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# Associative Recognition in a Patient With Selective Hippocampal Lesions and Relatively Normal Item Recognition

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**ABSTRACT: Previous work (Mayes et al., Hippocampus 12:325–340, 2002) found that patient YR, who suffered a selective bilateral lesion to the hippocampus in 1986, showed relatively preserved verbal and visual item recognition memory in the face of clearly impaired verbal and visual recall. In this study, we found that YR's Yes/No as well as forced-choice recognition of both intra-item associations and associations between items of the same kind was as well preserved as her item recognition memory. In contrast, YR was clearly impaired, and more so than she was on the above kinds of recognition, at recognition of associations between different kinds of information. Thus, her recognition memory for associations between objects and their locations, words and their temporal positions, abstract visual items or words and their temporal order, animal pictures and names of professions, faces and voices, faces and spoken names, words and definitions, and pictures and sounds, was clearly impaired. Several of the different information associative recognition tests at which YR was impaired could be compared with related item or inter-item association recognition tests of similar difficulty that she performed relatively normally around the same time. It is suggested that YR's familiarity memory for items, intra-item associations, and associations between items of the same kind was mediated by her intact medial temporal lobe cortices and was preserved, whereas her hippocampally mediated recall/recollection of these kinds of information was impaired. It is also suggested that the components of associations between different kinds of information are represented in distinct neocortical regions and that initially they only converge for memory processing within the hippocampus. No familiarity memory may exist in normal subjects for such associations, and, if so, YR's often chance recognition occurred because of her severe recall/recollection deficit. Conflicting data and views are discussed, and the way in which recall as well as item and associative recognition need to be systematically explored in patients with apparently selective hippocampal lesions, in order to resolve existing conflicts, is outlined.**


**KEY WORDS: associative memory; medial temporal lobes; hippocampus; familiarity; recollection**

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## INTRODUCTION

The literature on the effects of relatively selective hippocampal lesions on item recognition in humans is conflicting (see Mayes et al., 2002). In brief, some patients show clear item recognition as well as recall deficits (Zola et al., 1986; Reed and Squire, 1997; Manns and Squire, 1999; Manns et al., 2003), whereas others show clear recall deficits, but relatively normal item recognition (Vargha-Khadem et al., 1997; Baddeley et al., 2001; Mayes et al., 2001, 2002; Holdstock et al., 2002a). The reasons for these conflicting results have not yet been resolved, although the use of different tests in different patients is, at best, only a partial explanation (see Mayes et al., 2002). Most likely, the reasons relate to patients having different extents, locations, and kinds of hippocampal lesions; varying extents, kinds, and locations of extra-hippocampal damage and/or dysfunction; and/or differing degrees of functional or strategic reorganization of critical memory abilities. As Mayes et al. (2002) discuss, resolution will require the use of state-of-the-art structural and functional magnetic resonance imaging (fMRI) methods and administration of an agreed range of memory and other cognitive tests in additional patients who differ significantly from each other in the relative extents of their item recognition deficits.

Not only is it disputed whether recall is more impaired than item recognition following selective hippocampal lesions, it is also disputed whether these lesions disrupt associative recognition more than item recognition (e.g., Cave and Squire, 1991; Vargha-Khadem et al., 1997). In patients with impaired item recognition (e.g., those of Cave and Squire), it is necessary to use a matching procedure in which amnesics are given easier test conditions (e.g., more learning opportunity is given or testing is at shorter delays) than their controls to produce equivalent item recognition in patients and their controls. If patients show impaired associative recognition under these conditions, it is argued that associative recognition is more impaired than item recognition. The validity of this conclusion, however, depends on the matching procedure not affecting one kind of memory more than the other in normal subjects. This is hard to establish with confidence (see Mayes et al., 1985).

Only in patients with relatively preserved item recognition is it feasible to avoid the use of a possibly con-

founded matching procedure, and, instead, test patients under identical conditions to those used with their matched control subjects. When three such patients, who had relatively selective hippocampal lesions, were tested in this way, Vargha-Khadem et al. (1997) found that they showed not only fairly normal item recognition, but also fairly normal associative recognition for associations between pairs of words, pairs of nonwords, and pairs of faces. Associative recognition was examined using a procedure in which foils comprised recombinations of studied items, so that correct recognition could not be based on finding both items in a pair familiar from the study session. Recognition of object-location and face-voice associations was also examined using this recombination procedure. Both kinds of associative recognition were impaired in the patients. However, these results do not necessarily mean that normal hippocampal function is more important for object-location and face-voice associative recognition than it is for item recognition: First, all three patients suffered their hippocampal damage early and may have undergone functional or strategic reorganization of some of their memory abilities (see Manns and Squire, 1999; Maguire et al., 2001). Second, the single dissociation might arise not because of qualitative differences in the processing demands of the two kinds of recognition, but because associative recognition tasks are usually more difficult than item recognition.

Kroll et al. (1996) also used a recombination procedure to examine Yes/No recognition memory for associations between syllables of known words (e.g., study "valley" and "barter" and test either with these target words, new words, or the syllabic recombination "barley") or components of schematic faces. A patient who was reported to have bilateral hippocampal damage following an anoxic episode could discriminate between studied words or faces and completely novel foils, as well as a group of older adults, but was significantly impaired at discriminating between studied items and recombination foils (although there may have been a ceiling effect with the studied versus novel discriminations). The patient showed this pattern of deficit for both the word and face items. These results suggest that hippocampal lesions disrupt the ability to form intra-item associative memories. However, the greater disruption of the patient's ability to discriminate in memory between targets and target recombinations could have been an effect of difficulty because the normal subjects also found this task harder than discriminating in memory targets from novel foils. In addition, the patient was impaired at discrimination of studied patterns comprising several components from recombination foils. It is unclear whether this test required memory for intra-item associations or inter-item associations because the patterns may not have been perceived as items. If the test required inter-item memory for associations between similar kinds of items (e.g., words, nonwords, or faces), Vargha-Khadem et al.'s (1997) patients probably would not have been impaired. In contrast, if the test tapped memory for associations between different kinds of information (e.g., objects and their locations or pattern features and their locations), the patients studied by Vargha-Khadem and colleagues would have been impaired.

The first aim of this report was to examine whether the findings of Vargha-Khadem et al. (1997) also applied to the patient, YR, who suffered her relatively selective hippocampal damage in adulthood and, consequently, was less likely to have shown appreciable reorganization of her memory functions. YR has been shown to perform close to the mean level of her control subjects on a large number of item recognition memory tests (Mayes et al., 2002). The second aim was to examine whether single dissociations between item recognition and certain kinds of associative recognition would occur even when normal subjects found the item recognition tests as difficult as the associative recognition tests. The third aim was to compare YR's recognition of intra-item associations, associations between similar kinds of items, and associations between different kinds of information. The final aim was to examine YR's associative recognition using procedures that did not involve recombination foils, but made performance likely to be dependent on memory for associations for other reasons.

## METHODS

### Subjects

Patient YR has had a memory impairment since 1986, when, at the age of 49 years, she was given an opiate drug to relieve severe back pain, which may have caused an ischemic infarct. Her memory impairment immediately followed this incident and has persisted since that time.

Volumetric analysis of YR's 3D T1-weighted radiofrequency spoiled gradient echo (SPGR) MRI scan has shown a reduction in the volume of her hippocampus of about 50% bilaterally, with no visible damage to other brain regions. This hippocampal volume reduction extended uniformly along the entire anteroposterior axis of the structure (Fig. 1). YR's neuropathology is described in detail elsewhere (Holdstock et al., 2000; Mayes et al., 2001, 2002). In summary, outside the hippocampus, the volumes of YR's left and right parahippocampal gyrus, corrected for intracranial volume, were slightly above the mean level of her control subjects. In addition, YR's corrected volumes of gray and white frontal matter on both sides of the brain were within normal limits. On the left, these volumes were slightly greater than the mean of her control subjects, whereas on the right, these volumes were slightly below the mean of her control subjects. The corrected volumes of YR's parietal neocortex were within normal limits although just over a standard deviation below the control mean.

We have now measured the volume of YR's temporal lobe using coronal images. Anteriorly, the temporal lobe was determined on the slice first showing the temporal brain tissue. The posterior limit was defined as corresponding to the end of the hippocampal tail where the lateral ventricles split into the frontal and temporal horns. The corrected volume of YR's right temporal lobe was reduced by 0.4% relative to the mean of her eight control subjects, who were the same as those used for the measures made earlier. Her left temporal lobe volume was reduced by 4.8% relative to the control mean. In both cases, her temporal lobe volumes, which were 0.5 and 0.04 standard deviations (SDs) below the control mean for left and right temporal lobes respectively, were clearly very similar to those of the normal subjects to whom she was matched. This was the case even though YR's scan showed visible

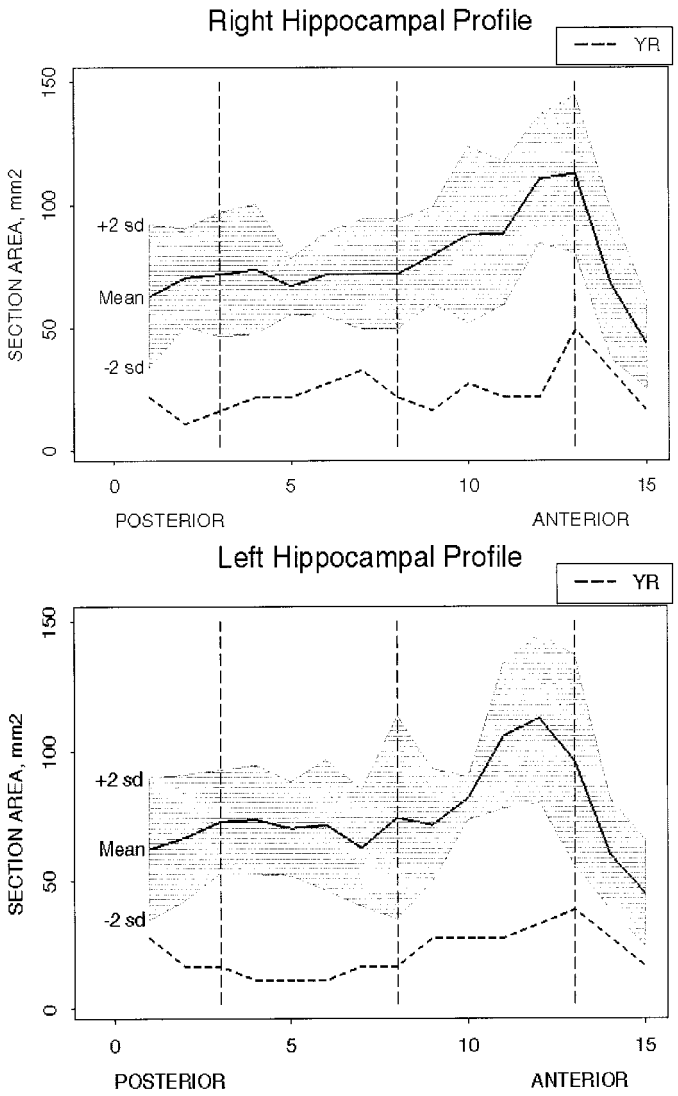


**FIGURE 1. Hippocampal section area for patient YR (dashed line), and the mean section area for eight age- and sex-matched healthy controls (solid line), is plotted as a function of section position through slices 1–15. The shaded region, which marks the posterior and anterior ends of the right and left hippocampus, extends between 2 SDs above and below the mean for controls.**

susceptibility artifacts arising from the interface between the inferior surface of the temporal lobes and the Mastoid air cells, which may have led to an uncertain amount of underestimation of her temporal lobe volume.

To our knowledge, volumes of the perirhinal and entorhinal cortices have not yet been reported in any patient with relatively selective hippocampal damage. One reason for this is that identifying reliable MRI markers for the boundaries of these cortices is extremely difficult. Further cross-validation studies using histology with post mortem tissue need to be completed to refine the procedure developed by Insausti et al. (1998). Nevertheless, we have attempted to measure these volumes in YR and in three control subjects, who were slightly younger, but matched to her in intelligence, using the boundaries defined by Insausti et al. (1998). The procedure used is described in more detail in Mayes et al. (2003). The findings should be viewed with caution, but the corrected volumes of YR's left and right perirhinal as well as entorhinal cortices were close to the mean values of her control subjects in every case. Her left and right entorhinal cortex volumes were slightly greater than those of all three control subjects, whereas her left and right perirhinal cortex volumes were slightly greater than those of two of her control subjects. The possibility that YR has hard-to-detect damage somewhere else in the brain other than the hippocampus can obviously not be excluded. However, our MRI-based measures have revealed no neocortical or medial temporal cortex region that shows detectable damage.

Psychometric assessment has shown that YR is of slightly above average intelligence with no evidence of decline from premorbid levels. Her performance on tests of executive function and visuospatial ability has been at normal levels. On standardized memory tests, such as the Doors and Names subtests of the Doors and People Test (Baddeley et al., 1994) and the Recognition Memory Test (RMT) (Warrington, 1984), she was impaired at recall, but within the normal range on tests of item recognition. (For a detailed description of her performance on psychometric tests, see Holdstock et al., 2000, 2002a,b; Mayes et al., 2001, 2002). On 43 item recognition tests and more than 34 free recall tests, YR performed just below her control subjects' mean score on the item recognition tests, but was significantly more impaired on the free recall tests (Mayes et al., 2002).

For the memory tasks described in the present report, YR's performance was always compared with that of control subjects matched to her in age and intelligence, and usually sex. Control groups usually contained 10 subjects, but varied in size from 6 to 12 normal subjects.

## MATERIALS AND PROCEDURE

### Part 1: Associative Recognition Tests with Recombination Foils

YR and matched control subjects were tested on 25 associative recognition tests. Three of the tests involved intra-item associations, four involved associations between items of the same kind, and 18 involved associations between information of different kinds. Tables 1–3, respectively, summarize the details of each of these kinds of tests.

#### *Intra-item associative recognition using recombination foils*

It is widely believed that item recognition is supported either by recollecting the contextual associations of studied items or by judging studied items increased relative familiarity, or both (see Yonelinas, 2002). Recognition in standard old/new item recognition tests may be facilitated by relative familiarity of any features of the items or of the associations between two or more of those features. In contrast, intra-item associative recognition can only be facilitated by relative familiarity of the associations between two or more item features. Greater impairment on the intra-item associative recog-

nition memory tests should, therefore, indicate that a patient has a specific difficulty in memorizing the associations between an item's features. In the verbal intra-item Yes/No recognition test described below, however, the intra-item associations would already be in memory and merely need strengthening to increase relative familiarity of these associations. In the face intra-item Yes/No and forced-choice tests, memory for these associations has to be created from scratch although the features can be fitted into a well-established facial template. The full basis for forming novel item representations is very poorly understood.

The verbal test used composite words as the items and the other used faces as the items. The verbal test was derived from the procedure used by Reinitz et al. (1996). Subjects were shown 30 composite words such as "earthquake" and "silkworm" and were then given a Yes/No recognition test comprising 10 of the studied composite words, 10 recombined composite words e.g., "earthworm"), and 10 new composite words. This made it possible to determine the subjects' ability to discriminate in recognition memory between studied and new words, and separately between old and recombined words.

The face intra-item associative recognition tests were derived from the procedure of Kroll et al. (1996) and required subjects to recognize studied faces that were nonfamous and novel at the time of study. At test, the faces had to be selected from among faces that were created by recombining the features of other studied faces. Task performance, therefore, depended on remembering face-feature associations. All faces, including the recombination stimuli, were constructed using the E-fit program created by Aspley Ltd. One test used a Yes/No format, and the other used a forced-choice format. Comparable nonassociative face recognition tests were created by requiring the studied faces to be selected from among totally new faces at test. In these tests, recognition of individual studied features was sufficient for performance to be successful. All of the above tests are also described in Table 1.

### *Recognition of associations between items of the same kind using recombination foils*

The same item associative recognition tests included recognition tests for word pairs, word triplets, and face pairs. Recombination foils were used in all cases. One of these tests has been reported in detail in another article (Mayes et al., 2001), as indicated in Table 2. All the word association recognition tests used a forced-choice format, whereas the face-face association test used a Yes/No recognition format.

### *Recognition of associations between different kinds of information using recombination foils*

The recognition tests for associations between information of different kinds are listed in Table 3. They included tests of the spatial position and temporal order of words and pictures, visual picture and auditory associations, visual picture and visually presented word associations, and associations between orthographic strings and meaning. Some of these tests have been reported in detail in other papers and are indicated as such in Table 3. Test selection was based on two principles. First, the components being associated were different kinds of information so that representation would probably be mediated by distinct neocortical regions. Second, a variety of different pairings of kinds of information to be associated were selected in order to determine to what extent any impairments were information specific.

## Part 2: Additional Associative Recognition Tests

YR has completed three further associative recognition tests that differed from those presented in Tables 1–3 because they did not use foils that were recombinations of the components of studied associations. Performance on these tests (described below) should nevertheless depend on remembering associative information.

### *Forced-choice recognition memory of faces with immediate and repeat test*

A face recognition memory test similar in format and difficulty to the RMT was completed with memory being tested immediately after presentation and again, using the same test materials, after a 5-min delay. This procedure is the same as that used by Aggleton et al. (2000). During the first (immediate) recognition test, relative familiarity can be used to distinguish between targets and foils because only one of each test pair has been studied recently. However, in the delayed test, targets and foils should have overlapping levels of familiarity so that subjects' accurate recognition on the delayed test may often have to depend on recollecting face-study context associations.

### *Associatively cued and uncued word recognition*

The procedure used was derived from that of Rabinowitz (1986). Forty pairs of words were presented to subjects. Each word pair was presented to subjects for 3 s. Subjects were asked to read the words and to try to remember them for a later memory test. No associative encoding instructions were given. In the memory test, which occurred after a short filled delay, words were presented to subjects one at a time. Half of the words had been studied in the presentation phase and the other half had not. Subjects had to indicate for each word, whether or not it had been seen in the study phase. YR's performance was compared with that of control subjects. The key manipulation was that at test half of the studied words were preceded by the word with which they were paired at study (associatively cued) and half were preceded by a different word (not associatively cued). Hit rates were derived for each condition, as was the false alarm rate for the foil data. Memory strength was measured using signal detection theory. Any bias in responding would have applied equally to each condition because the false alarm score was common to the two conditions.

### *Recognition memory for objects in scenes*

The abstract scene stimuli and procedure used with this paradigm were derived from Gaffan (1994). At study, subjects were asked to remember abstract computer generated shapes (foreground objects), each of which was presented within a unique computer-generated abstract scene. The scenes consisted of other simpler computer generated shapes such as circles, lines, letters,

*TABLE 1.*

*YR's Performance and the Performance of Her Matched Control Subjects on a Memory Test for Intra-Item Associations and a Corresponding Item Recognition Test**

| Test description | Paradigm | Delay[a] | Test choices[b] | Difficulty[c] | List length[d] | Control mean score[e] | YR's test score[e] | YR's z-score[f] |
|---|---|---|---|---|---|---|---|---|
| Intra-item association recognition | | | | | | | | |
| Selecting correct composite words, rejecting recombined composite words | YN | 15 | 2 | 77 | 30 | HR = 0.9, (0.07) FAR = 0.27 (0.27) | HR = 0.8, FAR = 0.35 | −0.8 |
| Selecting correctly combined face features, rejecting recombined face features | YN | 0 | 2 | 39 | 24 | HR = 0.88, (0.10) FAR = 0.51 (0.19) | HR = 0.88, FAR = 0.54 | −0.4 |
| Selecting correctly combined face features, rejecting recombined face features | FC | 20 s | 2 | 70 | 40 | 85 (7.07) | 80 | −0.7 |
| Item recognition | | | | | | | | |
| Old/new composite word recognition | YN | 15 min | 2 | 61 | 30 | HR = 0.9, (0.07) FAR = 0.09 (0.19) | HR = 0.8, FAR = 0.15 | −1.3 |
| Single face recognition | YN | 0 | 2 | 38 | 24 | HR = 0.82, (0.13) FAR = 0.29 (0.22) | HR = 0.88, FAR = 0.21 | 0 |
| Single face recognition | FC | 20 s | 2 | 80 | 40 | 94 (10.75) | 90 | −0.4 |

YN, yes/no test paradigm, performance measured as a d′ score; FC, forced choice test paradigm, performance measured as percentage correct; HR, hit rate; FAR, false alarm rate.

*Type of paradigm, study to test delay, and difficulty for control subjects are also displayed for each test.

[a]Delay from the end of the presentation of the study list to the start of test.

[b]Number of choices at test per studied item, for example, in a forced-choice test, in which three foils are presented with the studied item at test, the number of test choices is four; in a yes/no test in which 20 items are studied and 40 test items are presented (20 studied and 20 new), the number of test choices is two.

[c]Percentage score indicating where between chance and a perfect score the control subjects' mean score fell.

[d]Length of the study list.

[e]Hit rate and false alarm rate for yes/no tasks; percentage correct for forced-choice tasks; SDs in parentheses.

[f]YR's performance expressed as z-scores (i.e., the number of standard deviations that her performance fell above (+) or below (−) the control mean).

and numbers. Foreground and background shapes could be distinguished according to color, with foreground objects being warm hues of yellow through to red and the background shapes being blue and green in color.

Two kinds of recognition test conditions were used. In the test phase of the same condition, subjects were presented with the backgrounds they had studied. Within each background there were two foreground objects: the one presented in that background during the study phase and an object that was novel, although similar in style and structure to other foreground objects seen at study. The position of the studied foreground object within the background was also identical to its position at study.

*TABLE 2.*

*YR's Performance and That of Her Control Subjects on Four Memory Tests for Associations Between Items of the Same Kind, Along With Type of Paradigm**

| Test description | Paradigm type | Delay[a] | Test choices[b] | Difficulty[c] | List length[d] | Control mean score[e] | YR's test score[e] | YR's z-score[f] |
|---|---|---|---|---|---|---|---|---|
| Selecting correctly paired words from among re-paired words (Mayes et al., 2001) | FC | 0 | 2 | 50 | 20 pairs | 15 (3.0) | 14 | −0.3 |
| Selecting correctly paired words from among re-paired words | FC | 20 s | 2 | 67 | 40 pairs | 83.4 (12.6) | 62.5 | −1.7 |
| Selecting correct combinations of word triplets from among recombinations | FC | 30 min | 4 | 52 | 16 triplets | 64 (21.6) | 50 | −0.6 |
| Selecting correctly paired faces from among re-paired faces | YN | 0 | 2 | 18 | 5 × 12 pairs | HR = 0.58, (0.15) FAR = 0.39 (0.17) | HR = 0.53, FAR = 0.37 | −0.3 |

YN, yes/no test paradigm, performance measured as a d′ score; FC, forced choice test paradigm, performance measured as percentage correct; HR, hit rate; FAR, false alarm rate.

*Along with the paradigm, study to test delay and difficulty for control subjects for each test. For tasks described in more detail in other papers, reference is given in parentheses.

[a]Delay from the end of the presentation of the study list to the start of test.

[b]Number of choices at test per studied item, for example, in a forced-choice test in which three foils are presented with the studied item at test, the number of test choices is four; in a yes/no test in which 20 items are studied and 40 test items are presented (20 studied and 20 new), the number of test choices is two.

[c]Percentage score indicating where between chance and a perfect score the control subjects' mean score fell.

[d]Length of the study list.

[e]Hit rate and false alarm rate for yes/no tasks; percentage correct for forced-choice tasks; SDs in parentheses.

[f]YR's performance expressed as z-scores (i.e., the number of standard deviations that her performance fell above (+) or below (−) the control mean).

In the test phase of the different condition, subjects saw two foreground objects, presented within a background. However, this time the background was novel and had not been studied before. One of the foreground objects set against the background was from the studied set and the other was a new item, although similar in style and structure to other objects seen at study. Subjects were told at test that in this condition the backgrounds to be used at test were new and so should be ignored in making their decision about which foreground shape had been studied.

The different background condition makes it very unlikely that memories of object-background scene associations can be used to help foreground object recognition memory. Therefore, in this condition, subjects' foreground object recognition memory is probably tapped in a fairly pure way, as would be the case when objects are studied in isolation. In the same condition, however, subjects can use their memory for associations between foreground objects and background scenes to help their recognition memory for the objects. The difference in recognition memory between the two conditions gives an indication of the extent to which a subject has used associative memories in the same background condition.

The aim was to determine whether YR would be impaired in her ability to aid her recognition memory for foreground objects through the retrieval of object-background scene associations. To determine whether she had such an impairment, it was important to ensure that normal subjects showed a clear recognition memory advantage for foreground objects in the same condition. There was no guarantee that they would do so, however, because subjects were not forced to use memory for object-background scene associations so the procedure may be a less sensitive test of associative recognition than the recombination recognition tests.

To determine whether subjects' spontaneous encoding was sufficient to produce a clear recognition advantage for the same condition or whether directed encoding was necessary, 12 control subjects for YR were tested first in a spontaneous and then

*TABLE 3.*

*YR's Performance and That of Her Matched Controls on Memory Tests for Associations Between Information of Different Kinds**

| Test description | Paradigm type | Delay[a] | Test choices[b] | Difficulty[c] | List length[d] | Control mean score[e] | YR's test score[e] | YR's z-score[f] |
|---|---|---|---|---|---|---|---|---|
| Selecting studied locations of studied words from among recombinations of studied words and locations | FC | 0 | 5 | 46 | 5 | 56.7 (13) | 25 | −2.4 |
| Selecting the studied temporal order of words from among recombinations of words and temporal position (Mayes et al, 2001) | FC | 0 | 2 | 50 | 20 word pairs | 75 (7.5) | 57.5 | −2.3 |
| Selecting the studied temporal order of words from among recombinations of words and temporal position (Mayes et al., 2001) | FC | 20 s | 5 | 75 | 1 set of words | 80 (13.5) | 35 | −3.3 |
| Selecting the definition studied with a specific word from among definitions studied with other words (Holdstock et al., 2002b) | FC | 30 min | 4 | 91 | 10 | 93 (13.4) | 30 | −4.7 |
| Selecting the definition studied with a specific word from among definitions studied with other words (Holdstock et al., 2002b) | FC | 24 h | 4 | 91 | 10 | 93 (14.9) | 50 | −2.9 |
| Selecting the studied temporal order of wallpaper patterns from among recombinations of patterns and temporal position (Mayes et al., 2001) | FC | 20 s | 5 | 76 | 1 set of patterns | 80.5 (12.5) | 55 | −2.0 |
| Selecting studied locations of pictures of line drawn objects from among recombinations of studied pictures and locations (Holdstock et al., 2002a) | FC | 40 s | 4 | 96 | 12 | 96.7 (7.0) | 58.3 | −5.5 |
| Selecting studied locations of pictures of line drawn objects from among recombinations of studied pictures and locations (Holdstock et al., 2002a) | FC | 30 min | 4 | 85 | 12 | 88.4 (11.2) | 16.7 | −6.4 |

*TABLE 3. (Continued)*

| Test description | Paradigm type | Delay[a] | Test choices[b] | Difficulty[c] | List length[d] | Control mean score[e] | | YR's test score[e] | | YR's z-score[f] |
|---|---|---|---|---|---|---|---|---|---|---|
| Selecting the studied combination of animal picture and visually presented occupation name from among recombinations of animal pictures and occupation names | YN | 0 | 2 | 73 | 52 (inc practice) | HR = 0.82 (0.09) | FAR = 0.09 (0.07) | HR = 0.5 | FAR = 0.36 | −2.6 |
| Selecting the studied combination of face photograph and voice from among recombinations of studied faces and voices | YN | 20 s | 2 | 45 | 16 | HR = 0.68 (0.04) | FAR = 0.28 (0.15) | HR = 0.44 | FAR = 0.38 | −2.6 |
| Selecting the studied combination of face photograph and voice from among recombinations of studied faces and voices | YN | 40 min | 2 | 41 | 16 | HR = 0.71 (0.17) | FAR = 0.30 (0.13) | HR = 0.50 | FAR = 0.38 | −1.4 |
| Selecting the studied combination of scene photograph and sound from among recombination of studied scene photographs and sounds | YN | 20 s | 2 | 63 | 20 | HR = 0.85 (0.14) | FAR = 0.23 (0.08) | HR = 0.60 | FAR = 0.45 | −2.0 |
| Selecting the studied combination of scene photograph and sound from among recombinations of studied scene photographs and sounds | YN | 25 min | 2 | 63 | 20 | HR = 0.83 (0.13) | FAR = 0.20 (0.13) | HR = 0.55 | FAR = 0.55 | −2.3 |
| Selecting the studied combination of face photograph and auditorily presented name from among recombinations of studied faces and names | YN | 0 | 2 | 68 | 3 | HR = 0.83 (0.10) | FAR = 0.15 (0.11) | HR = 0.87 | FAR = 0.40 | −1.5 |
| Selecting the studied combination of face photograph and auditorily presented name from among recombinations of studied faces and names | YN | 5 s | 2 | 60 | 3 | HR = 0.83 (0.10) | FAR = 0.22 (0.09) | HR = 0.53 | FAR = 0.47 | −2.5 |

*TABLE 3. (Continued)*

| Test description | Paradigm type | Delay[a] | Test choices[b] | Difficulty[c] | List length[d] | Control mean score[e] | | YR's test score[e] | | YR's z-score[f] |
|---|---|---|---|---|---|---|---|---|---|---|
| Selecting the studied combination of face photograph and auditorily presented name from among recombinations of studied faces and names | YN | 10 s | 2 | 72 | 3 | HR = 0.81 (0.11) | FAR = 0.09 (0.12) | HR = 0.73 | FAR = 0.62 | −2.5 |
| Selecting the studied combination of face photograph and auditorily presented name from among recombinations of studied faces and names | YN | 20 s | 2 | 67 | 3 | HR = 0.82 (0.15) | FAR = 0.15 (0.07) | HR = 0.74 | FAR = 0.87 | −3.1 |
| Selecting the studied combination of face photograph and auditorily presented name from among recombinations of studied faces and names | YN | 30 s | 2 | 57 | 3 | HR = 0.75 (0.11) | FAR = 0.19 (0.09) | HR = 0.54 | FAR = 0.40 | −2.4 |

YN, yes/no test paradigm, performance measured as a d′ score; FC, Forced choice test paradigm, performance measured as percentage correct; HR, hit rate; FAR, false alarm rate.

*Along with the type of paradigm, study to test delay, and difficulty for control subjects for each test. For tasks described in more detail in other papers, references are given in parentheses.

[a]Delay from the end of the presentation of the study list to the start of test.

[b]Number of choices at test per studied item, for example, in a forced-choice test where three foils are presented with the studied item at test, the number of test choices is four; in a yes/no test where 20 items are studied and 40 test items are presented (20 studied and 20 new) the number of test choices is two.

[c]Percentage score indicating where between chance and a perfect score the control subjects' mean score fell.

[d]Length of the study list.

[e]Hit rate and false alarm rate for yes/no tasks; percentage correct for forced-choice tasks; SDs in parentheses.

[f]YR's performance expressed as *z*-scores (i.e., the number of standard deviations that her performance fell above (+) or below (−) the control mean).

in a directed encoding condition. In the spontaneous encoding condition, subjects were simply told at study that they should try to remember the foreground object in each scene for a later memory test. In the directed encoding condition, subjects were told that they should try to remember the foreground object in each scene for a later memory test, but that they should also look at where it was within the scene. Each condition comprised 40 scenes, divided into two sets of 20 trials each. Presentation time was 10 s per scene. The subjects completed the tasks in a counterbalanced order to eliminate the possibility that effects could be material specific. As only the directed encoding condition produced a clear advantage for recognition, YR was run in this condition and her performance compared with that of a further group of control subjects all 11 of whom completed the task in the same order as YR.

As the control subjects' recognition was not much above chance in the different background condition when directed encoding was used, and our goal was to increase the sensitivity of the test, a second experiment was run in which more scene stimuli were used, and subjects were given more opportunity to encode the scenes. YR's performance was compared with that of 10 age- and IQ-matched control subjects. For the encoding of each scene, subjects were allowed 15 s to describe where the foreground object was in relation to four background shapes.

Testing was split into two experimental sessions. In session 1, subjects first received 15 practice trials for the "same" condition.

This was followed by 45 trials for the "different" condition, which were split into three sets of 15 trials. Finally, there were 45 trials for the "same" condition, which were again split into three sets of 15 trials. In session 2, first, there were 15 practice trials for the "same" condition. Second, 45 trials for the "same" condition were presented, which were split into three sets of 15 trials. Third, 45 trials for the "different" condition were presented which were split into three sets of 15 trials.

## RESULTS

### Part 1: Associative Recognition Tests With Recombination Foils

#### *Recognition of intra-item associations*

Throughout the present report, we consider YR's performance to be impaired if it falls more than 1.96 SDs below the control mean. To check whether YR tended to be more impaired on some kinds of test than on others because the more impaired tests were more difficult, we used an operational definition of difficulty. According to this definition, difficulty was measured as a percentage score indicating where between chance (0%) and perfect memory (100%) the control mean fell (so that lower scores indicate greater difficulty). For this difficulty measure, Yes/No recognition was scored as proportion of hits minus proportion of false alarms. When the proportion of false alarms was equal to or greater than the proportion of hits, recognition was considered to be at chance at the difficulty score was zero.

The results from the three intra-item associative recognition memory tests are shown in Table 1 together with the results of their corresponding item recognition memory tests. None of these item recognition tests were reported in Mayes et al. (2002). On the composite word Yes/No recognition test on which performance was measured using a signal detection procedure, YR scored 0.8 SDs below the mean score of her control subjects when ability to discriminate between studied words and recombined words was measured. Her ability to discriminate between studied and new composite words was 1.3 SDs below the mean score of her control subjects. Like her control subjects, YR made more false alarms to the recombination foils than to the new foils. Her false alarm rate was 0.3 SDs above the mean level of her control subjects both when the foils were completely new composite words and also when they were recombined composite words. Therefore, there was no evidence that YR was more impaired at rejecting foils that were recombinations of studied words than she was at rejecting completely composite words. According to our criterion for impairment, YR was not impaired on either the intra-word associative recognition or the word item recognition measure, although her performance on both measures was worse than the mean level of her control subjects. More strikingly, YR did slightly better on intra-word associative recognition than she did on the otherwise comparable word item recognition test.

On the face intra-item Yes/No associative recognition test, which used recombinations of face features as foils, YR's performance was 0.4 SDs below the control mean and, therefore, could not be described as impaired according to our criterion. The corresponding old/new Yes/No face recognition task, which required studied faces to be selected from among totally new faces at test, was found to be somewhat easier by YR's control subjects; therefore, we were unable to closely match the difficulty of the two recognition tests. On this corresponding test, YR's performance was very close to the mean of her control subjects. As with the composite word recognition tasks, YR and her controls made more false alarms to associative recombination foils than to completely new foils in the face recognition task as well as the composite word recognition task. On the face tasks she made slightly fewer false alarms than her controls with the new foils (0.4 SDs below the controls' mean false alarm rate) and slightly more false alarms with the recombination foils (0.2 SDs above the controls' mean false alarm rate). Relative to her control subjects, YR's overall and false alarm scores on the recombination and old/new versions of these face recognition test were similar and close to her control subjects' mean scores.

On the face intra-item forced-choice associative recognition test, YR's performance was 0.7 SDs below the control mean and, therefore, could not be described as impaired according to our criterion. The corresponding old/new forced-choice face recognition task, which required studied faces to be selected from among totally new faces at test, was found to be somewhat easier by YR's control subjects so we were unable to closely match the difficulty of the two recognition tests. On this corresponding test, although YR's performance was slightly below the mean of her control subjects, it was closer to the mean than was her performance on the recombination test. Performance on the recombination forced-choice test fell slightly further below the control mean than did the Yes/No recombination test.

#### *Recognition of associations between information of the same kind*

YR's mean recognition performance on tests of associations between items of the same kind was 0.7 SDs below her control group's mean. There was no significant correlation between test difficulty for control subjects and YR's performance (Pearson correlation: $-0.73$, $P > 0.05$). However, the small number of tests should be noted (the result shows a trend for YR's recognition to be more impaired for easier tests).

Considering YR's performance on the forced-choice word pair and word triplets tests, her mean performance on these three tests was 0.87 SDs below the control mean. The item recognition tests she had performed that used stimuli most similar to the stimuli used in these word association recognition memory tests were six word recognition tests (Mayes et al., 2002). YR's mean performance on these tests, which was 0.84 SDs below her control groups' mean performance, was closely comparable to her performance on the word association recognition memory tests. Item recognition was easier for control subjects than verbal associative recognition. Difficulty was 75 for the item recognition tests and 56.3 for the associative recognition tests. A one sample *t*-test comparing single word recognition difficulty scores for controls with

their difficulty scores on the three verbal associative recognition tests showed that they found the associative word recognition memory tests significantly more difficult than the single word recognition memory tests ($t = 2.431$, $df = 7$, $P < 0.05$).

In an attempt to match the difficulty level of the associative and item recognition tests more closely, YR's performance on 12 slightly less comparable item recognition tests was examined. These tests included the six recognition tests of words (already mentioned), four recognition tests for names, and two recognition tests for words that required additional judgments (e.g., Remember/Know judgments). Her performance on these tests was 0.49 SDs below her control subjects' mean score, which did not differ significantly from her performance on the verbal associative recognition memory tests (independent sample *t*-test: $t = 0.421$, $df = 13$, $P > 0.05$). The difficulty level score of these 12 verbal item recognition memory tests was 66, which was somewhat higher than the difficulty level of 56.3 of the verbal associative recognition memory tests. In other words, the item recognition tests tended to be slightly easier. However, this difference was not significant (independent sample *t*-test: $t = 1.03$, $df = 13$, $P = 0.322$). Associative word recognition was, therefore, comparable to verbal item recognition, even when the two sets of tests did not differ significantly in difficulty.

On the associative Yes/No recognition test that required recognition of whether two faces had been seen together at study, YR's mean performance was just 0.3 SDs below the control mean. This level of performance was significantly worse than that on the seven recognition tests for individual faces reported by Mayes et al. (2002) and the two face recognition tests reported in Table 1 (one sample *t*-test of z-scores on nine face recognition tests and one face-face recognition test; $t = 2.48$, $df = 8$, $P = 0.038$).

The individual face recognition memory tests were significantly easier for control subjects than the associative face recognition tests. The mean difficulty score for the individual face recognition memory tests was 52.5, whereas that for the associative test was 18 (one sample *t*-test of performance on nine face recognition tests against mean face-face associative recognition performance: $t = 6.332$, $df = 8$, $P < 0.001$).

### *Recognition of associations between information of different kinds*

A comparison of Tables 2 and 3 demonstrates the striking difference in YR's performance on associative tests involving the same kinds of information (e.g., word-word and face-face pair associations) and tests in which associations between different kinds of information have to be remembered. Whereas YR's mean performance on the four recognition tests for associations between information of the same kind was 0.73 SDs below the control mean, her mean performance on the 18 tests of recognition for associations between information of different kinds was 2.91 SDs below the control mean, and therefore clearly impaired. Furthermore, inspection of Table 3 shows that YR's performance was clearly impaired (i.e., more than 1.96 SDs below the control mean) on all but two of the eighteen tests. One of these tests examined recognition of face-voice associations at 40-min delay. For this test there was a floor effect because YR's performance was at chance, but the recognition of her control subjects had fallen to a level insufficiently above chance to allow her to be significantly impaired on our criterion.

The other test probably relied heavily on working memory. In order to focus on YR's long-term memory for associations between information of different kinds, her performance on this test was omitted from the analysis. This was the recognition test for face-name pairings after a 0-s delay. As only three pairs of faces were presented before test, and memory was tested immediately, it was considered that performance on this test would have received a considerable contribution from working memory, which was not the focus of this paper. However, for the sake of completeness, YR's performance on this task at the 0-s delay is included in Table 3. Interestingly, although her performance at this delay was not significantly impaired according to our criterion, it would be unsafe to conclude that, at 1.5 SDs below her control group mean, it was completely normal. If so, there may have been a significant contribution from longer term memory to performance or her hippocampal lesions may have mildly disrupted working memory for face-name associations. Her performance for all subsequent filled delays was, however, more than 2 SDs below the control mean and clearly impaired by our criterion.

YR's mean performance on the remaining seventeen recognition tests for associations between information of different kinds was 3 SDs below the control mean. The mean difficulty score of these tests for control subjects was 67. A Spearman's correlation showed a significant relationship between task difficulty for control subjects and YR's performance on these seventeen tests (Spearman's $rho = -0.64$, $P < 0.05$). The correlation was, however, in the opposite direction to that which would be expected if YR's performance became worse on harder tests. YR's performance was more impaired (i.e., further below the control mean) for tests that control subjects found easier.

The "different information" associative recognition tests varied in retention interval from zero s to 24 h. The effect of delay on YR's performance was therefore examined. A Spearman test showed no significant relationship between performance and delay ($rho = -0.179$, $P > 0.05$). Similarly, when tests were split into two categories: those with study-test delays of ≤60 s ($N = 12$) and those with study-test delays of greater than 60 s ($N = 5$), YR's performance was found not to vary significantly between the two categories of test ($t = 0.809$, $df = 4.7$, $P > 0.05$). Equal variances were not assumed, as Levene's test showed that the assumption of equal variances was violated).

A comparison was also made between YR's performance on forced-choice ($N = 8$) and Yes/No ($N = 9$) associative recognition tests. A *t*-test showed a trend for YR's performance to be poorer relative to her controls on forced-choice ($SD = -3.7$) than on Yes/No ($SD = -2.4$) tests, but this did not reach significance on a two tailed test ($t = -2.25$, df 8.04, $P = 0.054$, equal variances were not assumed, as Levene's test showed that the assumption of equal variances was violated). The mean retention interval was longer for forced-choice (median = 30 s; range = 0 s to 24 h) than Yes/No tests (median = 20 s (range = 0 s to 40 min)). However, as seen above, there appeared to be no relationship between study-

test delay and YR's performance so it is unlikely that this can account for the trend for forced-choice test performance to be poorer than Yes/No performance. The forced-choice tests were also slightly easier than the Yes/No tests (75% and 60%, respectively, between chance and perfect performance). Given the negative relationship between performance and difficulty described above, this may account for the trend. It might be thought that the relationship between performance and difficulty reflected a forced-choice/Yes/No difference. However, the Pearson correlation of −0.56 between YR's performance and test difficulty when the effect of test mode was partialled out was still significant ($P < 0.02$). In contrast, the correlation of +0.3 between YR's performance and test mode when test difficulty was partialled out was insignificant ($P = +0.22$).

In order to minimize the possibility that YR's greater impairment in recognition memory for associations between different kinds of information relative to item recognition memory was unrelated to the specific demands of storing and retrieving these kinds of association, seven of the associative tests were run within the same session as separate, but matching item recognition tests. These tests included word-temporal order recognition at 20-s delay, word-definition associative recognition at 24-h delay, wallpaper pattern-temporal order recognition at 20-s delay, object drawing-location recognition at delays of 40 s and 30 min, and face-voice association recognition at 20-s delay. Within a maximum of one week from the time that she did these tests, YR was given a test of word recognition, a test of word definition recognition, a test of wallpaper recognition, two tests of object recognition, and a test of object recognition respectively. Details of these tests, and YR's performance on them, are given in Mayes et al. (2002, their table 1). Each of these item recognition tests used corresponding materials, paradigm types (forced-choice or Yes/No recognition), numbers of test choices, and list lengths to the associative recognition tests to which they were matched. An attempt was also made to match the item and associative recognition tests as closely as possible for difficulty by manipulating how similar the foils were to their corresponding target (see Holdstock et al., 2002a). The mean difficulty score for the item recognition tests was 65.4 and that for the associative tests was 77.3, indicating that on average the item recognition tests were slightly harder. Whereas YR scored very close to the control subjects' mean level across all the item recognition tests (+0.03 SDs), she scored on average 3.6 SDs below the control subjects' mean on the associative recognition tests. Across the tests, the discrepancy between YR's item recognition and associative recognition performance on the matched pairs of tests was always greater than 2 SDs (indicating less impaired item recognition performance). It was least for the matching word definition recognition tests (2.13 SDs) and greatest for the matching pairs of object and object-location recognition tests (6.03 and 7.23 SDs, respectively).

There was also evidence that YR's recognition of associations between different kinds of information was significantly more impaired than her recognition of associations between similar kinds of information even when the two kinds of tests were closely matched. The second test described in Table 3, which tapped recognition of the temporal order in which each member of a set of word pairs were presented, was run within the same session as a closely comparable test of recognition of word pairs (see Mayes et al., 2001). The two tests were equivalently difficult and were both forced-choice tests using the same number of study pairs and the same delay. Despite this, YR was over 1.96 SDs more impaired on the test of recognition of temporal order of each word in the series of word pairs. The first test described in Table 3, which tapped recognition of the spatial position of series of word pairs, was also equivalent in difficulty to the above word pair recognition test, and also used a forced-choice recognition procedure with the same number of word pairs and the same delay although it had four foils per target rather than the one foil used in the word pair recognition test. YR was also more than 1.96 SDs more impaired on this recognition test for the spatial position of word pairs. These results strongly suggest that YR was significantly more impaired when she had to recognize the temporal order or the spatial position of word pairs than when she had to recognize arbitrary associations between word pairs, and that this difference was specific to the information that had to be remembered.

## Part 2: Additional Associative Recognition Tests

### *Forced-choice recognition memory of faces with immediate and repeat test*

The mean control performance was 46.6/50 (SD = 2.6) and 43.6/50 (SD = 4.9) for immediate and delayed tests, respectively. YR's performance was close to the control group's mean on the immediate test (46/50). Her performance on the repeated test was more impaired and although the level of performance (37/50) was not significantly impaired (1.35 SDs below the control mean), her 9-point drop in performance from the immediate to the repeated test was 2.4 SDs larger than the mean drop of 3 points (SD = 2.5) shown by the controls.

### *Associatively cued and uncued word recognition*

As already indicated in the Methods section, any bias in responding would have applied equally to the associatively cued and not associatively cued conditions because a single false alarm measure was used. YR's d′ score in the nonassociatively cued word recognition condition was 2.0 SDs above her control group's mean score. Her results on this test were not included by Mayes et al. (2002, their table 1), but the test is basically one of verbal item recognition. YR's results, therefore, add to the number of verbal item recognition tests on which she scores above the mean level of her control subjects (and in this case significantly so). In contrast, in the associatively cued word recognition condition, her score was significantly impaired (2.2 SDs below her control group's mean score). Whereas everyone in YR's control group benefited from the associative verbal cueing, YR showed no benefit at all.

### *Recognition memory for objects in scenes*

Performance for the control subjects, following directed encoding is shown in Table 4. Under spontaneous encoding instructions, there was little advantage for recognition in the same versus the

*TABLE 4.*

*Recognition Memory for Studied Objects of YR and Two Groups of Control Subjects**

| Subjects | Directed encoding same | Directed encoding different |
|---|---|---|
| YR | 60 | 60 |
| Counterbalanced controls | 77.5 (6) | 62.5 (11) |
| Same order controls | 75 (8.75) | 57.5 (11.5) |

*Tested with objects set in the same context as at study and also set in a different context from study. All scores are expressed as percentages with control subjects' mean scores (SDs in parentheses).

different condition. Following directed encoding, however, a clear recognition advantage was obtained. YR was, therefore, given the directed encoding instructions. Relative to the control subjects who completed the directed encoding condition in a counterbalanced fashion, YR's performance was impaired in the "same" condition (2.87 SDs below the control mean), but not in the "different" condition (0.23 SDs below the control mean). To ensure that YR was compared with control subjects who were tested in exactly the same way, she was compared with another group of control subjects who completed the directed encoding condition in the same order as herself. Relative to these control subjects, YR showed a strong trend toward impairment in the same condition (1.64 SDs below control mean), whereas in the different condition, her recognition was slightly better than that of her control subjects (0.22 SDs above her control subjects' mean).

In a modified version of the test in which fuller encoding and more scene stimuli were used, YR's recognition memory was 1.3 SDs below the control mean in the "different" condition, which did not reach our criterion of impairment of 1.96 SDs below the control mean. In contrast, in the same condition her performance was 2.82 SDs below the control mean and was, therefore, clearly impaired. The performance of YR and her control group is presented in Table 5.

## DISCUSSION

### YR's Pattern of Associative Recognition Performance

The pattern of YR's associative recognition memory performance on the tests that used recombination foils was relatively clear. YR showed relatively normal recognition on the word and face intra-item associative recognition memory tests, scoring 0.6 SDs below the mean of her control subjects. Her mean performance on these tests was the same as that which she showed on comparable tests of old-new face and composite word recognition (−0.6 SDs) and only slightly worse than her overall old/new item recognition performance (−0.5 SDs). In this respect, her performance differed from that of the amnesics studied by Reinitz et al. (1996) and the bilateral hippocampal patient studied by Kroll et al. (1996), although it was similar to that of the bilateral hippocampal patient of Henke et al. (1999). Like the patients of Vargha-Khadem et al. (1997), her recognition memory for associations between similar kinds of items was relatively intact (0.7 SDs below the mean of her control subjects) and as good as her item recognition (0.5 SDs below the mean of her control subjects), whereas her recognition memory for associations between different kinds of information was significantly impaired (2.9 SDs below the mean of her control subjects) and often at or around chance levels. YR was significantly more impaired at this form of associative recognition memory than she was at either item recognition memory (where there was a discrepancy of 2.4 SDs) or recognition memory for associations between items of the same kind (where there was a discrepancy of 2.2 SDs). A significant discrepancy score was maintained between performance on item and "different information" associative recognition tests even when these tests were closely matched on a variety of variables such as difficulty and paradigm type. The discrepancy score, therefore, probably relates specifically to the demands of storing and recognizing associations between different kinds of information. So YR's memory deficit seems to involve mainly her free recall and her recognition of associations between different kinds of information. This latter impairment is not confined to associations between items and spatial or temporal information.

YR's performance on the three recognition tests that did not use recombination foils was broadly consistent with her performance on the recombination foil recognition tests. In so far as associatively cued word recognition can be regarded as a form of associative recognition, however, it constitutes an exception to YR's relatively normal recognition of associations between items of the same kind. This is discussed below in relation to our theoretical account of YR's memory impairment.

In the rest of this Discussion, we will interpret YR's associative recognition performance in terms of the roles of the hippocampus and medial temporal lobe cortices (MTLC) in recall/recollection and familiarity memory, consider how well this account fits with the Norman-O'Reilly model (Norman and O'Reilly, 2003), and discuss unresolved difficulties with this kind of account. We then briefly list some rival views of hippocampal mnemonic functions, describe other data (some of which is conflicting) on the effects of hippocampal lesions on associative recognition memory, and finally consider how future research will need to be done to resolve current disagreements between rival accounts about the relative

*TABLE 5.*

*Recognition Memory for Studied Objects of YR and Control Subjects Run in the Same Way**

| Subjects | Same | Different |
|---|---|---|
| YR | 60 | 56 |
| Controls | 80.6 (7.3) | 66.7 (8.2) |

*Tested with the objects set in the same context as at study and also set in a different context from study. All scores are expressed as percentages, with control subjects' mean scores (SDs in parentheses).

effects of hippocampal lesions in humans on recall, item recognition and different kinds of associative recognition.

## Interpretation of YR's Associative Recognition Results

Over many tests, we have found that YR was more impaired at recall than she was at recognition memory for items, intra-item associations, and associations between items of the same kind. Recall is a form of memory in which subjects incidentally or deliberately use encoded information as a cue to retrieve additional information from memory. It is, therefore, a form of associative memory in which memory links allow encoded memory cues to mediate the retrieval of associated information. These links can involve intra-item associations, arbitrary associations between similar kinds of items, or associations between different kinds of information. It is likely that YR was impaired at recalling information that depended on any of these kinds of associative links (see Mayes et al., 2002).

The dominant view of item recognition memory is that it depends on familiarity memory (which might be regarded as true recognition), but that it is also supported by a form of recall known as recollection (Mandler, 1980; Jacoby, 1991; for review, see Yonelinas, 2002). The familiarity memory process does not involve retrieving any information other than the encoded target information. It can be treated as a scalar signal produced particularly by the perirhinal cortex within the MTLC that tracks the similarity of the encoded test information to information in memory (see Norman and O'Reilly, 2003; Brown and Aggleton, 2001). In monkeys, about one-fourth of neurons in this region show long-lasting response reductions to stimuli seen once, and these response reductions are central to a plausible neural network model of familiarity (Bogacz et al., 2001). Consistent with this, fMRI data in humans indicates that encoding that leads to familiarity is accompanied by increased perirhinal cortex activity (Davachi et al., 2003), whereas familiarity itself is accompanied by decreased perirhinal cortex activity (Henson et al., 2003; Montaldi et al., 2003).

It seems likely, but it remains unproved, that item familiarity depends on the familiarity of both the item features and the associations between them. Whether familiarity memory also exists for associations between items of the same kind, and for associations between different kinds of information is an open issue. Recollection is usually treated as a form of episodic memory. As such, it is defined as a form of recall in which the subject incidentally or deliberately uses encoded target information (items or any kind of association) as a cue to retrieve associated information about the study episode. This retrieved information is diagnostic of the target information having been encountered before and, in particular, in that study episode. In the present report, because many people use the term in this way, we define episodic memory as including reference to personally experienced context, particularly spatiotemporal context (see Mayes and Roberts, 2001). However, there is no reason why a semantic form of recollection should not also exist that may well depend on many of the same brain structures as episodic recollection. Semantic recollection would be a form of recall in which encoded factual target information cues the subject (deliberately or incidentally) to retrieve associated factual information, which may help confirm that the target fact is true.

Holdstock et al. (2002a) argued, on the basis of eight Remember/Know recognition tests, that YR's item familiarity memory, which was measured using signal detection theory (see Yonelinas, 2002), seemed to be completely unimpaired regardless of whether one assumes a relationship of redundancy, independence, or exclusivity between recollection and familiarity. As recollection is a form of recall and YR was impaired at other kinds of recall, it is likely that she was also impaired at recollection. Assessments of YR's recollection were problematic, however, because, possibly like patient Jon (see Baddeley et al., 2001), her grasp of the concept of recollection was poor. For example, when she felt that she had previously seen an item on a screen she reported it as remembered even though questioning indicated that she had recalled no specific information. In one Remember/Know recognition test of abstract patterns, we asked subjects to justify their remember judgments. On this test, YR's recollection, which was measured as proportion of remember hits minus proportion of remember false alarms (see Yonelinas, 2002), was 7.2 SDs below the mean level of her control subjects. YR's control subjects were able to recall their item-specific thoughts during encoding of nearly all the studied patterns, and were also often able to recall from approximately where in the list a studied item came. In contrast, YR was unable to recall list position of items at all and was only able to recall her thoughts during encoding of a very small minority of abstract patterns. This strongly suggests that her recollection was impaired when precautions were taken to ensure that remember responses were based on recall.

Our finding that YR's familiarity memory is preserved, whereas her recollection is impaired is consistent with several other pieces of evidence. First, although encoding that leads to recognition with source memory has been found to activate the hippocampus, encoding that leads to recognition without source memory has not (Davachi et al., 2003). Encoding that leads to familiarity has been reported to activate the perirhinal cortex to a similar extent, regardless of whether this is accompanied by source memory (Davachi et al., 2003). At test, familiarity alone has been reported not to activate the hippocampus, whereas recollection did (Eldridge et al., 2000). Second, Duzel et al. (2001) have argued that the hippocampally lesioned patient, Jon, lacked the late positive event-related potential component that indexes recollection in normal subjects, but showed preservation of the so-called N400 effect that may index familiarity in normal subjects. Third, Yonelinas et al. (2002) estimated familiarity and recollection in patients who suffered hypoxia following cardiac arrest. Whether estimates of familiarity and recollection were based on structural covariance modeling, analysis of remember/know responding, or analysis of receiver operating characteristics of recognition, the patients showed preserved familiarity memory and impaired recollection. Although brain imaging was not possible with MRI, the hypoxic etiology in combination with its relative mildness and the kind of memory deficits shown by these patients makes it likely that they had relatively selective hippocampal damage. Structural equation modeling suggested that, as

hippocampal damage increased with coma duration, recollection progressively declined, whereas familiarity did not.

However, familiarity deficits as severe as recollection deficits have been found, using the remember/know procedure, in seven patients, six of whom showed evidence of hippocampal damage, but parahippocampal gyrus volumes within the normal range by Manns et al. (2003). Inspection of Figure 1b from Yonelinas et al. (2002) shows that some of the 56 studied cardiac arrest patients resembled YR in showing relatively intact recognition, but clearly impaired recall (suggesting intact item familiarity, but impaired recollection), whereas other patients were clearly impaired on recognition as well as recall (suggesting impaired item familiarity). These data, therefore, suggest that hippocampal damage can lead to both patterns of deficit (as well as gradations between them). Provided that duration of coma was a good correlate of extent of hippocampal damage, as Yonelinas et al. assumed, the lack of correlation between coma duration and familiarity, suggests that impaired familiarity in the patients was associated with damage or dysfunction in extra-hippocampal structures that play a key role in mediating familiarity. Four of the patients of Manns et al. (2003) had less than a 30% hippocampal size reduction (one had a 10% reduction and one had no reduction, but focal lesions) and AB has not been given an MRI scan. Although, with smaller lesions at least, their precise location in the hippocampus is likely to determine degree of disruption of normal function, it is surprising that patients with such small lesions showed marked impairments in familiarity and recognition relative to YR and Jon, both of whom have suffered destruction of almost half the hippocampus.

YR's recognition memory for intra-item associations and associations between arbitrarily linked items of the same kind was equivalent to her item recognition memory (based on comparisons of studied and unstudied items). She showed, at most, a mild deficit for both these forms of recognition memory. Assuming that she was impaired at all forms of recall (including recollection), this suggests that familiarity can be based not only on components of items, but also on associations between components of items and on associations between arbitrarily linked items of the same kind. It should be noted that, although current views allow that there may be familiarity memory for unitized items (including item components and intra-item associations), allowing familiarity for non-unitized associations between items would require a major change (e.g., see Yonelinas, 2002). If brief learning did not lead to the unitization of the item-item associations described in Table 2, YR's results suggest that both forms of familiarity exist, and also make it likely that she showed preservation of both. YR's significantly greater recognition memory impairment for associations between different kinds of information (which was comparable to her recall impairment), however, suggests that this form of memory receives little, if any, support from familiarity and depends primarily, if not solely, on recollection.

## Fit Between YR's Results and the Norman and O'Reilly Computational Model

This interpretation of YR's memory impairment closely corresponds to a computational model of recognition memory, which postulates that recall (and the form of recall known as recollection) critically depends on the hippocampus (Norman and O'Reilly, 2003; O'Reilly and Norman, 2002). The model proposes that this structure makes distinct (pattern separated) representations even of similar inputs after only one or two presentations. The pattern separated representation of episodes and facts facilitates their pattern completion, i.e., recall. In contrast, the MTLC and the neocortex assign similar representations to similar stimuli in order to extract the shared structure of events. These structures are unable to support recall of information that has only been encountered on one or two occasions because they do not differentiate the representations of different information sufficiently. They do, however, support familiarity memory for the information they represent. Only the hippocampus can support recall of information that has been encountered just once or twice. If it is damaged, the model predicts that recall of any kind of association should be impaired. The model does allow that the MTLC can support recall of information that has been studied a large number of times.

The model predicts that MTLC can support familiarity memory not only for features of items, but also for associations, which implies that patients with hippocampal damage should perform above chance on associative recognition tests. The model also predicts that controls should perform better than patients, who can only use familiarity memory, because controls can also use one component of an association to cue recall of the rest. If what is recalled matches the test association, it is highly diagnostic of the item having been studied (recall-to-confirm). If what is recalled mismatches the test association (e.g., when given A-D, cue with A and recall A-B), this is highly diagnostic of the association not having been studied provided each component occurred in only one pair at study (recall-to-reject).

The size of control subjects' advantage will clearly be a function of how well they use recall-to-confirm and recall-to-reject. When control subjects do not make optimal use of available cues, or the materials do not foster recollection of diagnostic details, the model predicts that patients will show relatively spared performance. One such situation, identified by Norman and O'Reilly (2003), is when subjects are asked to choose between two pairs that share an item (forced-choice shared-item testing: study A-B, C-D, test A-B vs. A-D so that subjects are typically asked "Was A studied with B or D?"). Norman and O'Reilly argue that control subjects tend to adopt a strategy of cueing with the shared item (A) on these tests. This strategy is suboptimal for two reasons. First, it gives subjects only one shot to get the right answer (use A to cue recall of B) rather than also use D to cue recall of C. Second, by only cueing with one rather than both items, control subjects deprive themselves of information about the conjoint familiarity of the pair. Both these factors should reduce control subjects' advantage on forced-choice shared-item tests.

Some results presented in the present work are consistent with the predictions of the Norman and O'Reilly model as outlined above. The finding that YR performed well above chance on Yes/No and forced-choice recognition tests involving intra-item associations, and tests involving associations between items of the same kind, is consistent with the model's prediction that MTLC familiarity can support some degree of associative recognition. Fur-

thermore, the finding that YR was relatively unimpaired on forced-choice recognition of associations between items of the same kind (all tests of which used the forced-choice shared-item testing format) is consistent with the model's prediction that patients like YR should show relative sparing on these tests.

However, other results presented here appear to be in tension with Norman and O'Reilly's model. First, YR's performance was at or around chance on half of the forced-choice recognition memory tests of different information associations, and her performance on Yes/No recognition memory tests of these kinds of associations was similarly poor (her performance on eight of the nine Yes/No recognition tests of different information associations was at or around chance). These results are inconsistent with the model's claim that MTLC-mediated familiarity can support above-chance associative recognition memory. Second, YR's spared performance on Yes/No associative recognition of composite words, faces, and face-face associations is not specifically predicted by the model; while the model predicts that patients may show spared associative recognition in some circumstances (e.g., forced-choice shared-item tests), the default prediction is that associative recognition should be impaired. We will address each of these points in turn.

The finding that recognition memory for different information associations was usually at chance is clearly contrary to Norman and O'Reilly's model. However, it can easily be accommodated within their framework if we add an additional postulate that different domain-specific processing streams do not converge fully in MTLC, and that only the hippocampus can rapidly form arbitrary associative memories across these processing streams. As a result, little or no MTLC-mediated associative familiarity memory can be created to support recognition of associations between different types of information after one or two study trials (Norman and O'Reilly, 2003, acknowledge this possibility).

YR's relatively spared Yes/No recognition of face-face associations may be explicable in terms of floor effects on recall provided even control subjects in this experiment were not able to use single faces to cue detailed recall of the associated face. This possibility is supported by the very poor recognition performance of the control subjects on this test. The model predicts that, when cued recall is poor in controls, performance will be relatively spared in patients. Detailed recall would have been far easier after a brief study exposure if famous faces or unrelated words had been used instead of unknown faces, because, after brief study exposures, subjects can probably recall associated names or words much better than previously unknown faces.

YR's relatively spared Yes/No recognition of intra-face and intra-word associations could have occurred because she may not have had to form new associations between previously unrelated stimuli, but could instead have used conjunctive representations already present in her cortex. In the latter situation, the model predicts relatively spared Yes/No associative recognition performance. For example, the pairings "earth + quake," "silk + worm," and "earth + worm" would activate well-established knowledge relating to earthquakes, silkworms, and earthworms so that the re-paired foil "earth + worm" can easily be rejected because "earth" coupled with "worm" activates semantic features (e.g., "dirt") that were not activated by "earth" in the context of "quake," or "worm" in the context of "silk." Furthermore, there is extensive evidence that regions of cortex code for conjunctions of face features rather than individual features (e.g., Searcy and Bartlett, 1996), so that re-paired studied face feature lures can be rejected on the grounds that they activate cortical "feature conjunction detectors" that were not activated at study. This kind of conjunctive encoding may well explain YR's good recognition of the composite words and intra-face associations (see Yonelinas et al., 1999, for evidence that familiarity supports memory for intra-face associations).

In summary, Norman and O'Reilly's model needs to be modified so as to distinguish recognition of intra-item associations and associations between items of the same kind from recognition of associations between different kinds of information. It is less clear whether this modified model can explain all of the conditions in which YR's associative recognition was good. Her relatively intact Yes/No recognition memory for same item and intra-item associations may be explicable in terms of floor effects on recall (with face-face tests) and the presence of conjunctive representations in cortex (with intra-face and intra-word tests), but these conclusions are post-hoc. Future associative recognition testing will need to ensure that (1) subjects are forced to use newly acquired associative memories, (2) testing conditions allow adequate opportunity for using hippocampal recall/recollection mechanisms to aid recognition (i.e., recall is above floor), and (3) control subjects make optimal use of available cues (i.e., use each individual item to cue recall of the other pair item, and cue jointly with the paired items to assess their conjoint familiarity). When all three of these conditions are met, the model predicts that patients like YR will show impaired (but above-chance) Yes/No same item associative recognition.

YR's deficits on the three tests that did not use recombination foils are all consistent with the Norman and O'Reilly modified model. First, her impairment on the retest of face recognition (relative to her first testing) was clear and also consistent with the finding of Aggleton et al. (2000) that fornix-sectioned patients were also impaired. At first testing, YR's good recognition on this test and on other face recognition tests reported by Mayes et al. (2002) probably depended heavily on her familiarity memory for the studied faces. As already discussed, this is a form of memory at which she may well be normal (see Mayes et al., 2002; Holdstock et al., 2002a). At retest, however, subjects probably do not find relative familiarity to be a very useful diagnostic because both targets and foils are similarly familiar. So, they have to rely more heavily on recollection of associations between test faces and source information that links them to the study context. Normal performance, therefore, requires the use of a kind of recall (recollection) that is based on memory for associations between faces and information that was encoded during the study episode, which would have been impaired in YR.

Second, YR's impaired performance on the associatively cued word recognition test can be traced to the fact that associative cues were presented (temporally) before the target word at test. Given this fact, and the fact that the target word was often preceded by an unassociated word, it is probable that control subjects' improved word recognition (when given a cue that was paired with the target

at study) depended on a recall process that was operating with little intentional guidance: Incidentally recalling a word associated with one that you have just recognized should lead to the recalled word being recognized when it appears, whereas without the coincidental recall, it might otherwise not have been. When recognition of the studied words was not aided by associative cueing from words that had been paired with the target words at study, YR's performance was as good as that of her control subjects. The finding that YR failed to benefit from the presence of associative cues (whereas controls did benefit) can be explained in terms of the idea that, due to her hippocampal damage, cues did not trigger recall of targets in YR (but they did in controls). One prediction arising from this explanation is that presenting the associative cue word at the same time as the target word should have markedly improved YR's recognition of the target word, because she could have used her intact familiarity memory for word-word associations.

Third, YR's good performance in the different context condition of the objects in scenes recognition task is consistent with her relatively normal recognition of studied visual items (see Mayes et al., 2002). It is also consistent with the unimpaired performance shown by the fornix-transected monkeys in Gaffan's (1994) Experiment 3, which was similar to our different context condition. YR's object recognition in this condition was probably strongly dependent on familiarity memory for visual objects (which was preserved in YR). In the same context condition, YR showed a tendency towards impaired recognition in the first study and her deficit was significant in the second study. This is consistent with the impairment shown by the fornix-transected monkeys in Gaffan's (1994) Experiments 2, 4, and 5 in which the objects were shown in constant backgrounds. Unlike her controls, YR may not have benefited from same vs. different context testing because the hippocampus is needed to form object-scene association memories (a kind of different information association). YR's deficits in the same context condition may have been relatively small because the task did not specifically require subjects to pay attention to scene "context" when trying to recognize objects so controls may have minimally attended to scene information at test. Gaffan's (1994) findings with fornix-transected monkeys suggest that similar results will be found in humans who have selective fornix transection from colloid cyst surgery.

## Unresolved Issues About Our Interpretation of YR's Pattern of Associative Recognition

It has been proposed above that YR's hippocampal damage has impaired her recall and recollection of all kinds of association, but that her intact MTLC and neocortex subserve normal familiarity memory for item features, intra-item associations, and associations between items of the same kind. It has also been proposed that only the hippocampus, however, can make memory representations of different information associations (given limited exposure to the association); as such, MTLC-mediated familiarity cannot support associative recognition on "different information" tests. These proposals provide a good account not only of YR's performance on the recombination associative recognition tests, but also on the additional associative recognition tests. However, three questions need to be answered in order to characterize more fully what the account is claiming.

The first question relates to the difference between memory for intra-item associations and both inter-item and different information associations. Unlike Norman and O'Reilly (2003), Yonelinas (2002) has proposed that Yes/No recognition of intra-item (unitized) associations is well supported by familiarity memory, but that Yes/No recognition of associations between items of the same kind is not (see Yonelinas, 1997). This proposal suggests that, unless associations between items of the same kind are unitized, little or no familiarity memory is possible. Caldwell and Masson (2001) have found that normal subjects showed significant familiarity memory for object-location associations. According to the generalization of Yonelinas's proposal that unitization of associative memories is necessary (as well as sufficient) for familiarity memory, this finding suggests that familiarity memory can support even recognition for associations between different kinds of information provided the associations are unitized. In contrast, our view is that unitization of memories for associations between items of the same kind is not a necessary condition for significant familiarity. Our view does allow, however, that unitization of memories for different information associations, if it occurs, should be sufficient to produce significant familiarity.

The problem in distinguishing between Yonelinas' proposal and our own is that the criteria for identifying memory representations of unitized associations are poorly specified, and, to avoid circularity, these criteria cannot include whether familiarity is present. Weak evidence that an associative memory has been unitized is provided if the association feels like a single entity. Using this as a criterion, two faces might be seen as a pair of two faces that were seen together earlier (i.e., not unitized), but there may be no clear feeling about an object-location association so introspected unitization is probably an insufficient criterion for identifying whether an association is unitized. If learned associations are strongly felt to be unitized and can be shown to carry certain measurable costs (e.g., greater difficulty in recognizing components or in learning new combinations of components) relative to equally well learned associations that are strongly felt to be nonunitized, then progress will be possible.

Were such unitization criteria agreed, it would need to be shown that they apply to familiarity for, not recollection of a specific association. Recollection is of overlapping, but also additional information, so the familiarity and recollection memories may differ with respect to whether they are unitized. However, elaborately encoded mediating links do not affect the information on which familiarity memory for an association is based. The reason is simple: familiarity does not involve recall so the feeling of familiarity is based solely on what aspects of the association's components are re-encoded at test. The information that subjects elaborately encode when trying to form a memory association (e.g., visual imagery links between unrelated words) is unlikely to influence directly whether any resultant familiarity memory is based on a unitized associative memory. Nevertheless, as long as unitization criteria remain unagreed, exactly what factors facilitate the formation of unitized associations will be uncertain.

The second question concerns how associations between different kinds of information (for several kinds of which YR's recognition was clearly impaired) should be operationally defined and whether all recognition memory meeting this definition will be clearly impaired following hippocampal damage. According to our view, there is little or no MTLC-mediated familiarity memory for these associations so recognition must depend on hippocampally mediated recollection. The associations comprise components that constitute different kinds of information and include not only spatiotemporal information, but also associations with no spatiotemporal content such as those between faces and voices, and between words and their meaning. It seems likely, therefore, that YR's semantic as well as episodic recognition memory was impaired whenever it involved different information associations (see Holdstock et al., 2002b).

In our view, the key difference between same item and different information associations is that same item informational components converge for familiarity memory processing in the MTLC, whereas different information components do not. This means that the same/different distinction of the kind required by our account, depends only on the information that will be available for a possible familiarity memory judgment. Information that has to be recalled (recollected) and that depends on elaborate encoding (e.g., forming a visual image that unifies two words) is irrelevant. Even if one focuses on the components of possible familiarity judgments, the borderline between same item and different information associations is blurred as is illustrated by three recent reports about the effects of hippocampal damage on associative recognition, the nature of which was uncertain. It has been reported that hippocampal patients were no more impaired at house-face recognition than they were at nonassociative house-face recognition (Stark et al., 2002; Stark and Squire, 2003). The third report of Simons et al. (2002) found that extent of hippocampal damage in semantic dementia patients did not correlate with extent of impairment at associative recognition of studied sofa-door pairings.

We propose that different information associations should be regarded as those in which the components are represented in distinct neocortical regions. Functional neuroimaging might help identify whether this is so. If YR's recognition memory was impaired for all associations between different kinds of information, then only the hippocampus should be able to form memory representations of all these associations after one or two presentations. Over time through a slow learning process, many believe that both episodic and semantic different information associative memories form in the neocortex (e.g., Squire and Alvarez, 1995; but see Nadel and Moscovitch, 1997). If such slow neocortical (and perhaps MTLC) binding does occur, it would presumably involve memory representations that are sufficiently distinct to support recall as well as familiarity memory. Murre's (1997) proposal that neighboring neocortical modules are an exception to the rule that such modules are only sparsely connected suggests that deficits may not be so severe for different information associations represented in neighboring modules even after only a few learning trials. A possible example of such preservation of a kind of different information association is egocentric spatial memory, which Burgess et al. (2002) have argued is preserved relative to allocentric spatial memory (Holdstock et al., 2000; King et al., 2002). However, the case for this is not yet made because it has been shown that monkey hippocampal neurons respond to egocentric spatial cues (Feigenbaum and Rolls, 1991) and patient testing has not attempted to match egocentric and allocentric tasks for the number of associations that would have to be recollected to support recognition memory.

The third question concerns whether there are circumstances in which the hippocampus supports, not only recall/recollection, but also familiarity and, if so, to what extent it can do so. Given that it has been proposed that certain different information associations only fully converge for memory-relevant processing in the hippocampus, MTLC-mediated familiarity memory for such associations should not exist or at least be minimal even in normal subjects. However, if the hippocampus can mediate familiarity memory for different information associations (and, by extension, other associations), some familiarity of this kind should support recognition memory in normal subjects. Norman and O'Reilly's model does allow that a damaged hippocampus might sometimes merely echo an input pattern rather than use the input to complete a larger memory. This would be equivalent to hippocampal familiarity. According to the model, such echoing should be rare when the hippocampus is intact because of its facility at pattern completion. If this is correct, then subjects should nearly always be able to report that their successful recognition of these associations is based on recollection of additional information that confirms their decision. However, it remains to be determined to what extent normal subjects report that briefly studied different information associations merely feel familiar. If this kind of familiarity memory is well above chance relative to other kinds of familiarity memory, it should be slow like recollection (see Yonelinas, 2002) because it requires processing through additional hippocampal synaptic steps (see Brown and Bashir, 2002).

## Conflicting Views

Our view about the effects of hippocampal lesions that is based on the pattern of YR's recognition and recall deficits is different from other hypotheses about the effects of hippocampal damage and, relatedly, of hippocampal mnemonic functions. In the present study, we briefly consider several related views that are similar to our own, as well as one view that is more distinct. It has been proposed that hippocampal lesions directly disrupt acquisition of episodic, but not semantic, memories (e.g., see Vargha-Khadem et al., 1997; Baddeley et al., 2001). This view is similar to ours except that it postulates that the hippocampus is not needed for the normal acquisition of semantic associations. According to this view, any deficit in acquiring factual memories shown by patients with hippocampal lesions must result because, unlike normal subjects, these patients cannot boost their memory for studied facts by recollecting the episodic contexts in which those facts were learned. Kesner (1998) has also suggested that the hippocampus makes pattern separated representations that are primarily concerned with creating spatiotemporal markers in memory so that lesions should primarily disrupt spatiotemporal and episodic

memory. Similarly, Burgess et al. (2002) stress the role of the hippocampus in episodic memory and place particular emphasis on the importance of this structure for certain kinds of spatial (and perhaps temporal) memory. This position may imply that hippocampal lesions will disrupt recognition of associations involving certain kinds of spatiotemporal information more than all other kinds of association. Much more distinct from our position is the view of Squire and colleagues that hippocampal damage disrupts recognition of items and associations equally, and, more generally, that it disrupts equally recall and recognition of recently acquired episodic and semantic memories (Stark et al., 2002; Squire and Zola, 1998). According to this view, familiarity-based item memory as well as overtly associative recognition and recall/recollection all depend on forming associations in memory, and this task is mediated by both the hippocampus and the MTLC.

## Other Relevant Studies

The view that hippocampal lesions disrupt different information associative recognition memory, but leave recognition memory for same item associations relatively preserved is not only supported by the findings with YR and Vargha-Khadem et al.'s (1997) three early onset cases, but is also supported by evidence from monkeys. Thus, fornix lesions in monkeys have been shown to disrupt rapid learning of nonspatial associations between visual stimuli and specific motor responses (Brasted et al., 2003). Although the effects of fornix and hippocampal lesions probably differ in some respects, both lesions may disrupt learning of associations, which appear to involve different kinds of nonspatial information. In contrast, Murray et al. (1993) found that hippocampally lesioned monkeys learned and then recognized associations between visual stimuli at a relatively normal rate, whereas monkeys with bilateral rhinal cortex lesions were severely impaired. However, learning was slow so may have used different neural mechanisms from the ones used by humans to acquire same item associations rapidly. An earlier study by Murray and Mishkin (1985) even suggested that lesions involving the hippocampus had a much less severe effect on cross-modal recognition memory than larger lesions that severely damaged the MTLC. Cross-modal recognition memory has not yet been tested in human patients with relatively selective hippocampal lesions.

However, although the patients of Vargha-Khadem et al. (1997) showed a very similar pattern of performance to YR, this was not true of the hippocampal patients tested by Squire and colleagues. These latter patients were clearly impaired at item recognition as well as recall (Zola et al., 1986; Reed and Squire, 1997; Manns and Squire, 1999), and, as discussed above, Manns et al. (2003) found seven of these patients to show familiarity deficits as severe as their recollection deficits. Stark et al. (2002) studied four patients for three of which there was MRI evidence that the size of the hippocampus was reduced more than that of the parahippocampal gyrus. The fourth patient was AB for whom no MRI evidence about the selectivity of hippocampal damage is available. These patients showed impairments in Yes/No recognition memory for single faces and single houses and similar impairments for Yes/No recognition memory of house-face associations. When the patients were given extra study repetitions, both their item and associative recognition matched that of their control subjects.

Stark and Squire (2003) used the procedure of Kroll et al. (1996) that is described in the Introduction, to show that three of Stark et al.'s patients (including AB) were similarly impaired on house-face associative and nonassociative recognition when a slightly different testing procedure was employed. Using the same procedure, these investigators also found that these patients had similar associative and nonassociative recognition memory deficits for disyllabic words (e.g., fickle), nonword composites of monosyllabic words (e.g., jambark), unrelated monosyllabic word pairs (e.g., jam and bark), and object pair pictures (e.g., a picture of a guitar and a boot). Conjunctions of syllables that make words and nonwords correspond to intra-item associations and conjunctions of unrelated word pairs and object picture pairs correspond to same item associations. As indicated above, it is unclear whether house-face associations should be regarded as associations between different kinds of information in our sense or as same item associations. Henke et al. (1997) have found that encoding house-face associations produced not only more hippocampal, but also more MTLC, activation than nonassociative encoding of house-face information. Although these data are correlational, they suggest that recognition of house-face associations can be supported by MTLC-mediated familiarity as well as hippocampally mediated recollection. This suggestion is consistent with Stark and Squire's (2003) finding that reducing recognition response time to 2 s (which would primarily affect recollection-see Yonelinas, 2002) led to control subjects' house-face associative and nonassociative recognition matching that of the hippocampal patients. The patients tested by Stark and his colleagues showed similar sized deficits for recognition of intra-item associations, same item associations, items, and house-face associations. Although YR showed a similar relative pattern of performance, her recognition memory deficits for items, intra-item associations, and associations between items of the same kind were at most mild, whereas the patients of Stark and his colleagues showed clear deficits for all these kinds of recognition as well as recognition of house-face associations. It remains unclear whether these patients would be even more impaired at recognition of associations between different kinds of information than at recognition of items, intra-item associations, and same item associations. Such comparisons could not be made under the same conditions as those used for control subjects because the patients would be scoring too close to floor levels even on item recognition tests (see Stark et al., 2002).

One other patient, DF, with relatively selective bilateral hippocampal damage has been given an extensive range of memory tests over a period of 18 months following a hypoxic episode caused by exposure to carbon monoxide poisoning (Henke et al., 1999). DF's left hippocampal damage appeared to be similar to that shown by YR, although his right hippocampal damage was rather less extensive. He also showed bilateral atrophy of the globus pallidus and his parahippocampal gyral volume in both hemispheres was about two thirds of the mean parahippocampal gyral volume of three control subjects. The patient initially presented with a severe global amnesia, but across four subsequent memory testing sessions over the next 18 months, there was a marked, but

differential, recovery of memory abilities. Unlike the bilateral hippocampal patient of Kroll et al. (1996) and more like YR, DF's recognition of intra-item associations was relatively good even four to six months following his hypoxic episode and appeared normal when 10–15 months had passed since his brain injury. His recognition of items (in comparisons of studied and new items) as well as his recognition of intra-item associations was less impaired than his recall of words and spatial associations. These forms of recall also recovered little over the 18 months following the hypoxic episode, whereas recognition did. Unfortunately, recombination recognition tests were not used to test spatial association recognition, the other kinds of different information associative recognition used with YR, or recognition of same item associations so direct comparisons with YR are difficult.

Nevertheless, the data from DF are of interest because they indicate that a patient with relatively (but certainly not completely) selective bilateral hippocampal damage suffered in adulthood can show relatively preserved item and intra-item associative recognition, but impaired recall and spatial memory similar to YR. So there are at least two cases of relatively late onset hippocampal damage that show a pattern of memory impairment similar to that of Vargha-Khadem et al.'s (1997) patients. The pattern cannot, therefore, always result from re-organization of function following an early lesion. DF did show some improvement in memory over the 18 months following his lesion. YR may have shown a similar pattern of initial improvement, but we were unable to test for this possibility because we began testing her many years after her initial brain damage when her memory condition was stable. When improvement occurs in adulthood, it is most likely to reflect physiological recovery rather than the re-organization of brain functioning although some degree of strategic adaptation to impairment may have played a minor role.

## CONCLUSION

In summary, YR, a patient with relatively selective hippocampal damage, showed good recognition not only of items, but also of intra-item associations and associations between items of the same kind, but a clear impairment not only of recall, but also of recognition of associations between different kinds of information. These results suggest that YR's intact neocortex and MTLC (and particularly her perirhinal cortex) mediate her preserved familiarity memory not only for unitized representations of items, but also for nonunitized representations of associations between items of the same kind. Consistent with a modification of Norman and O'Reilly's model (2003, the results also suggest that familiarity memory may not support recognition of different information associations because their components only fully converge for memory processing in the hippocampus. This structure is critical for recall of briefly studied information including recollection of different information associations.

However, evidence about hippocampal memory deficits is conflicting. Resolution requires that control subjects and a series of patients with relatively selective hippocampal lesions are tested in exactly the same way on a battery of well-controlled and matched recognition, familiarity, and recollection (and where appropriate recall) tests of memory for studied items as well as intra-item, similar item, and different information associations. The tests should, for example, be relatively easy with a large and similar number of SDs between the control subjects' mean score and chance so that there is an equal opportunity for patients to show large deficits. It will be critical to identify not only extent of hippocampal damage (see Mayes et al., 2002) and, where possible, its location (Small et al., 2000), but also extent of extrahippocampal damage/dysfunction, particularly in the MTLC, in these patients. Progress will depend on showing that patients have similar memory deficits unless there is evidence of extra-hippocampal damage/dysfunction, reorganization of brain function or development of effective mnemonic strategies. If this is achieved, it becomes possible to identify with confidence the effects of different extents/kinds of hippocampal damage on different kinds of associative memory. Future work should also clarify the different information/same item association and unitized/nonunitized distinctions by exploring how these forms of memory are supported by recollection and/or familiarity following brief study in normal subjects. Functional MRI could be used to determine whether associative versus nonassociative encoding of different information components will only activate the hippocampus, whereas such contrasted encoding of pairs of items of the same kind will also activate the perirhinal cortex, as our interpretation implies.

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