Differential spatial memory impairment after right temporal lobectomy demonstrated using temporal titration

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Summary
In this study a temporal titration method to explore the extent to which spatial memory is differentially impaired following right temporal lobectomy was employed. The spatial and non-spatial memory of 19 left and 19 right temporal lobectomy (TL) patients was compared with that of 16 normal controls. The subjects studied an array of 16 toy objects and were subsequently tested for object recall, object recognition and memory for the location of the objects. By systematically varying the retention intervals for each group, it was possible to match all three groups on object recall at sub-ceiling levels. When memory for the position of the objects was assessed at equivalent delays, the right TL group revealed disrupted spatial memory, compared with both left TL and control groups (P < 0.05). MRI was used to quantify the extent of temporal lobe resection in the two groups and a significant correlation between hippocampal removal and both recall of spatial location and object name recall in the right TL group only was shown. These data support the notion of a selective (but not exclusive) spatial memory impairment associated with right temporal lobe damage that is related to the integrity of the hippocampal functioning.

Keywords: spatial memory, temporal titration, right temporal lobectomy

Abbreviations: ANCOVA = analysis of covariance; NART-R = National Adult Reading Test—revised; TL = temporal lobectomy

Introduction
Studies in which the function of the mesiotemporal lobe region in primates were investigated confirm a major role for this region in episodic memory. In non-human primates, lesion studies suggest that the most important structures are the hippocampus, the entorhinal cortex, the parahippocampal cortex and the perirhinal cortex (Zola-Morgan et al., 1986; Squire et al., 1990; Squire, 1992; Alvarez et al., 1995). In humans, large bilateral lesions affecting these structures cause profound global amnesia (Scoville and Milner, 1957), but moderate memory impairment has also been observed when lesions are confined mainly to the hippocampus (Press et al., 1989; Squire et al., 1990).

In contrast, unilateral temporal lobe lesions do not produce a full amnestic syndrome, but have specific effects on verbal, visual and spatial memory functioning (Smith, 1989). Studies of patients following unilateral temporal lobectomy (TL), an operation involving removal of the hippocampus, amygdala and surrounding structures, indicate that the left temporal lobe contributes to performance on tasks requiring verbal learning and memory (Corsi, 1972; Smith and Milner, 1981; Petrides, 1985), whilst the right temporal lobe is implicated in tasks requiring memory for items that are difficult to verbalize, such as visuospatial material (Corkin, 1965; Milner, 1965; Smith and Milner, 1981, 1989; Jones-Gotman, 1986a, b; Goldstein et al., 1989; Kesner et al., 1992; Piggot and Milner, 1993; Morris et al., 1995a, b; Feigenbaum et al., 1996; Abrahams et al., 1997). Prevalent amongst the deficits seen following right TL are those that are primarily spatial in nature (see Schacter and Nadel (1991) for a review). Consistent with this, in other species the hippocampal formation also appears to be strongly implicated in spatial memory functioning, as postulated by O’Keefe and Nadel’s cognitive mapping theory (O’Keefe and Nadel, 1978; O’Keefe, 1991). In humans it has been proposed that the right hippocampus specifically is responsible for the computation and storage of spatial information (O’Keefe and Nadel, 1978; Abrahams et al., 1997).
Evidence for a specific spatial memory impairment comes from a series of studies investigating memory for location. In a landmark study, Smith and Milner (1981) directed patients with either right or left TL to name and estimate the price of 16 toy objects arranged in various locations on a blank sheet of paper. Immediately following price estimation, subjects were tested on object recall, object recognition and recall of object location, assessed via the subjects’ reconstruction of the array. Both the right and left TL patients showed normal object name recall; however, the right TL group showed a selective impairment in recall of object location. Testing was repeated after a 24 h delay. At this time point a different pattern of results emerged: both left and right TL groups were impaired in the recall of object names; however, the right TL group was again the only group to show disrupted memory for item location. Moreover, the spatial deficit demonstrated by the right TL group was contingent upon the radical excision of the hippocampal region and was severe even in the immediate condition. These data suggest that memory for the spatial location of items is disproportionately impaired relative to memory for the items themselves in right TL patients. Subsequent studies have confirmed the existence of the spatial location deficit in this group of patients, using either similar techniques (Smith and Milner, 1989; Pigott and Milner, 1993) or paradigms designed to test allocentric, or view-independent spatial memory (Feigenbaum et al., 1996; Abrahams et al., 1997).

Whilst spatial memory impairment appears to be specific to the right hippocampal formation in humans, deficits following right TL in other aspects of memory, for example, object recall and visual recognition memory (Smith and Milner, 1981, 1989; Morris et al., 1995a, b; Abrahams et al., 1997), do not suggest an exclusive role (Morris et al., 1996). Although the same neuronal structures may be supporting more than one type of memory functioning, it is not clear in humans to what extent they rely on dissociated systems within the same structures. For example, is spatial memory a separate system utilizing the same neuronal architecture, or an example of a broader class of declarative memory that happens to be more heavily represented in the right hemisphere? The presence of ‘place cells’ in the rodent hippocampus (e.g. O’Keefe and Dostrovsky, 1971) and view-independent cells in the non-human primate brain (e.g. Feigenbaum and Rolls, 1991) supports the suggestion of a separate processing system operating in the same neuronal structures. On the other hand, it is possible to model the spatial ‘properties’ of hippocampal neurons within the framework of a domain-general computational structure, rather than one that is pre-organized for spatial information processing (McClelland and Goddard, 1996). In humans, at least, the right hemisphere appears to be dominant in relation to spatial memory, suggesting some differentiation.

In this study a temporal titration method was used to differentiate spatial from other forms of memory within the right unilateral TL group. With this method, the retention interval is varied systematically between groups to match performance on one type of memory function (in this case, object recall and recognition) with a subsequent test for a deficit in another memory type (here, spatial location). This technique has been used previously to explore spatial memory in global amnesia (with presumed bilateral lesions). Cave and Squire (1991) used a modification of the Smith and Milner (1981) paradigm in which amnesiacs were tested at 5 min and compared with controls tested after a 3–5 week delay. In this case, object recall was matched between the two groups following titration, but they were also found to be matched on spatial location memory.

### Aims

In the current study, a modified version of the Smith and Milner (1981) task was used in both left or right temporal lobectomy patients. Following Cave and Squire (1991), object recall memory was matched between patient and control groups by titrating the retention interval between groups. In this experiment, however, the more mild memory impairment on object recall meant that the relative retention intervals when comparing the different groups were of the same order of magnitude (1–3 h), an important factor when comparing memory function (Mayes et al., 1991; Squire, 1992). In the patients used, approximately the anterior two-thirds of the hippocampus was removed. Using structural MRI it was possible, however, to measure natural variations in the size of the operation in order to investigate whether spatial memory impairment was sensitive to the degree of hippocampal removal. Accordingly, anatomical rating of five divisions of the temporal lobe were undertaken and the subsequent measurements correlated with memory performance.

### Method

#### Subjects

The study included 38 patients who had undergone a unilateral TL at the Neurosurgical Unit, Maudsley Hospital, London, UK, for the treatment of intractable complex partial epilepsy. These consisted of 19 left TL and 19 right TL patients. The standard en bloc resection (Falconer, 1971) was conducted. This involves removal of between 5.5 and 6.5 cm of temporal lobe tissue from the anterior pole in the posterior direction, with relative sparing of the superior temporal gyrus in the language dominant hemisphere. Additional mesiotemporal structures are removed, including the amygdala and approximately the anterior two-thirds of the hippocampus.

The patients were seen at a minimum of 6 months post-operatively. Any subject with a National Adult Reading Test—revised (NART-R; Nelson and Willison, 1991) predicted IQ of less than 85 was excluded, as was any subject under the age of 16 or over 60 years of age. The time since operation, age of onset of epilepsy and post-operative seizure...
Table 1 Subject characteristics

<table>
<thead>
<tr>
<th></th>
<th>LTL (N = 12)</th>
<th>RTL (N = 11)</th>
<th>CON (N = 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/female</td>
<td>8/11 (67%)</td>
<td>10/9 (91%)</td>
<td>8/8 (100%)</td>
</tr>
<tr>
<td>Handedness (right)</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Mean age (SD)</td>
<td>30 (9)</td>
<td>34 (9)</td>
<td>32 (11)</td>
</tr>
<tr>
<td>NART-R</td>
<td>100</td>
<td>106</td>
<td>102</td>
</tr>
<tr>
<td>Mean time since operation (SD)</td>
<td>4 (3)</td>
<td>5 (4)</td>
<td>–</td>
</tr>
<tr>
<td>Mean time since onset of regular seizures (SD)</td>
<td>7.3 (3)</td>
<td>11.6 (9)</td>
<td>–</td>
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<tr>
<td>Engel seizure frequency</td>
<td></td>
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<tr>
<td>Class I</td>
<td>12</td>
<td>11</td>
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<td>Class II</td>
<td>5</td>
<td>4</td>
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<td>Class III</td>
<td>2</td>
<td>4</td>
<td>–</td>
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<tr>
<td>Class IV</td>
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RTL = right temporal lobectomy; LTL = left temporal lobectomy; CON = normal control. Age and time variables are reported in years.

The performance of the patients was compared with a group of 16 normal controls, who were screened to exclude cases with psychiatric and/or neurological disorders. The age and IQ exclusion criteria adopted with the patients was used. Overall, they were matched with the patients for age, sex ratios, handedness and estimated NART-R intelligence (see Table 1). One-way analyses of variance confirmed that no significant differences existed between the groups on any of these measures.

All subjects gave informed written consent for both neuropsychological testing and scanning. Ethics approval for the project by the Ethical Committee (Research), St George’s Hospital, London.

Materials

The test was based on one described by Smith and Milner (1981) and subsequently employed by Cave and Squire (1991). The test objects comprised 16 small toys (bucket, chair, pair of mugs, trousers, shoes, car, sewing machine, picture, bag, vase, keyboard, waistcoat, ghetto-blaster, clock, frying pan, table lamp), with one additional practice item (table). A sheet of paper 60 cm square was used as the background upon which they were placed. Before testing the toys were distributed on the paper background with the constraint that they should be evenly but pseudorandomly distributed such that there was no obvious relationship between neighbouring objects. A different spatial arrangement of the objects was used for each subject. Figure 1 shows one such arrangement of the toys on the paper. For the purpose of subsequent measurement, the position of each toy was lightly outlined on the paper.

Procedure

Initially the array of test objects was covered, with only the practice object revealed in the foreground. The subjects were sat facing this arrangement and given the test instructions. They were told that the procedure tested their ability to estimate prices, and they would estimate the average real price of objects represented by the toys. They had to name each object and give a corresponding price value. A pencil was provided for them to point to the toy they were naming, but they were told not to touch the objects during the test. The subjects then tried this procedure with the practice object. Prompting was given, if necessary, until it was clear that the subject understood the instructions.

The array of 16 toys was then revealed, and the subjects asked to name and price each toy in any order. The experimenter corrected any name that was not the same as that on the recognition test (see below). They were prompted or slowed such that they all spent approximately 10 s looking at each toy. When all 16 toys had been evaluated, the array was covered. The experimenter gave no hint that there would be any further testing. Following a scheduled delay, however, three retention tests were administered. Both of the TL groups had shorter delays than the normal controls, since delayed object name recall is sensitive to both left and right temporal lobectomy (Smith and Milner, 1981). However, since left TL subjects have been shown to be more impaired in terms of object name recall than right TL subjects (Smith and Milner, 1981), the delay for the left TL group in the present study was shorter (1 h) than that for the right TL group (2 h). The controls were tested after 3 h.

Following the retention interval, there were three tests of memory function.

(i) Object recall, in which the subjects had to write down the names of as many toys that they could remember within a period of 3 min. The measure used was the total number of items recalled correctly.

(ii) Recognition memory, in which a written recognition test was administered, for which the name of each target item was presented visually in combination with three distractor items. The distractors were real-world objects, similar to the target objects. Subjects were required to underline the target name. The measure used was the total number of target items selected.

(iii) Spatial memory, in which the subjects were given a new background sheet of paper and the 16 toys. They had to place the toys in the same positions as they had been in during the price estimation task. The location of each of the toys was outlined in pencil once the task had been completed, for subsequent measurement. Here the method was adopted, following Smith and Milner (1981, 1989) and Cave and
J. A. Nunn et al.

Squire (1991), which involved measuring the absolute distance between the location of each toy at the time of the price estimation task and the location in which it was subsequently placed by the subject during the spatial recall test. To achieve this, the two pieces of paper showing the positions of the objects were superimposed in the same orientation. Straight-line distances between the centres of each object were then measured and averaged.1

Determination of baseline spatial recall
Following Cave and Squire (1991), a group of 19 healthy control subjects [mean age (SD) = 28 (6)] participated in an additional control condition to determine baseline (chance level) performance in the spatial memory task. Subjects were given the 16 toys and a fresh 60 cm sheet of paper and simply asked to place the toys on the paper in any way they chose. No further instructions or explanations were given until the toys had been arranged. Again, the locations of each of the toys was outlined in pencil once the task had been completed.

Structural scanning
The patients were scanned using a GE 1.5 Tesla MRI system at St George’s Hospital, London. Sagittal and coronal localizers were constructed using 10 mm slices with a 1 mm interslice gap [TR (recognition time) = 3000 ms; TE (echo time) = 12 ms; FOV (field of vision) = 24 cm]. The main coronal scanning sequence (3D SPGR: TR = 35 ms; FOV = 20 cm; flip = 35°) covered the length of the brain anteriorly–posteriorly with 128 1.5 mm contiguous slices. The coronal plane was established by tilting the head of the subject and ensuring orientation using the localizing scans. The brain was oriented such that the coronal plane was at right angles to the approximate plane of the hippocampus anteriorly–posteriorly.

Structural measurement
The MRI scans were used to provide an estimate of the extent of resection of various sectors of the temporal lobe, the differences between patients relating to natural variations in the accuracy of the operation. The MRIs were downloaded on to a SUN network system for inspection using ANALYZE software (Robb and Barillot, 1989).

A development of the 20 compartment model of the temporal lobe (Awad et al., 1989) was used in the resection evaluation, in order to determine the extent of resection of various sectors of the temporal lobe. A series of 29 slices were selected, covering the length of the hippocampus on the non-operated side (total length 4.5 cm). These were then split into five regions within the temporal lobe as follows: (i) superior lateral, corresponding to the region of the superior temporal gyrus, with the lower boundary the superior temporal sulcus; (ii) inferolateral, including the middle temporal and lateral portion of the inferotemporal gyrus; (iii) basal, including the mesial inferotemporal gyrus and fusiform gyrus;
(iv) parahippocampal, covering the parahippocampal gyrus region; (v) hippocampal, the region of the hippocampal formation, including the subiculum. Regions i–iii were identified systematically using a radial division technique as illustrated in Fig. 2. This technique (developed for the purposes of this study) involved taking the 1.5 mm image slice just posterior to the last slice showing amygdala tissue on the unoperated side.

A central point was then positioned just above the middle portion of the white matter tract in the temporal stem. A horizontal line was then drawn in the lateral direction. A further line was drawn from the central point so that it passed through the neck of the collateral sulcus. The angle between the horizontal and collateral sulcus lines was bisected by a further line. Next, a mirror image of these lines was constructed across the midline, in the operated hemisphere, with the same y coordinate for the central point and the same horizontal distance from the midline. The superior lateral region was defined as tissue above the horizontal line and below the region of the sylvian fissure. The inferolateral region was between the horizontal and the bisection line. The basal region was the region between the latter and the collateral sulcus line. The positions of the parahippocampal and hippocampal regions were judged by eye, by comparison with the unoperated side.

Each region was then rated in terms of the integrity of the neuronal tissue using the following scoring system: 0, total resection/no hippocampal tissue present; 1, a partial resection; 2, predominantly intact; and 3, intact/all tissue present. For rating 1 at least one-third of the tissue had to be missing; otherwise, if there was clear tissue alteration, but less than one-third, it was rated as 2.

A total score for each region was obtained by summing the ratings from each of 30 slices (total length = 4.5 cm). Thus, for example, complete sparing in any region would be rated 90 (rating of 3 multiplied by 30 slices), whilst complete resection would be rated 0. In practice, the rating scale is set so that a middle range score represents a substantial lesion.

The scans for all of the patients were rated by the second author (F.J.X.G.), a further nine were rated by the fourth author (R.G.M.). The criteria for rating were discussed in detail beforehand, followed by independent ratings. Pearson correlation coefficients were calculated to ascertain the inter-rater reliability of the ratings for the total score computed for each measure. The correlations were all above 0.97 and highly significant in each case.

**Statistical analysis**

All analyses were performed using SPSS for Windows. The two memory measures, object name recall and spatial recall, were analysed using an analysis of covariance (ANCOVA). Correlational analyses used Spearman’s rank coefficient because of the non-interval nature of the temporal lobe resection data.

**Results**

**Object recall and recognition**

Figure 3 shows mean percentage correct recall and recognition of the objects. All three groups (left TL, right TL and controls) were matched on recall at sub-ceiling levels, by the technique of manipulating delays. The three groups also appeared to be matched in terms of recognition scores; however, given the very high level of performance (c. 96%) a ceiling effect may be masking real differences in recognition performance, and statistical analyses were not performed on the recognition data.

**Spatial recall**

The recall of location was measured by the mean absolute displacement of the objects. The question of interest was whether the spatial memory performance of the right TL group was the same as that of the control group, who were tested after a longer delay (3 h) than either the right TL group (2 h) or the left TL group (1 h). As demonstrated in Fig. 4, right TL patients were much worse at recalling spatial location than either the left TL or control groups. The mean baseline score (chance level) obtained by subjects who had simply placed the objects on the background sheet without having seen them previously was 24.3 cm. Thus, all groups were more accurate than by chance alone.

**ANCOVA**

An ANCOVA was conducted to compare the group means on spatial recall with the object recall measure used as a covariate. Groups differed significantly \( F(2,50) = 6.33, P = 0.004 \). As there were three pairwise comparisons, we used the more stringent significance level of 0.01 for these comparisons. The right TL group differed significantly from the left TL group \( t(50) = 3.32, P = 0.002 \) and control group \( t(50) = 2.71, P = 0.009 \), whilst the left TL and control groups did not differ significantly \( t(50) = 0.48, P = 0.634 \). The standard ANCOVA assumes the slope of the relationship between the covariate and the dependent variable is the same for each group (see Wright, 1997). A separate slope was fitted to the data for each group, but this did not improve the fit significantly \( F(2,48) = 1.07, P = 0.351 \).

A one-way ANCOVA of spatial memory with age at test, age at onset of regular seizures and NART-R scores as covariates was also conducted to ensure that the observed spatial deficit in the right TL group was not confounded with these variables. The main effect of covariates was not significant \( P > 0.05 \).

**Lesion analysis**

The mean score for the different regions (superior lateral, inferolateral, basal, hippocampal and parahippocampal) are given in Table 2. The mean rating for each of the five regions...
Fig. 2 Representative right TL patient and compartmentalization of representative 1.5 mm MRI slices using the ANALYZE program. The sequence shows every sixth slice. The radial segmentation is explained fully in the text: within the temporal lobe and in the anticlockwise direction there exists (i) the superiorlateral; (ii) inferolateral; (iii) basal; and (iv) mesiotemporal segments. The same radial segmentation was used across the temporal lobe to measure intactness of structures (see Method for details).
**Fig. 3** Recall and recognition memory performance for the left (LTL) and right (RTL) unilateral temporal lobectomy groups, compared with the control (CON) group. Error bars represent standard deviations.

**Fig. 4** Spatial memory performance measured in terms of the mean absolute displacement of the objects for the left (LTL) and right (RTL) unilateral temporal lobectomy groups, compared with the control (CON) group. Error bars represent standard deviations.

**Table 2** Mean temporal lobe excision ratings

<table>
<thead>
<tr>
<th></th>
<th>LTL (n=19)</th>
<th>RTL (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SL (SD)</td>
<td>27 (9.2)</td>
<td>29.9 (15)</td>
</tr>
<tr>
<td>Range</td>
<td>7–44</td>
<td>11–65</td>
</tr>
<tr>
<td>IL (SD)</td>
<td>16.6 (9.6)</td>
<td>20.5 (12)</td>
</tr>
<tr>
<td>Range</td>
<td>0–32</td>
<td>2–41</td>
</tr>
<tr>
<td>Basal (SD)</td>
<td>11 (6.5)</td>
<td>12.7 (8.4)</td>
</tr>
<tr>
<td>Range</td>
<td>0–20</td>
<td>2–32</td>
</tr>
<tr>
<td>Hippocampal (SD)</td>
<td>2.9 (3.3)</td>
<td>3.5 (4.7)</td>
</tr>
<tr>
<td>Range</td>
<td>0–11</td>
<td>0–16</td>
</tr>
<tr>
<td>Parahippocampal (SD)</td>
<td>6 (4.7)</td>
<td>10.8 (9.3)</td>
</tr>
<tr>
<td>Range</td>
<td>0–17</td>
<td>0–37</td>
</tr>
</tbody>
</table>

Note that the lower the rating the greater the amount of tissue removed. The scale ranges between 90 (complete sparing) and 0 (complete lesion across region). SL = superior lateral; IL = inferolateral; RTL = right temporal lobectomy; LTL = left temporal lobectomy.

reflects quite large removals, since even the highest ratings (and therefore the smallest removals) were just under 30, which would correspond to a 'partial resection' for the region in question.

A series of Mann–Whitney U tests showed that there were no significant differences between the two patient groups in terms of the extent of resection in any of the regions (all P > 0.05). See Fig. 5 for an illustration of a sequence of coronal slices covering the hippocampal region.

The total scores for the five temporal lobe regions were then correlated against the visual and spatial recall measures for the two separate groups. Thus, 20 correlations were performed in total. For the right TL group, two significant correlations were found: firstly, between the extent of resection in the hippocampus and spatial recall (r = −0.58, P < 0.05); second, between the degree of resection in the hippocampus and object name recall (r = 0.51, P < 0.05). The negative association shows that larger hippocampal resection was associated with greater spatial memory impairment, as measured by absolute displacement. The positive correlation shows that larger hippocampal resection was associated with less object recall. No significant correlations were revealed between the degree of resection in other temporal lobe subdivisions and measures of object and/or spatial recall. We suggest caution in interpreting these multiple correlations. A stricter significance level could have been used, but because of the small numbers of subjects, we maintained the significance level at 0.05. Otherwise the probability of a Type 2 error would have been too high.

For the left TL group no significant correlations were found between any memory measure and the degree of resection in any temporal lobe subdivision. Figure 6 shows scatter plots of right and left hippocampal excision ratings and spatial recall.

**Discussion**

The present study was designed to assess whether memory for spatial location was disproportionately impaired following unilateral TL, and whether any deficit could be related to the amount of tissue removed in the temporal lobe, particularly the hippocampal region. Normal control subjects and both TL groups were matched on object name recall, a non-spatial task, by the technique of temporal titration (manipulating the retention interval). The right TL group subsequently demonstrated a larger deficit in terms of spatial recall than would have been expected given their level of object memory performance. This deficit was significant compared to both left TL and control mean group performance. A feature of the current study was the use of a recall format for both the object name and spatial memory tests, which obviates the difficulty in interpretation that arises if visual recognition is compared with spatial recall, due to the different sensitivities of the two formats.

The correlations between the extent of temporal lobe resection and behavioural data showed an association between recall of spatial location and the degree of excision in the hippocampus in the right TL group. An association was also found in this group between the amount of hippocampal tissue removal and object name recall. No significant...
Fig. 5 MRI sequence covering the whole of the hippocampus on the operated side and illustrating the remaining hippocampus on the other side for a representative right TL patient. The coronal sequence includes every third 1.5 mm thick slice.
Fig. 6 Scatter plots of right (top) and left (bottom) hippocampal excision ratings and spatial recall in terms of mean displacement (cm). Right hippocampal excisions and spatial recall were negatively correlated ($r = -0.58$, $P < 0.05$). Left hippocampal excisions and spatial recall were not significantly correlated.

correlations were observed in the left TL group between any temporal lobe region and any behavioural measure.

The results of the present investigation confirm and extend the findings of Corsi (1972), Rains (1981) and Smith and Milner (1981) by showing, firstly, a selective deficit in right TL subjects during the recall of spatial location, and second, a correlation between right hippocampal removal and both spatial and object name recall. The finding of a correlation between right hippocampal removal and spatial recall mirrors the results of several studies at the Montreal Neurological Institute, where ‘small’ versus ‘large’ hippocampal removal has also been shown to be related to spatial memory impairment, for example, on the Smith and Milner (1981, 1989) spatial task. Differences in technique, however, mean that the results are not entirely comparable. Whereas in the present study the measurement technique exploited natural variations in the extent of removal within the same type of operation, in the Montreal studies, hippocampal lesions are classed as small if the hippocampus is spared entirely or if the removal does not exceed the pes hippocampus. Large hippocampal lesions are those in which the removal extends beyond the pes into the main body of the hippocampus or the corresponding part of the hippocampal gyrus. In the current study, all the patients would be categorized as having ‘large’ hippocampal lesions under the Montreal scheme, since approximately the anterior two-thirds was removed.

The lack of a correlation between either spatial location or object name recall and other TL regions suggests that the hippocampus, rather than other, adjacent temporal lobe regions, may be critical for normal memory performance. This idea contrasts with findings from studies using non-human primates which have implicated the parahippocampal region in memory. For example, lesions of the parahippocampal gyrus and perirhinal cortex (which together can be viewed as an interface between the sensory cortices of the brain and the hippocampal formation), but sparing the hippocampus and amygdala, produce severe memory impairments in monkeys (e.g. Zola-Morgan et al., 1989; for reviews, see Mishkin and Murray, 1994; Murray, 1996). Importantly, because the parahippocampal and perirhinal lesion produced more severe impairment than a lesion involving the hippocampal formation and parahippocampal cortex [the ‘selective’ hippocampal lesion of Zola-Morgan et al. (1989)], and at least as severe an impairment as that observed following lesions of the hippocampal formation, amygdaloid complex and surrounding cortices (Zola-Morgan and Squire, 1985), the perirhinal lesion does not simply disconnect areas significant for memory. Furthermore, because the perirhinal cortex is the only component of the perirhinal lesion that is not included in the selective hippocampal lesion, the more severe impairment associated with the perirhinal lesion indicates that the perirhinal cortex itself must make an important contribution to memory function.

Perhaps the critical role of the perirhinal cortex (which is completely removed in the en bloc resection) is responsible for the lack of correlation between the right parahippocampal gyrus and memory and spatial memory function. However, Bohbot et al. (1997) have recently shown that three patients with selective lesions of the right parahippocampal gyrus were impaired on a spatial navigational task. The discrepancy between the present results and that of Bohbot et al. (1997)
may be explicable in terms of the different nature of the two tasks: whereas Bobbot et al. (1997) assessed allocentric spatial memory, we assessed egocentric spatial memory.

Non-temporal areas may also contribute to object and location memory. The deficits observed on these tasks in diencephalic amnesiacs show that these object and location tests are not specifically sensitive to hippocampal damage (Cave and Squire, 1991). Moreover, converging evidence suggests that the parietal lobes are a possible site for the encoding of spatial location. Damage to this area results in deficits on a variety of spatial tasks, and has been interpreted as the loss of comprehension of the overall spatial framework of a group of objects and their allocentric properties (Butters et al., 1972; Ratcliff and Newcombe, 1973; Levine et al., 1985). A number of pathways between the parietal lobes and the hippocampus have been identified (e.g. Jones and Powell, 1970; Seltzer and Pandya, 1976). From studies on non-human primates, Ungerleider and Mishkin (1982) suggest that memory for a location occupied by a particular object requires the association of the separately stored representations of object and place in temporal and parietal cortex, respectively, and that the hippocampus is the structure that mediates this association.

Although the spatial memory impairment is selective for the right TL group, this does not mean that this group are exclusively impaired on spatial memory. Previous studies have shown impairments in non-spatial tasks, including object recall and visual recognition memory. Indeed, in the current experiment, the right TL group showed a correlation between hippocampal excision and object name recall. This suggests that the right hippocampus is involved in the delayed retrieval of visual information to mediate verbal recall, corroborating the results of Jaccarino (1975) and Smith and Milner (1981).

This finding also ties in neatly with Jones-Gotman and Milner's (1982) report of the contribution of the right temporal lobe to image-mediated verbal learning. In addition, it confirms extant reports of visual memory deficits in right TL patients (Rains, 1981; Morris et al., 1995a, b; Abrahams et al., 1997) by demonstrating that the right hippocampus is not exclusively involved in spatial operations. This is in contrast to O'Keefe and Nadel's (1978) cognitive mapping hypothesis, which holds that in humans, the right hippocampus specializes in the computation and storage of spatial information. Nevertheless, the finding is consistent with the notion put forward in relation to both animals and humans that the hippocampus plays a disproportionately large role in spatial memory (Parkinson et al., 1988; Ono et al., 1991; Morris et al., 1996).

Object name recall may be non-lateralized because objects undergo dual encoding, forming both a verbal and visuospatial memory trace of the item (Paivio, 1971; see also Abrahams et al., 1997). Such dual encoding may not be relevant for the spatial recall task, so that spatial memory may depend solely on the right hippocampal region. As the left medial temporal lobe structures were intact in the right TL patients, this could explain why object recall was less disrupted than spatial recall in this patient group. If so, it remains possible that bilateral hippocampal lesioned patients [such as those reported by Press et al. (1989) and Squire et al. (1990)], might be equally impaired at object recall and spatial recall. To eliminate this possibility with right TL patients, one would have to compare spatial recall with another kind of non-verbal memory that is not disrupted in left TL patients.

Relevant to this line of thinking is the question of whether the left TL patients are unimpaired on the spatial recall task. A conclusion to this question cannot easily be derived from the results of the present study, because the left TL group was tested after 1 h compared with 3 h for the control group. However, Smith (1989), in a review of the relevant literature, suggests that left TL patients are not impaired on a variety of visuospatial tasks, and other studies of spatial memory conducted with the same patient sample as ours (e.g. Abrahams et al., 1997) show normal memory for spatial information in left TL patients.

A *prima facie* anomaly can be seen in the data for the right TL group: that group showed an impairment in spatial recall but not in recall for object names. However, significant correlations of performance with removal from the right hippocampus were found for both memory measures. Reconciling these findings prompts the possibility that the right TL group were in fact impaired at object recall names (although not as much as for spatial recall), but this does not show up because of the titration method (the right TL group were tested after 2 h and controls after 3 h). Other data obtained for the same population of patients indicate that the right TL group may well be impaired at object recall: on a different task, right TL patients were impaired on object recognition when performance was assessed without the use of the titration method (Abrahams et al., 1997). If the right TL group were impaired on object recall in the present study, then the significant correlation is consistent with the lesion.

To what extent does the deficit in spatial memory observed in the right TL group translate into spatial memory impairment in everyday life? On the face of it, in percentage terms the memory displacement in the right TL group relative to the controls is not huge. However, it may be that the spatial configuration within a small array provides sufficient cueing to minimize the observed deficit on the task. Alternatively, the real impairment is small in these patients and therefore phenomenologically less meaningful. One way to explore this issue further would be to compare the extent of deficit shown on this type of task with self-report of everyday memory loss (Goldstein and Polkey, 1992; Ivnik et al., 1993) or performance on naturalistic tasks in which the patient has to navigate a novel environment (Maguire et al., 1996).

No correlation was observed in the left TL group between any temporal lobe region and object name recall. One might have been expected given that Smith and Milner (1981) found deficits on this task in their left TL patients. However, deficits in object name recall seemed to be unrelated to the degree of hippocampal removal; patients with either small or large hippocampal excisions showed impairments (Smith et al., 1997) assessed allocentric spatial memory, we assessed egocentric spatial memory.
and Milner, 1981). It appears that removal of the temporal neocortex alone is sufficient to cause a deficit. Perhaps any damage to the left temporal lobe produces a deficit; if that were the case, correlations would not reveal a relationship.

The main finding in the present study, namely that in right TL patients memory for the location of objects was worse than memory for the objects themselves, despite controlling for the problem of differential sensitivities of the tasks to overall memory impairment, is consistent with other studies of amnesia in which dissociation of spatial from other forms of memory with the aid of the matching procedure have been attempted (Mayes et al., 1991; Shoqeirat and Mayes, 1991; MacAndrew and Jones, 1993) with one notable exception (Cave and Squire, 1991). The latter researchers used the same task, but applied it to patients with either bilateral hippocampal or diencephalic damage, and as a consequence of the more severe memory deficits associated with global amnesia, titrated delays between the presentation of the material and the test varied from 5 min (amnesiacs) to between 3 and 5 weeks (controls). Their results showed an equivalent impairment of spatial and non-spatial memory in amnesiacs. It is probable that discrepancies between these studies relate to the gross differences in the delays used between studies. In the Cave and Squire (1991) study, the amnesic patients were tested after 5 min, and compared with controls tested after 3–5 weeks. Although it has been suggested that information may be stored in the hippocampus for several years (Nadel, 1991), it is likely that following long delays information may be retrieved from neocortical sites rather than the hippocampus (Squire, 1992). Thus, the information processing demands for controls and amnesiacs may be different when there is a significant differential in delays. In this context it is interesting to note the contrasting results of Shoqeirat and Mayes (1991) who used a shorter retention interval in their amnesic patients. They achieved matching in an object recognition memory task by using increased exposure for the amnesiacs and found a differential impairment in memory for the spatial location of the same objects.

The current findings can be considered in relation to declarative/relational theories of hippocampal-based memory, which do not differentiate between memory systems across modalities (Squire and Cohen, 1979; Squire, 1982; Squire, 1992; Cohen and Eichenbaum, 1993). Squire and his co-workers favour an associationist explanation of hippocampal function, which focuses on the acquisition of information about the relationships among stimuli. On the basis of memory performance following well-defined limbic or diencephalic lesions, these theorists have discriminated between ‘declarative memory’ (semantic and episodic memory: ‘knowing that . . . ’) and ‘procedural memory’ (skilled performance: ‘knowing how . . . ’), the former mediated by temporal lobe structures, notably the hippocampus, the latter by diencephalic regions, chiefly the thalamus (Squire et al., 1990). According to this view deficits in spatial memory represent an example of a broader impairment in declarative memory, with the same physiological substrate as other types of long-term memories.

Whilst part of the same neuronal architecture, as would be suggested by the associationist view, the present results indicate that long-term spatial episodic memory is dissociable even within the same temporal lobe. This is consistent with physiological studies of non-humans, where ‘place cells’ in rodents and ‘allocentric’ cells in non-human primates have been observed (e.g. O’Keefe and Dostrovsky, 1971; Feigenbaum and Rolls, 1991), indicating specialized function within the hippocampus. As in non-human research, however, it seems that the right hippocampal formation is not exclusively involved in spatial operations; rather, the findings, in keeping with previous investigations of patients with unilateral TL, suggest a differential involvement.

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