Pergamon

Neuropsychologia, Vol. 33, No. 12, pp. 1583–1596, 1995
Elsevier Science Ltd
Printed in Great Britain
0028-3932/95 $9.50 + 0.00

0028-3932(95)00145-X

THE PERFORMANCE OF AMNESIC SUBJECTS ON TESTS OF DELAYED MATCHING-TO-SAMPLE AND DELAYED MATCHING-TO-POSITION

J. S. HOLDSTOCK, C. SHAW* and J. P. AGGLETON†

Department of Psychology, University of Durham, Science Laboratories, South Road, Durham DH1 3LE, U.K.; *Centre for Health Services Research, University of Newcastle Upon Tyne, 21 Claremont Place, Newcastle upon Tyne NE2 4AA, U.K.; and †School of Psychology, University of Wales, P.O. Box 901, Cardiff CF1 3YG, U.K.

(*Received* 28 *November* 1994; *accepted* 7 *August* 1995)

Abstract—Forced-choice tests of recognition have become the favoured behavioural method for the assessment of models of amnesia in nonhuman primates, yet the profile of deficits shown by human amnesic subjects remains uncertain. The present study explored the performance of 12 amnesic subjects on two delayed matching-to-sample tasks. Experiment 1, which used retention delays of between 2 and 60 sec, confirmed that amnesia impairs such tasks, even when there is only one item to be remembered. The results also highlighted the need to match levels of performance before the effects of delay can be interpreted. In Experiment 2 care was taken to eliminate ceiling effects and to match the subjects at the shortest delay (3 sec). This was achieved by giving the control subjects harder versions of the same task. The amnesic subjects still showed a faster rate of forgetting for abstract patterns, indicating that this is a genuine feature of amnesia. In contrast, the amnesic subjects' performance on a spatial matching-to-sample task was not differentially affected by delays of up to 40 sec. There was no evidence that the amnesic subjects were disproportionately impaired on this spatial task, nor could the different aetiological groups be distinguished by their patterns of DMS performance.

Key Words: amnesia; memory; recognition; spatial memory.

INTRODUCTION

Our understanding of the pathology of anterograde amnesia has been considerably advanced by studies examining the effects of selective temporal lobe and diencephalic lesions in nonhuman primates. The most influential behavioural test of memory used to assess such lesions has been delayed nonmatching-to-sample (DNMS). The basic task examines the ability of an animal to select between two stimuli, one of which has just been presented to the animal and so is familiar, while the other is novel. It has become widely accepted that a deficit on the DNMS task is a prerequisite for any animal model of anterograde amnesia [35, 37]. This view is supported by studies showing that similar tests of recognition memory are sensitive to anterograde amnesia in human subjects [5, 6, 33].

A number of recent analyses have, however, questioned the use and interpretation of the DNMS task as a measure of amnesia in monkeys [7, 29]. One problem is that the

†Address for correspondence: School of Psychology, University of Wales College of Cardiff, P.O. Box 901, Cardiff CF1 3YG, U.K.

performance of control animals is often at, or close to, ceiling levels, so obscuring the magnitude of any lesion-induced deficit. Furthermore, the scores of control and experimental animals may differ at the easiest (shortest delay) conditions, so making it very difficult to interpret any delay-dependent lesion effects [30]. Even when the scores do not differ at the shortest delay the results may be compromised by different amounts of training [30]. A related issue concerns the possibility that the very severe deficits shown by monkeys with lesions of the rhinal cortex may principally reflect perceptual rather than mnemonic impairments [11]. As a consequence there is uncertainty as to the relationship between DNMS deficits in monkeys with medial temporal lesions and the pattern of memory loss found in clinical states of anterograde amnesia.

The present study re-examined the performance of amnesic subjects on tests of recognition memory modelled on the DNMS paradigm. Its purpose was to uncover the pattern of deficits associated with amnesia in the light of these various shortcomings. Critical features of the present study, therefore, included the attempt to avoid ceiling effects on even the shortest delay conditions and the desire to obtain equivalent scores for the amnesic and control subjects on these same, easier conditions. Subjects were deliberately tested across a span of delays known to be sensitive to primate models of temporal lobe and diencephalic amnesia [4, 7, 23, 38]. Unlike most studies with monkeys, a delayed matching-to-sample (DMS) design was used throughout the present study. This version was selected because the choice of nonmatching for monkeys follows from the discovery that monkeys show a spontaneous preference for novelty. In contrast, it has been found that human subjects have a strong bias to match [5] and so DMS might be regarded as a better analogue. An associated advantage is that the DMS design helps to minimise those errors that reflect a failure to remember to apply the appropriate rule (matching).

The first task (Experiment 1) required subjects to perform a matching task with delays between sample and test of between 2 and 60 sec and a list of only one stimulus (i.e. only one sample stimulus was shown prior to it being tested for recognition). Previous studies using a list of just one have resulted in almost perfect scores by the control subjects [5, 6, 33], the ceiling effects making it impossible to appreciate the extent of the deficit associated with amnesia. For this first task we therefore used abstract designs and ensured that the sample stimulus and the novel (S-) stimulus were alike in appearance. Both the control and amnesic subjects were tested with the same stimuli.

A different procedure was used in Experiment 2, the primary aim of which was to ensure comparable levels of performance over the shortest retention delays. This was achieved by testing control subjects on a harder version of the same task. For this, we constructed several series of stimuli that systematically varied in the degree to which they resembled one another. This allowed the difficulty of the recognition task to be manipulated and so made it possible to match the performance of the amnesic and control subjects over the shortest delays. As a consequence it was possible to compare the effect of increasing the retention delay in two groups with equivalent levels of performance at the shortest delay and at the same time, avoid ceiling effects. This task design also made it possible to compare the recognition of spatial and nonspatial stimuli. The rationale for this part of the study stems from neuropathological evidence pointing to the critical involvement of the hippocampal system in anterograde amnesia [32, 36], combined with the finding that the effects of selective hippocampal damage in animals are much more pronounced on spatial rather than nonspatial tests of memory [1, 24, 26]. This discovery has led a number of

researchers to compare spatial with nonspatial memory in amnesics. While some studies have found no evidence of a difference [9, 18], others have reported a disproportionate deficit on the spatial components of a memory task [20, 31].

The final consideration concerned the relationship between DMS performance and the underlying neuropathology. For this reason, the study included amnesic subjects with a variety of confirmed or suspected patterns of brain injury. In all cases the amnesias were thought to have been caused by damage in either the temporal lobe or the diencephalon. In the case of Experiment 2 special interest focused on the performance of subject BJJ on the spatial and nonspatial stimuli. This man had suffered quite selective bilateral damage to the mamillary body region [10], and in the light of this region's close association with the hippocampus and in view of evidence from lesion studies in monkeys [3, 16] it might be expected that this subject would perform disproportionately worse on the spatial task.

EXPERIMENT 1

Method

Subjects. The subjects consisted of 12 amnesic patients (AMN) and 12 healthy control subjects (CON). The amnesic group could be subdivided into those suffering from alcoholic Korsakoff's syndrome (AKS) and those with amnesia due to a mixture of other aetiologies (referred to as 'mixed amnesics' or group MA).

The Korsakoff group consisted of seven subjects (two female) with a mean age of 60 years (53–67). The mixed amnesic group consisted of three male subjects who had suffered viral encephalitis (J.T., B.D., G.H.), a female subject (A.M.) with bilateral thalamic damage following a vascular accident and a male subject (E.W.) who had suffered a colloid cyst in the third ventricle. These five subjects had a mean age of 45 years (25–69, see Table 1). All three post-encephalitic subjects suffered primarily from memory problems and these had forced them out of work. A detailed case history of one of the post-encephalitic subjects (B.D.), who appears to suffer from a

Table 1. Details of the amnesic subjects in terms of aetiology, age, National Adult Reading Test (NART) full scale IQ, WAIS—R*, three index scores of the WMS—R†, number correct on the Warrington Recognition Memory Test‡ (RMT) and number of categories correctly sorted on the Wisconsin Card Sorting Test (WCST)

				WAIS—R			WMS—R			RMT		WCST
Subject	Aet.	Age	NART FIQ	FIQ	VIQ	PIQ	GM	ATT/C	DR	W	F	No. Cat.
H.K.K.	AKS	63	100	85	82	91	62	90	55	28	29	2
R.S.	AKS	57	109	105	104	105	51	81	50	30	38	5
S.M.	AKS	67	101	96	98	95	72	107	61	30	38	3
B.P.	AKS	57	103	95	94	99	72	111	51	38	38	6
B.J.	AKS	65	101	101	103	97	64	101	64	28	29	3
H.K.	AKS	53	119	101	100	88	74	87	51	24	33	0
T.C.	AKS	57	106	80	80	80	50	60	58	30	24	2
B.J.J.	MB	33	105	101	103	99	80	130	54	43	46	6
E.W.	CC	69	105	95	94	97	74	84	64	29	28	0
B.D.	PE	64	110	104	107	104	57	60	70	32	30	3
B.T.	PE	41	105	91	91	91	80	66	61	33	37	3
G.H.	PE	25	NA	99	101	97	77	95	50	33	27	4
A.M.	Thal	40	119	NA	NA	NA	51	91	50	36	42	6
Means		53	107	96	96	95	66	89	57	32	34	3
S.D.		14	6.4	7.6	8.6	6.9	11.2	20.4	6.7	4.9	6.6	1.8

*FIQ = full scale IQ, VIQ = verbal IQ, PIQ = performance IQ.
†GM = general memory, ATT/C = attention/concentration, DR = delayed recall.
‡W = words, F = faces.
NA, information is unavailable. Aetiology key: AKS = alcoholic Korsakoff syndrome, PE = post encephalitic, CC = colloid cyst, Thal = thalamic damage, MB = mamillary body damage.

semantic memory loss for living things [14], has already been published. In two cases (A.M. and E.W.) the region and extent of brain damage had been surveyed using magnetic resonance imaging (MRI). In subject A.M. there was evidence of a bilaterally symmetrical lesion in the medial thalamus. It is probable that it involved the more rostral and ventral parts of nucleus medialis dorsalis along with adjacent nonspecific nuclei such as nucleus parafascicularis. The lesion may also have involved the region of the internal medullary lamina and the mamillothalamic tract. The MRI of subject E.W. showed extensive enlargement of the ventricles resulting in marked shrinkage of the thalamus. The fornix and septum appeared to be absent while the hippocampi appeared slightly shrunken. There was evidence of a right frontal haematoma and more general signs of cortical thinning.

Amnesic subjects were assessed with the Wechsler Adult Intelligence Scale—Revised (WAIS—R) and National Adult Reading Test (NART) to obtain estimates of present and premorbid IQ, respectively. One of the post-encephalitic subjects (G.H.) had a speech impediment and did not attempt the NART, while subject A.M. was unavailable for testing on the WAIS-R. Memory was assessed with the revised version of the Wechsler Memory Scale (WMS—R) and the Warrington Recognition Memory Test (RMT) [34]. A measure of frontal lobe function was obtained using the Wisconsin Card Sorting Test [15]. The performance of individual amnesic subjects on these tests is shown in Table 1.

The mean psychometric scores (range in parentheses) for the AKS subjects (Table 1) on these tests were: WAIS—R VIQ 94 (80–104), PIQ 94 (80–105), FSIQ 95 (80–105), NART FSIQ 106 (100–119), WMS-R general memory index 64 (50–74), WMS—R attention/concentration index 91 (60–111), WMS—R delayed memory index 56 (50–64), RMT words 30 (24–38), RMT faces 33 (24–38) and for the Wisconsin Card Sorting Test the mean number of categories correctly sorted was 3 (0–6) and the number of perseverative responses was 44 (20–85). Mean psychometric scores (range in parentheses) for the mixed amnesic subjects (Table 1) were: WAIS-R VIQ 98 (91–107), PIQ 97 (91–104), FSIQ 97 (91–104), NART FSIQ 110 (105–119), WMS—R general memory index 68 (51–80), WMS—R attention/concentration 79 (60–111), WMS—R delayed memory index 59 (50–70), RMT words 33 (29–36), RMT faces 33 (27–42) and for the Wisconsin Card Sorting Test the mean number of categories correctly sorted was 3 (0–6) and the number of perseverative responses was 40 (15–88).

The mean age of the control group (six male, six female) was 53 years (range 39–61). Psychometric testing of the control group was limited to the NART [25] and the mean NART full scale IQ of the group was 110 (range 99–122). The NART scores of the control subjects did not differ from those of the amnesics [t (21) = 1.17, n.s.].

Stimulus. Subjects performed a delayed matching-to sample task in which the stimuli were black and white photocopies of abstract painted patterns designed by the experimenters. Each pattern filled a 14×10 cm rectangle. During the sample phase a single pattern was presented in the centre of an A4 sheet of paper. At recognition two patterns (both 14×10 cm) were presented side by side on a sheet of A4 with a gap of 5 mm between them. The patterns, which were designed to be difficult to label verbally, were bound into a book.

Procedure. Each trial consisted of two stages. The subject was first presented with a single 'sample' stimulus for 2 sec. The page was then turned over to reveal an uneven dark pattern that served as a standard mask during every trial. After a predetermined interval the sheet was turned over revealing two patterned rectangles. One of the patterns was that presented as a sample; the other was a similar but new pattern. The subject was required to point to the pattern that had just been presented. There were five durations of retention interval between sample presentation and recognition test, these were: 2, 5, 10, 30 and 60 sec. Each delay was tested for 12 trials per session in a counterbalanced sequence. The task used trial unique stimuli, that is each pattern was presented on one trial only. The stimuli and their order were kept the same throughout the experiment.

Results

Figure 1 shows the mean percentage correct scores of the control (CON), Korsakoff (AKS) and mixed amnesic (MA) groups over the five delays. It can be seen that both amnesic groups performed poorly and that an impairment was apparent across all delays. Analyses were conducted using first the raw scores and then the scores after arcsine transformation. This somewhat unusual step followed from the debate as to whether transforming the results of such tests can produce qualitatively different patterns of results [7, 30].

An analysis of variance (ANOVA) using the raw scores for the control (CON), Korsakoff group (AKS) and mixed amnesic group (MA) with the factors group and delay showed a significant effect of group [F (2, 21) = 9.86, $P = 0.01$]. This reflected the superior performance of the CON subjects over both the AKS and the MA groups (Newman–Keuls, both $P < 0.05$). The two amnesic groups did not, however, differ from one another. There was also a significant effect of delay [F (4, 84) = 7.54, $P < 0.001$] and a group by delay interaction [F (8, 84) = 2.57, $P < 0.05$].

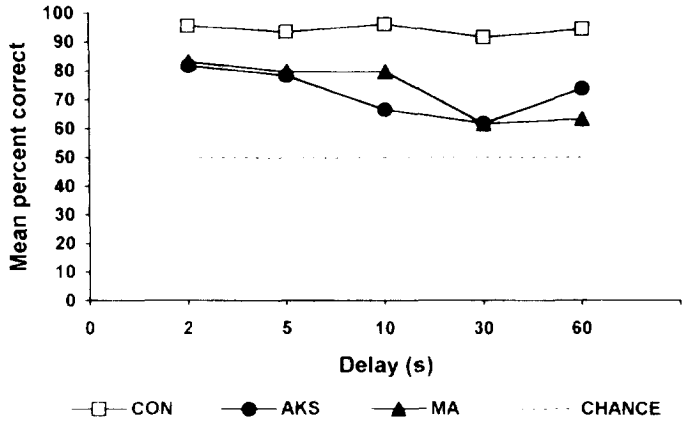

Fig. 1. Experiment 1: Mean percentage correct scores of the control (CON), Korsakoff (AKS) and mixed amnesic (MA) groups at delays of 2, 5, 10, and 60 sec on the delayed matching-to-sample task. Chance performance (50% correct) is indicated.

Newman–Keuls tests indicated that the performance of both amnesic groups (AKS, MA) was significantly affected by delay. For the AKS group performance after 2 sec was better than that after 10 and 30 sec, while performance after 5 sec was significantly better than that after 30 sec ($P<0.05$). Similarly for the MA group, more items were recognised after delays of 2, 5 and 10 sec than after delays of 30 and 60 sec ($P<0.05$). These findings indicate that the delay effect and the group by delay interaction reflected the abnormal performance of both amnesic groups.

The preceding analyses were then repeated following arcsine transformation of the data. Analyses on the CON, AKS and MA scores showed that although there were still highly significant effects of group [$F(2, 21)=11.04$, $P=0.001$] and delay [$F(4, 84)=6.10$, $P<0.001$], there was now no group by delay interaction [$F(8, 84)=1.33$, n.s.]. The same pattern of results was found when the AKS and MA groups were combined to form a single amnesic group (AMN). That is, analyses using the raw scores found a significant group by delay interaction, but this effect disappeared after arcsine transformation of the data. It should also be added that the AMN scores for the shortest delay (2 sec) differed from those of the CON group [$t(22)=2.24$, $P<0.05$].

Discussion

Both the Korsakoff and the mixed amnesic groups of subjects were found to be impaired on the performance of a forced-choice recognition task that involved the retention of just one stimulus at a time. This was consistent with a number of previous studies that have used either DMS or DNMS designs to test recognition memory [5, 6, 33] and, taken together, they indicate that this class of task is sensitive to a wide range of amnesias of different aetiologies. The results from Experiment 1 also served to highlight some of the difficulties and debates concerning the performance of amnesics of this class of tests.

A frequent drawback with tests of recognition that involve just one stimulus at a time is that they are too easy, producing ceiling effects. While the abstract stimuli used in Experiment 1 were designed to be difficult to distinguish and all of the control subjects

made some errors, their overall level of performance (about 95%) was still very high. In fact this level of performance is very similar to that obtained by normal monkeys tested over similar delays on standard versions of the DNMS task [29]. Nevertheless, this level of performance still makes it difficult to appreciate the severity of the amnesic deficit. Related to this is the problem of interpreting the delay-dependent effects.

There was clear evidence that the percentage correct scores of the amnesic subjects were affected by delay, unlike those of the control subjects. This pattern of results appears consistent with previous, similar studies [5, 6, 33]. The interpretation of this delay effect is, however, complicated by evidence that the amnesic subjects were impaired at even the shortest (2 sec) delay. This, combined with the finding that transformation of the data eliminated the group by delay interaction indicated that the present result did not provide unambiguous evidence of faster forgetting among the amnesic subjects. To test this possibility it is necessary to compare the effects of delay after comparable levels of performance have been obtained. This was examined in Experiment 2 in which task difficulty was manipulated so as to ensure that the control subjects did not outperform the amnesics at the shortest delay, while at the same time avoiding ceiling effects. This was achieved by testing the normal subjects with stimuli that were more difficult to discriminate than those presented to the amnesics, so making it harder for the controls to recognise the sample stimulus even though all other features of the task were identical for the two groups.

EXPERIMENT 2

Method

Subjects. The Korsakoff and control groups remained the same as in Experiment 1. An additional subject (B.J.J.) was, however, included in the mixed amnesic group. This subject was of particular interest as he had suffered a bilateral traumatic accident in the region of the mamillary bodies [10]. His performance on a range of psychometric tests is shown in Table 1. Recent MRI and positron emission tomography (PET) studies have confirmed the presence of bilateral mamillary body damage but have also indicated that his left hippocampus displays abnormal hypoactivity (Kapur, personal communication).

Stimuli and Apparatus. Subjects were tested on two delayed matching-to-sample tasks which used trial unique stimuli. One task required recognition of a pattern (nonspatial) and the other required recognition of location (spatial). Both tasks used a MacIntosh PowerBook 170 for stimulus presentation and data collection. The screen on this computer measures 21.5 × 13.5 cm.

The nonspatial stimuli were composed of nonrepresentational patterns with an average size of 3.5 × 3.5 cm. These patterns were radially symmetrical and all were unique (Fig. 2). The stimuli for the spatial task consisted of black squares which were identical on every trial. For the easy and moderate versions of the task the sides of the squares were 1 cm long and in the hard version the side of each square was 0.7 cm.

Design. Each task had three levels of difficulty ('easy', 'moderate' and 'hard') which differed in the ease with which the choice stimuli could be discriminated from the sample stimulus (Fig. 2). By testing controls on a harder version of the task, performance at the shortest delays could be equated and ceiling effects eliminated. For the pattern (nonspatial) task, difficulty was manipulated by varying the number of features by which the choice stimuli varied (i.e. in the hard version the patterns shared all but one or two features whereas in the easy version the stimuli had only one or two features in common). For the spatial task, difficulty was increased by placing the choice stimuli closer to the correct target location.

Eight amnesic subjects completed the easy version of the nonspatial task, the remaining five subjects (three from the mixed aetiology group) were at ceiling levels on the easy version and were therefore tested with the moderate version of the task. The amnesic subjects were tested on the spatial task at the same level of difficulty as that completed for the nonspatial task. The control subjects completed both the moderate and hard versions of each task.

Both the nonspatial and spatial tasks consisted of 60 trials at each level of difficulty. These were divided into a set of 28 trials followed, after an interval, by a second set of 32 trials. For the majority of subjects the two sets of trials were completed during the same testing session. All subjects completed the nonspatial task before the spatial

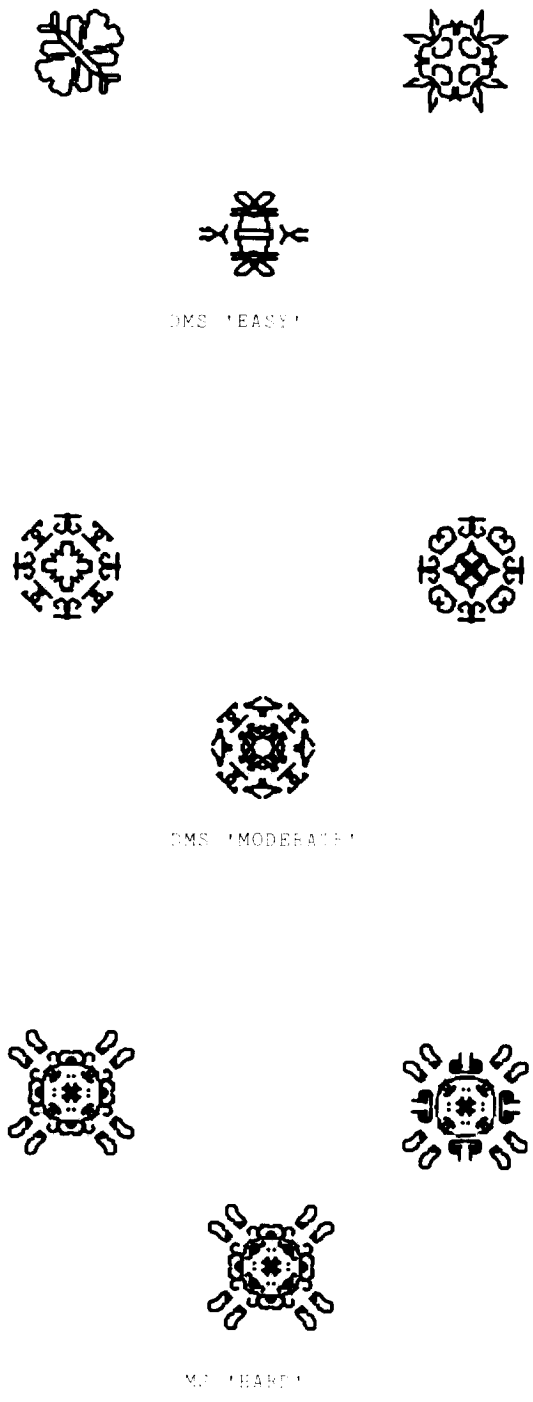

Fig. 2. Examples of patterns (as seen in the choice phase of Experiment 2) from the easy (top), moderate (middle) and hard (bottom) versions of the nonspatial (pattern) delayed matching-to-sample task (DMS).

task. The order in which control subjects completed the moderate and hard versions of the tasks was counterbalanced.

Procedure. Nonspatial (pattern) DMS—During the acquisition phase a single complex pattern (Fig. 2) was presented in the centre of the computer screen for 4 sec. This presentation time was selected as there is evidence that amnesics show preserved encoding of pictures for exposure times of up to at least 6 sec of the to-be-remembered item [19]. Presentation of the stimulus was followed by an unfilled interval of either 3, 10, 20 or 40 sec, in a random sequence. At the end of the interval three complex patterns (the sample pattern and two new patterns, Fig. 2) were presented in a triangular arrangement on the computer screen. Subjects used the 'trackball' to position the cursor over the pattern they thought had been presented at acquisition (the sample). They then pressed the 'trackball button' to select the pattern. Auditory and visual feedback was given by the computer to indicate whether the choice was correct. The auditory feedback was either a cheerful tune (correct) or a dull tone (incorrect). The visual feedback consisted of the presentation of the word 'correct' or 'wrong' in the centre of the screen.

The task was self paced. Each trial was initiated by the subject who moved the cursor into a box drawn on the computer screen and then pressed the trackball button to produce the next sample stimulus. Each of the four durations occurred 15 times throughout the sequence of 60 trials and these were in a different random order for each subject.

Spatial DMS—For this condition the computer was positioned on a turntable. The region immediately surrounding the computer screen was covered with a uniform card to prevent obvious features on the monitor being used as landmarks. During the acquisition phase a single square was presented on the computer screen for 4 sec. This was followed by an unfilled interval of either 3, 10, 20 or 40 sec given in a random sequence. During the interval the screen was turned away to stop the subject from fixating on the critical location. One second before completion of the interval the screen flashed and the computer was turned back to its original position in front of the subject. Three identical squares appeared on the screen, one of which was in the same location as that presented at acquisition (the sample). Subjects were required to move the cursor to the position occupied by the sample and press a button on the keyboard to receive feedback about the correctness of their choice. The next sample stimulus appeared on the screen immediately after feedback had been given.

Data analysis. The first set of analyses examined the comparability of the performance levels on the pattern and spatial DMS tasks for the different degrees of task difficulty. This was achieved by comparing the performance of the control subjects on the moderate and hard versions of the pattern and spatial tasks over the five retention intervals.

The second set of analyses compared the scores of the amnesic and control subjects. As the amnesics were only tested on one level of difficulty (easy or moderate) task difficulty could not be a factor in the analysis. These scores were then compared, in separate comparisons, with the 'moderate' and 'hard' scores of the control subjects. The amnesic subjects were divided into a Korsakoff group and a mixed amnesic group.

Results

Comparison of levels of difficulty of spatial and nonspatial tasks (control subjects only): An ANOVA, with factors of difficulty, task and delay was carried out to compare the scores of only the control subjects on the moderate and hard versions ('difficulty') of the spatial and nonspatial ('task') DMS tests (Figs 3 and 4). As expected, there was a significant main effect of difficulty [$F(1, 11) = 144.09$, $P < 0.001$], but there was no main effect of task [$F(1, 11) = 0.01$]. The latter result showed that the overall scores on the spatial and nonspatial tasks were comparable. Furthermore, there were no differences between the 'moderate' spatial and nonspatial scores, or between the 'hard' spatial and nonspatial scores (Newman–Keuls, $P > 0.05$). There was, however, evidence of a crossover interaction between difficulty and task [$F(1, 11) = 17.44$. $P < 0.005$] as the moderate version of the nonspatial task was slightly easier than the equivalent spatial task, while the reverse was true for the hard level.

In view of the concern over ceiling effects it should be noted that the mean score (out of 60) for the moderate nonspatial DMS was 51.8 (86.3%) and for the moderate spatial DMS was 49.3 (82.2%). For the hard tasks it was 38.6 (nonspatial) and 41.6 (spatial). The control subjects were not tested on the easy version of the tests as pilot testing showed that they made virtually no errors. For all of these tasks chance was 20 out of 60.

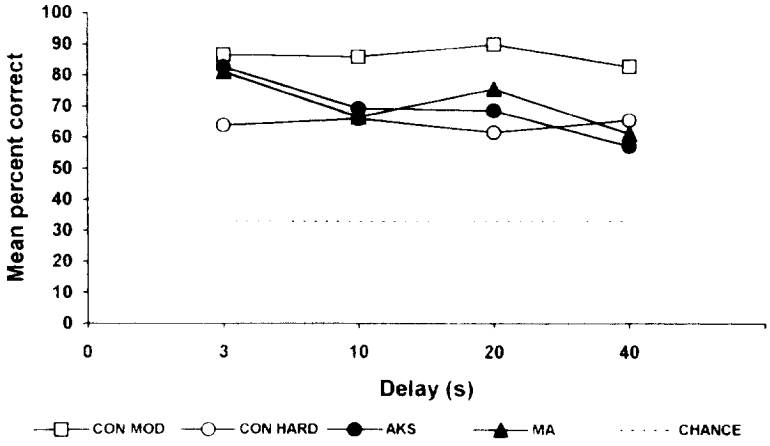

Fig. 3. Experiment 2: Mean percentage correct scores of the control (CON), Korsakoff (AKS) and mixed amnesic (MA) groups at delays of 3, 10, 20 and 40 sec on the nonspatial (pattern) delayed matching-to-sample task. Control performance is plotted for the moderate and hard versions of the task, whereas scores for the two groups of amnesic subjects are from either the easy version (five AKS and three MA subjects) or the moderate version (two AKS and three MA subjects) of the task. Chance performance (33% correct) is also indicated.

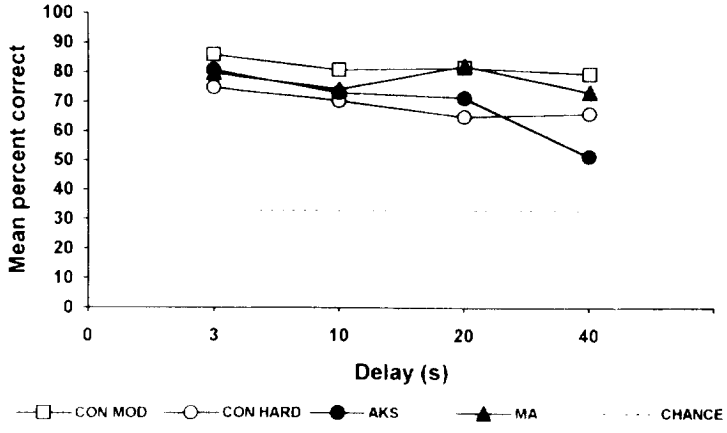

Fig. 4. Experiment 2: Mean percentage correct scores of the control (CON), Korsakoff (AKS) and mixed amnesic (MA) groups at delays of 3, 10, 20 and 40 sec on the spatial delayed matching-to-sample task. Control performance is plotted for the moderate and hard versions of the task whereas scores for the two groups of amnesic subjects are combined from the easy version (five AKS subjects and three MA subjects) and the moderate version (two AKS and three MA subjects) of the task. Chance performance (33% correct) is also indicated.

Amnesics vs controls: From Figs 3 and 4 it can be seen that one of the chief aims of the experiment was achieved. That is, the scores of the amnesic subjects on the shortest delay (3 sec) were bracketed between those of the control subjects on the 'moderate' and 'hard' test versions. At the same time, the amnesics' scores were not compromised by ceiling effects.

Two sets of ANOVAs were calculated with the between factor of group (control, Korsakoff and mixed amnesics) and the within factors of task (nonspatial and spatial) and

delay. The first set used the scores of the control subjects on just the moderate versions of the spatial and nonspatial tasks, the second set used the equivalent control scores from just the hard versions. Following from Experiment 1 these analyses used arcsine transformations of the scores.

Neither set suggested a significant main effect of task, and there were no significant group by task interactions. The latter results indicated that the amnesic subjects were not disproportionately impaired on the spatial (or nonspatial) tasks (Figs 3 and 4). There was, however, a significant effect of delay. This was found both for the comparisons using the 'moderate' control scores [$F(3,66)=9.34$, $P<0.001$] and for the 'hard' control scores [$F(3,66)=10.67$, $P<0.001$]. There was also a significant interaction between group and delay for the comparisons with both the 'moderate' control data [$F(6,66)=2.63$, $P<0.025$] and the 'hard' control data [$F(6,66)=3.57$, $P<0.005$]. These interactions reflected the greater rate of forgetting shown by the amnesic subjects. For the analysis comparing the performance of the amnesics with the performance of the controls tested on the moderate version there was also a significant main effect of group [$F(2,22)=5.48$, $P=0.012$], reflecting the poorer overall performance of the amnesic subjects (Figs 3 and 4). Exactly the same set of significant and nonsignificant results were found when the same analyses were repeated using the untransformed scores.

Nonspatial (pattern) DMS: Separate analyses were carried out to compare the performance of the AKS and MA subjects with that of the CON group on the moderate and hard versions of the nonspatial task (Fig. 3). For the moderate control scores a significant group effect was found [$F(2,22)=6.33$, $P<0.01$] and subsequent Newman–Keuls tests showed that while both of the amnesic groups performed worse than the controls ($P<0.05$) they did not differ from each other. There was also a main effect of delay [$F(3,66)=7.56$, $P<0.001$] which interacted significantly with group [$F(6,66)=2.25$, $P<0.05$]. This interaction reflected the fact that while the performance of the CON subjects did not decline with delay, the scores of the amnesic groups became lower. Thus, the scores of the AKS group were significantly better after the shortest (3 sec) delay than after any of the longer delays, while the scores of the mixed amnesics were significantly better after the 3 sec delay than after the delays of 10 or 40 sec. The scores of the amnesic groups did not differ from those of the controls on the shortest delay.

The same series of analyses were repeated with the control scores from the 'hard' test version. There was now no significant main effect of group, but there was still an effect of delay [$F(3,66)=7.96$, $P<0.001$] which again interacted with group [$F(6,66)=3.69$, $P<0.005$].

When the set of analyses were repeated using the raw scores exactly the same set of significant results were found. That is, the amnesic groups showed a steeper rate of forgetting than the control subjects for both the 'hard' and 'moderate' test versions.

Spatial DMS task: The first analysis considered the performance of the AKS and MA groups using the control scores from the 'moderate' spatial task for comparison purposes (Fig. 4). There was no clear effect of group [$F(2,22)=2.71$, $P=0.09$], but there was an effect of delay [$F(3,66)=3.55$, $P=0.019$] which was due to the poorer levels of performance after 40 sec. This principally reflected the scores of the AKS group. Unlike the nonspatial task the interaction between group and delay failed to reach significance [$F(6,66)=1.49$, $P=0.19$]. *Post hoc* investigations showed that the scores of the control group did not differ from those of the two amnesic groups at the shorter delays, the only difference occurring at 40 sec when the AKS group differed

from both the CON and the MA groups. There were no group differences for the scores at the shortest delay.

Exactly the same pattern of results was found when the set of analyses were repeated for the 'hard' control data. Once again, analyses using the raw scores also provided the same set of significant results.

Particular interest focused on the performance of subject B.J.J. who had suffered quite selective mamillary body damage. This subject was unimpaired on the nonspatial task, scoring 13, 14, 14, 14 over the increasing delays on the moderate version. His overall score of 55 was, in fact, somewhat higher than the mean control score (51.8). Although B.J.J. made considerably more errors on the spatial task (scoring 9, 13, 12, 9) on the moderate task, his total score (43) was still within the range of the control subjects (mean 49.3, range 42–55), although it was now near the bottom end.

Discussion

It has been repeatedly observed that in order to compare meaningfully the rates of forgetting in normal and amnesic subjects it is essential to start with equivalent levels of performance. In order to ensure this, studies have typically allowed amnesic subjects a longer exposure time to the target stimulus [12, 17, 21, 31]. While this procedure has been valuable it can create potential problems. These include possible differences in encoding resulting from the increased exposure time and minor changes in the actual retention intervals for individual stimuli (as the samples now take longer to present). The inevitable increase in the duration of the experiment for the amnesic subjects may also affect other factors influencing task performance (e.g. levels of attention and the degree of interference between stimuli).

In the present study equivalent levels of performance were achieved by giving the control subjects slightly more difficult versions of the same task. The advantage of this manipulation is that it makes it possible to hold all other task parameters constant. It is, however, appreciated that this manipulation is not without its possible drawbacks, the major one being that the more difficult stimuli might promote the use of different encoding strategies. While this cannot be excluded it is the case that the control subjects' patterns of performance on the 'hard' and 'moderate' versions of the DMS tasks were always very similar, suggesting that they were performed in essentially the same way.

The design of Experiment 2 ensured two important goals. First, that the scores were not influenced by ceiling effects even though only one sample stimulus had to be retained for each trial and second, that the scores of the amnesics on the shortest delays were comparable to those of the controls. For the pattern (nonspatial) DMS it appeared that amnesia was associated with a faster than normal rate of forgetting, and that this was true both for the Korsakoff subjects and for the group with mixed aetiologies (Fig. 3). This impression was confirmed by the significant interaction between group and delay with both the moderate and hard control conditions. Furthermore, exactly the same patterns of results were found for the raw and the transformed data. This reflected the success of the manipulations to eliminate ceiling effects. This is especially important in the light of the claim that arcsine transformation can provide a much more accurate measure of delay-dependent effects on DNMS or DMS tasks [29], a view supported by the results from Experiment 1.

The results of the spatial DMS task were slightly different as there was no clear group effect and no group by delay interaction. The lack of an interaction may indicate the need

to use delays longer than 40 sec and this remains to be tested. At first sight the lack of a group effect appears more surprising, but this does not mean that the amnesics were unimpaired on this task. This is because the majority of the amnesic subjects were tested on the easiest version of the task. (We do not have control data for the easiest version as pilot studies showed that normal subjects made virtually no errors on this particular version of the task.) Of more interest is the fact that the mean scores of the two amnesic groups for the 3, 10 and 20 sec conditions fell between those of the control subjects for both the spatial and nonspatial DMS tasks (Figs 3 and 4). This, when taken into consideration with the equivalent control performance on the spatial and nonspatial tasks, means that the present study found no evidence that amnesic subjects were disproportionately impaired on the test of spatial memory. This conclusion is in agreement with a number of other recent studies [9, 18]. There is, however, some counter evidence to suggest that amnesics can show disproportionate deficits on the recall of stimulus location when compared with stimuli recognition [20, 31]. It may therefore be relevant that the present study compared two recognition judgements and so was able to provide a more direct comparison between spatial and nonspatial abilities.

These inconsistencies concerning the outcome of experiments comparing spatial and nonspatial memory suggest the existence of a number of variables that can influence the findings. One of the most likely concerns the site of pathology. There was in fact no overall difference between the two groups of amnesics in the present study, nor could any distinct subgroup be identified. In this regard the findings are consistent with other studies of spatial memory in mixed amnesic groups [20, 31]. The performance of B.J.J., who had sustained bilateral damage to the mamillary bodies [10], was however of especial interest. Descriptions of the effects of selective mamillary body lesions in rats and monkeys clearly indicate that damage in this region leads to deficits on spatial tasks even though nonspatial recognition is little affected [2, 3, 37]. Consistent with this, B.J.J. performed remarkably well on the nonspatial DMS task (overall 55 out of 60) and this agreed with his normal performance on the Warrington Recognition Memory task [10]. His scores on the spatial task (overall 43) were, however, considerably poorer. This drop in scores was unusual as the other amnesic subjects tended to perform slightly better on the spatial DMS task (mean difference in overall score +2.8). In fact, the difference in scores shown by B.J.J. (−12) was markedly greater than that of any of the other amnesics ($z = 2.4$), suggesting a disproportionate spatial impairment. In spite of this relative difference, his overall level of performance on the spatial task was not particularly deficient and was only at the low end of the control range. For this reason the proposal that mamillary body damage leads to particularly severe spatial deficits remains to be more fully tested.

The finding that amnesia was associated with a faster rate of forgetting of the patterned (nonspatial) stimuli is of direct relevance for other clinical studies of DNMS and DMS performance [5, 6, 33]. This is because these studies have used either objects or abstract patterns and hence have also focused on visual, nonspatial stimuli. While these earlier studies had also reported faster rates of forgetting [5, 6, 33] this conclusion could not be confirmed because of a failure to match performance levels at short delays. The results for the pattern DMS clearly indicate that faster forgetting is a genuine feature of amnesia when tested in this way and so should be expected in experimental models. Consistent with this, studies of DNMS performance in monkeys with medial temporal lesions [23, 27, 35, 37] have repeatedly indicated that these lesions do result in faster rates of forgetting. Unfortunately, scores at the shortest delays have rarely been properly equated, but in the

most appropriate cases it does appear that these lesions can result in steeper forgetting curves [7, 27, 35].

A final feature of the present study was the finding of an amnesic group deficit with delays of 5 sec or less (Experiment 1). This was consistent with a previous report showing that Korsakoff subjects can be impaired in nonverbal recognition tasks with retention intervals as short as 5 sec [8]. Inspection of the individual scores does, however, highlight the variability between amnesic subjects, some of whom appeared to perform the DMS task accurately at short delays. This relative sparing could not, however, by linked systematically with aetiology. In this regard subject B.J.J. was of especial interest as his recognition scores (especially on the nonspatial task) were very good, as were his Recognition Memory Test scores [10]. This case, and a small number of other examples [13, 22, 28] indicate that there is a subgroup of amnesics in whom recognition memory may remain intact. It will prove most valuable to determine the defining characteristics of this subgroup of amnesics.

Acknowledgements:—The authors wish to thank Narinder Kapur, John Gray, Angus McGregor, Daniel Collerton and Andrew Fairbairn for their invaluable assistance. This research was supported by a grant from the MRC.

REFERENCES

1. Aggleton, J. P., Hunt, P. R. and Rawlings, J. N. P. The effects of hippocampal lesions upon spatial and non-spatial tests of working memory. *Behav. Brain Res.* **19,** 133–146, 1986.
2. Aggleton, J. P., Hunt, P. R. and Shaw, C. The effects of mamillary body and combined amygdalar-fornix lesions on tests of delayed non-matching-to-sample in the rat. *Behav. Brain Res.* **40,** 145–157, 1990.
3. Aggleton, J. P. and Mishkin, M. Mamillary-body lesions and visual recognition in monkeys. *Exp. Brain Res.* **58,** 190–197, 1985.
4. Aggleton, J. P. and Mishkin, M. Visual recognition impairment following medial thalamic lesions in monkeys. *Neuropsychologia* **21,** 189–197, 1983.
5. Aggleton, J. P., Nicol, R. M., Huston, A. E. and Fairbairn, A. F. The performance of amnesic subjects on tests of experimental amnesia in animals: delayed matching-to-sample and concurrent learning. *Neuropsychologia* **26,** 265–272, 1988.
6. Aggleton, J. P., Shaw, C. and Gaffan, E. A. The performance of postencephalitic amnesic subjects on two behavioural tests of memory: Concurrent discrimination learning and delayed matching-to-sample. *Cortex* **28,** 359–372, 1992.
7. Alvarez-Royo, P., Zola-Morgan, S. and Squire, L. R. Impairment of long-term memory and sparing of short-term memory in monkeys with medial temporal lobe lesions: A response to Ringo. *Behav. Brain Res.* **52,** 1–5, 1992.
8. Cermak, L. S., Reale, L. and De Luca, D. Korsakoff patients' nonverbal vs verbal memory effects of interference and mediation on rates of information loss. *Neuropsychologia* **15,** 303–310, 1977.
9. Cave, C. B. and Squire, L. R. Equivalent impairment of spatial and nonspatial memory following damage to the human hippocampus. *Hippocampus* **1,** 329–340, 1991.
10. Dusoir, H., Kapur, N., Byrnes, D. P., McKinstry, S. and Hoare, R. D. The role of diencephalic pathology in human memory disorder. *Brain* **114,** 1695–1706, 1990.
11. Eacott, M. J., Gaffan, D. and Murray, E. A. Preserved recognition memory for small sets and impaired stimulus identification for large sets following rhinal cortex ablations in monkeys. *Eur. J. Neurosci.* **6,** 1466–1478, 1994.
12. Freed, D. M., Corkin, S. and Neal, J. C. Forgetting in H.M.: A second look. *Neuropsychologia* **25,** 461–471, 1987.
13. Hanley, J. R., Davies, A. D. M., Downes, J. J. and Mayes, A. R. Impaired recall of verbal material following rupture and repair of an anterior communicating artery aneurysm. *Cognit. Neuropsychol.* **11,** 543–578, 1994.
14. Hanley, J. R., Young, A. and Pearson, N. Defective recognition of familiar people. *Cognit. Neuropsychol.* **6,** 179–210, 1981.
15. Heaton, R. K. *Wisconsin Card Sorting Test Manual.* Psychological Assessment Resources Inc., Odessa, Florida, 1981.

16. Holmes, E. J. and Butters, N. An examination of the effects of mamillary-body lesions on reversal learning sets in monkeys. *Physiol. Psychol.* **11,** 159–165, 1983.
17. Huppert, F. A. and Piercy, M. Recognition memory in amnesic patients: A deficit of acquisition? *Neuropsychologia* **15,** 643–652, 1977.
18. MacAndrew, S. B. G. and Jones, G. V. Spatial memory in amnesia: Evidence from Korsakoff patients. *Cortex* **29,** 235–249, 1993.
19. Mayes, A. R., Downes, J. J., Shoqeirat, M., Hall, C. and Sagar, H. J. Encoding ability is preserved in amnesia: Evidence from a direct test of encoding. *Neuropsychologia* **31,** 745–759, 1993.
20. Mayes, A. R., Meudell, P. R. and Macdonald, C. Disproportionate intentional spatial-memory impairments in amnesia. *Neuropsychologia* **29,** 771–784, 1991.
21. Mayes, A. R., Pickering, A. and Fairbairn, A. Amnesic sensitivity to proactive interference: Its relationship to priming and the causes of amnesia. *Neuropsychologia* **25,** 211–220, 1987.
22. Moscovitch, J. Confabulation and the frontal systems: Strategic versus associative retrieval in neuropsychological theories of memory. In *Varieties of memory and consciousness: Essays in honour of Endel Tulving*, H. L. Roediger, III and F. I. M. Craik (Editors). Lawrence Erlbaum, Hillsdale, NJ, 1989.
23. Murray, E. A. and Mishkin, M. Visual recognition in monkeys following rhinal cortical ablations combined with either amygdalectomy or hippocampectomy. *Neurosci.* **6,** 1991–2003, 1986.
24. Nadel, L. The hippocampus and space revisited. *Hippocampus* **1,** 221–229, 1991.
25. Nelson, N. E. *The National Adult Reading Test*. NFER-Nelson, Windsor, 1985.
26. O'Keefe, J. and Nadel, L. *The Hippocampus as a Cognitive Map*. Clarendon Press, Oxford, 1978.
27. Overman, W. H., Ormsby, G. and Mishkin, M. Picture recognition vs. picture discrimination learning in monkeys with medial temporal removals. *Exp. Brain Res.* **79,** 18–24, 1990.
28. Parkin, A. J., Dunn, J. C., Lee, C., O'Hara, P. F. and Nussbaum, L. Neuropsychological sequelae of Wernicke's encephalopathy in a 20-year-old woman: Selective impairment of a frontal memory system. *Brain Cognit.*, **21,** 1–19, 1993.
29. Ringo, J. L. Memory decays at the same rate in macaques with and without brain lesions when expressed in d' or arcsine terms. *Behav. Brain Res.* **42,** 123–134, 1991.
30. Ringo, J. L. Spared short-term memory in monkeys following temporal lobe lesions is not yet established: A reply to Alvarez-Royo, Zola-Morgan and Squire. *Behav. Brain Res.* **59,** 65–72, 1993.
31. Shoqeirat, M. A. and Mayes, A. R. Disproportionate incidental spatial-memory and recall deficits in amnesia. *Neuropsychologia* **29,** 749–769, 1991.
32. Squire, L. R. Memory and the hippocampus: A synthesis from findings with rats, monkeys and humans. *Psych. Rev.* **99,** 195–231, 1992.
33. Squire, L. R., Zola-Morgan, S. and Chen, K. S. Human amnesia and animals models of amnesia: Performance of amnesic patients on tests designed for the monkey. *Behav. Neurosci.* **102,** 210–221, 1988.
34. Warrington, E. K. *The Recognition Memory Test*. NFER-Nelson, Windsor, 1984.
35. Zola-Morgan, S. and Squire, L. R. Medial temporal lesions in monkeys impair memory on a variety of tasks sensitive to human amnesia. *Behav. Neurosci.* **99,** 22–34, 1985.
36. Zola-Morgan, S., Squire, L. R. and Amaral, D. G. Human amnesia and the medial temporal region: enduring memory impairment following a bilateral lesion limited to field CA1 of the hippocampus. *Neurosci.* **6,** 2950–2967, 1986.
37. Zola-Morgan, S., Squire, L. R. and Amaral, D. G. Lesions of the hippocampal formation but not lesions of the fornix or the mamillary nuclei produce long-lasting memory impairment in monkeys. *Neurosci.* **9,** 898–913, 1989.
38. Zola-Morgan, S., Squire, L. R., Amaral, D. G. and Suzuki, W. A. Lesions of perirhinal and parahippocampal cortex that spare the amygdala and hippocampal formation produce severe memory impairment. *Neurosci.* **9,** 4355–4370, 1989.