuals with alcohol dependence) could also affect metabolic pathways in the brain by interfering with the complex chains of biochemical reactions that manufacture energy.

OUTCOMES

A Dutch series of 44 patients referred to either nursing home or specialist sheltered accommodation found that, although cognitive functioning was similar in the two groups, those in the nursing home group showed more evidence of deterioration in social functioning (Blansjaar *et al.*, 1992). Another study found that Korsakoff patients fared better in terms of social functioning and speed of information processing in a specialist rehabilitation ward than in a long-stay psychiatric ward (Ganzelves *et al.*, 1994). An Australian study found that about half of a series of 104 Korsakoff patients who underwent a rehabilitation programme were successfully placed in the community at 1–2 years following discharge from hospital (Leenane, 1986). Little is known about long-term outcomes as there are very few long-term follow-up studies. These patients are reported to have a normal life expectancy if they remain abstinent from alcohol.

CONCLUSION

It very often falls to the psychiatrist to coordinate the care for these patients, to arrange placement, follow-up and further assessment when necessary. Close working with the GP means that families can be supported. Older patients can be transferred to the Old Age Psychiatry Service, but there is a dearth of appropriate services in the UK for younger patients with memory disorders in general and for Korsakoff patients in particular. There are examples of good practice from The Netherlands and Australia that support the benefits of specialized provision.

REFERENCES

Aggleton JP, Brown MW. (1999) Episodic memory, amnesia and the hippocampal anterior thalamic axis [Review]. *Behav Brain Sci* **22**:425–44.

Aggleton JP, Saunders RC. (1997) The relationships between temporal lobe and diencephalic structures implicated in anterograde amnesia. *Memory* **5**:49–71.

Alzheimer's Society. (2007) *Dementia UK*: a report into the prevalence and cost of dementia prepared by the Personal Social Services Research Unit (PSSRU) at the London School of Economics and the Institute of Psychiatry at King's College London, for the Alzheimer's Society.

Baddeley AD, Kopelman MD, Wilson BA (2002) *Handbook of Memory Disorders*, 2nd edn. Chichester: Wiley.

Baddeley AD, Warrington EK. (1970) Amnesia and the distinction between long- and short-term memory. *J Verbal Learn Verbal Behav* **9**: 176–89.

Baddeley AD, Wilson BA. (1994) When implicit learning fails: amnesia and the problem of error elimination. *Neuropsychlogia* **32**:53–68.

Berlyne N. (1972) Confabulation. *Br J Psychiatry* **120**:31–9.

Blansjaar BA, Takens H, Zwinderman AH (1992) The course of alcohol amnestic disorder: a three-year follow-up study of clinical signs and social disabilities. *Acta Psychiatr Scand* **86**:240–6.

Butters N, Cermak LS. (1980) *Alcoholic Korsakoff's Syndrome: An Information-Processing Approach to Amnesia*. New York: Academic Press.

Cermak LS. (1984) The episodic-semantic distinction in amnesia. In Squire LR, Butters N (eds). *The Neuropsychology of Memory*. New York: Guildford Press.

Cohen NJ, Poldrak RA, Eichenbaum H. (1997) Memory for items and memory for relations in the procedural/declarative memory framework. *Memory* **5**:131–78.

Colchester A, Kingsley D, Lasserson D *et al.* (2001) Structural MRI volumetric analysis in patients with organic amnesia: 1. Methods and comparative findings across diagnostic groups. *J Neurol Neurosurg Psychiatry* **71**:13–22.

Cox S, Anderson I, McCabe L. (2004) *A Fuller Life: Report of the Expert Committee on Alcohol-Related Brain Damage*. Stirling: Dementia Services Development Centre.

Cutting J. (1978) The relationship between Korsakoff's syndrome and 'alcoholic dementia'. *Br J Psychiatry* **132**:240–51.

Day E, Bentham P, Callaghan R *et al.* (2008) *Thiamine for Wernicke–Korsakoff Syndrome in People at Risk from Alcohol Abuse (Review)*. The Cochrane Collaboration. Chichester: Wiley.

Department of Health. (2008) *Safe, Sensible Social-Consultation on Further Action*. London: Department of Health.

de Wardener HE, Lennox B. (1947) Cerebral beriberi (Wernicke's encephalopathy): review of 52 cases in a Singapore prisoner-of-war hospital. *Lancet* **1**:11–7.

d'Ydewalle G, Van Damme I. (2007) Memory and the Korsakoff syndrome: not remembering what is remembered. *Neuropsychologia* **45**:905–20.

Fama R, Pfefferbaum A, Sullivan EV. (2006) Visuoperceptual learning in alcoholic Korsakoff syndrome. *Alcohol Clin Exp Res* **30**: 680–7.

Ferran J, Wilson K, Doran M *et al.* (1996) The early onset dementias: a study of clinical and service need. *Int J Geriatr Psychiatry* **11**:863–9.

Fotopoulou A, Conway MA, Solms M. (2007) Confabulation: motivated reality monitoring. *Neuropsychologia* **45**: 2180–90.

Ganzelves PGJ, Geus BWJ, Wester AJ (1994) Cognitive and behavioural aspects of Korsakoff's syndrome: the effect of special Korsakoff wards in a general hospital. *Tijdschrift voor Alcohol Drugs en Andere Psychotrope Stoffen* **20**:20–31.

Gilboa A, Alain C, Stuss DT *et al.* (2006) Mechanisms of spontaneous confabulations: a strategic retrieval account. *Brain* **129**:1399–414.

Guerrini I, Thomson AD, Cook CCH *et al.* (2005) Direct genomic PCR sequencing of the high affinity thiamine transporter (SLC19A2) gene identifies three genetic variants in Wernicke–Korsakoff syndrome (WKS) research subjects of which two were not found in controls. *Neuropsychiatr Genet* **137B**:17–9.

Gupta S, Warner J (2008) Alcohol-related dementia: a 21st century silent epidemic. *Br J Psychiatry* **193**:351–3.

Harding A, Halliday G, Caine D *et al.* (2000) Degeneration of anterior thalamic nuclei differentiates alcoholics with amnesia. *Brain* **123**:141–54.

Harper C. (1983) The incidence of Wernicke's encephalopathy in Australia: a neuropathological study of 131 cases. *J Neurol Neurosurg Psychiatry* **46**: 593–8.

Harper C. (2006) Thiamine (vitamin B1) deficiency and associated brain damage is still common throughout the world and prevention is simple and safe. *Eur J Neurol* **13**:1078–82.

Harper C. (2007) The neurotoxicity of alcohol. *Hum Exp Toxicol* **26**:251–7.

Harper C, Gold J, Rodriguez M *et al.* (1989) The prevalence of the Wernicke–Korsakoff syndrome in Sydney, Australia: a prospective necropsy study. *J Neurol Neurosurg Psychiatry* **52**:282–5.

Harper CG, Giles M, Finlay-Jones R. (1986) Clinical signs in the Wernicke–Korsakoff complex: a retrospective analysis of 131 cases diagnosed at necropsy. *J Neurol Neurosurg Psychiatry* **49**:341–5.

Hope LC, Cook CCH, Thomson AD (1999) A survey of the current practices of psychiatrists and accident and emergency specialists in the United Kingdom concerning vitamin supplementation for chronic alcohol misusers. *Alcohol Alcohol* **34**:862–7.

Huppert FA, Piercy M. (1978) The role of trace strength in recency and frequency judgements by amnesic and control subjects. *Q J Exp Psychol* **30**:347–54.

Jacobson RR, Acker C, Lishman WA. (1990) Patterns of neuropsychological deficit in alcoholic Korsakoff's syndrome. *Psychol Med* **20**:321–34.

Jacques A, Stevenson G. (2000) *Korsakoff'Syndrome and Other Chronic Related Brain Damage in Scotland*. Stirling: Dementia Service Development Centre.

Kok AF. (1991) Developments in the care of Korsakoff patients. *Tijdschrift voor Alcohol, Drugs en Andere Psychotrope Stoffen* **17**:3–9.

Kopelman MD. (1987) Two types of confabulation. *J Neurol Neurosurg Psychiatry* **50**:1482–7.

Kopelman MD. (1989) Remote and autobiographical memory, temporal context memory and frontal atrophy in Korsakoff and Alzheimer patients. *Neuropsychologia* **27**:437–60.

Kopelman MD, Lasserson D, Kingsley D *et al.* (2001) Structural MRI volumetric analysis in patients with organic amnesia: 2 Correlations with anterograde memory and executive tests in 40 patients. *J Neurol Neurosurg Psychiatry* **71**:23–8.

Korsakoff SS. (1887) Disturbance of psychic function in alcoholic paralysis and its relation to the disturbance of the psychic sphere in multiple neuritis of non-alcoholic origin. Quoted by Victor M, Adams RD, Collins GH. (1971) *The Wernicke–Korsakoff Syndrome*. Oxford: Blackwell.

Korsakoff SS. (1889a) Psychic disorder in conjunction with peripheral neuritis. Translated by Victor M, Yakovlev PI. (1955) *Neurology* **5**:394–406.

Korsakoff SS. (1889b) Etude medico-psychologique sur une forme des maladies de la mémoire. *Revue Philosophie* **20**:501–30.

Leenane KJ. (1986) Management of moderate to severe alcohol-related brain damage (Korsakoff's syndrome). *Med J Aust* **145**:136–43.

Lishman WA. (1998) Wernicke's encephalopathy. Organic psychiatry. *The Psychological Consequences of Cerebral Disorder*, 3rd edn. Oxford: Blackwell Science.

MacRae S, Cox S. (2003) Meeting the needs of people with Alcohol Related Brain Damage: a literature review on the existing and recommended service provision and models of care. University of Stirling: Dementia Services Development Centre.

Mair WG, Warrington EK, Weiskrantz L. (1979) Memory disorder in Korsakoff's psychosis: a neuropathological and neuropsychological investigation of two cases. *Brain* **102**:749–83.

Mayes AR, Downes JJ. (1997) What do theories of functional deficit(s) underlying amnesia have to explain? *Memory* **5**:3–36.

Mayes AR, Meudell PR. (1981) How similar is immediate memory in amnesic patients to delayed memory in normal subjects? A replication, extension and reassessment of the amnesic cueing effect. *Neuropsychologia* **19**:647–54.

Mayes AR, Meudell PR, Mann D *et al.* (1988) Location of lesions in Korsakoff's syndrome: neuropsychological and neuropathological data on two patients. *Cortex* **24**:367–88.

Meudell PA, Mayes AR, Neary D. (1979) Is amnesia caused by a consolidation impairment? In Oborne DJ, Gruneberg MM, Eiser JR (eds). *Research in Psychology and Medicine*, vol. **1**. London: Academic Press, 323–30.

Moscovitch M. (1982) Multiple dissociations of function in amnesia. In Cermak LS (ed). *Human Memory and Amnesia*. Hillsdale, NJ: Lawrence Erlbaum, 337–70.

Moscovitch M, Nadel L, Winocur G *et al.* (2006) The cognitive neuroscience of remote episodic, semantic and spatial memory. *Curr Opin Neurobiol* **16**:179–90.

Naik PC, Lawton J, Brownell LW. (2000) Comparing general practitioners and specialist alcohol services in the management of alcohol withdrawal. *Psychiatr Bull* **24**:214–5.

NHS Quality Improvement Scotland. (2008) *Understanding Alcohol Misuse in Scotland*. Scottish Emergency Department Alcohol Audit (SEDAA). www.nhshealthquality.org.

Postma A, Van Asselen M, Keuper O *et al.* (2006) Spatial and temporal order memory in Korsakoff patients. *J Int Neuropsychol Soc* **12**:327–36.

Ramayya A, Jauhar P. (1997) Increasing incidence of Korsakoff's psychosis in the east end of Glasgow. *Alcohol Alcohol* **32**: 281–5.

Reed LJ, Lasserson D, Marsden P *et al.* (2003) [18]FDG-PET findings in the Wernicke–Korsakoff syndrome. *Cortex* **39**:1027–45.

Royal College of Psychiatrists. (2006) *Services for Younger People with Alzheimer's Disease and Other Dementias*. Council Report CR 135. London: Royal College of Psychiatrists.

Schnider A. (2003) Spontaneous confabulation and the adaptation of thought to ongoing reality. *Nat Rev Neurosci* **4**:662–71.

Shimamura AP, Jernigan TL, Squire LR. (1988) Korsakoff's syndrome: radiological (CT) findings and neuropsychological correlates. *J Neurosci* **8**:4400–10.

Smith DM, Atkinson RM (1995) Alcoholism and dementia. *Int J Addict* **30**:1843–69.

Smith JS, Kiloh LG (1981) The investigation of dementia: results in 200 consecutive admissions. *Lancet* **1**:824–7.

Smith I, Hillman A. (1999) Management of alcohol Korsakoff syndrome. *Adv Psychiatr Treat* **5**:271–8.

Squire LR. (2006) Lost forever or temporarily misplaced? The long debate about the nature of memory impairment. *Learn Mem* **13**:522–9.

Sullivan EV, Deshmukh A, Desmond JE *et al.* (2000) Cerebellar volume decline in normal aging, alcoholism, and Korsakoff's syndrome: relation to ataxia. *Neuropsychology* **14**:341–53.

Thomson AD, Cook CCH, Guerrini I *et al.* (2008) Wernicke's encephalopathy: 'Plus ca change, plus c'est la meme chose'. *Alcohol Alcohol* **43**:180–6.

Torvik A, Lindboe CF, Rogde S. (1982) Brain lesions in alcoholics. *J Neurol Sci* **56**:233–48.

Victor M, Adams RD, Collins GH. (1971) *The Wernicke–Korsakoff Syndrome*. Philadelphia, PA: F.A. Davis.

Victor M, Adams RD, Collins GH. (1989) *The Wernicke–Korsakoff Syndrome and Related Neurological Disorders due to Alcoholism and Malnutrition*. Philadelphia, PA: F.A. Davis.

Warrington EK, Weiskrantz L. (1968) New method of testing long-term retention with special reference to amnesic patients. *Nature* **217**: 972–4.

Warrington EK, Weiskrantz L. (1970) Amnesic syndrome: consolidation or retrieval? *Nature* **228**:628–30.

Wernicke C. (1881) Die acute haemorrhagische poliencephalitis superior. In Wernicke C (ed.) *Lehrbuch der Gehrinkrankheiten*. Berlin: Fischer, 229–42. Translated and republished by Brody IA and Wilkins RH. (1968) *Archives of Neurology* **19**:228–32.

Wong A, Moriarty KJ, Crompton S *et al.* (2007) Wernicke–Korsakoff syndrome: who cares? *Gastroenterol Today* **17**:46–9.

World Health Organisation. (2007) *WHO Expert Committee on Problems Related to Alcohol Consumption*. Second Report. Geneva: World Health Organisation.