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Clinical Tests of Memory

MICHAEL D. KOPELMAN

This study compared the performance of groups Alzheimer, Korsakoff, and depressed patients and a group of healthy controls at various clinical tests of memory, and wide differences were found in the discriminatory power of the different tests. In addition, the patterns of performance of the Alzheimer and Korsakoff groups differed, and to some extent this was understandable in terms of what is known about the nature of organic amnesia. Depressed patients showed relatively mild impairments, which were not correlated with the severity of their depression.

There have been various attempts to develop memory tests which would differentiate patients with organic disorders from those with functional diagnoses or from healthy controls. The Wechsler Memory Scale (Wechsler, 1945) was developed in part for this purpose, but it is cumbersome to administer and subject to a number of criticisms (Erickson & Scott, 1977; Prigatano, 1978; Schacter & Tulving, 1982; Warrington, 1982). Various other tests or combinations of tests have also been employed for this purpose; in general, evidence of their reliability and concurrent validity (in terms of clinical diagnosis) has been satisfactory (Williams, 1968; Whitehead, 1973; Kendrick *et al*, 1979). In particular, the use of a simple paired-associate learning test has been successfully employed in discriminating dementing from non-dementing elderly patients (Inglis, 1959; Isaacs & Walkey, 1964; Priest *et al*, 1959; Irving *et al*, 1970). More recently, Coughlan & Hollows (1984) demonstrated that a battery of six verbal and visual memory tests could differentiate a mixed group of neurological patients (aged under 65 years) from depressed patients and healthy controls.

There are three principal difficulties with such studies. Firstly, they have usually employed heterogeneous samples of organic patients. There is evidence that the nature of the memory impairment in amnesic patients may differ between diagnostic groups (Lhermitte & Signoret, 1972; Luria, 1976; Cutting, 1978a; Huppert & Piercy, 1979; Butters & Cermak, 1980), and in particular, that the underlying memory deficits may be more extensive in dementing disorders than in the more discrete amnesic syndromes (Miller, 1973; Butters & Cermak, 1980; Weingartner *et al*, 1983; Kopelman, 1985a, b). This means that tests which discriminate for one diagnostic group of patients may not do so for another. Secondly, many studies have also employed a heterogeneous group of functional patients, which gives rise to further problems of interpretation, and these studies have not always used healthy controls as a comparison group to assess the extent of any impairment within the functional sample. Thirdly, most studies have been content to demonstrate statistically significant differences between the mean scores of their groups, and data have not been presented in a form which allows the relative discrimination of different tests to be easily compared (other than in terms of the degree of statistical significance).

A more serious problem is that there is considerably less evidence regarding the validity of everyday tests employed by clinicians than there is regarding more formal, psychometric assessments. Shapiro *et al*. (1956) found that delayed (5-min) recall of a name and address failed to distinguish an elderly group of psychiatric patients with memory impairment from those without amnesic difficulties. Likewise, Warburton (1963) showed that a majority of (mentally) healthy subjects over the age of 40 failed the so-called Babcock sentence test, making its clinical usefulness very doubtful. Withers & Hinton (1971) developed three forms of a Clinical Test of the Sensorium, which included various memory items and which has been employed in a number of clinical studies (Johnstone *et al*., 1976); their tests did indeed appear to discriminate between patients with a brain syndrome and healthy controls. However, the validation study included only six patients with a brain syndrome, and the mean age of these patients was 20 years older than that of the controls (Hinton & Withers, 1971).

The present study employed a clinical test of memory and orientation and several verbal learning tests to examine discrete groups of dementing,

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organic amnesic, and functional patients as well as a group of healthy controls. The clinical test of memory and orientation was the Gresham Questionnaire (Institute of Psychiatry, 1973), which was adapted for outpatient as well as inpatient use. The verbal learning tests were selected as being *either (i)* ones commonly employed in clinical practice, *or (ii)* more formal tests, which might easily be administered by a clinician at the bedside. The subject groups were each homogeneous for diagnosis, consisting of Alzheimer patients (dementing group), alcoholic Korsakoff patients (amnesic group), and hospitalised depressed patients (functional group).

Method

Subject groups

Alzheimer patients were diagnosed according to clinical history and examination, with physical investigations to exclude other possible causes of dementia. In addition, it was required that patients should have psychometric evidence of generalised cognitive impairment and CT scan (computerised axial tomographical) evidence of cortical atrophy. None of the patients was hypertensive and none had a history of cerebrovascular disease. Mean duration of symptoms was 2.9 years (range 6 months to 5 years). Mild extrapyramidal symptoms were elicited in 5 out of 16 cases, primitive reflexes in 5 out of 16, and either impaired copying and drawing or frank apraxic signs in 12 out of 13 tested. One further patient was excluded because a changed pattern of symptoms at a 2-year follow-up suggested another cause of dementia. The Alzheimer patients were asked to do Raven's Coloured Progressive Matrices (Raven *et al*, 1977), and Intelligence Quotients (IQ) were obtained from Raven's age-related tables. If the patient's IQ was ≥ 75 on this screening, he or she was retested on those sub-tests of the Wechsler Adult Intelligence Scale (WAIS) employed by Savage *et al* (1973) and a pro-rated full scale IQ obtained. The patient with the highest IQ (full scale = 116) had deteriorated by 21 points over an 11-month period. As reported elsewhere (Kopelman, 1985b), Alzheimer patients had a significantly larger mean ventricular-brain ratio (VBR) on CT scan ($t = 4.36$, $P < 0.001$) and a significantly greater rating of cortical atrophy ($t = 3.61$, $P < 0.01$) than the Korsakoff patients.

Korsakoff patients were selected to conform as closely as possible to the acute onset group described by Cutting (1978b). Eight out of 9 cases in which the mode of onset was known had had an acute onset of the disorder (i.e. less than 8 weeks between onset of symptoms and admission). The patients had a similar age- and sex-distribution to Cutting's sub-group, reflecting the different age- and sex-distribution of this disorder from Alzheimer-type dementia. With respect to Wernicke symptoms, 12 out of 16 cases had a recorded history of nystagmus and/or ophthalmoplegia, all cases had a history of ataxia and of disorientation in time, and 10 a history of peripheral neuropathy. All had an alcoholic aetiology, with a mean duration of heavy alcohol abuse of 24 (range 10 to 37.5) years. Median time 'dry' was 24 weeks (range 8 weeks to 12 years), and although some patients had shown a degree of improvement on repeated psychometric testing, all were severely incapacitated by their memory disorder—either living in institutions or heavily dependent on institutional support.

Depressed patients all had a clinical diagnosis of a primary depressive disorder: mood change was prominent and biological symptoms invariably present. Onset had been acute or subacute in all cases, and the severity of the depression was such that they were all hospitalised inpatients during a 3-month period (August to October 1984). Mean Hamilton Depression score (Hamilton, 1960) was 28.1 ± 4.1 (range 20–35). The sample was selected so that it would overlap in terms of sex-distribution (8 M:8 F) and age (mean 60.6, range 42 to 74 years) with the Alzheimer and Korsakoff patients. Patients who had had ECT within the last 3 years, any evidence of organic impairment, or any history of recent alcohol abuse were excluded from the sample. Thirteen of the 16 patients were taking antidepressant medication, one lithium, six phenothiazines, and seven benzodiazepines (usually as night sedation); only two patients were yet to be started on any medication. In none of the patients were memory symptoms so prominent that a diagnosis of pseudodementia had been considered; however, on direct questioning, virtually all the patients complained of forgetfulness.

Control subjects were selected to match the depressed patients and to overlap with the Alzheimer and Korsakoff patients in terms of sex- (8 M:8 F) and age-distribution (mean 60.4, range 38 to 73 years). It was possible to subdivide the control group into an Alzheimer comparison group (2 M:6 F, mean age 66.25, range 55 to 73 years) and a Korsakoff comparison group (6 M:2 F, mean age 54.5, range 38 to 67 years), although this did not prove necessary for present purposes. The control subjects consisted of healthy elderly subjects living in sheltered accommodation and younger subjects from the MRC Applied Psychology Unit Research Panel and from the Institute of Psychiatry non-academic staff.

Tests employed

Gresham questionnaire (Shapiro *et al*, 1956; Institute of Psychiatry, 1973): a clinical interview designed to assess memory and orientation (especially in the elderly), and, in the present study, adapted for outpatient as well as inpatient use. The amended questionnaire is available from the author on request. Maximum score = 43.

Wechsler logical memory (Wechsler, 1945): recall of the contents of a short paragraph, immediately and after 45 min

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delay. Maximum score = 23. Percentage retention = 45 min score ÷ immediate score.

Paired-associate learning (Isaacs & Walkey, 1964; Priest *et al*, 1969): a very simple paired-associate test, previously found useful in assessing elderly and dementing patients, and consisting of three very easy paired-associates (e.g. east–west) and three more difficult paired associates (e.g. gold-lead). Maximum score = 18.

Name and address (Withers & Hinton, 1971): an 8-word name and address to be recalled immediately (repeated by the examiner until one perfect recall or a maximum of five learning trials had occurred) and after 4 min delay. Maximum score = 8.

Anomalous sentences test (adapted from Newcombe & Marshall, 1967; Newcombe, 1969): Subjects were asked to repeat immediately back to the examiner two normal sentences and six anomalous sentences. Four sentences had normal syntax but aberrant semantics (e.g. 'Colourless green ideas sleep furiously'); one sentence provided the opportunity for semantic confusions ('Wasn't the rich uncle advised by the nice manager?'); and one was a random word-string ('Not in tree to the ran lake with'). All eight sentences were read to the subject before testing proper began. Each sentence was then re-read to the subject, who was required to repeat it verbatim, and there was a maximum of four learning trials for each sentence. Maximum score for test (perfect recall) = 32.

Digit span forward (Wechsler, 1945): assessed according to the procedure of the Wechsler memory scale. Performed on two occasions (usually a week apart) and mean score taken.

Supraspan (Zangwill, 1943; Miller, 1973): digit span was established, and then the subject was required to learn a sequence two digits greater than his/her immediate span. Number of learning trials for perfect recall recorded up to a maximum of 10.

Babcock sentence (Babcock, 1930; Zangwill, 1943): number of learning trials required for perfect recall of the Babcock sentence, up to a maximum of 10.

Results

Table I shows that the four groups were approximately matched for premorbid IQ, as evaluated by a reading test (Nelson & O'Connell, 1978). Whilst the Alzheimer group had a substantially lower current IQ ($F = 24.3$, $P < 0.001$), the other three groups did not differ significantly from one another ($F = 0.94$, NS). The Korsakoff patients and the depressed group both showed, at most, very trivial deterioration in terms of general intellectual function.

Table II shows the mean scores of the four groups at all the tests except Supraspan and the Babcock sentence. All

TABLE I
Summary description of samples

	Healthy controls (C) (n = 16)	*Depressed patients (D) (n = 16)*	*Korsakoff patients (K) (n = 16)*	*Alzheimer patients (A) (n = 16)*
Sex ratio	8 M:8 F	8 M:8 F	13 M:3 F	4 M:12 F
Mean age (years)	60.4(±10.5)	60.6(±9.2)	56.5(±7.1)	65.6(±6.8)
(range)	(38–73)	(42–74)	(38–66)	(56–75)
Premorbid IQ estimate by NART[1,2] mean (±s.d.)	108.5(±9.3)	107.6(±8.3)	106.3(±11.5)	105.9(±9.6)
Full scale IQ[3] mean (±s.d.)	107.3(±12.3)	103.7(±5.9)	101.8(±12.3)	71.4(±17.2)
(range)	(84–124)	(87–122)	(81–124)	(48–116)
Deterioration index[2] (NART − IQ) Mean (±s.d.)	0.3(±6.9)	3.9(±7.5)	5.4(±8.7)	32.7(±18.4)

[1]New Adult Reading Test: Nelson & O'Connell (1978).
[2]Data available for $n = 14$ for each of controls, Korsakoffs and Alzheimers: $n = 16$ for depressed patients.
[3]For method of determination in the Alzheimer group, see text.

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TABLE II

Mean scores of clinical groups on memory tests, and statistical significance of differences between groups

	Healthy controls (C)	*Depressives (D)*	*Korsakoffs (K)*	*Alzheimers (A)*	*ANOVA F*	*ANOVA P*	*Non-organic[1] versus organic[2]**	*C versus D**	*D versus K**	*K versus A**
Gresham										
Orientation	8.0	7.7	3.4	5.0	33.2	<0.001	<0.001	NS†	<0.001	<0.05
Remote personal	11.7	10.9	6.0	6.9	63.75	<0.001	<0.001	<0.02†	<0.001	NS
Recent personal	10.1	10.0	2.1	3.4	139.5	<0.001	<0.001	NS	<0.001	<0.05
General events	10.6	9.4	3.9	3.8	54.5	<0.001	<0.001	NS	<0.001	NS
Total score	40.0	38.0	15.3	19.2	170.2	<0.001	<0.001	0.02†	<0.001	<0.05
Logical memory										
Immediate recall	12.1	9.3	4.1	3.2	46.5	<0.001	<0.001	<0.02	<0.001	NS
Delayed recall	9.9	6.8	0.4	0.3	84.3	<0.001	<0.001	<0.01	<0.001	NS
Percentage retention	81.8	73.1	9.8	9.4	149.8	<0.001	<0.001	NS	<0.001	NS
Paired-associate learning										
Very easy pairs	8.9	8.3	8.1	5.6	20.6	<0.001	<0.001	<0.05†	NS	<0.001
More difficult pairs	8.3	6.9	5.1	3.25	15.0	<0.001	<0.001	<0.02†	<0.05	NS
Total score	17.2	15.2	13.1	8.8	22.5	<0.001	<0.001	<0.02†	NS	<0.01
Name and address										
Delayed recall (4 min)	6.9	6.0	2.1	1.7	33.1	<0.001	<0.001	NS	<0.001	NS
Anomalous sentences										
Total Score	26.1	25.8	23.9	15.8	11.8	<0.001	<0.001	NS	NS	<0.001
Digit span										
Forward	6.4	6.7	6.5	5.4	**6.5	<0.001	<0.02	NS	NS	<0.01

*t-tests. Two-tailed level of significance given for all tests cited.

**Co-varying for age = 5.65; $P < 0.005$.

†Mann Whitney U-test employed when variance within groups could not be assumed to be homogeneous (tested by F_{max} statistic).

[1]C + D.

[2]K + A.

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TABLE III

Number of subjects in each group failing to score at cut-off point on memory tests (n = 16 in each group)

	Healthy controls (C)	*Depressives (D)*	*Korsakoffs (K)*	*Alzheimers (A)*	χ^2	*P*	*Non-organic*[1] *versus organic*[2]	*C versus D**	*D versus K**	*K versus A**
Gresham										
Orientation < 7	0	1	15	12	44.2	<0.001	<0.001	NS	<0.001	NS
Remote personal < 10	0	1	16	15	56.5	<0.001	<0.001	NS	<0.001	NS
Recent personal < 8	0	0	16	16	64.0	<0.001	<0.001	NS	<0.001	NS
General events < 7	0	0	15	13	50.3	<0.001	<0.001	NS	<0.001	NS
Total score < 32	0	0	16	16	64.0	<0.001	<0.001	NS	<0.001	NS
Logical memory										
Immediate < 7	0	5	15	15	42.6	<0.001	<0.001	NS	<0.001	NS
Delayed < 5	0	3	16	16	54.2	<0.001	<0.001	NS	<0.001	NS
Retention < 50%	0	0	16	16	64.0	<0.001	<0.001	NS	<0.001	NS
Paired-associates										
More difficult pairs < 6	0	3	8	12	23.0	<0.001	<0.001	NS	NS	NS
Total score < 14	0	3	8	14	30.3	<0.001	<0.001	NS	NS	NS
Total score < 16	3	8	10	15	18.8	<0.001	<0.001	NS	NS	NS
Name and address										
Learning trials > 2	2	3	2	13	25.0	<0.001	<0.01	NS	NS	<0.001
Delayed recall score < 6	0	7	15	14	37.1	<0.001	<0.001	<0.02	<0.01	NS
Anomalous sentences										
Score < 16	1	0	1	8	19.4	<0.001	<0.01	NS	NS	<0.02
Score < 22	4	3	5	13	16.5	<0.001	<0.01	NS	NS	<0.02
Supraspan (+2)										
Learning trials > 5	11	12	14	14	2.6	NS	NS	NS	NS	NS
Learning trials > 10	5	11	8	13	9.4	<0.05	NS	NS	NS	NS
Babcock sentence										
Learning trials > 5	9	14	13	16	10.7	<0.02	NS	NS	NS	NS
Learning trials > 10	6	8	12	15	13.2	<0.01	<0.001	NS	NS	NS

[1] C + D.

[2] K + A.

* χ^2 with Yates's correction.

the tests discriminated at a very high level of statistical significance between the non-organic (control + depressed) and organic (Korsakoff + Alzheimer) groups. The most discriminating tests were the Gresham in terms of recent personal memory ($F = 139.5$) and total score ($F = 170.2$) and Wechsler logical memory in terms of percentage retention ($F = 159.8$). Despite this, some interesting and important differences between the tests emerged when the performance of individual groups was compared (see Table II).

Depressives scored lower than healthy controls at all tests except digit span. Differences were small, but were statistically significant for Gresham remote personal memory and total score, Wechsler logical memory (immediate and delayed recall), and paired-associate learning. There were no significant correlations between the depressives' Hamilton scores and their performance at any of the memory tests.

Both Korsakoff and Alzheimer patients were significantly impaired, relative to depressives, at the Gresham and logical memory tests, paired-associate learning of more difficult pairs, and delayed recall of a name and address. However, there were no significant differences between the Korsakoff and depressive groups at digit span, paired-associate learning of very easy pairs, or the anomalous sentences test.

The Alzheimer group was significantly impaired on each of these last three tests, relative to the Korsakoff group, and also relative to the other two groups. The only tests at which Alzheimer patients scored significantly higher than Korsakoff patients were the orientation and recent personal memory scales of the Gresham, and the Gresham total score.

Table III shows the relative discrimination between the groups by the different tests at selected cut-off points. Data for the Supraspan and Babcock sentence tests are included, showing the numbers of subjects in each group who failed at these tests after five and after 10 learning trials. The cut-off points for the other tests are those which gave the best discrimination between the non-organic and the organic groups. Also shown for the paired-associate total score is the cut-off point (less than 16) which Priest *et al* (1969) reported to discriminate maximally between organic and functional patients.

The three most discriminating tests (Gresham recent personal memory score below 8, Gresham total score below 32, and Wechsler logical memory percentage retention less than 50%) all gave perfect differentiation between the non-organic and organic groups in the present sample. Most of the other tests gave statistically significant discrimination between the non-organic and organic groups, but the paired-associate learning test was unsatisfactory, in that it failed to discriminate significantly between depressed and Korsakoff patients. The Supraspan and Babcock sentence tests gave very poor discrimination.

Using these cut-off points, more depressives scored within the impaired range on most tests than did healthy controls, but the difference was statistically significant only for delayed recall of a name and address. Alzheimer patients were impaired significantly more frequently than Korsakoff patients (and also than the other two groups) at learning a name and address within two trials and at the anomalous sentences test.

Discussion

The samples employed in the present study were relatively small, but, unlike those in many other studies, homogeneous for diagnosis. Moreover, the Alzheimer and Korsakoff groups both displayed a severe memory impairment (revealed by their clinical histories, as well as by their Gresham and logical memory performance). Those tests which failed to differentiate these patients clearly from depressives or healthy controls are therefore very unlikely to be of diagnostic value in assessing individual cases with a milder degree of memory impairment.

Non-organic versus organic groups

Although virtually all the tests differentiated between these two groups at a statistically significant level, the results revealed wide variability in their discriminatory power.

The Gresham and Wechsler logical memory tests gave by far the best discrimination. Both tests have previously been validated in studies employing a prospective component (Shapiro *et al*, 1956; Whitehead, 1973). This indicates the clinical usefulness of a memory and orientation questionnaire such as the Gresham, but also reminds us that impairment on such a scale is by no means diagnostic of dementia: the Korsakoff group scored significantly lower in terms of total score than the Alzheimer group ($t = 2.16$, $P < 0.05$). The usefulness of the Wechsler logical memory test is corroborated by the recent finding of Sunderland *et al* (1983) that impairment at this test is correlated more strongly with the severity of everyday memory symptoms reported by questionnaire than is performance at other psychometric tests. Sunderland *et al* (1983) examined severe head injury patients, and the memory questionnaire was completed in each case by both the patient and a relative.

Delayed recall of a name and address also gave satisfactory discrimination; and the paired-associate learning test differentiated between the non-organic and organic groups, as Priest *et al* (1969) had earlier found. However, this latter test illustrated the hazards of comparing heterogeneous groups, because the total test score failed to differentiate at a statistically significant level between the depressed and Korsakoff samples. This particular paired-

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associate test contains word-pairs of a very high or a somewhat lower degree of association. Recall of paired-words of very high associative status (eg east-west) can hardly be construed as a test of new learning, and indeed it has previously been reported that Korsakoff patients are relatively unimpaired at recalling high-associate paired words (Wechsler, 1917; Warrington & Weiskrantz, 1982). The present results were consistent with that observation: the Korsakoff patients were unimpaired at recalling the very easy pairs (of high associative status), but were significantly impaired at the more difficult pairs (of lower associative status). By contrast, Alzheimer patients were impaired at recalling both the very easy and the more difficult paired associates.

The Supraspan and Babcock sentence tests gave very poor discrimination, the results confirming Warburton's (1963) observation that healthy controls over 40 frequently perform very poorly at such tests. Though these tests are still widely employed in clinical practice, the present results suggest that they should be abandoned.

Controls versus depressives

Various previous authors have noted impairment by depressed patients relative to healthy controls on memory and other cognitive tests (Whitehead, 1973; Weingartner *et al*, 1981). Cohen *et al* (1982) reported that the degree of impairment was closely related to the severity of depression, as assessed by various rating scales (including the Hamilton), whereas Friedman (1964) and Coughlan & Hollows (1984) found that impairment was mild and had no significant association with the severity of depression. The present study is consistent with the latter observations. Depressives performed worse than healthy controls at all tests except digit span, the differences being statistically significant in some instances, but the degree of impairment tended to be relatively small and there was no significant correlation with Hamilton scores.

Alzheimer versus Korsakoff patients

The tests at which Alzheimer, but not Korsakoff patients were severely impaired were those which required immediate recall of a relatively small quantity of verbal material: viz, digit span, immediate recall of a name and address, recall of very easy paired-associates, and the anomalous sentences test. It has been argued elsewhere that Alzheimer, but not Korsakoff patients have a severe impairment of immediate or primary memory, also known as short-term or working memory (Miller, 1971, 1973; Wilson *et al*, 1983; Kopelman, 1985a, b). The primary memory store is assumed to have a very limited capacity, and to hold information for a few seconds only before most of it is filtered out and decays, a relatively small proportion being encoded into a secondary, more permanent memory store (Hunter, 1964; Craik, 1971; Baddeley, 1976). Given that the present Alzheimer patients were not dysphasic, an impairment of primary (or working) memory may best account for their deficit at those tests which Korsakoff patients were able to perform satisfactorily. This interpretation with respect to the anomalous sentences test will be discussed in greater detail elsewhere (Kopelman, 1986).

Weingartner *et al* (1983) have recently proposed that the memory disorder of Alzheimer-type dementia differs from that of Korsakoff's syndrome in that it involves a deficit of semantic as well as of episodic memory. Semantic memory refers essentially to stored, conceptual knowledge of the world, as distinct from a stored record of personal experiences (Tulving, 1972; Baddeley, 1964). As such, it is a conglomerate term, encompassing, for example knowledge of the use of language and syntax, and of personal details (e.g. date of birth, height, and weight), and worldly information (e.g. being able to name the present prime minister). The present results on relevant Gresham questionnaire items indicate that the Korsakoff group's conceptual knowledge of the world was, in some respects, at least as impaired as that of the Alzheimer group. Thus, a crude distinction between the memory disorders of the two conditions, based on the episodic/semantic dichotomy, is unlikely to be very useful.

Conclusion

The present study revealed very wide differences in the discriminatory power of various clinical tests of memory: the most satisfactory were of memory and orientation questionnaire (the Gresham) and the Weschler logical memory test. Other tests—Supraspan and the Babcock sentence—were very unsatisfactory and would best be abandoned.

To a substantial degree, the differing patterns of performance by the Alzheimer and Korsakoff groups could be understood in terms of what is already known about the nature of organic amnesia. Alzheimer, but not Korsakoff, patients were impaired at tests which appeared to depend heavily upon an intact immediate or primary memory. Moreover, Korsakoff patients were able to recall

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paired-associates without difficulty when the pairs were of high associative status. This study confirmed those previous ones which have suggested that, although depressed patients are impaired at memory tests, the impairment is not marked and is not correlated with the severity of the depression.

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Michael D. Kopelman, BA, MB, MRCPsych, ABPS. *Wellcome Trust Lecturer, Institute of Psychiatry, De Crespigny Park, Denmark Hill, London SE5 8AF.*

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