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Item Recognition Is Less Impaired Than Recall and Associative Recognition in a Patient With Selective Hippocampal Damage

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ABSTRACT: This article explores the recall, item recognition, and associative recognition memory of patient B.E., whose pattern of retrograde amnesia was reported by Kapur and Brooks (1999; Hippocampus 9:1–8). Structural magnetic resonance imaging (MRI) has shown that B.E. has bilateral damage restricted to the hippocampus. The structural damage he had sustained was accompanied by bilateral hypoperfusion of the temporal lobe, revealed by positron emission tomography (PET), and which single photon emission computed tomography (SPECT) suggested was greater in the left than the right temporal lobe. B.E. showed a global anterograde amnesia for verbal material, but he displayed some sparing of nonverbal item recognition relative to nonverbal recall and associative recognition. His performance on an item recognition task that used the remember/know procedure and another that involved repetition of the test phase, to reduce the difference between the familiarity of the targets and foils, suggested that his relatively spared nonverbal item recognition may have been mainly supported by familiarity. This finding is consistent with the view that the anterior temporal lobe, including the perirhinal cortex, can support familiarity-based memory judgments (Brown and Bashir, 2002; Philos Trans R Soc Lond B 357:1083–1095). B.E.'s data also highlight the importance of functional as well as structural scan information for interpreting the pattern of memory deficits shown by patients with selective hippocampal structural lesions. © 2004 Wiley-Liss, Inc.

KEY WORDS: recollection; familiarity; memory; medial temporal lobe

INTRODUCTION

The medial temporal lobes (MTL) are known to play a critical role in declarative memory (memory for facts and events), but it is currently unresolved whether the hippocampus and the adjacent MTL cortices (defined here as the entorhinal, perirhinal, and parahippocampal cortices) make distinct contributions to memory and, if so, what these contributions are. The nature of the memory deficit following selective bilateral hippocampal damage or bilateral fornix damage in humans has varied considerably across cases. In some patients, selective hippocampal damage has been reported to impair both recall and recognition (Reed and Squire, 1997; Manns and Squire, 1999; Manns et al., 2003; Cipolotti et al., 2001). These data have been interpreted as supporting the view that the MTL functions as a highly integrated memory system in which both recognition and recall are dependent on the hippocampus (Squire and Zola-Morgan, 1991). Other investigators have reported a deficit in recall but, at most, only a mild impairment of recognition of individual items, such as words, faces, objects, and abstract patterns, following fornix damage (McMackin et al., 1995) and relatively selective hippocampal damage (Vargha-Khadem et al., 1997; Henke et al., 1999; Holdstock et al., 2002a,b; Mayes et al., 2002). It has been argued that this pattern is consistent with alternative views put forward by Aggleton and Brown (1999) and Norman and O'Reilly (2001) (see also O'Reilly and Norman, 2002); these views postulate that the hippocampus mediates recall and recollection (the type of recall that contributes to recognition) whereas regions of the neocortex can support familiarity-based memory decisions. Electrophysiological studies have shown that neurons in the anterior inferior temporal lobe have the response properties necessary to support familiarity judgments (Brown and Bashir, 2002). These findings, in combination with lesion studies, have led Aggleton and Brown (1999) to suggest that familiarity-based recognition decisions may be mediated by a system that includes the perirhinal cortex, dorsomedial thalamic nucleus and frontal cortex. The assessment of an item's familiarity and the recollection of information about the study event are thought to be distinct and probably independent processes that contribute to recognition memory (Yonelinas, 2002). Both processes may normally contribute to the recognition memory decision but under some circumstances familiarity alone may be sufficient for good recognition performance (see Norman and O'Reilly, 2001; O'Reilly and Norman, 2002).

The models of Aggleton and Brown (1999) and Norman and O'Reilly (2001) (see also O'Reilly and Norman, 2002) predict that residual recognition memory following hippocampal damage is mediated by familiarity. The computational model proposed by Norman and O'Reilly (2001) (see also O'Reilly and Norman, 2002) makes specific predictions about the conditions under which familiarity alone will be able to support good recognition memory performance. According to their model, when targets and corresponding related foils are very similar, familiarity is sufficient to distinguish between targets and corresponding related foils in a forced-choice paradigm. However, familiarity is not sufficient to distinguish between targets and corresponding related foils in a yes/no paradigm, making performance under these conditions heavily dependent on recollection. Consistent with this prediction, patient Y.R., who had relatively selective bilateral hippocampal damage, was impaired at yes/no item recognition, but not at forced-choice item recognition

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when targets and corresponding related foils were very similar (Holdstock et al., 2002a). Further support has been provided by studies that have measured recollection and familiarity more directly. Patient Y.R. showed normal levels of familiarity, as measured by the remember/know procedure (Holdstock et al., 2002a), but impaired recollection when justification of her remember responses was required. Attempts to use the remember/know procedure with patient Jon, who was one of the young patients reported by Vargha-Khadem et al. (1997), were unsuccessful because he appeared to have difficulty understanding the concept of recollection (Baddeley et al., 2001). However, in an event-related potential study of word recognition, Jon showed a normal event-related potential (ERP) index of familiarity, but the ERP index of recollection was absent (Duzel et al., 2001). Furthermore, Yonelinas et al. (2002) found that patients with mild hypoxia, and assumed hippocampal damage, were impaired at recollection but not at familiarity, whereas patients with large MTL lesions were impaired at both recollection and familiarity. However, it should be noted that the patients described by Manns et al. (2003), who had a global anterograde amnesia following relatively selective hippocampal damage, were impaired at both recollection and familiarity as measured by the remember/know procedure.

Functional imaging studies have also provided evidence consistent with the view that the hippocampus mediates recollection whereas the perirhinal cortex can support familiarity (for review, see Rugg and Yonelinas, 2003). Davachi et al. (2003) showed that activation at encoding in the hippocampus and posterior parahippocampal cortex predicted later recollection of the source of a recognized item (word), but did not predict later item recognition. In contrast, activation at encoding in the perirhinal cortex predicted later word recognition, but not later source recognition (Davachi et al., 2003). Similarly, Ranganath et al. (2003) reported that activity at encoding in a region corresponding to the entorhinal or perirhinal cortex predicted subsequent familiarity, measured by recognition confidence ratings, whereas activity at encoding in the hippocampus and posterior parahippocampal gyrus predicted subsequent recollection, measured by source judgment. Further evidence has been provided by studies that have imaged individuals during retrieval. In a study that used the remember/know procedure, greater activation at retrieval was found in the hippocampus and parahippocampal gyrus for items that were assigned remember responses than for those assigned know responses (Eldridge et al., 2000). Greater hippocampal activation at retrieval was also reported in response to correctly recognized study items for which the correct source (study location on the screen) was identified relative to those for which the remembered source was incorrect (Cansino, 2002). With relevance to the proposed role of the perirhinal cortex in the mediation of familiarity, a meta-analysis of four studies, showed decreased activation in the anterior MTL cortex for items that had been previously experienced in the experimental session (experimentally familiar) relative to items that had not been experienced before during the experimental session (experimentally novel) (Henson et al., 2003).

Although patient Y.R. (Holdstock et al., 2002a,b; Mayes et al., 2002) and the patients described by Vargha-Khadem et al. (1997) showed a relative sparing of item recognition, they did not show a general sparing of recognition memory. Certain types of associative recognition were clearly impaired in these patients. Whereas they showed good recognition of word pairs and face pairs they were impaired at recognizing associations between different kinds of information such as the locations of objects and the voices corresponding to particular faces (Vargha-Khadem et al., 1997; Holdstock et al., 2002a; Mayes et al., 2004). The model of Norman and O'Reilly (2001) (see also O'Reilly and Norman, 2002) allows that both the neocortex and the hippocampus are sensitive to conjunctions and that the hippocampus is involved in associative recognition only when this requires recollection. According to their model, under certain circumstances neocortical familiarity will be sufficient to support associative recognition. This can explain the normal word pair and face pair association recognition shown by the patients. However, for the model to explain the patients' deficits, it is necessary to make the additional assumption that certain types of information (e.g., object and location information) only converge fully in the hippocampus (O'Reilly and Norman, 2002). Recognition of these associations would always depend on recollection because neocortical familiarity for associations of these types of information would not be available (for a fuller discussion of these issues, see Mayes, 2004). Others, however, have found a sparing of item recognition relative to a deficit in associative recognition both when the same type (face–face) and when different types (face–word) of information have to be associated (Turriziani et al., 2004). The disproportionate deficit in associative recognition relative to item recognition (Vargha-Khadem et al., 1997; Holdstock et al., 2002a; Mayes et al., 2004; Turriziani et al., 2004) may reflect the importance of the hippocampus in the formation and storage of particular kinds of associations, as well as its importance for recollection. However, a disproportionate deficit of associative recognition, relative to item recognition, following hippocampal damage has not been consistently reported. Stark et al. (2002) reported that both yes/no item recognition (recognition of individual faces and houses) and yes/no associative recognition for house–face pairs was impaired in four patients, three of whom had MRI confirmed bilateral damage to the hippocampus with only limited volume reduction of the parahippocampal gyrus. Further, when the difference between the item recognition performance of the control subjects and the patients was reduced by giving the patients increased exposure (Stark et al., 2002), or requiring the control subjects to respond under time pressure (Stark and Squire, 2003), associative recognition was not disproportionately impaired relative to item recognition in the patients. Additionally, Simons et al. (2002) report that, for patients with semantic dementia, there was no significant correlation between hippocampal volume and performance on a source discrimination test and on an associative recognition test for pairings of doors and sofas.

Therefore, the current evidence concerning the nature of the involvement of the hippocampus in recognition memory is conflicting. Some patients have shown a global anterograde amnesia following relatively selective hippocampal damage, which has included an impairment of familiarity (Manns et al., 2003). Other patients have shown a relative sparing of item recognition and recognition of associations between stimuli of the same type (e.g., two faces) as well as a sparing of familiarity. Further cases need to be explored to determine to what extent the latter pattern is a frequent consequence of relatively selective hippocampal damage. In addition, to enable comparison between cases, these patients should be tested on tasks that have been completed by other patients with hippocampal damage already reported in the literature. In the present study, we explore the recall, item recognition, and associative recognition memory of a patient, B.E., for whom structural MRI has revealed bilateral damage restricted to the hippocampus accompanied by bilateral hypoperfusion of the temporal lobe, as measured by positron emission tomography (PET), and which single photon emission computed tomography (SPECT) has suggested may be greater in the left than the right temporal lobe. The pattern of B.E.'s memory performance is discussed in relation to that of patient Y.R. (e.g., Holdstock et al., 2002a,b; Mayes et al., 2002), who has also completed the tests in the battery. Further, we investigate whether any residual memory shown by B.E. is mediated to a larger extent by familiarity than residual recollection.

MATERIALS AND METHODS

Subjects

Patient B.E. has been described by Kapur and Brooks (1999). He is an ex-college lecturer, who developed viral encephalitis in 1991. There were no positive findings to indicate that the encephalitis was due to herpes simplex virus, but antiviral treatment was given. The encephalitis was accompanied by loss of memory for recent events, an odd sense of smell and déjàvu. He also experienced two grand mal seizures shortly after admission. A computed tomography (CT) scan carried out on admission, and a magnetic resonance imaging (MRI) scan carried out 11 days later were reported to be normal; however, electroencephalography (EEG) investigations at that time indicated bilateral temporal lobe abnormalities.

A second MRI scan was carried out in May 1992 following the protocol described by Kapur et al. (1994), which provided more detailed information about MTL structures. Two neuroradiologists, who were blind to the neuropsychological findings, reviewed the scans independently and reported the presence of bilateral atrophy to the hippocampus. All other brain regions were reported as intact. B.E. has since declined to take part in further scanning and therefore 3D imaging to estimate brain region volumes has not been possible. However, the T1-weighted MRIs from 1992 were considered of sufficient quality to allow us to estimate the volume of the hippocampus and the temporal lobe. Unfortunately, the quality of the images was not sufficient for us to estimate the volume of the parahippocampal gyrus (the region comprising entorhinal, perirhinal, and parahippocampal cortices). To minimize error, the hard copies of the T1-weighted coronal MRIs were digitized. Stereological measurements, using the Cavalieri method in combination with point counting (García-Finana et al., 2003; Roberts et al., 2000), were made using ANALYZE (Mayo Foundation, Minneapolis, MN) and EasyMeasure imaging analysis software. All volumetric measurements were taken on coronal images. Anteriorly, the temporal lobe was defined as the first slice showing temporal brain tissue. The posterior limit of the temporal lobe was defined as the slice corresponding to the end of the hippocampal tail, where the lateral ventricles split into the frontal and temporal horns. The temporal lobe volume measure included both the hippocampus and the gray and white matter of the temporal lobe cortices. The estimated volumes of B.E.'s hippocampi and temporal lobes are shown in Table 1; the volumes of these structures, estimated from 3D scans, for seven age-matched male control subjects are also displayed. B.E.'s hippocampus volume was 3.08 SD and 2.97 SD below the control mean on the left and the right, respectively. His hippocampus was 39% smaller than the control mean on the left and 37% smaller on the right. In contrast, his estimated temporal lobe volume was only 1% and 2% smaller than the control mean on the left and right, respectively. Therefore, there is clear evidence from the MRIs that his hippocampus is substantially reduced in volume bilaterally whereas his temporal lobe volumes are very close to the control mean.

TABLE 1.

Hippocampal and Temporal Lobe Volume (ml) Measures for B.E. and the Mean Volume of These Structures for Matched Control Subjects With the Standard Deviation Indicated in Brackets

	Hippocampus		Temporal lobe[b]	
	Left	Right	Left	Right
B.E.	1.80	1.95	67.20	73.27
Control mean[a]	2.94 (0.37)	3.08 (0.38)	68.02 (5.23)	74.87 (4.13)

[a] Age and sex matched.

[b] This measure includes hippocampus and gray and white matter of the temporal cortices.

A fluorodeoxyglucose (FDG) PET scan carried out in January 1993, 18 months after B.E. had suffered from the virus, confirmed that there was bilateral hypometabolism in the MTL (Kapur and Brooks, 1999), which may have affected the MTL cortices as well as the hippocampus. A SPECT scan carried out 2 months earlier (in December 1992) also showed bilateral hypometabolism in the temporal lobe. In addition, it was the radiologist's opinion that SPECT showed a 25 % greater reduction in perfusion in the left compared to the right temporal lobe. The limited spatial resolution of the PET and SPECT scans makes it difficult to determine precisely which regions of the temporal lobe were affected by the reduction in perfusion, but it appears that this was not restricted to the hippocampus and MTL cortices.

Previous neuropsychological testing (Kapur and Brooks, 1999) showed that B.E. had an estimated premorbid full-scale IQ of 112, estimated using the NART-R (Nelson, 1982), and a current full-scale IQ of 128, as measured by the WAIS-R (Weschler, 1981). Hence, there was no evidence of a decline in IQ from premorbid levels. (In our experience, the NART-R commonly underestimates the premorbid IQ of intelligent people.) On standardized memory tests, B.E. showed impaired recall (WMS-R: Weschler, 1987;

TABLE 2.

Order of Tests Administered in Each Test Session

Order	Task
Session 1	
1	Forced-choice object recognition with 40-s delay
2	Object-location recognition with 30-min delay
3	Yes/no wallpaper pattern recognition
4	Object-location recall after 40-s delay
5	Object recall after 30-min delay
6	Forced-choice wallpaper pattern recognition
7	Recall of the temporal order in which wallpaper patterns were presented
Session 2	
1	Object-location recognition with a 40-s delay
2	Forced-choice object recognition after a 30-min delay
3	Recognition of the temporal order in which wallpaper patterns were presented
4	Object recall with a 40-s delay
5	Object-location recall with a 30-min delay
6	Yes/no object recognition
Session 3	
1	Presentation of picture and topographical memory test stimuli
2	Presentation of story for story recall test
3	Yes/no recognition of line drawn patterns (easy version)
4	Story recall test
5	Recognition memory test with retest
6	Presentation of story for story recognition test
7	Yes/no recognition of line-drawn patterns (moderate version)
8	Story recognition test
9	Forced-choice pattern recognition with remember/know procedure
10	Picture and topographical recognition test

AMIPB: Coughlan and Hollows, 1985) and impaired recognition of verbal information (Recognition Memory Test [RMT]: Warrington, 1984), but his face recognition score on the RMT was within the normal range (Kapur and Brooks, 1999). The present study investigated his recognition memory in more detail and focused particularly on nonverbal memory to explore the generality of the finding of spared face recognition on the RMT to other nonverbal recognition tests.

B.E. completed the memory tests, reported in this article, on two occasions that were separated by 3 years. The tests administered on the first occasion were split into two sessions (sessions 1 and 2) and the tests administered on the second occasion were given within a single session (session 3). Overlapping groups of male control subjects completed the test batteries from the three sessions. Sessions 1 and 2 were each 1.5 h in duration. B.E. completed these sessions in 1 day (one session in the morning and the other in the afternoon). Control subjects completed the sessions on separate days, which were, on average, 1 week apart. Session 3 was 2 h in duration. Table 2 shows the order in which the tests were administered in each session.

Control subjects were drawn mainly from Liverpool University and worked in teaching, technical and administrative positions. Eleven control subjects completed the tests from sessions 1 and 2. These subjects had a mean age of 54.1 years (SD 6.2), which was within 0.2 SD of B.E.'s age at the time of testing (53 years). The control group had a mean full-scale IQ, which was estimated using the NART-R of 115.9 (SD 7.0). B.E.'s premorbid IQ as predicted by the NART-R was 0.56 SD below the control mean, and his current IQ measured by the WAIS-R was 1.73 SD above the control mean.

Eight control subjects completed the tests from session 3. The control subjects had a mean age of 54.9 (SD 3.6), which was comparable to B.E.'s age of 56 during test session 3. The mean NART-R full scale IQ of the control group was 121.5 (SD 5.8). Three of these subjects had also completed the test battery from sessions 1 and 2.

Neuropsychological Test Battery

B.E. was tested on a battery of recall and recognition memory tests for verbal and nonverbal material. These tests are briefly described below.

Verbal recall and recognition

Recall of a short story comprising 20 facts was tested after a filled delay of 10 min. The delay was filled by a pattern recognition task. In scoring, 1 point was allocated to each correctly recalled piece of information, 0.5 points were allocated to each recalled point of information that was partially correct (e.g., recall of the first name but not the surname of a character in the story), and 0 was allocated to each incorrect piece of recalled information. Recognition of a separate short story was tested after a 10-min delay, which was filled by a pattern recognition task. Memory was tested using a four-choice forced-choice recognition task comprising 12 questions about facts from the story. For example: What was the couple's surname? (1) Howe, (2) Hinde, (3) Hill, (4) Hurd. The stories were selected from those used by Isaac and Mayes (1999).

Nonverbal item recognition

Object recognition. Recognition of line-drawn pictures of natural and manmade objects was tested using the forced-choice and yes/no procedures described by Holdstock et al. (2002a). In these tasks, the targets and their corresponding related foils were very similar (for examples, see Holdstock et al., 2002a). In each task, 12 pictures were studied twice for 3 s per exposure. Four-choice forced-choice recognition was tested after delays of 40 s and 30 min. Yes/no recognition was tested after a 40-s delay only. In the yes/no task, the 12 studied (target) pictures and 36 foils were randomly intermixed and each picture was presented individually during the memory test. To encourage subjects to make a decision about each test picture that was independent of their decisions concerning the preceding pictures in the test list, four of the studied (target) pictures occurred twice in the test list and four occurred three times in the test list. Targets had to be detected each time they were presented at test, but only the subjects' response to the first occurrence of each target was scored and included in the analysis. The 40-s delays were filled with mental arithmetic and the 30-min delay was filled with unrelated tests.

Wallpaper pattern recognition. The stimuli and procedure of Mayes et al. (2001) were used. Ten patterns like those often seen on wallpaper were studied individually for 2 s each. Memory was tested after a delay of 15 s. The delay was filled with an odd/even judgment task. In the forced-choice paradigm, subjects had to select the studied pattern from among four simultaneously presented foil patterns. In the yes/no paradigm, patterns were presented individually at test, and the 10 studied (target) patterns were randomly intermixed with 40 foils.

Picture recognition after 2-h delay. Subjects studied the 60 photographs from the study sets of the Picture and Topographical Memory tests from the Camden Memory Test (Warrington, 1996). At the end of the test session, which was approximately 2 h, the test phase of each task was administered. Each task involved a three-choice forced-choice recognition test. In the Picture test, the foils were photographs of different scenes; in the Topographical test, the foils were the same scene photographed from different views.

Line-drawn pattern recognition. Yes/no recognition of line-drawn patterns was tested using two tasks that differed in the similarity of the targets and their corresponding related foils. These tasks used the stimuli from the “easy” and “moderate” difficulty conditions of Holdstock et al. (1995), but with a yes/no rather than a forced-choice paradigm. A total of 20 patterns were studied in each condition. In the “easy” discrimination condition, the patterns were presented once for 5 s and in the “moderate” discrimination condition the patterns were presented three times for 5 s on each occasion. To aid encoding, subjects reported aloud what each picture reminded them of. Memory was tested after a 40-s retention interval during which the subject counted backward in threes from a given number. At test, pictures were presented individually and the 20 studied (target) pictures were randomly intermixed among 40 foils (each target picture was modified twice to produce two foils).

Associative recognition of nonverbal information

Object-location recognition. Forced-choice recognition of the locations in which line-drawn pictures were presented on a circular tabletop was tested using the procedure of Holdstock et al. (2002a). A total of 12 pictures were presented on a circular tabletop. The subject’s attention was directed to each picture twice for 3 s each time. Following delays of 40 s and 30 min, recognition of the position of the object pictures was tested. A different set of objects and different locations were used for each delay. At test, subjects were given circular pieces of card that were one-half the diameter of that of the tabletop. Each card showed a studied object in four locations: the location it occupied at study and those that had been occupied by three other studied pictures. Subjects had to indicate the location in which that picture had been presented at study. The short delays were filled with mental arithmetic, and the 30-min delay was filled with unrelated tests.

Forced-choice recognition of the temporal order in which patterns were presented. The temporal order in which wallpaper patterns were studied was tested using the procedure and materials described by Mayes et al. (2001). Subjects studied five patterns similar to those found on wallpaper for 5 s each. Following a 15-s delay, which was filled with an odd/even judgment task, subjects were presented with a card on which they were shown the five studied patterns in five different orders. Subjects had to indicate in which of these orders the patterns had been presented at study. The procedure was repeated for a further 19 sets of patterns.

Recall of nonverbal stimuli

Recall of line-drawn pictures. Recall of line-drawn pictures of natural and manmade objects was tested using the materials and procedure of Holdstock et al. (2002a). A total of 12 pictures were presented twice for 3 s per picture on each occasion. Memory was tested after filled delays of 40 s and 30 min. Separate study materials were used for the test at each delay. At test, subjects were asked to list the objects that were presented in the study set. The short delays were filled with mental arithmetic and the 30-min delay was filled with unrelated tests.

Recall of the object-location associations. Recall of the locations in which line-drawn pictures were presented on a circular tabletop was tested using the procedure of Holdstock et al. (2002a). A total of 12 pictures were presented on a circular tabletop. The subject’s attention was directed to each picture twice for 3 s each time. Following filled delays of 40 s and 30 min, recall of the position of the object pictures was tested. A different set of objects and different locations were used for each delay. At test, subjects were given a circular piece of card that was one-half the diameter of that of the tabletop and appropriately scaled-down copies of the pictures. Subjects were told that the circle of card represented the tabletop and to place the pictures on the card in the positions in which they had been studied. One picture was placed in position at a time; its position was recorded, and then it was removed before the next picture was placed in position. Different sets of objects and positions were used for each delay. The short delays were filled with mental arithmetic, and the 30-min delay was filled with unrelated tests.

Recall of the temporal order in which patterns are presented. The temporal order in which wallpaper patterns were studied was tested using the procedure and materials described by Mayes et al. (2001). Eight patterns of the type used for wallpaper were presented to subjects one at a time for 5 s. After a filled retention interval of 15 s, the eight patterns were laid out from left to right in front of the subject in an order that had a zero correlation with the study presentation order. Subjects rearranged the patterns into their remembered study order. The correlation between recalled study order and actual study order was calculated. This procedure was repeated with four further sets of patterns.

Tasks used to tap recollection and familiarity

RMT immediate and repeat test. The faces subtest of the Recognition Memory Test (RMT) (Warrington, 1984) was administered to subjects in the standard way. At 10 min after the initial memory test, face recognition was retested. In the retest, targets were paired with the same foils and presented in the same order as in the original test. The individual items from the original study set were not re-presented between the initial and repeat test. Aggleton et al. (2000) reported that patients with bilateral fornix damage, following removal of a colloid cyst, performed at a comparable level on an immediate test of the RMT to patients who had undergone colloid cyst surgery but had not sustained damage to the fornix. In contrast, the performance of the patients with damage to the fornix was significantly worse than that of the patients with intact fornices when the recognition test was repeated. Aggleton et al. (2000) argued that good performance on the initial recognition test can be achieved by comparing the relative familiarity of the studied item and its foil; however, in the repeat test, as both the studied item and its foil are now familiar, reliance on a comparison of their relative familiarity is less effective. It is therefore predicted that if a patient bases their recognition decisions on familiarity to a larger extent than healthy individuals, there will be a greater reduction in their performance on the repeat relative to the initial test than for healthy control subjects.

Forced-choice recognition of abstract patterns using the remember/know procedure. Subjects studied a total of 40 line-drawn patterns, which were divided into two study lists of 20 items. Each pattern was presented three times for 5 s on each occasion. Subjects reported aloud what the pattern or individual features in the pattern reminded them of. Memory was tested after a 40-s delay using a three-choice forced-choice recognition test. The two foils were created by changing a number of the features in the studied pattern. After indicating which of the three simultaneously presented patterns had been studied, subjects were required to indicate either that (1) they remembered specific information about studying that pattern, e.g., what it reminded them of, its position in the study set; (2) the pattern looked familiar, and they were sure that they had seen it but could not remember anything specific about studying it; or (3) they were guessing. Subjects were required to justify all remember responses. A forced-choice, rather than a standard yes/no procedure was used because, as will be seen in the Results section, B.E. performed more poorly on yes/no than forced-choice recognition tests. The aim was to determine whether his correct responses on forced-choice recognition tests were based to a larger extent than in healthy individuals on familiarity than recollection.

RESULTS

For all tests, B.E.'s performance was considered to be impaired if it was >1.96 SD worse than the control mean (type 1 error probability of 0.05, two-tailed test).

Verbal Memory

As shown in Table 3, B.E.'s recall and forced-choice recognition of a short story were impaired. These data are consistent with a previous report that B.E. is impaired at both recalling and recognizing lists of words (Kapur and Brooks, 1999).

Nonverbal Memory

Forced-choice item recognition

B.E.'s performance was unimpaired on four of the seven forced-choice item recognition tests that were administered. The tests for which his memory was relatively preserved required the recognition of objects, wallpaper type patterns, and faces and had retention intervals that varied from 0 s to 30 min.

Of the three tests on which B.E. was impaired, two required recognition of photographs of scenes after long retention delays of 2 h, and one required the recognition of abstract line-drawn patterns after a short delay with an accompanying remember/know judgment. B.E.'s recognition of the photographs from the Topographical subtest of the Camden Memory Test was at chance after the 2-h delay. However, his recognition of the photographs from the Picture subtest and his recognition of line-drawn patterns, although impaired, was well above the chance level of performance, which was 33% correct (Table 3).

A difficulty measure was calculated for each test that indicated where between chance and perfect performance the control mean fell (see Holdstock et al., 2002a). A higher score on this measure indicates an easier test for the control subjects. There was no indication that the forced-choice item recognition tests on which B.E. was unimpaired (difficulty scores ranged from 44% to 80%) were easier for the control group than those on which he was impaired (difficulty scores ranged from 63% to 86%).

Yes/no item recognition

As shown in Table 3, B.E.'s performance did not reach the criterion for impairment on three of the four yes/no item recognition tests when d' (Green and Swets, 1966) was used as the performance measure. His scores on these tests were 1–2 SD below the control mean. The data were also analyzed using, as the performance measure, proportion of hits minus proportion of false alarms. Although the pattern of performance over the tests was the same as for the d' measure, B.E.'s performance was impaired on two of the tests and close to the criterion of impairment on the remaining two (z-scores were -1.82 and -1.94 for the object recognition and pattern recognition task involving quite different foils and -2.29 and -4.56 for the pattern recognition task involving quite similar foils and the wallpaper pattern recognition task, respectively). The yes/no recognition tests were of comparable difficulty for the control subjects to the forced-choice item recognition tests (difficulty scores ranged from 57% to 64%).

Associative recognition

As shown in Table 3, B.E. was impaired at recognizing the spatial locations occupied by specific objects at study after delays of

TABLE 3.

For Each of the Memory Tests: Retention Interval, Mean Difficulty of Test for Control Subjects, B.E.'s Raw Score, Mean Raw Score of Matched Control Subjects, and B.E.'s Performance Expressed as a z-score[a]

Memory test	Delay	Test difficulty (SD in parentheses)	B.E.'s score	Control mean (SD in parentheses)	B.E.'s performance expressed as a z-score
Verbal memory					
Story recall[b]	10–15 min	58 (22.5)	0	58 (22.5)	−2.58*
FC recognition of story facts[b]	10–15 min	79 (12.5)	25	84.2 (9.2)	−6.43*
Nonverbal memory					
Forced-choice item recognition					
FC object recognition[c]	40 s	44 (22.8)	50	58 (17.1)	−0.49
FC object recognition[c]	30 min	49 (26.5)	50	61.4 (19.8)	−0.58
FC wallpaper pattern recognition[d]	15 s	78 (23.1)	100	82.7 (18)	+0.93
Face recognition (RMT)	0 s	80 (8.7)	100	89.8 (4.3)	+2.38
FC recognition of abstract line drawn patterns	40 s	81 (11.4)	60	87.5 (7.7)	−3.57*
Picture recognition[e]	2 h	86 (8.6)	60	90.4 (5.8)	−5.24*
Topographical recognition[e]	2 h	63 (13.8)	26.7	75.4 (9.2)	−5.29*
Yes/no item recognition					
YN object recognition[c]	40 s	58 (18.4)	0.67	1.85 (0.75)	−1.57
YN wallpaper pattern recognition[d]	15 s	57 (9.7)	0.32	1.87 (0.56)	−2.76*
YN line-drawn pattern recognition (different targets and foils)	40 s	64 (16.0)	1.02	1.99 (0.71)	−1.36
YN line-drawn pattern recognition (similar targets and foils)	40 s	57 (14.3)	0.89	1.80 (0.54)	−1.69
Associative recognition					
FC object-location recognition[c]	40 s	74 (25.5)	25	80 (19)	−2.89*
FC object-location recognition[c]	30 min	80 (17.8)	16	85 (13)	−5.15*
Wallpaper pattern temporal order recognition[d]	15 s	69 (16.2)	35	75 (13)	−3.13*
Recall					
Object recall[c]	40 s	83 (13.2)	8	83 (13)	−5.66*
Object recall[c]	30 min	67 (20.5)	0	67 (20)	−3.26*
Object-location recall[c]	40 s	74 (6.6)	11.2	4.4 (1.1)	−6.08*
Object-location recall[c]	30 min	72 (9.6)	14.6	4.8 (1.6)	−6.02*
Wallpaper pattern temporal order recall[d]	15 s	70 (15.0)	−0.29	0.70 (.15)	−6.55*

FC, forced choice; YN, yes/no.

*z-score of −1.96 or larger.

[a] The raw score is percentage correct performance for all tasks apart from yes/no recognition tasks, where the reported raw score is d′, object-location recall where the raw score is distance from correct location, and pattern temporal order recall where the raw score is the correlation between correct order and recalled order. Negative scores indicate that performance is poorer than the control mean.

[b] Isaac and Mayes (1999).

[c] Holdstock et al. (2002a).

[d] Mayes et al. (2001).

[e] Stimuli taken from the Camden Memory Test (Warrington, 1996).

40 s and 30 min. He was also impaired at recognizing the temporal order in which patterns were presented. B.E.'s performance was at chance for the object-location recognition tests and slightly above chance (which was 20%) for the temporal order recognition test.

Recall

B.E. was impaired at recalling a set of 12 studied objects after delays of 40 s and 30 min (Table 3). He was also impaired at recalling the spatial locations occupied by specific objects at study after delays of 40 s and 30 min and at recalling the temporal order in which patterns were presented (Table 3).

Summary of performance on item recognition, associative recognition, and recall tests

In summary, B.E. had clearly impaired recall and associative recognition, but some sparing of item recognition. His performance was above the control mean on two of the seven forced-choice item recognition tests and within 1 SD of the control mean on a further two of the forced-choice item recognition tests. Although his performance fell >1 SD below the control mean for all four yes/no item recognition tests, when d′ was used as the performance measure, his mean performance was not significantly impaired according to our criterion. The dissociation between relatively preserved item recognition, but clearly impaired recall and associative recognition after short delays is illustrated by B.E.'s performance on two subsets of the tests, which required recall and item recognition for the same types of stimuli and recall and/or recognition of the spatial or temporal positions of these stimuli. In addition, for one of these subsets of tests the tasks were manipulated so that, for healthy control subjects, the item recognition tests were more difficult than the recall and associative recognition tests. Thus, any sparing of item recognition could not be explained by these tests being easier than the recall and associative recognition tests.

The first battery involved forced-choice and yes/no recognition of wallpaper type patterns, forced-choice recognition of the temporal order in which wallpaper type patterns were presented and recall of the order in which such patterns were presented. (For the performance of patient Y.R., who has relatively selective hippocampal damage, on these tests, see Mayes et al., 2001.) The associative recognition task was slightly harder than the forced-choice item recognition task for control subjects (control mean associative recognition performance was only 0.65 SD below the mean for the item recognition task). B.E.'s performance on this battery is shown in Figure 1A. His performance was ≥3 SD below the control mean and clearly impaired for the temporal order recall and recognition tests but he performed numerically above the control mean on the forced-choice pattern recognition test. B.E.'s performance on the item recognition test differed from his performance on the temporal order recall and recognition tests by >4 SD. In contrast, and unlike patient Y.R., his performance on the yes/no pattern recognition test was clearly impaired.

The second battery comprised forced-choice and yes/no recognition of objects, recall of objects, forced-choice recognition of the locations of objects and recall of the locations of objects. (For the performance of patient Y.R. on these tests, see Holdstock et al., 2002a.) The control subjects performed more poorly on the object recognition tests than on the associative recognition tests and the object recall tests. Despite this, B.E. performed well within 1 SD of the control mean on the forced choice object recognition tests but was clearly impaired on the recall and associative recognition tests in the battery (Fig. 1B). His performance on the forced-choice item recognition tests was 2.3–5.6 SD better than that on the recall and associative recognition tests. This is consistent with the pattern of performance shown by patient Y.R. However, unlike Y.R., patient B.E. was not clearly impaired on the yes/no object recognition test when performance was measured by d′. His performance was >1 SD worse on the yes/no than the forced-choice recognition test, but it fell within our criterion for impairment. B.E.'s performance on the yes/no object recognition test was 1.3–4.5 SD better than performance on the recall and associative recognition tests.

Familiarity and recollection

RMT with retest. The difference between performance on the immediate and repeat memory test was calculated for B.E. and eight matched male controls. The control group showed a mean drop of two points from immediate to repeat testing. In contrast, B.E. showed a drop of 6 points, which was 3.05 SD larger than that for the controls.

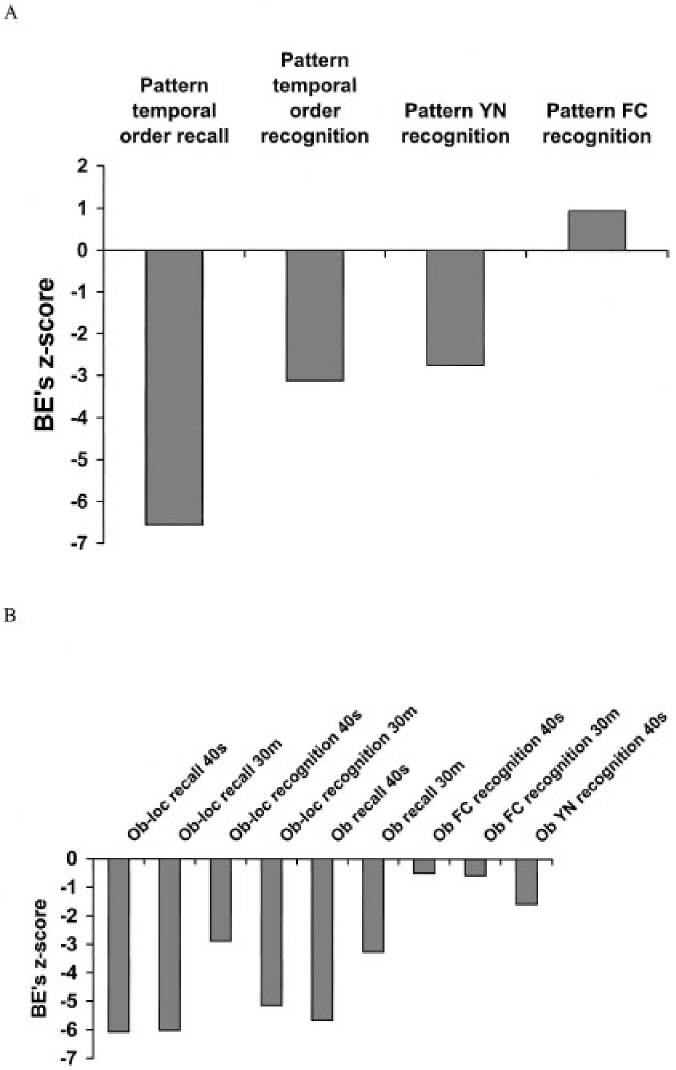

FIGURE 1. **A: B.E.'s performance, plotted as z-scores, for recall of the temporal order in which patterns were studied, recognition of the temporal order in which patterns were studied, yes/no recognition of studied patterns and forced-choice recognition of studied patterns. For the yes/no recognition test performance was measured using d′. B: B.E.'s performance, plotted as z-scores, for recall of studied object locations (Ob-loc recall), recognition of studied object locations (Ob-loc recognition), recall of studied objects (Ob recall), forced-choice recognition of studied objects (Ob FC recognition) and yes/no recognition of studied objects (Ob YN recognition). For all tests, apart from the yes/no recognition test, performance after delays of 40 s and 30 min is reported. For the yes/no recognition test, performance, which was measured using d′, is reported after a 40 s delay only.**

Forced-choice recognition using the remember/know procedure. B.E. was impaired on this recognition task relative to the control group but performed well above chance. To determine whether B.E.'s correct responses were mediated by familiarity to a larger extent than those of the control subjects, the pattern of remember, know, and guess responses produced by B.E. and the control group for correctly recognized patterns was examined. These data are shown in Table 4. For the control group, most of the correctly recognized patterns attracted "remember" responses

TABLE 4.

Number of Remember, Know, and Guess Responses Made by B.E. for Correctly and Incorrectly Recognized Items on Forced-Choice Pattern Recognition Task and Mean Number of Remember, Know, and Guess Responses Made by Control Subjects for Correctly and Incorrectly Recognized Items on This Task (Standard Deviation in Parentheses)

	Correct remember	Correct know	Correct guess	Incorrect remember	Incorrect know	Incorrect guess
No. of responses made by B.E.	8	13	3	1	5	10
Mean no. of responses made by control group	27 (8.3)	3.75 (3.5)	4.25 (3.7)	1.25 (1.4)	1.25 (1.8)	2.5 (1.7)

(0.76); i.e., specific information could be reported about the event of studying that item. An approximately equal proportion of correctly recognized patterns were assigned "know" and "guess" responses (0.11 and 0.13, respectively). In contrast, B.E. provided "remember" responses for 0.33 of the patterns he recognized correctly, which was 2.18 SD below the control mean but provided "know" responses for 0.54 of the correctly recognized patterns, which was 3.93 SD above the control mean. The proportion of "guess" responses that B.E. made for correctly recognized items (0.13) was the same as the control mean.

To determine whether B.E. was able to use recollection and familiarity to discriminate between studied items and foils, we calculated, for B.E. and his controls, the difference between the number of correct and incorrect remember responses, the number of correct and incorrect know responses, and the number of correct and incorrect guess responses that were made. The difference between B.E.'s correct and incorrect remember responses was 7, which was 2.26 SD below the control mean of 25.75; the difference between his correct and incorrect know responses was 8, which was 1.88 SD above the control mean of 2.5; and the difference between his correct and incorrect guess responses was −7, which was 3.5 SD below the control mean.

The data suggest that his correct item recognition responses were based on a feeling of familiarity more often than his matched control subjects. Although he could discriminate between studied items and foils using recollection, recollected information was available to him on significantly fewer trials than for the controls. The feeling of familiarity on which the majority of his correct responses were based enabled him to successfully discriminate between studied items and foils as a larger number of "know" responses were made for correctly than incorrectly recognized items. Although B.E. relied more on familiarity than on recollection in making his recognition decisions, this does not mean that his familiarity was entirely normal. Rather, it shows that, as recollected information was available on only a few trials, on the majority of trials he was relying on familiarity.

DISCUSSION

B.E.'s pattern of memory performance suggests that he has a global anterograde amnesia for verbal information in which both recall and recognition are clearly impaired. In contrast, for nonverbal material he shows some sparing of item recognition, which may be mediated by familiarity to a large extent, relative to recall and associative recognition.

It was previously reported that B.E. was impaired both at recalling and recognizing lists of words, using standardized tests with retention intervals ranging from zero to 30 min (Kapur and Brooks, 1999). The data reported in the present study show that this finding extends to the recall and recognition of a short story after a 10-min delay. B.E. had no memory for the verbal material after this retention interval; he was unable to recall any information from one story and he performed at chance on a four-choice forced-choice recognition test of a second story. As B.E.'s structural hippocampal lesion was probably equivalent bilaterally, the difference between the pattern of his performance on verbal and nonverbal item recognition tests cannot be easily explained by his detectable structural lesion. However, his global anterograde amnesia for verbal information could be explained by dysfunction in the temporal lobe beyond the hippocampus, which SPECT suggested may have been greater in the left than the right hemisphere.

For nonverbal material B.E. showed some sparing of item recognition both relative to recall and relative to recognition of associations between objects and locations and between patterns and their temporal order. B.E.'s forced-choice item recognition was variable, with performance above or close to the control mean for four of the tests and impaired on the remaining three tests. His performance on the yes/no item recognition tests was more consistent, and varied from 1.57 to 2.76 SD below the control mean when measured by d'. When the retention intervals of the forced-choice and yes/no tests were made more comparable by excluding the forced-choice tests with 2-h delays, B.E.'s mean performance on the forced-choice item recognition tests was just 0.27 SD below the control mean whereas his performance on the yes/no item recognition tests was 1.85 SD below the control mean. When a threshold measure was used, B.E.'s mean yes/no item recognition performance was significantly impaired (−2.65 SD below the control mean). B.E.'s yes/no item recognition therefore appears to be considerably poorer than his forced-choice item recognition.

Although B.E.'s nonverbal item recognition performance was impaired on four of the 11 tests, his performance was above chance for all but the topographical recognition test. The deficit on the topographical task may reflect an involvement of the hippocampus in memory for this specific type of material, although this is inconsistent with data from patients Y.R. and Jon who were both unimpaired on this task. Alternatively, it could reflect a deficit in nonverbal item recognition after delays of longer than a few minutes in B.E. This is different to patient Y.R.'s performance which was unimpaired on this task even after 24 h. The reason for this difference in the patients' performance is uncertain but may relate to the hypometabolism detected in the temporal lobe for B.E.

In contrast to B.E.'s relatively spared nonverbal item recognition, B.E.'s recall and associative recognition were both clearly impaired and at, or close to, chance for the majority of tests. This dissociation between some preservation of item recognition and clearly impaired recall and associative recognition was strengthened by his performance on two subsets of tests that assessed these three aspects of memory using parallel versions of the same stimulus materials. Furthermore, in one of these subsets of tests, item recognition was harder for control subjects than recall and associative recognition, suggesting that the preservation of item recognition performance on this test battery was not attributable to these tests being easier than those on which B.E. was impaired. B.E.'s disproportionate deficit in recall and associative recognition, relative to item recognition, is consistent with the patterns of performance shown by patient Y.R. (Holdstock et al., 2002a,b; Mayes et al., 2002), patient D.F. (Henke et al., 1999), and the young patients described by Vargha-Khadem et al. (1997). Further, his greater impairment of associative than item recognition is consistent with the pattern of performance displayed by the patients with hippocampal pathology reported by Turriziani et al. (2004), although it should be noted that the nature of the associative recognition tasks differs between studies. B.E.'s performance on the nonverbal tasks, like the performance of these other patients, is therefore consistent with the view that the hippocampus is critical for recollection whereas neocortical regions are sufficient to support familiarity-based memory decisions (Norman and O'Reilly, 2001, see also, Holdstock et al., 2002a; Mayes et al., 2002). Furthermore, B.E.'s chance level of performance on the forced-choice object-location recognition test is consistent with the proposal that information of some kinds may only fully converge for memory processing in the hippocampus (see Norman and O'Reilly, 2001; Mayes et al., 2004). According to Norman and O'Reilly (2001), if such information had converged prior to the hippocampus, good forced-choice recognition of object-location associations would be possible on the basis of familiarity. Data from B.E., Y.R., and Jon suggest that recognition of such associations will always depend on recollection because cortical familiarity for associations for these types of information will not be available (see Mayes et al., 2004). However, given that the associative recognition tests administered to B.E. involved associations between different kinds of information only, the current study was unable to address whether recognition of associations between information of the same kind can be spared by hippocampal damage.

According to Aggleton and Brown's (1999) model, familiarity is mediated by a brain system that includes association cortices but also, critically, the perirhinal cortex, dorsomedial thalamus, and the prefrontal cortex. Volumetric measures confirmed that B.E.'s temporal lobe was only 1% or 2% below the control mean volume, suggesting that there was no gross atrophy or damage to this region as a whole. According to neuroradiologists' reports his MTL cortex, including the perirhinal cortex, was also intact. The information that is available therefore suggests that, for B.E., the regions proposed to be involved in mediating familiarity are structurally intact at a gross level, although, as volumetric measures of the MTL cortices were not possible, we cannot exclude the possibility that there were small volume reductions of these regions, which were undetectable by visual inspection. In contrast, the hippocampus, which has been proposed to be critically involved in recollection, was significantly reduced in volume bilaterally. B.E.'s at, or close to, chance performance on recall and associative recognition tests may therefore be explained by his hippocampal lesion, whereas his above chance performance on the nonverbal item recognition tests may have been mediated by his MTL cortex and, in particular, the perirhinal cortex. However, B.E.'s relatively poor performance on verbal item recognition tests, yes/no item recognition tests and three forced-choice item recognition tests suggest that his familiarity may not be entirely normal. Rather, for patient B.E., familiarity may have been spared relative to recollection but may not have been spared absolutely. Although there was no detected structural damage to the cortex, as discussed above, both PET and SPECT revealed bilateral hypometabolism in the temporal lobe, which may have affected familiarity. According to SPECT, although not PET, hypometabolism was less in the right than the left hemisphere, which is consistent with a greater relative sparing of item recognition, and familiarity, for nonverbal information.

Although B.E.'s familiarity may not have been entirely normal, evidence from the RMT retest paradigm and the remember/know paradigm suggested that he relied on familiarity to a larger extent than control subjects in making his recognition memory decisions. His performance on the RMT dropped by a significantly larger amount than that of the controls from the initial test to the retest. As discussed earlier, it has been argued that the retest relies more on recollection of the association of the item to its study context than the initial test (Aggleton et al., 2000). However, as the target would have been seen twice during the test session whereas the foil would have been seen only once, the target may have been slightly more familiar than the foil. Therefore, some discrimination between the target and foil on the basis of familiarity may have been possible during the retest but this is likely to have been more difficult than in the initial test. The larger drop in B.E.'s recognition from the initial test to the retest is consistent with this view. However, B.E.'s recognition performance in the retest of the RMT was still very high indicating that, if he was relying primarily on familiarity, this can still support good levels of recognition in this paradigm.

In the forced-choice item recognition test, which used a remember/know procedure, B.E.'s performance was impaired relative to his matched controls but was still considerably above chance. He was therefore able to discriminate between targets and foils but not as well as controls. B.E. classified a smaller proportion of his correctly recognized items as "remember" responses and a larger proportion as "know" responses than controls. More "remember" and "know" responses were made for correctly recognized items than for incorrectly recognized items indicating that both residual recollection and familiarity enabled him to successfully discriminate between studied and unstudied items. However, recollected information was only available to B.E. on a few trials. He therefore appeared to be relying to a larger extent than the controls on familiarity in making his recognition decisions.

B.E.'s nonverbal item recognition, although above our criterion of impairment on most tests was below the control mean on nine of the 11 tests. Similarly, patients Y.R., Jon, and D.F. performed below the control mean on some tests, but at the control mean on others (Mayes et al., 2002; Vargha-Khadem et al., 1997; Baddeley et al., 2001; Henke et al., 1999). This below control mean performance in patients is perhaps not surprising if they were relying primarily on familiarity to support their recognition memory decisions, even if familiarity was at normal levels. Familiarity may be able to support above chance and good levels of item recognition under a number of conditions (Norman and O'Reilly, 2001). However, if recollection and familiarity are independent processes (Yonelinas, 2002) and both can contribute to recognition memory decisions in control subjects, this may allow control subjects to outperform a patient who has available only familiarity.

The control subjects had another possible advantage over B.E. They potentially had available both verbal and nonverbal mnemonic information, which may have contributed to their nonverbal recognition memory decisions. In contrast, B.E.'s verbal memory was impaired when tested by both recall and recognition. This would have put him at a disadvantage on nonverbal item recognition tests relative to controls if they verbally, as well as, visually encoded features of the visual stimuli into memory. This could therefore potentially explain why his performance was below the control mean on the majority of the nonverbal item recognition tests. B.E.'s verbal memory deficit may also have contributed to his recall and associative recognition deficits for nonverbal material. This may be particularly true of the object recall test, which is likely to be verbally as well as visually encoded, as subjects know they will have to produce the names of the objects at the test. It is less likely to have contributed to the spatial and temporal order recall and recognition tests. In the former, the locations would have been difficult to verbally encode due to lack of local landmarks; in the latter, the patterns were difficult to distinguish between verbally. Therefore, although B.E.'s verbal memory deficit may have contributed to his deficit in recall and associative recognition of nonverbal information, it is unlikely to entirely explain these deficits.

Comparison of B.E.'s performance with that of patient Y.R. who had completed the same tests revealed a number of differences. One difference that has already been discussed was their differing performance on the topographical memory test. A second difference was their performance on the yes/no object recognition test, which used very similar targets and corresponding related foils. Consistent with the model of Norman and O'Reilly (2001, see also O'Reilly and Norman, 2002), patient Y.R. showed good forced-choice item recognition but impaired yes/no item recognition when targets and foils were very similar. In contrast, her yes/no item recognition was unimpaired on other tests, which used less similar targets and corresponding related foils. However, B.E. did not show this pattern of memory performance. His yes/no item recognition was poorer than his forced-choice item recognition. However, it was no poorer for the yes/no object recognition test, which used very similar targets and corresponding related foils than it was for the other tests, which used less similar targets and foils. B.E.'s data are therefore potentially in tension with the predictions of the Norman and O'Reilly model; however, given the limited number of yes/no item recognition tests that were administered, caution is warranted. It is interesting to note that B.E.'s overall yes/no item recognition was poorer than that of Y.R. (1.85 SD below the control mean compared with 0.4 SD below the control mean for Y.R., using d' to measure discrimination accuracy in both patients). One possible reason for this may be that B.E.'s control subjects used recollection to a large extent in all the yes/no recognition tests and this put them at an advantage relative to B.E. on all of the tests and not just that in which targets and corresponding related foils were very similar. Consistent with this interpretation, it has been suggested that healthy individuals use recollection to a larger extent in yes/no than forced-choice recognition tests (Parkin et al., 1994; Bastin and Van der Linden, 2003), although such a difference was not found by Khoe et al. (2000). Alternatively, B.E.'s yes/no item recognition when targets and foils were very similar may have been supported by residual recollection that was insufficient to support normal associative recognition but sufficient to support above chance levels of item recognition when it was difficult to use familiarity.

The differences between the performance of patients Y.R. and B.E. on the forced-choice tests with long delays and on the yes/no item recognition tests serve to highlight the variability in the pattern of memory deficit that may result from focal structural damage to the hippocampus. The reasons why the pattern of performance has differed between these and other patients is currently unknown and may relate to a number of factors, including reorganization of function, the extent and location of pathology within the hippocampus, the presence of pathology outside the hippocampus, premorbid differences in memory ability, and individual differences in the strategies used.

Compensation due to early onset of pathology has been proposed as an explanation for patient Jon's unimpaired item recognition (Manns and Squire, 1999; Maguire et al., 2001). However, like patients Y.R. and D.F., B.E.'s hippocampal damage occurred late in life and so, like these other patients, his memory performance is no more likely to be affected by compensation than the patients with global anterograde amnesias described by Squire and his colleagues (e.g., Reed and Squire, 1997) and by Cipolotti et al. (2001).

In relation to the extent and location of brain pathology, B.E.'s data suggest that differences in extent of hippocampal damage are unlikely to explain the different patterns of performance shown by different patients. B.E.'s hippocampus was reduced in volume by a comparable amount to that of the patients reported by Squire and colleagues who, unlike B.E., showed a global amnesia. However, the possibility that the patients differ in the exact location of structural damage to the hippocampus and that this explains their differing memory patterns cannot be excluded. In contrast, B.E.'s data suggest that dysfunction outside the hippocampus may be an important factor in explaining why the patients' patterns of performance have differed. The PET and SPECT data suggest that dysfunction was not restricted to the hippocampus in this patient and the SPECT data suggest that there was greater disruption of cortical function in the left than the right temporal lobe. As discussed earlier, this may explain some of the differences between the memory test performance of Y.R. and B.E., although functional imaging data were not available for Y.R., so a direct comparison between patients is not possible. Functional imaging data have also not been reported for the patients in the literature who have shown deficits in item recognition memory following hippocampal damage. It is therefore unknown whether, in addition to the relatively focal damage to the hippocampus reported for these patients from structural MRI, there is dysfunction in cortical regions, which is not visible as structural brain changes. The exception is patient VC who was shown to have hypometabolism in the right thalamus and right parietal areas on an FDG PET scan (Kapur et al., 1999). Therefore, the possibility that the global anterograde amnesia reported for these patients may be explained by the disruption to the functioning of regions beyond the hippocampus cannot be eliminated. B.E.'s data therefore highlight the importance in future work of both functional and structural imaging of patients with apparently selective hippocampal damage.

The final possibility that will be considered is that different patients and different groups of control subjects have used different strategies to complete similar tasks. Some patients may base their recognition memory decision on residual and, possibly inaccurate, recollection whereas others may be willing to rely on familiarity. If familiarity is sufficient to support good performance on a test, those patients who base their recognition decision on a feeling of familiarity may outperform those who use residual recollection, particularly if this is inaccurate. A reliance on such different strategies may therefore result in considerable variability in patients' performance.

The control groups matched to different patients may also differ in the strategies they use on recognition tests. For example, younger control subjects may use more elaborative encoding strategies than older subjects in memory tasks (Naveh-Benjamin, 2000; Perfect and Dasgupta, 1997; for review, see also Yonelinas, 2002). Similarly, and consistent with the reported relationship between explicit memory performance and IQ (Rapport et al., 1997; Meiran et al., 1995; Reber et al., 1991; Waldmann et al., 1991), control subjects with higher IQs may use more elaborative encoding strategies than do those with lower IQs. Elaborative encoding has been reported to benefit recollection more than familiarity (Rugg and Yonelinas, 2003); consistent with this, aging has been found to have a greater detrimental effect on recollection than familiarity (see Yonelinas, 2002). Therefore, some control groups may use recollection to a larger extent than others. B.E.'s IQ, and that of his control group, was considerably higher than that of Y.R. and her control group. B.E.'s control subjects may, therefore, have been more likely to have used recollection than Y.R.'s controls, particularly on the yes/no item recognition tests for nonverbal material. If the patients' recognition memory is based primarily on familiarity then, when compared with the performance of a control group who use both familiarity and accurate recollection, their performance will be more impaired than when compared with a control group who do not have such high levels of recollection available. This is unlikely to explain the differences between the performance of the patients reported by Squire and his colleagues, and Y.R. and Jon, because these patients and their matched controls had more comparable IQs. Nevertheless, this possible interpretation of the difference between Y.R. and B.E.'s pattern of performance suggests that in future work more control should be placed over the strategies that normal individuals can use to perform a task.

In summary, patient B.E. has equivalent bilateral volume reductions of the hippocampus accompanied by bilateral hypoperfusion of the temporal lobe, which may be greater in the left than the right hemisphere. Memory testing showed that he had some sparing of nonverbal item recognition relative to recall and associative recognition, but a global anterograde amnesia for verbal material. B.E.'s pattern of performance was not identical to patients Y.R. (Mayes et al., 2002) and Jon (Vargha-Khadem et al., 1997), but, like them, he showed a relative sparing of nonverbal item recognition, at short delays. This relative sparing of item recognition may have been supported to a large extent by familiarity. This is consistent with the view that familiarity is not critically dependent on the integrity of the hippocampus but, rather, can be mediated by cortical regions including the perirhinal cortex.

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