

# PERCEPTUAL AND MNEMONIC MATCHING-TO-SAMPLE IN HUMANS: CONTRIBUTIONS OF THE HIPPOCAMPUS, PERIRHINAL AND OTHER MEDIAL TEMPORAL LOBE CORTICES

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## ABSTRACT

Two questions were addressed by the present study. The first was whether the previously reported item recognition deficit which is shown by amnesic patients may be due to a perceptual rather than a memory deficit. To address this question a group of amnesic patients were tested on a 14-choice forced-choice visual item recognition test which included a “simultaneous” condition in which the sample remained visible during the matching decision and a zero second delay. Eacott, Gaffan and Murray (1994) have reported an impairment in simultaneous matching-to-sample following perirhinal damage in monkeys. In our amnesic patients, a deficit was found only after filled delays of 10 seconds or longer and this was also the case for a subgroup of patients whose damage included the perirhinal cortex. The second question, which arose from the model of Aggleton and Brown (1999), was whether performance on the DMS task would remain intact following selective damage to the hippocampus. We tested a patient with bilateral damage to the hippocampus on the 14-choice DMS task and found that her performance was not significantly impaired at delays of up to 30 seconds.

Key words: item recognition, amnesia, hippocampus, perirhinal cortex

## INTRODUCTION

A deficit in recognition memory has been considered to be a central feature of anterograde amnesia (Parkin and Leng, 1993). As a result, object recognition tests have been used extensively to assess animal models of this memory deficit. The favoured format of these tasks has involved the presentation of a single sample item and then, after a delay of varying duration, the presentation of the previously seen item along with a new (novel or less familiar) item. The animal has either to select the previously seen item (delayed-match-to-sample – DMS) or, more often, to select the new item (delayed-nonmatch-to-sample – DNMS) in order to receive a reward. Early studies showed that large medial temporal lobe (Mishkin, 1978; Zola-Morgan, Squire and Mishkin, 1982) and large medial diencephalic lesions (Aggleton and Mishkin, 1983a, 1983b) impaired DNMS performance. Recently, studies have investigated more specifically the contribution to performance of structures within these regions. The use of more

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selective lesions have pointed to the perirhinal cortex as being the medial temporal lobe region critical for object recognition memory of this sort (Meunier, Bachevalier, Mishkin et al., 1993; Meunier, Hadfield, Bachevalier et al., 1996). In contrast, aspiration lesions of the hippocampus have produced only a mild DNMS impairment (Murray and Mishkin, 1986; Zola-Morgan and Squire, 1986; Zola-Morgan, Squire and Amaral, 1989; Zola-Morgan, Squire, Clower et al., 1993). Further, more precise stereotaxic lesions of the hippocampus, which produce less incidental damage to adjacent cortex, have left DNMS performance intact at delays of up to 60 seconds (Alvarez, Zola-Morgan and Squire, 1995). DNMS was impaired after longer delays during which the animal was removed from the test apparatus (Alvarez et al., 1995), but it was not impaired at delays of up to 40 minutes when the animals remained in the test apparatus during all retention intervals (Murray and Mishkin, 1996).

The fornix is a major efferent pathway of the hippocampus which connects this structure with the mammillary bodies and anterior thalamic nuclei. Together these structures make up what has been referred to as the extended hippocampal system (Aggleton and Brown, 1999). Like hippocampal damage, fornix transection has been demonstrated to have little or no effect on DNMS and DMS in monkeys (Bachevalier, Parkinson and Mishkin, 1985; Bachevalier, Saunders and Mishkin, 1985; Gaffan, Sheilds and Harrison, 1984; Zola-Morgan et al., 1989) and no effect on DNMS performance in rats (Aggleton, Hunt and Shaw, 1990; Rothblat and Kromer, 1991; Shaw and Aggleton, 1993). In fact, in monkeys, a double dissociation has been demonstrated between the effects of perirhinal lesions and fornix lesions on memory. Perirhinal lesions had a much greater effect on DNMS performance than fornix transection, whereas fornix transection impaired performance on a spatial memory task on which perirhinal lesions had little effect (Gaffan, 1994). Lesions of the parahippocampal cortex have been found not to cause a DNMS deficit (Meunier et al., 1996; Ramus, Zola-Morgan and Squire, 1994) and, similarly, lesions of the adjacent entorhinal cortex have only a very mild or transient effect on DNMS performance (Leonard, Amaral, Squire et al., 1995; Meunier et al., 1993). Within the diencephalic region, damage to the medial dorsal nucleus of the thalamus, to which the perirhinal cortex projects, has been shown to disrupt item recognition (see Aggleton and Brown, 1999). In contrast, lesions to the mammillary bodies, structures thought to form part of the extended hippocampal system, have been found to leave DNMS performance intact (Aggleton and Mishkin, 1985; Aggleton et al., 1990; Zola-Morgan et al., 1989).

The importance of the perirhinal cortex in object recognition has also been suggested by electrophysiological studies. In the study of Brown, Wilson and Riches (1987), 15 percent of cells in the inferomedial temporal cortex, which included the perirhinal and entorhinal cortices, responded more strongly to the first presentation of a stimulus than to subsequent presentations. These cells therefore appeared to be discriminating between unfamiliar and familiar item stimuli. Brown et al. (1987) found no such cells in the hippocampus or subiculum. These findings have been supported by the results of more recent studies (for a review, see Brown and Xiang, 1998).

The evidence from the animal literature which suggests that the perirhinal

and hippocampal regions make different contributions to memory led Aggleton and Brown (1999) to propose the existence of two memory systems. One memory system, comprising the perirhinal cortex and dorsomedial nucleus of the thalamus, was proposed to be important for familiarity-based item recognition. In contrast, a second system which Aggleton and Brown (1999) refer to as the extended hippocampal system was thought to be critical for successful recall of new episodic information, but to be unnecessary for successful item recognition when this was dependent on stimulus familiarity (Mandler, 1980). Aggleton and Brown (1999) considered forced-choice recognition tasks such as DMS and DNMS to be tasks which are likely to be tapping this aspect of recognition. The extended hippocampal memory system was suggested to comprise the hippocampus, mammillary bodies and anterior thalamic nuclei.

Aggleton and Brown's theory predicts that, in humans, deficits in recall and recollection will be seen following lesions restricted to structures within the extended hippocampal system, but that item recognition on tasks in which relative familiarity contributes substantially to the memory decision will remain intact. In contrast, Aggleton and Brown's theory predicts that item recognition will be impaired following damage to the perirhinal cortex or the dorsomedial nucleus of the thalamus.

Although the findings from the lesion and electrophysiological studies described above have highlighted the importance of the perirhinal cortex in visual item recognition (Aggleton and Brown, 1999), a study by Eacott et al. (1994) has questioned whether this is a selective deficit of recognition memory or one of perceptual processing of visual information that results in a memory deficit. Although these authors found that monkeys with rhinal cortex lesions were impaired at delayed-match-to-sample (DMS) when trial unique stimuli were used, they also found that rhinal lesions impaired performance when there was no delay between sample and test and in a "simultaneous" condition in which both the sample and test items were visible while the matching decision was made. As these latter two conditions made no demands on memory this poor performance must have been due to a perceptual deficit. Subsequent studies have shown that concurrent discrimination learning is impaired by perirhinal cortex damage when a large set of discriminations have to be learned (Buckley and Gaffan, 1997), a large number of foils are used (Buckley and Gaffan, 1997) or the rewarded item is presented in different views on different trials (Buckley and Gaffan, 1998). When small sets, few foils and the same views of an item were used, no concurrent discrimination learning deficit was seen after perirhinal damage. It has been argued that the manipulations which resulted in a deficit "increased the demands that these tasks placed on object identification" (Buckley and Gaffan, 1998). Buckley, Booth, Rolls et al. (1998) have also shown that perirhinal cortex damage impaired monkeys' ability to select the odd-one from among six pictures: five showing different views of a single object and the other showing a different object. They could, however, select the odd-one when the five pictures of the single object were identical views. In considering the animal literature, Murray and Bussey (1999) have suggested that the perirhinal cortex plays a role in both perception and memory. They propose that its perceptual role is that of representing "complex conjunctions of stimulus features" (Murray

and Bussey, 1999, p. 148) and that this is the final stage in the ventral visual processing stream.

Consistent with the animal literature, studies of item recognition in human amnesia have found that large medial temporal lobe lesions or large diencephalic lesions impaired performance on tests of forced-choice item recognition modelled on the DNMS and the DMS procedures used with monkeys (Aggleton, Nicol, Huston et al., 1988; Squire, Zola-Morgan and Chen, 1988). Furthermore, when performance of control and amnesic subjects has been matched at an initial delay, and performance of the controls is well below ceiling, both medial temporal lobe and diencephalic (Korsakoff) amnesics have been demonstrated to forget visual item information at an accelerated rate on an analogue of the DMS task (Holdstock, Shaw and Aggleton, 1995). Such accelerated forgetting has also been demonstrated in a number of other forced choice and yes/no recognition memory studies (Carlesimo, Sabbadini, Fadda et al., 1995; Downes, Holdstock, Symons et al., 1998; Mayes, Downes, Symons et al., 1994; Squire, 1981; Huppert and Piercy, 1979). This accelerated forgetting strongly suggests that poor performance in the amnesics is due to a deficit in memory. However, an additional perceptual deficit cannot be ruled out. None of these studies used either a simultaneous condition or immediate memory test (i.e. a 0s delay), rather, initial performance was measured at delays of between three seconds and 10 seconds and in the majority of cases the amnesic patients were given extra exposure to the stimuli in order to match their performance at this initial delay with that of the control group. However, a recent study (Buffalo, Reber and Squire, 1998), which investigated the effects of perirhinal damage on object recognition, did include very short initial delays. It was found that two patients whose damage included this region were unimpaired when recognition was tested after delays of zero and two seconds but were impaired at later delays. These results therefore indicated that, contrary to the results from animal studies (Eacott et al., 1994; for a review, see Murray and Bussey, 1999), in humans, the perirhinal cortex may have a role in memory, but not perception. This finding, if replicable, suggests that one should be careful in generalising from monkeys to humans. In the first part of the present study we investigated further the possibility that the poor recognition performance of amnesic patients could be due to a perceptual deficit by testing a group of amnesics of mixed aetiology, including four patients with damage to the perirhinal cortex, on a DMS task which included both a simultaneous condition and a 0s delay.

The second question which was investigated in the present study was Aggleton and Brown's (1999) prediction that damage to the extended hippocampal system will not impair performance on item recognition tasks such as DMS even though recall of information will be impaired. There is some evidence in support of Aggleton and Brown's prediction. In their meta-analysis of studies which assessed recognition memory using the Recognition Memory Test (RMT) (Warrington, 1984), Aggleton and Shaw (1996) found that patients with damage restricted to the hippocampus, fornix or mammillary bodies were impaired at recall as assessed by the WMS-R, but were only mildly impaired, or even in some cases unimpaired, at item recognition tested by the RMT. The RMT consists of two recognition tests, one of words and one of faces. Each test

uses a 2-choice forced-choice recognition paradigm for 50 items and so is equivalent to a DMS task with a list length of 50. A similar finding was reported by Vargha-Khadem, Gadian, Watkins et al. (1997), who found that three young people with relatively selective hippocampal pathology were unimpaired at two-choice forced-choice item recognition whilst being amnesic for the recall of episodic information and impaired at recognising object-location and face-voice associations. Consistent with this finding, Volpe, Holtz and Hirst (1986) reported impaired recall but apparently intact yes-no recognition in a group of patients who had suffered a cardiac arrest, an event which results in preferential pathology in limbic structures such as the hippocampus (Volpe et al., 1986). Another relevant finding is that of McMackin, Cockburn, Anslow et al. (1995) whose data suggested that bilateral fornix damage resulted in only a mild impairment of recognition memory (assessed by the RMT). As described above, it is within the fornix that efferents from the hippocampus travel to the mammillary bodies and the anterior nucleus of the thalamus and when this fibre pathway is lesioned, a similar pattern of memory deficits is obtained to that found after hippocampal lesions (see Gaffan, 1994). The findings of these studies are all consistent with the prediction which arises from Aggleton and Browns' (1999) model.

However, there are also some apparently conflicting findings. Reed and Squire (1997) described the recognition memory performance of six patients who were reported to have selective damage of the hippocampal formation (hippocampus proper, dentate gyrus, subiculum and entorhinal cortex), including one patient whose damage appeared to be restricted to the CA fields of the hippocampus. Recognition memory was reported to be impaired in these patients. Reed and Squire's (1997) paper considered performance on a range of recognition tests whereas all but one (Volpe et al., 1986) of the studies supporting Aggleton and Browns' model used a two-choice forced-choice recognition paradigm. The conflicting findings highlight the need both to test further patients with selective hippocampal damage and to use other item recognition tests in addition to the two-choice forced-choice design to determine the extent to which previously reported findings generalise to other recognition paradigms.

In the present study, we tested a patient, YR, who has relatively selective bilateral hippocampal damage, on the DMS task completed by the group of amnesic patients of mixed aetiology. Patient YR has been found to be unimpaired on the RMT (Warrington, 1984) and the recognition subtests of the Doors and People Test (D&P) (Baddeley, Emslie and Nimmo-Smith, 1994) despite showing a substantial recall deficit on the Wechsler Memory Scale-Revised and the recall subtests of the D&P (see Table I of the present paper). YR therefore showed the same pattern of impaired recall but unimpaired forced-choice item recognition as the patients described by Aggleton and Shaw (1996), McMackin et al. (1995) and Vargha-Khadem et al. (1997). The present study allowed us to investigate whether YR's item recognition would also be impaired on another forced-choice item recognition task which was designed to be difficult and to avoid ceiling effects in the control group by using a large number of foils (13) at test, used different stimulus materials to the RMT and D&P, and assessed memory over delays of up to 30 seconds.

In summary, there were two questions which the present study addressed. The first was whether the previously reported deficit in DMS in amnesic patients with perirhinal damage may be due to a perceptual deficit rather than a memory deficit (Eacott et al., 1994; Murray and Bussey, 1999). To address this question a group of amnesic patients were tested on a difficult 14-choice forced-choice visual item recognition test which included a "simultaneous" condition in which the sample remained visible during the matching decision and a zero second delay. The stimuli were abstract complex patterns which had to be discriminated from foils containing similar features. This discrimination required the representation of both the stimulus features and the way in which they were combined. A deficit in the perceptual processes necessary for this would impair performance in these two conditions. The second question, which arose from the model of Aggleton and Brown (1999), was whether performance on the DMS task would remain intact following selective damage to the hippocampus.

## MATERIALS AND METHODS

### *Subjects*

A group of 9 patients (2 female, 7 male) of mixed aetiology were tested. Three patients had suffered encephalitis (CF, RS, YW). These patients' pathology was investigated using Magnetic Resonance Imaging (MRI). CF was found to have complete damage to the amygdala, hippocampus, parahippocampal cortex, perirhinal cortex and entorhinal cortex on the right with additional partial damage in this hemisphere to the superior and middle temporal gyri, the occipito-temporal gyrus and the insular cortex. CF also had some damage to the amygdala, and the parahippocampal, perirhinal and entorhinal cortices on the left. RS's hippocampus was small throughout its length bilaterally with greater volume loss at the head. In addition, this patient had some damage to the parahippocampal cortex, perirhinal cortex and entorhinal cortex on the left and some damage to the perirhinal cortex on the right. RS also had some general cortical atrophy. Volume estimates for medial temporal lobe structures in this patient have been reported elsewhere (Holdstock, Mayes, Cezayirli et al., 1999a). In patient YW, the amygdala, hippocampus, parahippocampal gyrus, perirhinal and entorhinal cortices were almost completely destroyed on the right but were less extensively damaged on the left. There was extensive damage to both the inferior and middle temporal gyri on the right. On the left the inferior temporal gyrus was damaged but the middle and superior temporal gyri were relatively spared. There was some mild cortical atrophy of the frontal, and parietal lobes but no evidence of focal damage to these regions. A fourth patient (NM) had suffered from meningitis in 1969 and was found by MRI to have partial bilateral damage to the amygdala, hippocampus, parahippocampal cortex, perirhinal cortex and entorhinal cortex. Volume measures of medial temporal lobe structures in this patient have been provided elsewhere (Holdstock et al., 1999a). In addition, NM had some atrophy of the mammillary bodies, cerebellum, and in the superior frontal and parietal lobes. One patient had amnesia as a result of a posterior communicating artery aneurysm (CW) and a CT scan showed damage to the posterior temporal region, low density change in the right temporal region medially and a zone of reduced density in the occipital cortex. Two patients had had an anterior communicating artery aneurysm clipped (AB, RB). MRI data was only available for RB and showed high signal changes in the gyrus rectus and the medial orbital frontal gyri on the right which extended up to the head of the caudate nucleus. There was also cystic change in the genu of the corpus callosum and high signal in the anterior cingulate sulcus on the left. Atrophy of the frontal poles and high signal changes in the superior surface of the right temporal pole were also reported. The final two patients had Korsakoff's syndrome (RT, JT). Unfortunately scan information for these patients was not available. The patient group had a mean age of 48.1 years (S.D. = 7.3).

The results of the psychometric assessment of the patients is shown in Table I. The

TABLE I  
*Details of Age, Aetiology and Performance on Standardised Tests of Intellectual Function and Memory for the Nine Patients Participating in the Group Study and for Patient YR [The test scores shown are predicted premorbid full scale IQ from the National Adult Reading Test-Revised (NART-R), index scores (mean of 100, SD of 15) from the Wechsler Adult Intelligence Scale-Revised (WAIS-R) and the Wechsler Memory Scale-Revised (WMS-R), percentile equivalents for scores on the Doors and People Test, number correct out of 50 on the Recognition Memory Test (RMT) with performance at less than the fifth percentile marked with an asterisk]*

NM	Aet.	Age	N-R	WAIS-R				WMS-R				Doors & People					RMT	
				FSIQ	VIQ	PIQ	GEN	ATT/C	DEL	P	D	S	N	W	F			
CF	PE	39	118	101	105	98	89	105	88	50	<1	<1	75	25-50	48	31*		
RS	PE	50	111	106	103	110	74	92	55	<1	10-25	<1	25	33*	33*			
YW	PE	55	96	100	103	96	63	118	<50	<5	<5	<1	<5	29*	23*			
NM	M	47	82	84	87	87	77	88	<50	<1	<1	<1	1	26*	32*			
CW	PAA	40	102	86	92	80	64	80	<50	<1	<1	<1	5	41	27*			
AB	AAA	47	107	89	93	86	65	74	50	<5	<1	<1	1	30*	28*			
RB	AAA	62	110	108	106	109	84	130	50	<5	50	1-5	<1	31*	38			
RT	K	50	98	104	106	102	87	93	62	<5	10	<1	1	31*	32*			
JT	K	43	85	90	91	92	78	90	59	<1	<1	<1	25	40	37			
YR		48	115	102	108	97	66	122	73	<1	50	1-5	99	45	48			

N-R = NART-R; FSIQ = full scale IQ; VIQ = verbal IQ; PIQ = performance IQ; VERB = verbal memory; VIS = visual memory; GEN = general memory; ATT/C = attention/concentration; DEL = delayed memory; P = people subtest; D = doors subtest; S = shapes subtest; N = names subtest; W = words; F = faces.

premorbid IQ of the patients was estimated using the NART-R (Nelson and Willison, 1991) and the group had a mean predicted full scale IQ of 101 (range 82-118). A measure of present full scale IQ was obtained using the Wechsler Adult Intelligence Scale – Revised (WAIS-R) on which a mean score of 96.4 (range 84-108) was obtained. Memory was measured using the Wechsler Memory Scale – Revised (WMS-R), the Doors and People Test (D&P) (Baddeley, Emslie and Nimmo-Smith, 1994) and the Recognition Memory Test (RMT) (Warrington, 1984). On the WMS-R the mean general memory index score was 75.7 (range 63-89), with mean index scores of 96.7 (74-130) for attention and concentration and 57.1 (range 50-88) for delayed memory. The mean raw score obtained by the amnesic group on the D&P was 7.8 (range 0-30) for the people subtest, 11.8 (range 8-18) for the doors subtest, 15.1 (range 8-36) for the shapes subtest and 13.4 (range 10-18) for the names subtest; these mean scores fell at less than the fifth percentile, first to fifth percentile, less than the first percentile and first to tenth percentile, respectively. The mean number of items recognised out of 50 on the RMT was 34 (range 26-48) for words and 31 (range 23-38) for faces.

The performance of the amnesic group was compared with a group of 9 control subjects (2 female, 7 male) who were well matched for age and estimated IQ. The mean age of the control group was 48.7 years (S.D. = 8.2). A t-test demonstrated that control and amnesic groups did not differ significantly in age [ $t(16) = 0.18, p > 0.05$ ]. The mean estimated full scale IQ of the control group was determined from the NART-R and was 101.2 (S.D. = 10.9). A t-test comparing the NART-R predicted full scale IQ of the control subjects with the WAIS-R full scale IQ of the amnesic patients revealed no significant difference [ $t(16) = 0.76, p > 0.05$ ].

The patient, YR, with relatively selective hippocampal damage was a clerical worker aged 59 at the time of testing. In 1986 she received an opiate drug to relieve a severe back pain and may then have suffered an ischaemic incident. Following this incident she suffered a memory impairment which has persisted for 12 years. A Magnetic Resonance Imaging (MRI) scan was obtained for patient YR using a 3D T1-weighted radio-frequency spoiled gradient echo (SPGR) sequence [TE = 9 ms, TR = 34 ms, flip angle = 45 degrees, matrix size =  $256 \times 192$ , 2 NEX, field of view = 20 cm, acquisition time = 27 minutes and 52 seconds] available on a 1.5T SIGNA whole-body magnetic imaging system (General Electric, Milwaukee, WI). The volumes of the hippocampus, parahippocampal gyrus, temporal lobe, parietal lobe and grey and white matter of the prefrontal lobe were estimated using the Cavalieri method of modern design stereology (Gundersen and Jensen, 1987) via stereology menus within Analyze (Mayo Foundation, Minnesota, USA) software running on a SPARC 10 workstation (SUN Microsystems, CA, USA). The scan revealed bilateral damage to the hippocampus throughout its entire length. Volume measures, corrected for intracranial volume were 2.25 S.D.s and 3 S.D.s smaller than the control mean on the right and left respectively. The amygdala was small but showed no sign of pathology and there were no other visible abnormalities within the medial temporal lobe. The volume of the temporal lobe was also normal. Grey and white matter volumes for the frontal lobe were normal and the volume of the parietal lobe was within two standard deviations of the control mean volume bilaterally (a more detailed report of the volumetric analysis of YR's scan is provided by Holdstock, Mayes, Cezayirli et al., 1999b).

YR's results from standardised tests of intellectual function and memory are shown in Table I. Psychometric testing revealed that YR has an IQ, assessed by the WAIS-R, which is a little above average and which is higher for Verbal than Performance tests. The difference between her premorbid IQ (measured by the NART-R) and her present IQ was less than 1 S.D. on the WAIS-R scale, so there was no indication of a significant decline in IQ in this patient. Memory testing showed that recall, measured by the two recall subtests of the Doors and People Test (Baddeley, Emslie, Nimmo-Smith, 1994) and the general and delayed memory indices of the WMS-R, was impaired. In contrast, recognition of visual and verbal items from the D&P and the RMT was unimpaired. YR's executive and visuospatial abilities were also assessed. She showed no impairment on verbal fluency (FAS) (Benton, 1968), Cognitive Estimates (Shallice and Evans, 1978) and the Wisconsin Card Sorting Test (WCST) (Heaton, 1981), all of which tap executive functions. Her performance on the FAS was 0.1 S.D.s below her control group's mean, on the CET was



0.69 S.D.S. below her control group's mean, and on the WCST the number of correct categories achieved was at the sixth to tenth percentile and number of perseverative errors was at the 88th percentile. YR's perception of objects and space, assessed by the Visual Object and Space Perception Battery (VOSP) (Warrington and James, 1991), the Judgement of Line Orientation test (Benton, Hamsher, Varney et al., 1983) and the "Little Men" Test of mental rotation (Ratcliff, 1979), was unimpaired. On the VOSP performance ranged from 18th to 76th percentile, on the Judgement of Line Orientation test performance was above the control mean as was performance on those conditions of the "Little Men" test requiring mental rotation (performance ranging from 0.05 to 0.5 S.D.s better than the control mean). Spatial reasoning, assessed using the Verbal and Spatial Reasoning Test (VESPAR) (Langdon and Warrington, 1995), was also unimpaired (50th-75th percentile).

As YR was older than most of the subjects making up the amnesic group, her performance was compared with that of a separate control group of a more appropriate age. The control group, which consisted of 11 females, had a mean age of 60 years (S.D. = 4.8) which was 0.21 standard deviations older than YR. The mean full scale IQ of the control group which was estimated from the NART-R was 110.5 (S.D. = 7) which was 1.2 standard deviations higher than YR's full scale IQ from the WAIS-R and 0.64 standard deviations lower than YR's estimated premorbid (NART-R) full scale IQ.

### *Apparatus and Stimuli*

Subjects were tested on a 14-choice visual delayed-match-to-sample task which used trial unique stimuli. The task was presented on a PC computer connected to a 39 cm × 29 cm touch screen. The stimuli were computer-generated monochrome complex abstract designs (ranging from 4 cm × 4.5 cm to 5 cm × 4.5 cm) which comprised a white pattern overlaid by a grey pattern. The stimuli were difficult to verbalise (see Figure 1). Stimulus complexity was similar to that of the stimuli used by Eacott et al. (1994), each of which comprised a large typographic character overlaid by a small typographic character.

### *Design*

Performance was investigated in seven conditions: a simultaneous condition and six delays. In the simultaneous condition the sample item remained visible while the matching decision was made and so did not necessitate memory. The delays were chosen to be consistent with those which have been used to assess animal models of amnesia and were of zero seconds, two seconds, five seconds, ten seconds, twenty seconds and thirty seconds. In the zero second condition the choice stimuli appeared immediately after the disappearance of the sample item.

Performance on the simultaneous condition and the zero second condition was assessed on 50 trials and for the remaining conditions subjects completed 20 trials. Each subject completed all the trials for one condition before moving on to the next condition. For the three longest delays a mental arithmetic task was interposed between study and test.

Each stimulus was seen only once throughout testing although other similar stimuli were used. The stimuli were allocated randomly to the seven conditions prior to the study. The stimuli seen within a particular condition were the same for all subjects. In the group study, each patient completed the conditions in a different random order. These same nine orders were used for the control group. Each patient was allocated a control subject of the same sex and similar age who completed the conditions in the same order to that amnesic. Patient YR and her controls completed the conditions in a different random order to the subjects in the group study.

### *Procedure*

In the simultaneous condition a stimulus was presented in the centre of the screen for 2.5 seconds. This sample stimulus then remained visible while the 14 choice stimuli appeared on the screen. The foils contained similar features to the target stimuli. The choice stimuli appeared in three rows, with one row above and one below the sample item (each

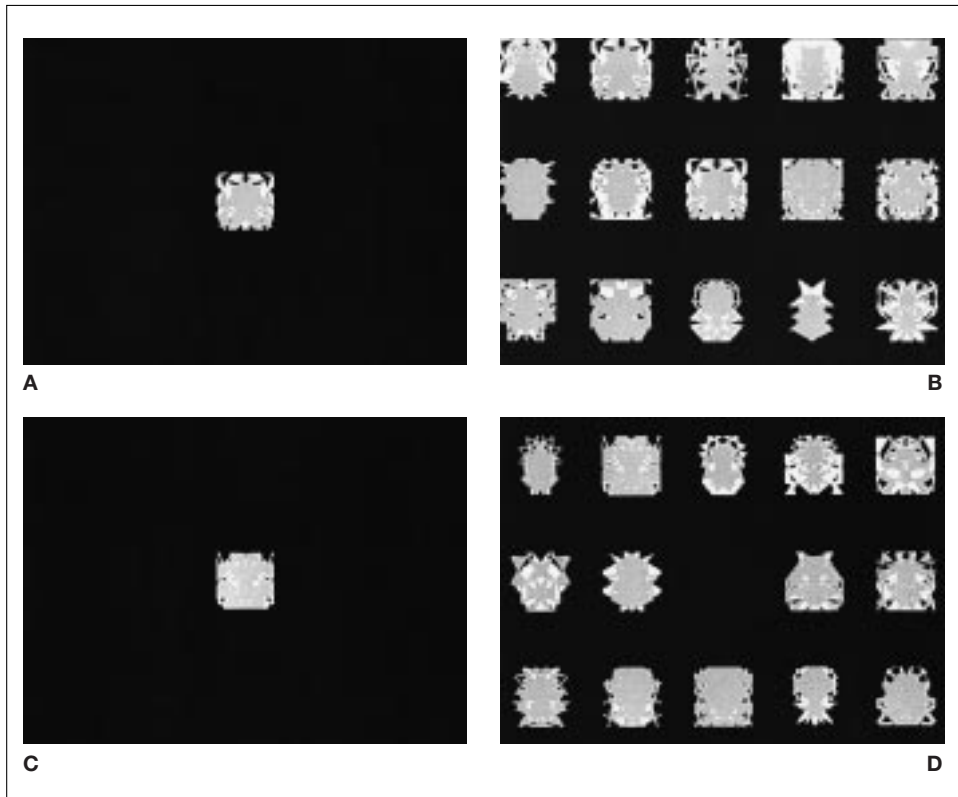


Fig. 1 – An example of the monochrome abstract patterns used for the match-to-sample task. A illustrates what subjects saw at presentation in the simultaneous condition; B illustrates what subjects saw at test in the simultaneous condition; C illustrates what subjects saw at presentation in the memory conditions; D illustrates what subjects saw at test in the memory conditions.

row consisting of five stimuli) and two stimuli to the left and two to the right of the sample stimulus on the middle row (see Figure 1). The subject was instructed to touch the design which matched the sample in the centre of the screen.

In the delay conditions a sample stimulus was presented in the centre of the screen for 2.5 seconds in exactly the same way as the simultaneous condition. The sample then disappeared and the screen remained blank for the duration of the delay. For retention intervals of zero seconds, two seconds and five seconds the delay was unfilled and subjects allowed to continue looking at the computer screen while waiting for the choice items to appear. For the three longer delays subjects were asked to complete mental arithmetic problems as quickly and accurately as possible. The problems, which were presented on A4 sheets of paper, required subjects to add, subtract, divide or multiply four numbers as quickly as possible and to write the answer alongside each problem. Following the delay the choice stimuli were presented in the same screen locations as in the simultaneous condition i.e. in the delay conditions the central position (which had been occupied by the sample) remained blank in the test phase (see Figure 1). Subjects selected the design which matched the previously presented sample.

In all conditions, an unlimited amount of time was allowed at test for subjects to make their decision and their response time was recorded. Sets of 4 practice trials were provided prior to each block of trials in order to ensure that the subject understood the requirements for that condition.

## RESULTS

Exploration of the results considered both percent correct scores and response time. All post hoc testing employed Tukey's HSD test.

The first analysis compared the percentage of correct responses made by the amnesic group and their healthy controls for each of the seven delays. A  $2 \times 7$  ANOVA with factors of group and condition showed a significant effect of group [ $F(16, 1) = 34.95, p < 0.001$ ] which was due to the amnesic group making fewer correct choices overall than the control group. There was also a significant effect of condition [ $F(96, 6) = 69.91, p < 0.001$ ]. Post hoc tests indicated that performance was significantly better in the simultaneous condition than in any of the delay conditions and was significantly better after any of the three shortest delays than after any of the three longest delays ( $ps < 0.05$ ). Condition was found to interact significantly with group [ $F(96, 6) = 22.39, p < 0.001$ ]. Post hoc tests compared the performance of the two groups in each condition. This revealed that the two groups differed significantly in performance only at the three longest delays. The analysis was repeated following arcsine transformation of the data which was performed because of the debate as to whether transforming the results of such tests produces a qualitatively different pattern of results (Alvarez-Royo, Zola-Morgan and Squire, 1992; Ringo, 1993). Consistent with a similar study of amnesic patients (Holdstock et al., 1995), the pattern of our results which was obtained after transformation of the scores was identical to that obtained with the untransformed data.

The analysis was repeated after selecting just those patients with MRI evidence of perirhinal damage ( $n = 4$ ) to compare with the control group ( $n = 9$ ). A very similar pattern of results was found as for the entire amnesic group; the patients with damage to the perirhinal cortex were only significantly impaired after the filled delays of 10 seconds or longer. The only difference that was obtained between this analysis and that of the entire amnesic group was that, for the perirhinal patients, post hoc tests showed that performance in the simultaneous condition did not differ from that at the three shortest delays. In addition, a  $2 \times 7$  ANOVA with factors of group and delay compared the perirhinal subgroup with the rest of the amnesic group. There was no significant effect of group [ $F(7, 1) = 1.71, p > 0.05$ ] and no significant interaction between group and delay [ $F(42, 6) = 1.58, p > 0.05$ ]. Figure 2 shows graphically the percent correct scores for the amnesic group split into patients with or without MRI evidence of perirhinal cortex damage and the control group.

Figure 2 also plots percent correct scores for patient YR and her control group for each of the seven conditions. YR's performance expressed as standard deviations from the control mean are shown in Table II. We have considered YR's performance to be impaired if her scores were more than 1.96 S.D.s worse than the control mean giving a type 1 error probability of 0.05, 2 tailed. YR's performance was not significantly impaired in any condition. At delays of 5 s, 10 s and 30 s her performance was over 1 S.D. below the mean of the control group but was within the control range for all conditions. A comparison of YR's scores with the mean of the amnesic group (see Table II) showed that YR's score was over 2 S.D.s better than the mean of the amnesic group at the 20 s delay and over 1 S.D. better for

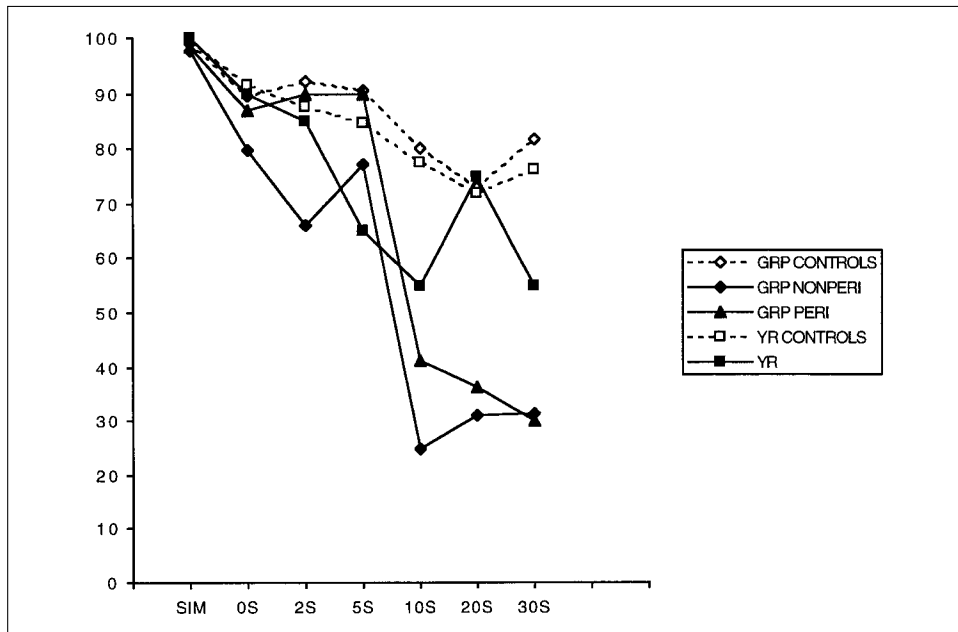


Fig. 2 – Graph displaying the percent correct scores from the simultaneous condition and each of the six delays for patient YR and the mean percent correct scores for her age and IQ matched control group (YR CONTROLS), the amnesic subgroup with perirhinal damage (GRP PERI), the amnesic subgroup with no confirmed perirhinal damage (GRP NONPERI) and a control group which was matched for age and IQ to the overall amnesic group (GRP CONTROLS).

delays of 10 and 30 seconds. These were the delays which were filled by the distractor task and were the conditions in which performance would be most likely to be tapping long-term memory. When YR's performance was compared with only those patients with MRI evidence of perirhinal damage, a similar pattern of superior performance was found for YR, which was over 2 S.D.s better than the perirhinal subgroup at the 20 second delay and 0.83 S.D.s better than the perirhinal group mean at the 10 second and 30 second delays.

An analysis was also performed on subjects' response times pooled over correct and incorrect responses. A  $2 \times 7$  ANOVA with factors of group (amnesic

TABLE II

*Number of Standard Deviations that YR's Mean Percent Correct Score was from the Control Mean (YR v Con), the Mean of the entire amnesic group (N = 9) (YR v Amn), and the Mean of Those Amnesics with MRI Evidence of Perirhinal Damage (N = 4) (YR v Peri) for each of the Seven Conditions of the Match-to-Sample Task [Positive scores indicate that YR was performing above the mean of that comparison group]*

Comparison	Sim.	0 s	2 s	5 s	10 s	20 s	30 s
YR v Con	– .47	– .26	– .39	– 1.5	– 1.6	+ .32	– 1.1
YR v Amn	+ .75	+ .7	+ .55	– 1.42	+ 1.12	+ 2.74	+ 1.14
YR v Peri	+ .5	+ .87	– 1.2	– 2.74	+ .83	+ 2.16	+ .83

group and control group) and condition was carried out. The analysis showed that the response time of the two groups did not differ significantly [ $F(16, 1) = 4.05$ ,  $p > 0.05$ ]. There was a significant effect of delay [ $F(96, 6) = 31.85$ ,  $p < 0.01$ ] which post hoc tests revealed was due to response time being significantly longer after filled delays of 10, 20 and 30 seconds than after the shorter delays and the simultaneous condition. The effect of delay did not interact significantly with group [ $F(96, 6) = 1.05$ ,  $p > 0.05$ ]. The response time, pooled over correct and incorrect responses, was also investigated specifically in the perirhinal group because, although percent correct scores gave no indication of a perceptual deficit in this group, an increase in response time would be consistent with such a deficit. Patient mean response times were very similar to those of the control subjects and an ANOVA with factors of group (control and perirhinal groups) and delay indicated no significant difference between the response time of the control and perirhinal group [ $F(11, 1) = .22$ ,  $p > 0.05$ ] and no significant interaction with delay [ $F(66, 6) = .58$ ,  $p > 0.05$ ].

In contrast to the amnesic group, YR's response time was significantly slower than her controls' for all conditions other than the simultaneous condition. As shown in Table III, which shows YR's response time expressed as the number of standard deviations above the control mean, this increased response time was particularly striking at the longer delays. Her mean response time (collapsed over correct and incorrect response) was 10.45, 12.96, 30.31, 39.3, 38.55 and 45.5 seconds at delays of 0 seconds, 2 seconds, 5 seconds, 10 seconds, 20 seconds, and 30 seconds, respectively, whereas the mean control response time for these delays were 5.01, 6.48, 6.41, 10.73, 12.23, 11.29, respectively. This increase in response time was found for both correct and incorrect responses (see Table III). As shown in Table III YR's response time was also significantly slower than the amnesic group at delays of zero seconds onwards. The results suggest that the intervals over which YR was remembering the stimuli were considerably longer than both her control group and the amnesic group. Due to this it is possible that YR's percent correct scores may be providing an underestimate of her performance.

TABLE III

*Number of Standard Deviations that YR's Mean Response Time, Collapsed over Correct and Incorrect Responses (Overall RT), was from the Control Mean (YR v Con) and the Amnesic Group Mean (YR v Amn) for each of the Seven Conditions. Number of Standard Deviations that YR's Mean Response Time, for Correctly Recognised Items (Correct RT) and for Incorrectly Recognised Items (Incorrect RT), was from the Control Mean. [Positive scores indicate longer response time].*

Comparison	Sim.	0 s	2 s	5 s	10 s	20 s	30 s
Overall RT							
YR v Con	1.18	2.4	2.1	8.69	7.6	6.5	10.5
YR v Amn	-.14	2.2	2.1	10.1	6.0	6.6	6.9
Correct RT							
YR v Con	1.18	2.3	3.2	6.9	5.3	6.6	7.2
Incorrect RT							
YR v Con	1.18	2.7	.94	5.9	4.5	4.2	6.7

## DISCUSSION

A group of amnesic patients of mixed aetiology, including four patients with MRI evidence of perirhinal cortex damage, were found to be unimpaired on a 14-choice visual matching-to-sample task when the sample item remained visible during the choice phase (simultaneous condition) and when the study-test interval was unfilled and of five seconds or less. In contrast, the performance of this group was significantly impaired after a delay of 10 seconds or longer during which rehearsal was prevented by a distractor task.

The unimpaired performance of the amnesic group in the simultaneous and zero second conditions confirms that the impairment in DMS found in amnesic patients is due to a deficit in memory rather than perception. The fact that the amnesic group were impaired only when study and test were separated by a filled delay suggests, consistent with other studies, that both encoding (e.g. Mayes, Downes, Shoqeirat et al., 1993; Smith and Milner, 1989; Shoqeirat and Mayes, 1991; Downes et al., 1998, Warrington and Baddeley, 1974) and short-term/working memory (e.g. Mayes and Meudell, 1983) were normal. The amnesic patients' impaired performance at the three longer filled delays indicates that long-term memory for this information was impaired because rehearsal was not possible and the delays were such that short-term memory was unlikely to be contributing to performance (see Downes et al., 1998, Isaac and Mayes, 1999). This deficit was seen as soon as long-term memory was being tapped, as marked by the introduction of the filler task, and in agreement with the bulk of the literature (for a review see Isaac and Mayes, 1999) this deficit did not appear to increase with time. The apparent accelerated loss of information by the perirhinal group between 10 s and 30 s delays was not statistically significant ( $t = 1.963$ ,  $p > 0.05$ ). However, as the patients' performance was impaired even at the first of the longer filled delays, scaling effects make it difficult to reliably compare the relative rate of forgetting of the amnesic and control groups.

As the findings of Eacott et al. (1994) specifically implicated the perirhinal cortex in perceptual processing we also examined the performance of four of the amnesic patients for whom we had MRI confirmation of perirhinal cortex damage. The mean percent correct scores of these patients was 98.5 (S.D. = 3) in the simultaneous condition and 87 (S.D. = 3.5) in the zero second condition. An analysis of variance which compared the performance of these four patients with the control performance on the simultaneous condition and each of the six delays indicated that the perirhinal damaged patients were only significantly impaired after the filled delays of 10 seconds or longer. No significant difference was found between perirhinal damaged patients and controls on the simultaneous condition or the zero second delay. In addition, the response time of the perirhinal group did not differ significantly from that of the control group at these or the longer delays. Due to ceiling effects, it may be argued that the simultaneous condition was not sensitive enough to reveal a deficit in our patient group and that a deficit would be visible if a more difficult discrimination task had been used. However, the subjects are clearly away from ceiling in the zero second condition and yet the amnesic group, and the subgroup with perirhinal damage, did not differ significantly in performance from the controls.

It is possible that a deficit in the simultaneous and zero second delay conditions is related to the extent of perirhinal damage, particularly that on the right given the visual nature of the task. The animal studies which have reported perceptual deficits following perirhinal cortex lesions have involved complete bilateral removal of this region so the effect of incomplete removal of the perirhinal cortex in monkeys is unknown. The extent of the patients' perirhinal damage was rated separately for the right and left hemispheres by a neuroanatomist on a scale ranging from 0 (no damage) to 5 (complete damage). Spearman rank order correlations between the extent of right perirhinal damage and percent correct scores did not approach significance for either the simultaneous ( $r_s = -.58$ ,  $p > 0.05$ ) or zero second ( $r_s = -0.71$ ,  $p > 0.05$ ) conditions, but they did suggest a trend for a relationship between extent of damage and performance.

However, because of the small group size, the correlational results should be interpreted with caution and more detailed inspection of the data indicates that the obtained trend may be misleading. For each of the simultaneous and zero second delay conditions three of the patients performed at around the control mean whereas the fourth patient performed at a slightly lower level. In each case the patient who performed more poorly was one of the two patients with complete right perirhinal damage. However, it was a different patient who performed poorly in each of the two conditions. So a stable deficit following right perirhinal cortex damage was not found. Furthermore, at the 2 s delay greater perirhinal damage was actually related, but not significantly, to better task performance ( $r_s = 0.71$ ,  $p > 0.05$ ) and at the 5 s delay there was zero correlation between extent of perirhinal damage and performance. Had the correlations from the simultaneous and zero second delays been indicating that more complete perirhinal damage resulted in a perceptual deficit, similar correlations would also have been expected for the two and five second delays which tapped short-term/working-memory.

The lack of a consistent deficit in the two patients with total right perirhinal cortex damage is illustrated clearly by the performance of the patient who was impaired in the simultaneous condition (YW). Although YW's deficit in the simultaneous condition was in agreement with Eacott et al.'s (1994) and Murray and Bussey's (1999) view, her performance was unimpaired in the zero, two and five second delay conditions and was actually better than the control mean in the two second delay condition. Also, her response time was faster than the control mean at these short delays suggesting that the few errors that she made may have been due to a speed-accuracy trade off. Therefore, a consideration of her performance from all four conditions provides no strong evidence for a perceptual deficit. So, our results suggest that total right perirhinal cortex damage is not sufficient to produce a perceptual deficit in humans for the kind of stimuli used in our task but we cannot exclude the possibility that such a deficit may only become apparent when complete damage to the perirhinal cortex is bilateral.

The results of Buffalo et al. (1998), however, indicate that our patients' unimpaired performance may not be due to incomplete damage to the perirhinal cortex. Buffalo et al. (1998) showed that complete bilateral damage to the

perirhinal cortex in two patients left item recognition unimpaired at delays of zero and two seconds. Our results are, therefore, consistent with another study of perirhinal cortex damage in humans (Buffalo et al., 1998), which seems not to agree with the animal literature (e.g., Eacott et al., 1994; Buckley et al., 1998).

An appropriate test of the hypothesised perceptual function of the perirhinal cortex should both be difficult for normal subjects and tap the right processes. The control subjects found our simultaneous discrimination task easier than Eacott et al.'s monkeys. This may have mattered. More important, however, is whether the tasks tap relevant perceptual processes. Perirhinal cortex lesions in monkeys do not cause a crude perceptual deficit. Concurrent discrimination learning for colours (Buckley, Gaffan and Murray, 1997; Buckley and Gaffan, 1997) and small sets of objects (Buckley and Gaffan, 1997; Thornton, Rothblat and Murray, 1997) are spared by such damage. Determining whether a task is tapping the appropriate perceptual processes will require fuller specification of Murray and Bussey's hypothesis. For the kind of stimuli we used, which were comparable to those used in Eacott et al.'s study, no perceptual deficit was found following perirhinal lesions. What we did find was that these patients were unable to maintain a representation of the stimuli in memory over a period of time during which rehearsal was prevented and performance was reliant on long-term memory. This finding is consistent with the view that the perirhinal cortex is involved in the recognition of visual stimuli which have been normally represented (Aggleton and Brown, 1999).

Unlike Buffalo et al. (1998), we found no significant difference between the item recognition performance of our amnesic patients with and without damage to the perirhinal cortex. Buffalo et al. (1998) report that item recognition was more impaired in their patients with perirhinal damage than in a group of amnesics comprising patients with Korsakoff's syndrome and MRI confirmed or suspected hippocampal damage. There are a number of differences between our study and the Buffalo et al. (1998) study which may account for this discrepancy. First, unlike Buffalo et al.'s patients, our patients did not have total *bilateral* perirhinal damage. It is possible that our patients' residual perirhinal cortex may have been able to process information sufficiently to keep the performance of these patients comparable to the other amnesic patients. We investigated this possibility with a Spearman's rank order correlation between the performance of our four patients with perirhinal damage at the 30 second delay and the rated extent of their perirhinal damage. Combining the rated perirhinal damage for the left and right hemispheres, ratings ranged from 8.5 to 2 out of a possible total of 10. Similarly there was a considerable range of percent correct scores from the memory test (5 to 65 percent correct). The correlation coefficient was very low ( $r_s = 0.11$ ) giving no indication of a relationship between extent of perirhinal damage and performance. A correlation of a similar magnitude was obtained when extent of right perirhinal damage only was considered ( $r_s = 0.24$ ). However, the availability of only a small number of data points did limit the power of the analysis.

Second, in our task rehearsal was blocked by the inclusion of a distractor task during the three longest retention intervals. This would have minimised the contribution to performance of short-term or working memory so that primarily



long-term memory would have been tapped. Such a rehearsal blocking task was not included in the design of Buffalo et al.'s study so one cannot exclude the possibility that their results are reflecting differences between patients in working memory or short-term memory.

Finally, and perhaps most importantly, Buffalo et al.'s mixed amnesic group had a different composition to the mixed group included in our study. Both studies included Korsakoff patients (four in the Buffalo et al. group and two in our group). However, whereas the other patients in our group had lesions which included cortical regions other than the perirhinal cortex, Buffalo et al.'s group included two patients who are reported to have selective hippocampal damage. The performance of our patient with selective hippocampal damage (YR) was not significantly impaired on the DMS task and was better than both the amnesic group and those patients with perirhinal damage. Our results therefore indicate that item recognition performance will differ depending on whether damage is restricted to the hippocampus or is more extensive. Given that YR's item recognition was unimpaired, the inclusion of two patients with reported selective hippocampal lesions in Buffalo et al.'s group may have inflated the amnesic group's mean level of performance. This cannot be determined from the data provided by Buffalo et al. If this was the case, however, then the difference between the performance of the amnesic and perirhinal groups in their study may have been reflecting a difference between the behavioural effects of selective hippocampal damage and more widespread damage, as found in the present study.

Patient YR was tested in order to address the issue of whether selective damage to the human hippocampus will leave item recognition unimpaired on tasks such as DMS. She was not significantly impaired on the DMS task at any delay. Her scores were within the control range at all delays and her performance was actually better than the control mean at the 20 second delay. This clearly indicates that she was not impaired on this forced-choice item recognition task. This intact item recognition was found in the context of a recall deficit which, at comparable delays, was as impaired as the amnesic group (WMS-R general memory index, D&P people and shapes subtests) and so cannot be explained by the severity of her memory disorder. This unimpaired performance in YR is particularly striking given that her response time is between 6.5 and 10.5 standard deviations longer than the control mean for the memory conditions. This would have increased the retention interval for YR relative to both her controls and the amnesic group and as a result YR's scores in the present study may actually underestimate her performance at delays comparable to those experienced by the controls. This may explain why her performance is below the control mean (although still within the control range) after two of the three filled delays. It is of interest to note that of the three filled delays, the one on which YR recognised more items than the control mean was that on which her response time was least slowed relative to the controls (although it was still significantly slower than the control mean).

YR's long response times were not due to a general slowness in processing and responding to stimuli, as her responses were not significantly slower than the control mean in the simultaneous condition and were slightly faster than the

amnesic group mean in that condition. Her response time was significantly slower than the control and amnesic groups only in the memory conditions. This slowness therefore appears to be related to her ability to make a decision based on the remembered information she has available. She is very aware that her memory is often impaired and this may have affected her confidence or willingness to make memory related decisions. Alternatively, YR's slow response times may indicate that her recognition performance depends on at least partially different processes to those used by healthy control subjects which take longer to complete. Therefore, although YR's results suggest that nonhippocampal systems have the capacity to support recognition memory, further research will be needed to address the related question of whether nonhippocampal systems alone normally support recognition memory in healthy subjects with intact hippocampal systems.

YR's item recognition was better than that of the amnesic group mean at all delays apart from five seconds and was more than one standard deviation better at the three longest delays. At the 20 second delay YR's performance was significantly better (i.e. greater than two standard deviations better) than the amnesic group. A similar pattern of results was found when YR's scores were compared with the subgroup of amnesics with perirhinal cortex damage. These considerable differences in performance between YR and the other amnesic patients were obtained even though YR and the amnesic group differed in a number of ways which would reduce any memory difference between them. These differences included: response time, which, as already discussed, would increase the retention interval for YR relative to the amnesic group; age – YR was older than the mean of the amnesic group; sex – the amnesic group and perirhinal subgroup were predominantly male and it has been shown that visuospatial abilities tend to be better in males than females (see Lezak, 1995). Memory for the difficult to verbalise abstract patterns used in the present study is likely to have relied considerably on visuospatial abilities. As this was the case an additional comparison was made. YR's performance was compared with that of one of the patients from the amnesic group (YW) who was female and of a similar age to YR. YW also had the most extensive damage to the perirhinal cortex of the patients included in our study (perirhinal damage was total on the right and was rated as 3-4 on the left where 0 = no damage and 5 = total damage) and so was of particular interest given Aggleton and Browns' model. As YW was a similar age to YR, both patients' scores were expressed as the number of standard deviations above or below the mean of YR's control group. YW's performance was found to be 2.09 S.D.s lower than YR's at the 10 second delay, 5.98 S.D.s lower at the 20 second delay and 2.67 S.D.s lower at the 30 second delay. YW was therefore considerably more impaired than YR at all three long delays.

In summary, our data showed that YR performed consistently better than the amnesics at the three longest delays and was over two standard deviations better than them at one of these delays, even though factors such as sex, age and response time meant that any comparison provided a conservative estimate of the memory differences due to their differing pathology. YR also performed considerably better than another female patient of a similar age (and with

comparable scores on the general memory index of the WMS-R and the recall subtests of the D&P) who has more extensive medial temporal lobe damage which includes the entire perirhinal cortex on the right and approximately 70% of the perirhinal cortex on the left. These findings, coupled with the fact that she performed better than the control mean at one of the longest delays (and within 1.96 S.D.s of the control mean at all other delays) and was within the control range at all delays, provides strong evidence that YR's object recognition memory is intact. Consistent with several other human studies (Aggleton and Shaw, 1996; McMackin et al., 1995; Vargha-Khadem et al., 1997), YR's scores indicate that selective damage to the hippocampus has little effect on forced-choice item recognition.

This conclusion is inconsistent with Reed and Squire's (1997) report that six patients with selective hippocampal damage were impaired on a variety of recognition memory tests. These patients had a recall deficit of similar severity to YR as measured by the general memory index of the WMS-R. It is difficult to directly compare the recognition memory of YR and Reed and Squire's patients because, apart from the RMT, they have not been tested on identical tests. However, YR has been tested on over 40 item recognition tests which have differed in paradigm (forced-choice or yes/no), number of foils, delay, and difficulty for healthy subjects (Mayes, van Eijk, Gooding et al., 1999). None of these variables were found to affect the normality of her performance. As these tests correspond to the kinds of item recognition tests used by Reed and Squire (1997), it is very likely that YR would perform normally on the item recognition tests on which Reed and Squire's patients are impaired. On the one test which all patients had completed, the RMT, YR's performance was better than Reed and Squire's patients.

The discrepancy may reflect a difference in the extent of the patients' pathology. Structural MRI has revealed pathology restricted to the hippocampus in YR. At post-mortem two of Reed and Squire's patients were found to have pathology extending into the entorhinal cortex and the location and extent of pathology is not known in one other patient. The possibility that there is significant pathology outside the hippocampus, not identified by MRI, and present only in patients with clear item recognition deficits, such as those of Reed and Squire, remains to be systematically explored.

Two conclusions arose from the results of the study. First, performance of a group of amnesic patients of mixed aetiology was impaired on a 14-choice DMS task only when filled delays were interposed between study and test indicating that amnesic patients' impairments on this task were due to memory rather than perceptual deficits. Exactly the same pattern of performance was found for that subset of patients with MRI evidence of perirhinal damage which suggests that in humans, if the perirhinal cortex has a perceptual role, this is not necessary for the representation of the complex visual stimuli that we used. Second, on this task which was highly sensitive to human amnesia, a patient with relatively selective damage to the hippocampus, and who has a recall deficit comparable to that of the amnesic group at short delays, was not significantly impaired and, in fact, performed better than the control mean at one of the longest delays. This therefore supports the view put forward by Aggleton and Brown (1999) that the

hippocampus is not necessary for successful item recognition and extends the range of item recognition tasks over which such nonimpaired performance has been found.

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