ALCOHOLIC KORSAKOFF'S PSYCHOSIS: A PSYCHOMETRIC, NEURORADIOLOGICAL AND NEUROPHYSIOLOGICAL INVESTIGATION OF NINE CASES

by

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SUMMARY

Nine patients who were admitted to Purdysburn Hospital with a clinical diagnosis of Korsakoff's psychosis were subjected to a series of psychometric tests, to electroencephalography (including P3 auditory evoked potential) and to computerised axial tomography. When compared with controls, the experimental group differed significantly in their psychometric scores in all but the comprehension, vocabulary and digit span subtests of the Wechsler Adult Intelligence Scale. A significant negative correlation was found between scores on the Digit Symbol Subtest and the degree of temporal lobe atrophy \((p < 0.01)\), and between Evans' Ratio and the Paired Associate Learning Test of the Wechsler Memory Scale \((p < 0.05)\). The P3 auditory evoked potential correlated significantly with a poor performance on the Digit Symbol Subtest. In all cases, cortical atrophy co-existed with ventricular dilatation and in none was intellectual impairment confined to short-term memory. The traditional criteria used in arriving at a diagnosis of Korsakoff's psychosis are called into question.

INTRODUCTION

In 1887 S. S. Korsakoff\(^1\) described the amnesic syndrome which now bears his name. Although the term 'Korsakoff's psychosis' is used by many in a restricted sense, to describe a memory defect accompanied by confabulation, it is evident from Korsakoff's writings that his patients exhibited a much wider range of mental symptoms, including delirium, anxiety, fear and depression. Evidence of a link between Korsakoff's psychosis and Wernicke's encephalopathy was provided by

103
Malamud and Skillicorn,\(^2\) when they showed that cerebral damage was indentical in both. At post-mortem, symmetrical lesions are found in the walls of the third ventricle, the periaqueductal region, the floor of the fourth ventricle, the medial dorsal and anteromedial nuclei of the thalamus, the pulvinar and the mamillary bodies. A great deal of discussion has centred on the question of the minimal lesion necessary for the production of amnesia. Victor, Adams and Collins,\(^3\) in their clinico-pathological study entitled *The Wernicke-Korsakoff syndrome*, stressed the importance of thiamine deficiency in the aetiology of this condition and suggested that a lesion involving the dorsomedial nucleus of the thalamus was of critical importance in its development. Their results could also be interpreted as showing that atrophy of both the dorsomedial nucleus and mamillary bodies was necessary for development of the amnesic syndrome. Bilateral lesions of the hippocampus and hippocampal gyrus lead to an amnesic syndrome similar to that found in Korsakoff's psychosis. The amnesia which results from diffuse cerebral damage is accompanied by intellectual impairment which tends to impede careful analysis of the memory disorder, and the size of the area damaged is thought to be more important than the site. The principal defect with both hypothalamic and hippocampal lesions is in recent memory. Disorientation in time is almost universal. Immediate memory, as tested by measuring the digit span, is preserved. A retrograde amnesia, extending for months or years before the onset of the illness, is also found.

This study looks at a group of nine patients in Purdysburn Hospital, Belfast, whose disorder at the time of admission was diagnosed as Korsakoff's psychosis (I.C.D. — 291.1). They were subjected to a series of psychometric tests, to electro-encephalography and to CT scanning. The stimulus for the study came from the work of Ron,\(^4\) who carried out CT scanning in a series of chronic alcoholic patients. She noted that clinically intact alcoholic subjects had learning difficulties resembling those encountered in Korsakoff's psychosis, and that these subjects had the largest ventricles. She suggested that the study be extended to include chronic alcoholics in whom brain damage was clinically apparent so that the possibility that alcohol-related organic psychosyndromes are part of a continuum might be explored.

**PATIENTS AND METHODS**

In October 1980, all hospital in-patients with a diagnosis of Korsakoff's psychosis were identified. Those aged over 60 years, and those with a history of head injury, epilepsy or severe functional illness, such as schizophrenia, were excluded. This left a group of nine patients — seven males and two females.

A typical history would be of a 54-year-old unemployed welder, living alone, and drinking often and heavily. He spent Christmas 1979 with his brother and 'behaved himself' until he was given a large sum of redundancy money. For the next five months he was scarcely ever sober. He was found unconscious at home by his brother, and admitted to an acute medical ward where he was described as 'hopelessly confused'. He was disorientated in time and place and was noted to be behaving strangely. He even poked the electric fire on one occasion, 'to get a bit more heat out of it'. No obvious neurological signs were elicited and physical investigations were normal, apart from liver function tests. He settled to a state of benign and placid affect, but remained disorientated. He recognised total strangers as friends and vice versa. Following his transfer to a psychiatric ward, his recent
memory was described as 'non-existent'. He said that King George V was the reigning monarch, and had to look at his library card to check his home address. He had been an avid reader, but was unable to recall the content of a book recently read, and produced an entirely fabricated account.

Routine physical examination, including neurological assessment, was carried out on each patient. The diagnosis was verified from the case notes and by interviewing the next of kin. The following psychometric tests were administered to all nine patients and controls by the same psychologist (as described by Lishman): 5

The Wechsler Adult Intelligence Scale (W.A.I.S.)
The Graham Kendall Memory for Designs Test.
The Williams Delayed Memory Test.
The Paired Associate Learning Test of the Wechsler Memory Scale.
The Modified Wisconsin Card Sorting Test.

Each subject was examined using the EMI CT5005 head scanner in the Royal Victoria Hospital, and the following measurements made by the same Consultant Radiologist.

*Evans' Ventriculo-Skull Ratio*: the maximum width of the frontal horns, divided by the maximum internal diameter of the skull, expressed as a percentage.

*Ventricular-Brain Ratio*: the ratio of ventricular area to maximum internal brain area, expressed as a percentage.

*Ventricular Size*: rated by the radiologist as small, medium or large.

*Cortical Atrophy Score*: rated by the radiologist as none (1), mild (2), moderate (3), severe (4). Ratings were made for each of the five cortical regions and a cumulative score calculated. The best possible cumulative score would be 5, the worst 20.

Routine electroencephalograms were carried out on all nine subjects. In addition the P3 component of the auditory evoked potential was investigated. Evoked potentials may be separated into stimulus-related components, which are sensitive to the physical characteristics of the stimulus, and event-related components which depend on the information content of the stimulus and appear only when the subject attends to a meaningful stimulus. The most prominent event-related potential is the P3 component, a positive wave which occurs at a latency of 300 to 500 msec. Goodin et al 6 showed an increased P3 latency in dementing subjects when compared with normals of the same age, and suggested that the magnitude of the latency change was large enough to provide a practical and objective measure of dementia in a clinical setting.

A control group of nine subjects, matched for age and sex, who either were teetotal or were occasional drinkers, of average intelligence, suffering from no serious psychiatric illness, and who were willing to participate without financial inducement, was found with some difficulty. Several were attending local services workshops and had previous histories of neurotic illness; the remainder were friends and relatives of patients in the hospital. The controls were not subjected to CT scanning. Statistical procedures were performed using the Statistical Package for Social Scientists (S.P.S.S.), in the Department of Medical Statistics, The Queen's University of Belfast.
RESULTS

In four of the nine cases, there was evidence of neurological impairment on physical examination at admission, including ataxia, nystagmus and peripheral neuropathy. All nine patients had presented with an acute confusional state, and with unequivocal evidence of alcoholism. A marked impairment of short-term memory was noted at, or shortly after, admission in every case. The average duration of in-patient care had been three years. In two of the nine cases, physical abnormalities were noted at the time of the study. One patient was severely ataxic with horizontal nystagmus, the other had peripheral neuropathy. On psychometric testing significant differences were found between cases and controls in 10 of the 13 tests (Table I).

TABLE I

Mean scores on Wechsler Adult Intelligence Scale for experimental group and controls

|                      | Korsakoff | Control |
|----------------------|-----------|---------|
| Verbal I.Q.          | 97.3      | 113.7   |
| Performance I.Q.     | 81.4      | 111.9   |
| Full-scale I.Q.      | 89.9      | 113.9   |
| Verbal performance discrepancy | 15.9 | 1.9   |
| Comprehension        | 9.2       | 11.6    |
| Arithmetic           | 8.4       | 12.8    |
| Similarities         | 8.0       | 11.8    |
| Digit span           | 8.9       | 11.4    |
| Vocabulary           | 10.3      | 12.2    |
| Digit symbol         | 3.7       | 8.5     |
| Picture completion   | 6.1       | 10.9    |
| Block design         | 5.4       | 10.7    |
| Object assembly      | 3.9       | 10.1    |

* p < 0.05
** p < 0.01
*** p < 0.001

Adjusted for pre-morbid I.Q.

These differences persisted after an analysis of covariance to allow for the higher pre-morbid I.Q. in the control subjects. Significant differences emerged in all the performance subtests (digit symbol, picture completion, block design and object assembly), indicating diffuse cerebral damage in the cases. The non-significant differences occurred in three of the five verbal subtests (comprehension, arithmetic, similarities, digit span and vocabulary) which are less vulnerable to brain damage and reflect the use of old knowledge. The absence of a significant difference in digit span — a measure of immediate memory — between cases and controls would be expected.

Significant differences were found in verbal and non-verbal memory tests (Table II). The cases were significantly less able to recall both verbal (Paired Associate
Learning) and visual (Williams Delayed Memory and Graham Kendall Memory for Designs) materials and performed poorly on the Modified Wisconsin Card Sorting Test, indicating frontal lobe damage.

**Table II**

*Mean scores on Psychometric Tests for experimental group and controls*

| Test                                          | Korsakoff | Control |
|-----------------------------------------------|-----------|---------|
| Williams Delayed Memory                       | 25.7      | 3.0     |
| Graham Kendall Memory for Designs             | 1.8       | -3.6    |
| Modified Wisconsin Card Sorting Test          | 30.4      | 3.1     |
| Paired Associate Learning                     | 6.0       | 11.9    |

* p < 0.05  
** p < 0.01  
*** p < 0.001  
Adjusted for pre-morbid I.Q.

On CT scanning, cortical atrophy was present in every case, with a mean total atrophy score of 9.8 (S D 1.9, range 7-12). The highest mean atrophy score for an individual region was for the parietal cortex (Table III).

**Table III**

*Cortical atrophy ratings for different cortical regions in experimental group*

| Cortical atrophy | None | Mild | Moderate | Severe | Mean |
|------------------|------|------|----------|--------|------|
| Temporal         | 2    | 6    | 1        | 0      | 1.9  |
| Parietal         | 2    | 4    | 3        | 0      | 2.1  |
| Insular          | 2    | 5    | 2        | 0      | 2.0  |
| Frontal          | 2    | 6    | 1        | 0      | 1.9  |
| Occipital        | 1    | 8    | 0        | 0      | 1.9  |

Evans ratio was originally devised for use with pneumoencephalograms in the coronal plane, but this name is also used for the equivalent ratio in the transverse plane on CT scanning. The mean ratio in the experimental group was 28.2%. Four subjects had an Evans’ ratio above 29.4% which was found by Haug to be the upper 95% confidence limit in a study of normal ventricles. All nine subjects in this study had an abnormal ventricular brain ratio (10% or more), using the normal data of Synek et al. Ventricular size in one subject was rated as small, in four as normal and in four as large. There was a significant positive correlation between the ventricular brain ratio and ventricle size (p < 0.01). Atrophy of the temporal cortex was significantly correlated with both the ventricular brain ratio and ventricle size (p < 0.05).

A significant negative correlation was found between scores on the digit symbol subtest of the WAIS and the degree of temporal lobe atrophy (p < 0.01).
A significant negative correlation was also found between Evans’ ratio and scores on the Paired Associate Learning Test of the Wechsler Memory Scale (p < 0.05). The relationship between cognitive deficits and neuropathological lesions at post-mortem or in biopsy specimens is not always close, and the same applies to abnormalities detected by pneumoencephalography. It would, therefore, be surprising if a very close correlation was present in the case of abnormalities detected by CT scan.

The routine electroencephalogram was reported as abnormal in six of the nine subjects, most often showing diffuse slowing. The EEG was normal in all nine controls. The mean P3 latency for the experimental group was 400 msec (range 295-540, S D 80). Four of the cases exceeded a value of 410 msec which would be the electrophysiological definition of dementia for this age group proposed by Goodin.6 The P3 latency was found to correlate significantly with a poor performance on the Digit Symbol Subtest of the WAIS (p < 0.01).

DISCUSSION

Tarter10 summarised four contemporary hypotheses regarding the nature of the neuropsychological disturbance in chronic alcoholics:

1. ‘Chronic Alcohol Consumption leads to diffuse or generalised cerebral damage’. On the whole, CT scan studies in alcoholics have confirmed the presence of cortical atrophy and dilated ventricles in a large proportion of alcoholics.11 There is no evidence of involvement of the posterior temporal or occipital areas in alcoholics, so the cerebral damage cannot be said to be diffuse.

2. ‘Alcoholics are relatively more disrupted in the right than left hemisphere of the brain’. There is no evidence from psychological research which would support this hypothesis. It is possible, however, that the observed deterioration in visuospatial as opposed to verbal ability is because visuospatial functions are more susceptible to cerebral pathology than the automatic and overlearned verbal processes.

3. ‘The chronic consumption of alcohol causes an acceleration of the ageing process’. There is some evidence that the performance of alcoholics on neuropsychological tests is analogous to a premature ageing process.12 While the analogy is a useful one, no information about the underlying mechanism can be deduced from it.

4. ‘Alcoholics suffer from frontal-limbic-diencephalic pathology’. There is a large body of evidence demonstrating that these brain regions are morphologically and functionally integrated. Pneumoencephalogram and CAT scan studies show evidence of frontal atrophy, and, on psychometric testing, alcoholics manifest impairment similar to that found in acute frontal lesions.

Paraventricular atrophy was found in a large group of ‘intact alcoholics’ when echoencephalography was used to measure the width of the third ventricle.13 Compared with non-alcoholic control subjects, alcoholics and Korsakoff patients perform poorly on visuoperceptual tasks, i.e. digit symbol tests and embedded figure tests. Invariably, the scores of the alcoholic group fall intermediate between those of the Korsakoffs and the controls.14 The Digit Symbol Subtest emerged as a particularly useful and sensitive indicator of brain damage and provided significant correlations with CT scan indices, and P3 latency. Isolated abnormalities in digit
symbol testing have been said to be characteristic of Korsakoff's psychosis.\textsuperscript{15} This could, however, be related to the test's sensitivity rather than its specificity for the amnesic syndrome. Ryan et al\textsuperscript{16} set out to investigate short-term memory in clinically intact chronic alcoholics, which other workers had consistently found to be normal. They did indeed uncover short-term memory deficits of the kind encountered in Korsakoff patients.

The reasons for thinking that the Korsakoff syndrome is caused by thiamine deficiency are that it is frequently associated with Wernicke's encephalopathy, and that tumours or other lesions in the brain may cause the amnesic syndrome. Although some Korsakoff patients improve concomitantly with thiamine therapy, treatment failures are common, indicating the need for a closer look at other causes. Since it is conceivable that this syndrome could arise from deficiency of several nutritional factors, or from some direct toxic effect of ethanol itself, and bearing in mind that they may act simultaneously, the cause is bound to remain obscure. There is, however, circumstantial evidence. Reviewers have been unable to find reports of any documented cases of permanent Korsakoff syndrome (with disturbed memory persisting for more than two or three months) in a patient with the Wernicke syndrome which was induced by malnutrition alone.\textsuperscript{17} There was no documented permanent mental disability in a large number of prisoners-of-war with longstanding malnutrition which had resulted in severe neurological disorders. One possible explanation is that ethanol is the causal factor, and that when patients finally present and are recognised as having Wernicke's encephalopathy they have already sustained recurrent and irreversible damage. This conclusion is supported by reports of patients dying and having the classical lesions at post-mortem but not exhibiting the signs attributed to Wernicke's encephalopathy.\textsuperscript{18} The Korsakoff syndrome has also been described in alcoholic patients when histological lesions were confined to the cerebral cortex. It is uncertain which of the diencephalic structures is more critical for memory formation, since not all patients with extensive anatomical involvement causing the Wernicke syndrome have the Korsakoff symptoms.\textsuperscript{19}

This study highlights the problems involved in defining and diagnosing Korsakoff's psychosis. Wernicke's encephalopathy is not a necessary prerequisite.\textsuperscript{3} The short-term memory defect considered pathognomonic of Korsakoff's psychosis has been demonstrated in clinically intact alcoholics.\textsuperscript{15} Diencephalic lesions at post-mortem do not correlate with symptomatology in life. A high percentage of clinically intact alcoholics show cortical atrophy and ventricular dilatation on CT scanning, which must render any diagnosis of Korsakoff's psychosis made on the basis of psychometric testing alone suspect, and the results of such research questionable. If Korsakoff's psychosis is defined as a severe short-term memory defect in the absence of any other intellectual impairment, with damage confined to the diencephalic region, it can be diagnosed with certainty only at post-mortem, and must surely be exceedingly rare. I have been able to find only one such case in the literature.\textsuperscript{20} In all nine cases in this study, cortical atrophy co-existed with ventricular dilatation, and in none was intellectual impairment confined to short-term memory.

While these problems of definition, diagnosis, and aetiology remain, the usefulness and validity of making a diagnosis of alcoholic Korsakoff's psychosis must be questionable.
I am indebted to Mrs Heather Grant for administering the psychometric tests to both patients and controls. Dr R Hutchinson carried out the CT scanning and measurements, Dr J Lumsden interpreted the electroencephalograms, and Mr C Patterson gave statistical and computing advice. I am also grateful to Professor George Fenton for his help and encouragement.

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110