PERGAMON

Neuropsychologia 37 (1999) 829–841

NEUROPSYCHOLOGIA

A cognitive activation study of memory for spatial relationships☆

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Received 22 September 1997; accepted 8 October 1998

Abstract

Twelve neurologically normal right-handed subjects were asked to remember the locations of eight representational drawings, presented one at a time, together with two landmarks (white squares), on a computer screen. Subjects were then scanned using positron emission tomography (PET) while performing forced-choice recognition of object location in four conditions, using either the original landmarks or two of the other objects as cues. In two conditions, the absolute location of the objects was unchanged from the time of encoding (fixed-array conditions), whereas in the other two, the location of the objects was shifted, although the spatial relationship among the objects and landmarks was maintained (shifted-array conditions). Subjects were also scanned in a control condition that made the same perceptual and motor demands as the recognition tasks but that had no mnemonic component. Compared to the control condition, all of the recognition tasks activated both the dorsal and ventral visual pathways bilaterally, but with notable asymmetries. In particular, activation in the right, but not left, inferior temporal gyrus (area 37) was observed when both shifted-array conditions were compared to their respective cue-matched fixed-array conditions. The recognition conditions with landmark cues were associated with focal increases in regional cerebral blood flow (rCBF) in the region of the right parahippocampal gyrus. The results support previous reports of involvement of the right mesial temporal region in object-location memory tasks, and suggest that right inferotemporal cortex is involved in extracting the invariant relational features of a visual scene.

Keywords: Frontal lobe; Hippocampal formation; Positron emission tomography; Temporal lobe; Visual pathways

1. Introduction

Being able to remember where things are in the world is crucial to the survival of many species. In particular, many kinds of rodents and birds depend on memory for object locations in order to solve ecologically important problems. It is not surprising that, in such species, a relatively large proportion of their brain mass is devoted to a structure that appears largely responsible for this type of memory: the hippocampus. For example, female cowbirds of some brood-parasitic subspecies must remember the location of potential host nests so that they can return, often days later, to lay their eggs. Such female cowbirds have larger hippocampi, on average, than conspecific males, and brood-parasitic cowbirds of both sexes have relatively larger hippocampi than non-brood parasitic cowbirds [52, 56]. Similarly, studies of food-storing behaviour in perching birds demonstrate a link between hippocampal size and the degree to which individual species rely upon memory for the location of scattered food caches [5, 6, 17, 22, 23]. Furthermore, hippocampal damage in food-storing birds impairs memory for the location of caches, although it does not interfere with caching behaviour itself [57]. In rats, spatial memory deficits are consistently observed after hippocampal lesions [33, 38, 43, 45, 51] and, in both rats and monkeys, many neurons in this region exhibit firing patterns that appear to reflect the spatial layout of a learned environment [24, 42–44, 49, 53, 54]. Lesion work in monkeys has shown that both bilateral hippocampectomy and transection of the fornix impair aspects of memory for object-place associations [14, 15, 47].

In human subjects, deficits in the recall of the location of familiar objects have been demonstrated after right anterior temporal-lobe resection, and this impairment is to some degree dependent upon extensive removal of the hippocampus and/or the parahippocampal gyrus [1, 9, 59–61]. No such deficits have been observed after left

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0028-3932/99/$ - see front matter
PII: S0028-3932(98)00136-5

anterior temporal-lobe resection, even when the procedure includes a radical excision of the hippocampus. Smith and Milner [59, 61] for example, tested subjects for their recall of object position after exposure to a spatial array of discriminable objects. Compared to neurologically intact subjects and patients with left temporal-lobe removals, patients with right temporal-lobe removals that encroached extensively upon the hippocampal formation had difficulty replacing the objects in their correct positions, after both short (4 min) and long (24 h) delays. No differences in group performance were evident at zero delay. Notably, the impairment in the right temporal-lobe lesioned patients was manifested in both a greater-than-average displacement of each object from its original position (its absolute position), and in an impaired recall of each object's position relative to its neighbours (its relative position).

Blood-flow activation studies provide corroborative evidence for preferential right-hemisphere involvement in various processes involving spatial memory, including memory for object location [29, 39, 46] and for topographical information [2, 30]. In these studies, activation in the right hippocampal/parahippocampal region has been observed more consistently during encoding conditions than during tests of recall or recognition (but see [46]). In a similar fashion, the results of another recent study suggest that the hippocampal region is more strongly activated when a subject views novel complex visual scenes, as compared to familiar ones [65]. Thus, the hippocampus and parahippocampal gyrus appear to be more involved in the encoding of new spatial-location information than in the retrieval of more familiar material.

Nevertheless, activation in the hippocampal/parahippocampal region is apparent during retrieval tasks under some conditions. Owen et al. [46] demonstrated a significant increase in cerebral blood flow in the right parahippocampal gyrus (entorhinal cortex) in a condition involving recognition of previously learned locations of particular objects on a computer screen, compared with a condition involving recognition of previously learned locations alone (without object information). Thus, this anterior region of the parahippocampal gyrus appears to play a role in the retrieval of information that links object to place. This is consistent with studies in non-human primates that implicate entorhinal cortex in memory for objects and locations [40], and that demonstrate selective responding of cortical units in this region to objects, locations, or a combination of both [54, 62]. Although significant activation was not observed in the hippocampus itself in this subtraction, it is still possible that the right hippocampus is critically involved in spatial memory. Both of the tasks used by Owen et al. [46] involved spatial memory, and thus both may have caused increases in rCBF in the hippocampus proper, which would not be evident in the subtraction. In fact, since memory for spatial-location is so biologically important, the hippocampus may be tonically active, continuously registering spatial-location information at an optimal level (see also [13, 19, 32]). Indeed, it has been postulated that spatial-location information is automatically encoded ([18, 31], but see [41]). Activation in the hippocampus may only be evident in conditions where the processing and memory loads on the hippocampus are greater than normal. Previous work with patients has suggested that the right mesial-temporal-lobe region is involved in organizing and integrating spatial information that is broken down at encoding [26], and this feature was incorporated into our tasks.

The present study is an elaboration of the Owen et al. [46] study, in which, again, we required subjects to retrieve information about the location of objects on a computer screen. The array of objects was encoded prior to scanning, but since the objects were presented one at a time, subjects never saw the entire array of objects as a whole. Using this method, we were able to examine retrieval of object-location under several conditions that varied in their spatial processing demands. In one condition, we 'moved' the array around the screen, so that subjects were required to recognize object-location on the basis of relative, rather than absolute, position cues. In another, we used a novel combination of stimulus items as cues for object-location recognition. A third condition combined both these two factors, and a fourth was formally identical to the one used in the previous study (Owen et al. [46]) and did not include either manipulation. Activation in each of the retrieval conditions was compared to activation in a visuomotor control condition that involved similar visual stimuli and motor responses but required minimal memory for spatial information. It was predicted that the right anterior parahippocampal gyrus would be involved in all retrieval conditions, consistent with previous studies [1, 46, 59–61]. Furthermore, by including a visuomotor control task, we were able to test the hypothesis that activation in the hippocampus itself would be evident when the retrieval conditions were compared to a task with minimal mnemonic requirements. Finally, we were able to examine the effects of increasing the spatial processing demands of the retrieval tasks on medial temporal-lobe activation.

2. Methods

2.1. Subjects

Six male and six female right-handed undergraduate volunteers with no history of neurological or psychiatric illness participated in the study. Each subject underwent five 60 s PET scans within a single session and a magnetic resonance imaging (MRI) scan on a different day. The ages of the subjects ranged from 18–33 years (mean age = 22.5 years). All subjects gave informed, written

consent for participation in the study after its nature and possible consequences had been explained to them. The study was approved by the Research and Ethics Committee of the Montreal Neurological Institute and Hospital.

2.2. Stimulus materials and procedure

The stimuli used in all five experimental conditions were digitized black and white representational drawings of common objects (brush, cake, glasses, bowl, candle, butterfly, hen, and bow), 5×5 cm in size, presented against a black background. In addition, there were two 'landmarks' (featureless white squares of the same dimensions as the object drawings) presented close to the centre of the screen (Fig. 1a). The stimuli were shown on a high resolution, touch-sensitive screen (39×29 cm), which was suspended approximately 50 cm above the subject and was therefore within comfortable reach.

2.2.1. Encoding

Approximately 10 min before the first scan, subjects learned the object-locations that they would be subsequently asked to recognize. The eight object drawings were presented, one at a time, each in its unique location on the screen. The four corners of the monitor were never used as object locations. Each drawing was presented together with the two 'landmarks', which maintained constant positions (Fig. 1b). The subjects were instructed to attend to each object as it appeared, to note its location relative to the two landmarks, and then to touch it. When an object drawing was touched, it disappeared, and the next object appeared 1 s later. The entire set of eight objects was shown four times, the order of presentation being randomized within each block of eight. The same object-locations were used for all subjects across all conditions, although the order in which the stimuli were presented was randomly varied across subjects.

After the encoding condition, subjects were scanned in

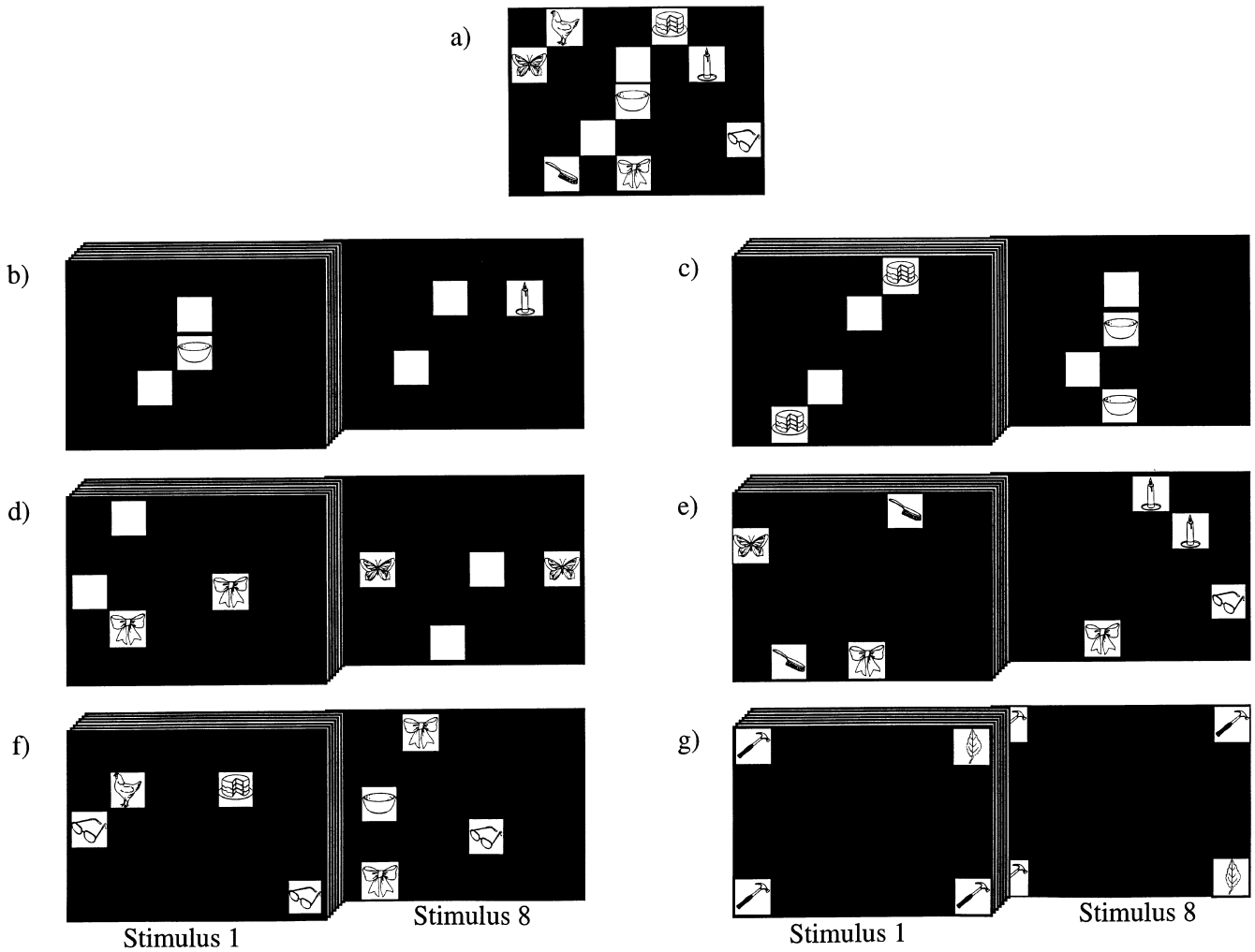

Fig. 1. Schematic drawings of the complete stimulus-landmark array, and of representative stimuli seen in each of the conditions. (a) The complete stimulus-landmark array. Note that subjects never saw the array in its entirety as presented here. (b) Encoding Object-Locations (10 min prior to first scan); (c) Retrieval of Fixed-array Location, Using Landmark Cues; (d) Retrieval of Shifted-array Location, Using Landmark Cues; (e) Retrieval of Fixed-array Location, Using Object Cues; (f) Retrieval of Shifted Array Location, Using Object Cues; (g) Visuomotor Control.

four recognition conditions and in the *Visuomotor Control* condition. The order in which these five tasks were performed across scans was randomized across subjects. Performance of each task began approximately 10 s before the onset of scanning. All subjects completed the same fixed number of trials in each condition, the performance lasting for approximately 90 s in total. Accuracy and latency data were collected throughout this task-performance period. Successive scans were separated by approximately 10 min, during which time the requirements of the next were explained to the subject. Subjects were instructed not to dwell too long on any particular stimulus during the scan (because each stimulus would be presented more than once), and to maintain a constant response rate of approximately one touch per second.

2.2.2. Retrieval of fixed-array object location, using landmark cues (fixed array with landmarks)

Eight pairs of stimuli were presented on the computer screen for forced-choice recognition, one pair at a time (Fig. 1c). Both stimuli were identical to one of the eight object drawings presented before scanning. Each pair of stimuli was presented together with the two white landmarks, which were placed in identical positions to those used during the pre-scanning encoding condition. For each pair of stimuli, one of the locations was identical to that occupied by that particular object in the encoding condition and the other location had been occupied by one of the other seven objects. Subjects were asked to touch the object in its correct location. Since none of the locations was novel, the choice had to be made on the basis of object-location, not on the basis of location alone. Immediately following a touch, both squares disappeared and the next pair was presented 1 s later. No feedback about accuracy of responding was given. The series of eight pairs was presented four times during the task-performance period, the order of presentation being randomized within each block of eight.

2.2.3. Retrieval of shifted-array object location, using landmark cues (shifted array with landmarks)

The procedure for this condition was identical to that for the condition described above, except that the array composed of the eight object drawings and the landmarks effectively shifted position from trial to trial, although all the individual elements maintained their spatial relationship to each other. Thus, the two landmarks moved to new positions on the screen each time a new pair of stimuli was presented for recognition, and subjects were asked to choose the correct object-location relative to the landmarks. The new array positions were chosen so that both of the forced-choice stimuli, although in previously learned locations relative to the landmarks, were in novel locations relative to the borders of the screen (Fig. 1d).

2.2.4. Retrieval of fixed-array object location, using object cues (fixed array with objects)

In this condition, the position of the array composed of the eight objects was held constant. As in the two retrieval conditions previously described, eight pairs of identical objects were successively presented on the screen and subjects were asked to touch the object in its correct location. In this case, the landmark cues were never visible. Instead, two other objects in their proper array positions were presented as cues. These cue objects changed from trial to trial (Fig. 1e).

2.2.5. Retrieval of shifted-array object location, using object cues (shifted array with objects)

As in the condition just described, two objects from the array were presented as cues to object locations, but this time the array composed of the eight objects shifted position from trial to trial (as in *Shifted array with Landmarks*). The cue objects were again different for each forced-choice recognition pair (Fig. 1f).

2.2.6. Visuomotor control

Two object drawings were used in this condition (a leaf and a hammer). On each trial, one leaf drawing and three hammer drawings were presented, one in each of the four corners of the screen. The subjects were instructed to respond by touching the leaf. Immediately following a touch, the four stimuli disappeared and reappeared 1 s later, randomly rearranged in the corner positions. Thirty-two such trials were presented during the task-performance period (Fig. 1g).

2.3. Scanning methods and data analysis

PET scans were obtained with the Scanditronix PC-2048 system, which produces 15 image slices at an intrinsic resolution of $5.0 \times 5.0 \times 6.0$ mm [11]. Regional CBF was measured by means of the bolus $H_2{}^{15}O$ method [50]. PET images were reconstructed using an 18-mm Hanning filter and normalized for global CBF value. A high-resolution MR image (160 contiguous 1 mm thick sagittal slices) was also obtained for each subject (Philips Gyroscan 1.5T), and each pair of MR and PET data sets was co-registered and resampled into a standardized stereotaxic co-ordinate system [63] by means of an automated feature-matching algorithm [7]. Individual PET subtraction images were obtained by calculating, voxel by voxel, the difference in normalized CBF between two conditions within subjects. The mean subtraction image volume was then obtained for each comparison, and a *t*-value was calculated at each voxel by dividing the mean CBF difference by the standard deviation pooled across all intracerebral voxels [69]. Individual MR images were also averaged, and merged with the averaged PET subtraction images to allow direction localization of regions with high *t*-values.

The presence of significant focal changes was tested by a method based on three-dimensional Gaussian random-field theory [69], which corrects for the multiple comparisons involved in searching across a volume. The threshold for reporting a peak as significant was set at $t = 3.5$ (corresponding to a probability of $P < 0.00046$, two-tailed, uncorrected). Correcting for multiple comparisons, this value yields a false positive rate of 0.69 in 200 resolution elements (each of which has dimensions $18 \times 18 \times 7.7$ mm), which approximates the total volume of cortex scanned. Given that a substantial literature of both lesion and functional imaging studies points to involvement of right mesial temporal-lobe structures in spatial memory processing in humans, we set the threshold for significance at $t = 3.00$ (corresponding to an uncorrected probability of $P < 0.0026$) for activation foci in this region.

3. Results

3.1. Behavioural data

Within-subjects ANOVAs were computed on the accuracy and latency data (see Table 1 for descriptive statistics). All subjects completed the *Visuomotor Control* task perfectly, and therefore data from this scan were not included in the accuracy ANOVA. The ANOVA on accuracy data revealed a significant effect of Scan ($F = 5.19$ (3,33), $P = 0.005$), with scores on the *Shifted array with Objects* task significantly inferior to scores on the other three tasks (post-hoc comparisons: Fs > 5.21 (1,33), Ps $< .03$). Planned weighted comparisons of the Fixed-array conditions with the Shifted-array conditions show that the former were performed significantly better than the latter ($F = 9.93$ (1,33), $P = 0.003$). In contrast, there was no difference between the Landmarks and Objects conditions ($F = 1.33$ (1,33), $P = 0.26$).

In a similar fashion, there was a significant effect of Scan in the reaction-time data ($F = 13.94$ (4,44), $P = 0.0001$). Post-hoc comparisons demonstrate significantly longer latencies in the *Shifted array with Objects* condition than in the other four conditions (Fs > 24.43 (1,44), Ps < 0.0001). Weighted planned comparisons of the Fixed-array tasks with the Shifted-array tasks show that the former were performed significantly faster ($F = 15.59$ (1,44), $P = 0.0003$). Furthermore, latencies were shorter for the Landmarks tasks than for the Objects tasks ($F = 17.98$ (1,44), $P = 0.001$). On average, between 16 and 21 stimulus items were presented across the four retrieval conditions during scanning. On this basis, it seems unlikely that any of the rCBF results can be attributed to a difference in the number of stimulus items presented.

Table 1
Mean accuracy and latency data for the five scanning conditions (± SD)

Condition	Percentage correct	Reaction time (s)
Visuomotor control	100 ± 0	1.65 ± 0.39
Fixed array with landmarks	97.1 ± 3.0	1.79 ± 0.52
Fixed array with objects	98.3 ± 2.7	1.87 ± 0.32
Shifted array with landmarks	95.6 ± 6.9	1.86 ± 0.39
Shifted array with objects	91.2 ± 7.3[1]	2.79 ± 0.85[2]

[1] Different from all other recognition conditions at Ps < 0.02
[2] Different from all other conditions at Ps < 0.0001.

3.2. Image subtractions

When blood flow in the *Visuomotor Control* condition was subtracted from that in the *Fixed array with Landmarks* condition (Table 2), a significant change was observed in an area of the right parahippocampal gyrus close to the hippocampus itself (Fig. 2a). No significant rCBF change was observed in the corresponding region of the left hemisphere. Other significant rCBF changes were located in the left mid-dorsolateral frontal cortex (Fig. 2b) and in a posterior region of the left inferior temporal gyrus. In addition, changes were observed bilaterally in posterior parietal cortex, the cerebellum, and in visual areas 17 and 18.

When blood flow in the *Visuomotor Control* condition was subtracted from that in the *Shifted array with Landmarks* condition (Table 3), a significant activation focus was observed at the border of the right parahippocampal gyrus and the hippocampus itself (Fig. 3a). Again, no

Table 2
Foci of rCBF change during retrieval of fixed-array location using landmark cues, compared with *Visuomotor control*

Brain region	Stereotaxic co-ordinates			
	x	*y*	*z*	*t*
Left hemisphere				
Middle frontal gyrus (area 8)	−39	17	30	3.73
Fusiform gyrus (area 37)	−43	−52	−17	3.67
Inferior parietal lobule (area 7)	−28	−62	41	5.03
Cerebellar vermis	−4	−68	−30	5.22
Precuneus (area 7)	−1	−74	50	3.94
Lingual gyrus (area 18)	−23	−87	−11	6.20
Cuneus (area 18)	−24	−88	9	3.89
Striate cortex (area 17)	−5	−92	−5	4.60
Right hemisphere				
Right hippocampus/ parahippocampal gyrus	36	−19	−23	3.31
Inferior parietal lobule (area 7)	35	−66	44	6.73
Cerebellar vermis	4	−76	−26	5.59
Lingual gyrus (area 18)	24	−87	−6	3.96
Striate cortex (area 17)	15	−90	5	6.03

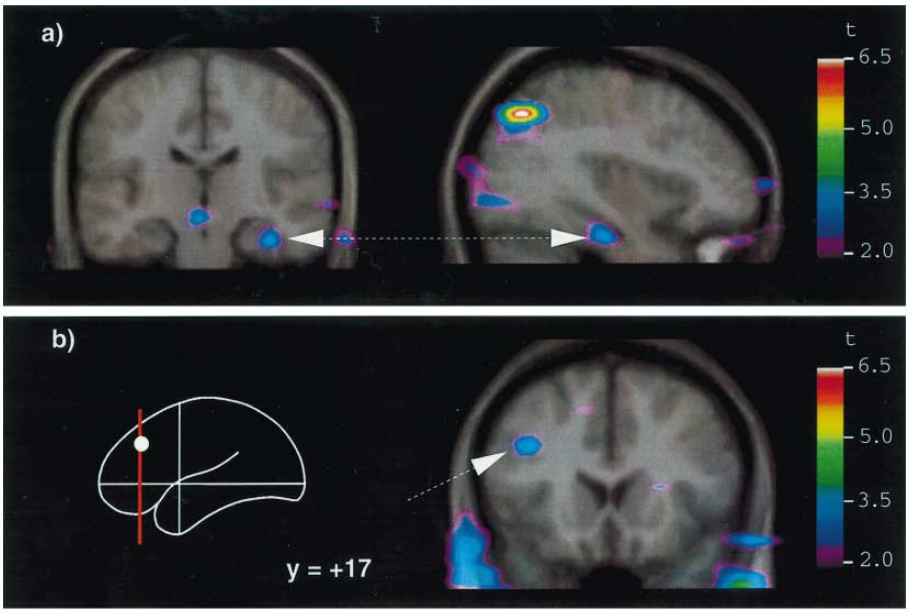

Fig. 2. The averaged PET images of the *Fixed array with Landmarks* minus *Visuomotor Control* subtraction are shown superimposed upon the corresponding averaged MRI scans, transformed into the standardized stereotaxic space of Talairach and Tournoux (1988). Areas of significant increases in blood flow are shown in this *t*-statistic image, whose range is coded by the colour scale placed to the right of the Figure. (a) The coronal section at $y = -21$ and the sagittal section at co-ordinate $x = +36$ illustrate the significant rCBF increase observed in the right parahippocampal gyrus close to the hippocampus. (b) The coronal section at co-ordinate $y = +17$ illustrates the significant rCBF increase observed in the mid-dorsolateral frontal cortex (Brodmann area [BA] 9/46). The intense bilateral activation at the bottom of the image is muscle artefact.

Table 3
Foci of rCBF change during retrieval of shifted-array location using landmark cues, compared with *Visuomotor control*

Brain region	Stereotaxic co-ordinates			
	x	*y*	*z*	*t*
Left hemisphere				
Anterior fusiform gyrus (area 36)	−32	−35	−24	3.88
Fusiform gyrus (area 37)	−44	−52	−17	4.89
Inferior parietal lobule (area 7)	−36	−56	45	5.18
Precuneus (area 7)	−12	−69	39	3.81
Precuneus (area 7)	−1	−74	47	3.60
Cerebellar vermis	−7	−56	−36	4.02
Cerebellar hemisphere	−27	−71	−27	4.59
Lingual gyrus (area 19)	−46	−73	−18	4.67
Lingual gyrus (area 18)	−21	−87	−11	6.25
Cuneus (area 18)	−25	−85	9	5.00
Right hemisphere				
Ventrolateral frontal cortex (areas 47/45)	29	27	0	3.53
Middle frontal gyrus (area 6/8)	36	15	59	3.92
Hippocampus/ parahippocampal gyrus	21	−14	−27	3.54
Inferior temporal gyrus (area 20/37)	51	−42	−12	5.13
Cerebellar vermis	4	−64	−30	4.60
Inferior parietal lobule (area 7)	34	−66	44	8.10
Lingual gyrus (area 18)	11	−78	−12	5.32
Striate cortex (area 17)	13	−88	0	5.38

significant rCBF change was observed in the corresponding region of the left hemisphere. Another significant unilateral activation was observed in right posterior inferior temporal cortex (area 20/37; Fig. 3b). Other significant CBF increases were observed bilaterally in posterior parietal cortex (Fig. 3c), cerebellum, fusiform gyrus and prestriate cortex. Significant foci were also observed in the left anterior fusiform gyrus (medial occipitotemporal gyrus), in right frontal regions, and in primary visual cortex on the right.

The *Fixed array with Objects* minus *Visuomotor Control* subtraction yielded significant foci bilaterally in posterior parietal cortex, cerebellum, fusiform gyrus and prestriate cortex, as in previously discussed subtractions. Activation was also observed in the left medial occipitotemporal gyrus, and in right striate cortex (Table 4).

In the *Shifted array with Objects* minus *Visuomotor Control* subtraction, activation was observed bilaterally in prestriate cortex, continuing ventrally into posterior temporal cortex on the right. This unilateral extension included a focus in the posterior inferior temporal gyrus (area 20/37; Fig. 4a) in a position similar to that seen in the *Shifted array with Landmarks* minus *Visuomotor Control* subtraction. Bilaterally symmetric foci were observed in mid-dorsolateral prefrontal cortex, posterior parietal cortex (Fig. 4b), and in the cerebellar vermis. The right primary visual cortex also yielded significant unilateral rCBF increases (Table 5).

When blood flow in the *Fixed array with Landmarks*

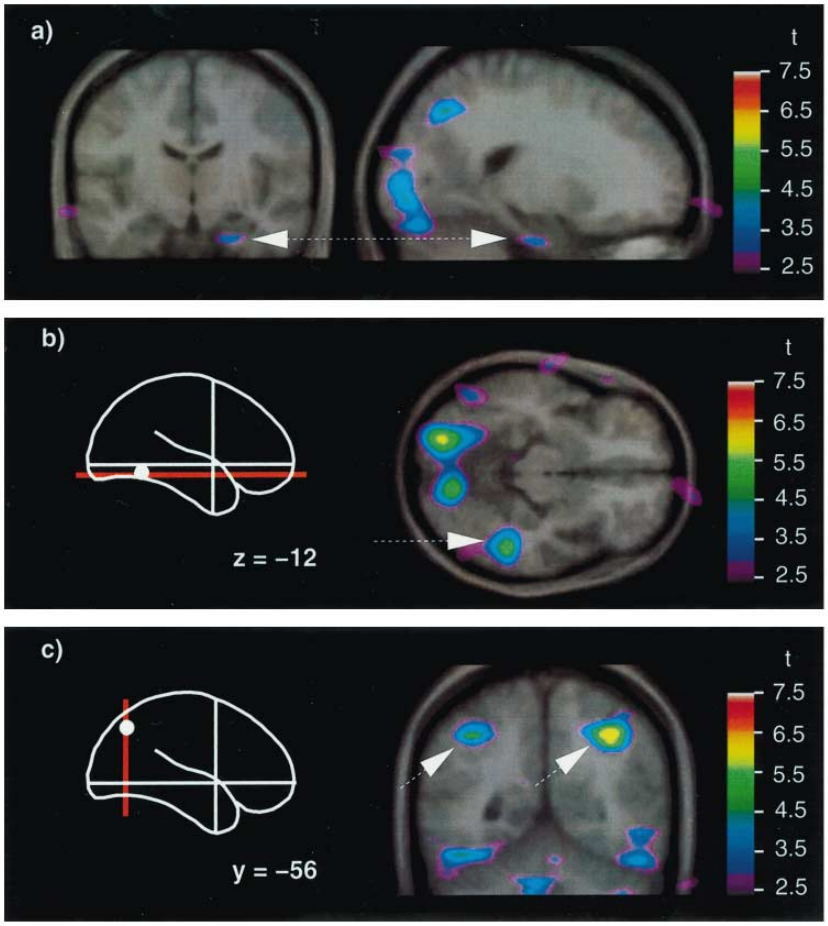

Fig. 3. Significant rCBF increases in the *Shifted array with Landmarks* minus *Visuomotor Control* subtraction. (a) The coronal section at $y = -14$ and the sagittal section at co-ordinate $x = +21$ illustrate the significant rCBF increase observed in the right hippocampus/parahippocampal gyrus. (b) The horizontal section at co-ordinate $z = -12$ illustrates the significant rCBF increase observed in right posterior inferotemporal cortex (BA 37), as well as bilateral activation in prestriate cortex (BA 18). (c) The coronal section at co-ordinate $y = -56$ illustrates bilateral activation along the two visual pathways: dorsally in posterior parietal cortex (area 7) and ventrally in posterior inferotemporal cortex (area 19).

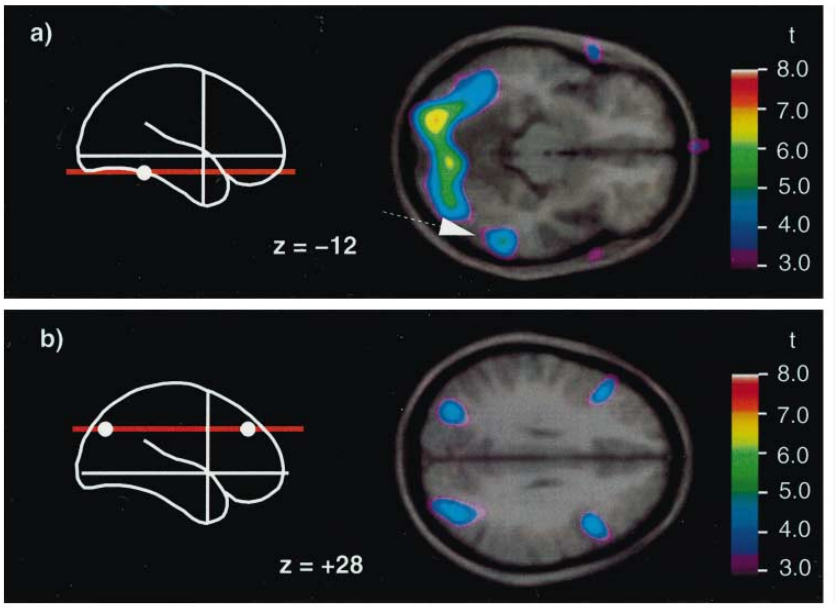

Fig. 4. Significant rCBF increases in the *Shifted array with Objects* minus *Visuomotor Control* subtraction. (a) The horizontal section at co-ordinate $z = -12$ illustrates the significant rCBF increase observed in right posterior inferotemporal cortex (BA 37), as well as bilateral activation in prestriate cortex (BA 18). (b) The horizontal section at co-ordinate $z = +28$ illustrates bilateral activation in posterior parietal cortex (BA 7) and in mid-dorsolateral frontal cortex (BA 9/46).

condition was subtracted from that in the *Shifted array with Landmarks* condition (Table 6), significant focal increases were observed in both cerebellar hemispheres (Fig. 5a). The right posterior inferior temporal cortex (area 37) activation, observed in both Shifted array minus *Visuomotor Control* subtractions, was also evident (Fig. 5b).

The *Shifted Array with Objects* minus *Fixed Array with Objects* subtraction also yielded a significant focus of activation in the right posterior inferior temporal cortex (area 37; Fig. 5c) (Table 7). Activation was also observed bilaterally in frontal regions, and in parietal cortex. Significant blood flow increases in left primary and prestriate cortical regions and the left fusiform gyrus were evident.

With respect to the hypotheses raised in the Introduction, two major findings emerge from these data. The first is unilateral activation centered on the anterior right parahippocampus in at least a subset of the retrieval conditions, notably in the two Landmark–Visuomotor Control subtractions. The second is consistent activation in right area 37 (posterior inferior/middle temporal gyrus) in the two Shifted tasks, compared to their Fixed analogues. We have concentrated on simple one-condition subtractions. However, the four retrieval conditions can also be analysed as a 2×2 factorial design ('Landmarks' vs 'Objects' and 'Shifted' vs 'Fixed'). We include here three supplementary analyses, which are driven in each case by a question deriving from the analysis of simple subtractions. Two of these supplementary analyses exploit the factorial nature of the retrieval conditions.

In order to determine whether the right anterior parahippocampal gyrus is involved in all of the retrieval tasks, we computed a weighted contrast comparing all retrieval tasks against the visuomotor control task. This revealed right posterior temporal and bilateral occipital, parietal and cerebellar activation, similar to that observed in the single comparisons of each of the recognition tasks

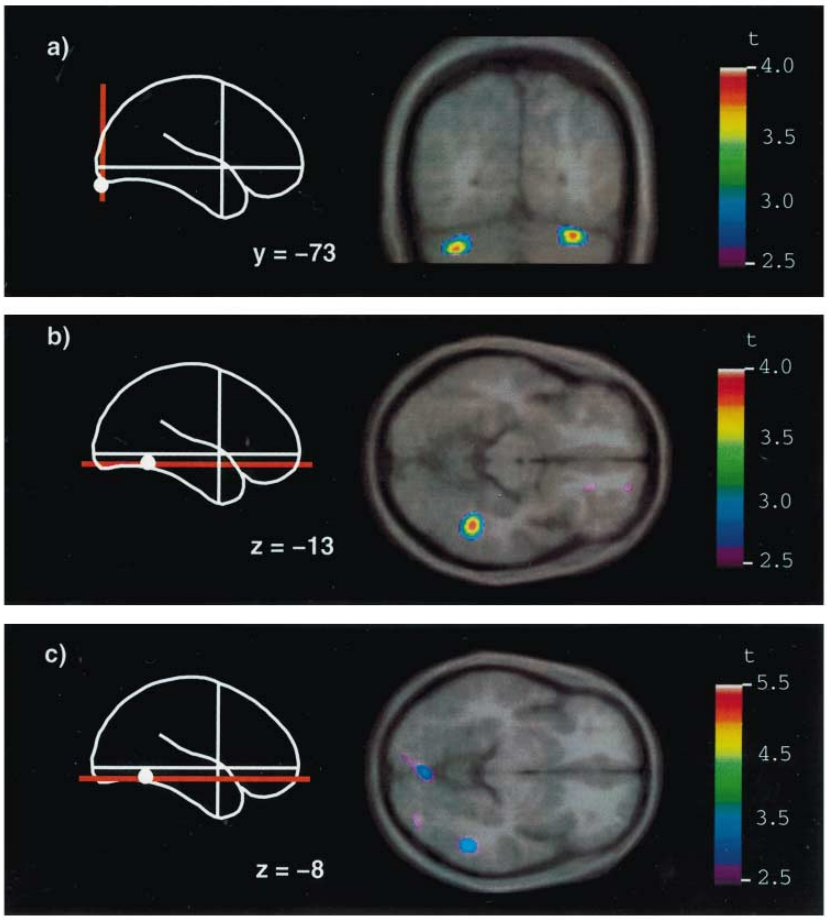

Fig. 5. Significant rCBF increases in the two higher-order subtractions. (a) The coronal section at co-ordinate $y = -73$ illustrates the significant rCBF increase observed bilaterally in the cerebellar hemispheres in the *Shifted array with Landmarks* minus *Fixed array with Landmarks* subtraction. (b) The horizontal section at co-ordinate $z = -13$ illustrates the significant rCBF increase observed in right posterior inferotemporal cortex (BA 37) in the *Shifted array with Landmarks* minus *Fixed array with Landmarks* subtraction. (c) The horizontal section at co-ordinate $z = -8$ illustrates the significant rCBF increase observed in right posterior inferotemporal cortex (BA 37) in the *Shifted array with Objects* minus *Fixed array with Objects* subtraction.

with the control task. In addition, a right anterior parahippocampal focus was observed (co-ordinates $x = 23$, $y = -11$, $z = -29$; $t = 2.89$). This peak is predicted from the Owen et al. [45] study, and so a correction for multiple comparisons is not necessary.

Table 4
Foci of rCBF change during retrieval of fixed-array location using object cues, compared with *Visuomotor Control*

Brain region	Stereotaxic co-ordinates			
	x	*y*	*z*	*t*
Left hemisphere				
Medial occipitotemporal gyrus (area 37)	−34	−45	−20	3.52
Cerebellar hemisphere	−8	−57	−29	4.39
Inferior parietal lobule (area 7)	−29	−66	44	4.53
Medial occipitotemporal gyrus (area 37)	−29	−68	−12	5.12
Lingual gyrus (area 18)	−19	−87	−11	6.28
Cuneus (area 18)	−27	−92	0	5.23
Right hemisphere				
Inferior parietal lobule (area 7)	32	−64	44	4.87
Medial occipitotemporal gyrus (area 37/19)	25	−74	−12	4.89
Cerebellar hemisphere	13	−78	−17	4.55
Striate cortex (area 17)	12	−90	6	6.61
Cuneus (area 18/19)	27	−92	20	4.11

Table 5
Foci of rCBF change during retrieval of shifted-array location using object cues, compared with *Visuomotor control*

Brain region	Stereotaxic co-ordinates			
	x	*y*	*z*	*t*
Left hemisphere				
Mid-dorsolateral frontal cortex (area 9/46)	−42	24	26	4.61
Inferior parietal lobule (area 7)	−38	−54	45	7.08
Inferior parietal lobule (area 7)	−12	−71	45	5.24
Cerebellar vermis	−1	−59	−29	4.28
Cerebellar hemisphere	−16	−76	−24	4.36
Lingual gyrus (area 18)	−34	−69	−17	5.90
Lingual gyrus (area 18)	−3	−85	−5	8.31
Cuneus (area 18)	−27	−88	9	7.23
Right hemisphere				
Middle frontal gyrus (area 8/9)	46	17	30	5.36
Middle temporal gyrus (area 37)	58	−44	−12	5.08
Inferior temporal gyrus (area 19/37)	51	−57	−20	4.05
Inferior parietal lobule (area 7)	32	−64	44	8.89
Inferior parietal lobule (area 7)	8	−68	51	5.73
Lingual gyrus (area 18)	34	−76	−14	5.42
Cerebellar vermis	4	−76	−30	5.23
Cuneus (area 18)	27	−88	21	5.03
Striate cortex (area 17)	12	−90	2	7.34

Table 6
Foci of rCBF change during retrieval of shifted-array location using landmark cues, compared with retrieval of fixed-array location using landmark cues

Brain region	Stereotaxic co-ordinates			
	x	*y*	*z*	*t*
Shifted array with landmarks—fixed				
Left hemisphere				
Lateral cerebellar hemisphere	−35	−78	−30	4.17
Right hemisphere				
Posterior middle temporal gyrus (area 37)	44	−45	−14	3.99
Lateral cerebellar hemisphere	29	−73	−23	3.87
Fixed array with landmarks—shifted				
Left hemisphere				
Insula	−38	−4	−9	3.67
Right hemisphere				
Prestriate cortex (area 19)	25	−68	−2	3.67

In examining the main effects of type of cue (Landmarks versus Objects) and array position (Shifted versus Fixed), we were motivated by the following questions: one, is right anterior parahippocampal activation significantly greater for Landmarks than for Objects? Two, is the right posterior temporal (area 37) peak evident in the Shifted conditions compared to the Fixed conditions? The weighted contrast comparing Landmarks tasks to Objects tasks yielded right medial orbitofrontal (area 11), right posterior inferior temporal (area 37) and bilateral anterior middle frontal (area 11) activation. No significant activation in the region of the right parahippocampal gyrus was observed. Thus, although the Landmarks tasks activated the anterior right parahippocampal region significantly compared to the control condition and the Objects tasks did not, the Landmarks tasks are not different from Objects tasks with respect to the magnitude of parahippocampal activation.

The weighted contrast comparing Shifted tasks to Fixed tasks yielded distributed activation in right parietal cortex (area 7/40), peaks in right middle frontal gyrus (area 8/9), right orbitofrontal cortex (area 11), right cerebellum, left inferior parietal lobule (area 7), left parahippocampal gyrus and left fusiform gyrus (area 20/36). In addition, as predicted, an activation focus was observed in right posterior temporal cortex (area 37: co-ordinates $x = 50, y = -49, z = -9; t = 4.16$). There was no significant activation in the right parahippocampal region.

4. Discussion

The main aim of the present investigation was to examine retrieval of object location under different spatial

Table 7
Foci of rCBF change during retrieval of shifted-array location using object cues, compared with retrieval of fixed-array location using object cues

Brain region	Stereotaxic co-ordinates			
	x	*y*	*z*	*t*
Shifted array with objects—fixed array				
Left hemisphere				
Mid-dorsolateral frontal cortex (area 9/46)	−44	27	21	3.87
Superior frontal gyrus (area 8)	−21	1	48	3.51
Supramarginal gyrus (area 39/40)	−44	−54	44	4.69
Inferior temporal gyrus (area 37)	−51	−54	−23	3.88
Precuneus (area 7)	−8	−68	48	3.78
Angular gyrus (area 39)	−35	−69	35	4.28
Striate cortex (area 17)	−9	−92	−3	3.56
Right hemisphere				
Orbitofrontal cortex (area 11)	28	48	−14	4.11
Superior frontal gyrus (areas 9/46)	48	34	24	3.64
Superior frontal gyrus (areas 6/8)	31	8	45	3.77
Mid-dorsolateral frontal cortex (area 9/46)	46	18	30	5.47
Posterior middle temporal gyrus (area 37)	51	−50	−8	3.53
Angular gyrus (area 39)	34	−64	39	4.41
Fixed array with objects—shifted array				
Left hemisphere				
Fusiform gyrus (area 37)	−50	−4	−9	4.19
Superior temporal gyrus (area 22)	−16	−56	−3	3.88
Right hemisphere				
Subcallosal gyrus (area 12/24)	4	10	−9	3.9
Insula	35	−4	12	4.06
Posterior insula	36	−25	3	3.6
Posterior superior temporal gyrus (area 22)	62	−40	9	3.8
Cuneus (area 18)	3	−76	29	4.46

processing demands. We hypothesized that activation in the hippocampus would be more evident when the retrieval task was made more demanding by requiring subjects to compute the spatial relationships among the stimulus items, either by requiring the retrieval of object location on the basis of relative, rather than absolute, position cues as in the Shifted tasks, or by requiring subjects to retrieve object-location on the basis of a novel combination of cue items as in the Objects tasks. Judging from their performance, subjects did find the *Shifted array with Objects* task, incorporating both manipulations, more difficult than the others.

In general, all retrieval tasks yielded similar patterns of blood flow when compared to the control condition. CBF increases were observed bilaterally in prestriate and posterior parietal cortex and in the striate cortex (more consistently in the right hemisphere than in the left) in all four recognition tasks. The weighted contrast comparing all four recognition tasks to the control condition also resulted in a small activation centred in the right anterior parahippocampal gyrus, bordering on the hippocampus. The stereotaxic co-ordinates of this activation focus are 5 mm away from the parahippocampal focus observed by Owen et al. [46] when rCBF during retrieval of object-locations was compared with that during simple location retrieval. This activation reached significance in only a subset of the simple subtractions, namely in those involving recognition on the basis of landmark cues. The stereotaxic co-ordinates of these activation foci were 7 mm (*Shifted array with Landmarks*) and 12 mm (*Fixed array with Landmarks*) away from the focus observed by Owen et al. [46]. These differences in location are not significant, given the resolution of the PET technique used in the current study and that by Owen et al. [46]. Furthermore, given the extensive blurring effected by the filter in this study (18 mm) and the proximity of the peak of activation to the hippocampus, one cannot say whether the right hippocampus was significantly activated during these tasks or not. Conclusions must be limited to the mesial-temporal-lobe region, without more specific anatomical detail. This region appears to be involved in retrieval of object-location information, regardless of whether the retrieval task emphasizes the positions of items relative to a fixed external reference frame (the screen, for example), as in the *Fixed array with Landmarks* task, or emphasizes the locations of items relative to each other (as in the *Shifted array with Landmarks* task).

Right mesial-temporal CBF did not increase disproportionately in the Shifted-array conditions compared to the Fixed-array conditions, or in the Object-cue conditions compared to the Landmark-cue conditions. In fact, the *Shifted array with Objects* task (incorporating both processing-demand manipulations, and which subjects found the most difficult) was not associated with significant blood-flow increase in the right parahippocampal region. Thus, our hypothesis that activation in the region of the hippocampus would increase when the task demands were increased is clearly not supported. These results suggest instead that the location of an object is automatically perceived relative to its surroundings. The spatial interrelationships of items in a visual scene may be automatically computed, providing some constancy to a perpetually shifting field of view. Several studies suggest that relative- and absolute-position tasks yield similar behavioural results [41, 59]. Further support for the automaticity of relative-position computation comes from studies showing that human newborns are able to perceive relative position [4], and that there are hippocampal place cells in the rat that respond to relative-position cues [44, 68].

The foci of CBF-change observed in the hippocampal region in this study contrast in both location and intensity

with the large differences observed in studies of topographical memory [16, 30]. In these studies, subjects were asked either to view [30] or to imagine [16] navigating through highly complex, three-dimensional scenes. In both cases, bilateral activation (more intense on the right) was observed in both parahippocampal and hippocampal regions. These data suggest that visual complexity and three-dimensionality may be required in order to elicit robust hippocampal activation. The functional imaging environment conventionally requires an experimenter to have control over all aspects of stimulus processing, so that task demands can be tightly matched across conditions. This typically leads (as in the present study) to highly simplified analogues of situations encountered in the real world, but the results of the topographical mapping studies mentioned above suggest that such simplification may also de-emphasize the obligatory role of medial temporal-lobe structures in stimulus encoding. If hippocampal activation is the goal, experimenters may have to compromise control over some aspects of the stimulus situation in order to achieve conditions that are more similar to those found in the real world. A promising approach was used recently by Aguirre and colleagues [2] who used functional magnetic resonance imaging to examine topographical memory using a virtual-reality maze. However, despite being three-dimensional, the stimulus environment in this study was homogeneous and many of the characteristics of the maze were learned prior to scanning. This may perhaps explain why these authors did not observe hippocampal activation (see also [30]).

All recognition tasks appeared to activate posterior parietal cortex bilaterally. This area is a component of the dorsal visual pathway, which has been implicated in the perception of spatial location, orientation and movement in lesion and unit-recording studies in monkeys [3, 10, 27, 67]. This area is richly interconnected with dorsolateral prefrontal cortex [48], and coactivation of dorsolateral prefrontal regions was observed, most strikingly when activation during the *Shifted array with Objects* condition was compared to that during *Visuomotor Control*.

All recognition tasks also activated right posterior inferotemporal cortex, a component of the ventral visual processing stream which is implicated in the perception of object identity. Functional activation studies also support the distinction in extrastriate cortex for the perception of objects and their spatial location [8, 20, 21, 39, 66]. Whereas most of the functional imaging studies of the two visual pathways have been perceptual in nature, Moscovitch and his colleagues [39] observed activation in the two visual streams during their PET study of spatial-location and object-identity recognition. They observed relatively greater parietal-cortex activity in the spatial-location recognition condition and relatively greater temporal-lobe activity in the object-identity condition, suggesting that the cortices involved in perception were also engaged by mnestic processes. The results of the current study also support this idea. In the Moscovitch et al. [39] study, activation in the two visual pathways was observed to be predominantly right-sided in both recognition conditions. In the current study, although activation in extrastriate and posterior parietal regions tended to be bilaterally symmetric, comparisons of blood flow during Shifted-array tasks to that during the Fixed-array analogues yielded right posterior inferotemporal foci (Brodmann area 37). Thus, we observe some lateralization of visual memory function within the neocortex. This finding is also consistent with previous studies that demonstrate material-specific memory deficits after right, but not left, anterior temporal-lobe resection [28, 35–37]. The posterior temporal region in which we observe these unilateral activation foci is a visual association area and may be involved in extracting the invariant features of a visual scene, before assembling those features into identifiable objects. Activation in a similar area was observed bilaterally in a recent study of shape-matching using unknown abstract objects [58], and other visual matching tasks yield predominantly right-sided activation in this region [12, 25, 34]. Thus, this area, particularly in the right hemisphere, appears to be involved in the analysis of visual information for the purposes of comparison with an item held in memory. The Shifted-array tasks also yielded frontal activation in the right hemisphere (in both dorsal and ventral regions), whereas the Fixed-array tasks did not. This activation may reflect the working memory processes involved in reorganizing and matching a percept to the stimulus array being held in memory, as would be necessary for accurate performance of the Shifted-array tasks. Furthermore, the lateralization of the results is generally consistent with previous functional blood-flow studies, which demonstrate a preferential involvement of right frontal cortex in retrieving information from memory [39, 55, 64].

Acknowledgements

We thank anonymous reviewers for helpful comments. This work was supported by the McDonnell-Pew Program in Cognitive Neuroscience and by the Medical Research Council of Canada through Grant MT 2624 and a Career Investigatorship award to B. Milner and through Special Project Grant SP-30 (co-ordinator A. Evans). Adrian Owen was supported by a Pinsent-Darwin Research Fellowship, and Joelle Crane was supported by a Medical Research Council of Canada Studentship.

References

[1] Abrahams S, Pickering A, Polkey CE, Morris RG. Spatial memory deficits in patients with unilateral damage to the right hippocampal formation. Neuropsychologia 1997;35:11–24.

[2] Aguirre G, Detre J, Alsop DC, D'Esposito M. The parahippocampus subserves topographical learning in man. Cerebral Cortex 1996;6:823–9.
[3] Andersen RA. Multimodal integration for stable representations of space in the posterior parietal cortex. Philosophical Transactions of the Royal Society, Series B, 1997;352:1421–8.
[4] Antell SE, Caron AJ. Neonatal perception of spatial relationships. Infant Behavior & Development 1985;8:15–23.
[5] Basil JA, Kamil AC, Balda RP, Fite KV. Differences in hippocampal volume among food storing corvids. Brain, Behavior & Evolution 1996;47:156–64.
[6] Clayton NS. The neuroethological development of food-storing memory: A case of use it, or lose it! Behavioural Brain Research 1995;70:95–102.
[7] Collins DL., Neelin P, Peters TM, Evans AC. Automatic 3D intersubject registration of MR volumetric data in standardized Talairach space. Journal of Computer Assisted Tomography 1994;18:192–205.
[8] Courtney SM, Ungerleider LG, Keil K, Haxby JV. Object and spatial visual working memory activate separate neural systems in human cortex. Cerebral Cortex 1996;6:39.
[9] Crane J, Milner B, Leonard G. Spatial-array learning by patients with focal temporal-lobe excisions. Society for Neuroscience Abstracts 1995;21:566.14.
[10] Desimone R, Ungerleider L. Neural mechanisms of visual processing in monkeys. In: Goodglass H, Damasio AR, editors. Handbook of Neuropsychology. Amsterdam: Elsevier, 1989. p. 267–300.
[11] Evans AC, Thompson CJ, Marrett S, Meyer E, Mazza M. Performance characteristics of the PC-2048: A new 15 slice encoded crystal PET scanner for neurological studies. IEEE Transactions on Medical Imaging 1991;10:90–8.
[12] Faillenot I, Toni I, Decety J, Grégoire M-C, Jeannerod M. Visual pathways of object-oriented action and object recognition: Functional anatomy with PET. Cerebral Cortex 1997;7:77–85.
[13] Fletcher PC, Frith CD, Grasby PM, Shallice T, Frackowiak RSJ, Dolan RJ. Brain systems for encoding and retrieval of auditory-verbal memory: An in vivo study in humans. Brain 1995;118:401–16.
[14] Gaffan D, Saunders RC. Running recognition of configural stimuli by fornix transected monkeys. Quarterly Journal of Experimental Psychology 1985;37B:61–71.
[15] Gaffan D, Harrison S. Place memory and scene memory: Effects of fornix transection in the monkey. Experimental Brain Research 1989;74:202–12.
[16] Ghaem O, Mellet E, Crivello F, Tzourio N, Mazoyer B, Berthoz A, Denis M. Mental navigation along memorized routes activates the hippocampus, precuneus and insula. NeuroReport 1997;8:739–44.
[17] Hampton RR, Sherry DF, Shettleworth SJ, Khurgel M, Ivy G. Hippocampal volume and food-storing behavior are related in parids. Brain, Behavior & Evolution 1995;45:54–61.
[18] Hasher L, Zacks RT. Automatic and effortful processes in memory. Journal of Experimental Psychology: General 1979;108:356–88.
[19] Haxby JV. Medial temporal-lobe imaging. Nature 1996;380:669–70.
[20] Haxby JV, Grady CL, Horwitz B, Ungerleider LG, Mishkin M, Carson RI, Herscovitch P, Shapiro MB, Rapoport SI. Dissociation of object and spatial visual processing pathways in human extrastriate cortex. Proceedings of the National Academy of Sciences of the United States of America 1991;88:1621–5.
[21] Haxby JV, Horwitz B, Ungerleider LG, Maisog JM, Pietrini P, Grady CL. The functional organization of human extrastriate cortex: A PET-rCBF study of selective attention to faces and locations. Journal of Neuroscience 1994;14:6336–53.
[22] Healy SD, Krebs JR. Development of hippocampal specialisation in a food-storing bird. Behavioural Brain Research 1993;53:127–31.
[23] Healy SD, Krebs JR. Food storing and the hippocampus in Paridae. Brain, Behavior & Evolution 1996;47:195–9.
[24] Hetherington PA, Shapiro ML. A simple network model simulates hippocampal place fields: II. Computing goal-directed trajectories and memory fields. Behavioral Neuroscience 1993;107:434–43.
[25] Horwitz B, Grady CL, Haxby JV, Schapiro MB, Mishkin M, Rapoport SI. Functional associations among human posterior extrastriate brain regions during object and spatial vision. Journal of Cognitive Neuroscience 1992;4:311–22.
[26] Jones-Gotman M. Memory for designs: The hippocampal contribution. Neuropsychologia 1986;24:193–203.
[27] Karnath H-O. Spatial orientation and the representation of space with parietal lobe lesions. Philosophical Transactions of the Royal Society, Series B, 1997;352:1411–20.
[28] Kimura D. Right temporal-lobe damage: Perception of unfamiliar stimuli after damage. Archives of Neurology 1963;8:264–71.
[29] Köhler S, McIntosh AR, Moscovitch M, Winocur G, Houle S. Functional interactions between human hippocampus and visual cortices related to long-term memory for spatial location and object identity. Society for Neuroscience Abstracts 1996;22:732.5.
[30] Maguire EA, Frackowiak RSJ, Frith CD. Learning to find your way: a role for the human hippocampal formation. Proceedings of the Royal Society of London B 1996;263:1745–50.
[31] Mandler JM, Seegmiller D, Day J. On the coding of spatial information. Memory & Cognition 1977;5:10–16.
[32] Martin A, Wiggs CL, Weisberg J. Modulation of human medial temporal lobe activity by form, meaning and experience. Hippocampus 1997;7:587–93.
[33] McDonald RJ, White NM. Hippocampal and nonhippocampal contributions to place learning in rats. Behavioral Neuroscience 1995;109:579–93.
[34] McIntosh AR, Grady CL, Ungerleider LG, Haxby JV, Rapoport SI, Horwitz B. Network analysis of cortical visual pathways mapped with PET. Journal of Neuroscience 1994;14:655–66.
[35] Milner B. Visual recognition and recall after right temporal-lobe excision in man. Neuropsychologia 1968;6:191–209.
[36] Milner B. Hemispheric specialization: Scope and limits. In: Schmitt FO, Worden FG, editors. The Neurosciences: Third Study Program. Boston: M.I.T. Press, 1973. pp 75–89.
[37] Milner B. Right temporal-lobe contribution to visual perception and visual memory. In: Iwai E, editor. Vision, Memory, and the Temporal Lobe. New York: Elsevier, 1990. p. 43–53.
[38] Morris RGM, Garrud P, Rawlins JNP, O'Keefe J. Place navigation impaired in rats with hippocampal lesions. Nature 1982;297:681–3.
[39] Moscovitch M, Kapur S, Köhler S, Houle S. Distinct neural correlates of visual long-term memory for spatial location and object identity: A positron emission tomography study in humans. Proceedings of the National Academy of Sciences of the United States of America 1995;92:3721–5.
[40] Murray EA, Gaffan D. Effects of lesions of rhinal cortex, hippocampus, or parahippocampal gyrus in rhesus monkeys on object and spatial reversals. Society for Neuroscience Abstracts 1993;19:186.7.
[41] Naveh-Benjamin M. Coding of spatial location information: An automatic process? Journal of Experimental Psychology: Learning, Memory & Cognition 1987;13:595–605.
[42] O'Keefe, J. Place units in the hippocampus of the freely moving rat. Experimental Neurology 1976;51:78–109.
[43] O'Keefe J, Nadel L. The Hippocampus as a Cognitive Map. Oxford: Clarendon Press, 1978.
[44] O'Keefe J, Speakman A. Single unit activity in the rat hippocampus during a spatial memory task. Experimental Brain Research 1987;68:1–27.

[45] Olton DS, Papas BC. Spatial memory and hippocampal function. Neuropsychologia 1979;17:669–82.
[46] Owen AM, Milner B, Petrides M, Evans AC. A specific role for the right parahippocampal gyrus in the retrieval of object-location: A positron emission tomography study. Journal of Cognitive Neuroscience 1996;8:588–602.
[47] Parkinson JK, Murray EA, Mishkin M. A selective mnemonic role for the hippocampus in monkeys: Memory for the location of objects. Journal of Neuroscience 1988;8:4159–67.
[48] Petrides M, Pandya DN. Projections to the frontal cortex from the posterior parietal region in the rhesus monkey. Journal of Comparative Neurology 1984;228:105–16.
[49] Quirk GJ, Muller RU, Kubie JL, Ranck JB. Jr. The positional firing properties of medial entorhinal neurons: description and comparison with hippocampal place cells. Journal of Neuroscience 1992;12:1945–63.
[50] Raichle JE, Martin WRW, Herscovitch P, Mintun MA, Markham J. Brain blood flow measured with intravenous H_2O^{15}. II. Implementation and validation. Journal of Nuclear Medicine 1983;24:790–8.
[51] Rawlins JNP, Olton DS. The septo-hippocampal system and cognitive mapping. Behavioural Brain Research 1982;5:331–58.
[52] Reboreda JC, Clayton NS, Kacelnik A. Species and sex differences in hippocampus size in parasitic and non-parasitic cowbirds. NeuroReport 1996;7:505–8.
[53] Rolls ET, O'Mara SM. View-responsive neurons in the primate hippocampal complex. Hippocampus 1995;5:409–24.
[54] Rolls ET, Miyashita Y, Cahusac PMB, Kesner RP, Niki H, Feigenbaum JD, Bach L. Hippocampal neurons in the monkey with activity related to the place in which a stimulus is shown. Journal of Neuroscience 1989;9:1835–45.
[55] Shallice T, Fletcher P, Frith CD, Grasby P, Frackowiak RSJ, Dolan RJ. Brain regions associated with acquisition and retrieval of verbal episodic memory. Nature 1994;368:633–5.
[56] Sherry DF, Forbes MR, Khurgel M, Ivy GO. Females have a larger hippocampus than males in the brood-parasitic brown-headed cowbird. Proceedings of the National Academy of Sciences of the United States of America 1993;90:7839–43.
[57] Sherry DF, Vaccarino AL. Hippocampus and memory for food caches in black-capped chickadees. Behavioral Neuroscience 1989;103:308–18.
[58] Smith EE, Jonides J, Koeppe RA, Awh E, Schumacher EH, Minoshima S. Spatial versus object working memory: PET investigation. Journal of Cognitive Neuroscience 1995;7:337–56.
[59] Smith ML, Milner B. The role of the right hippocampus in the recall of spatial location. Neuropsychologia 1981;19:781–93.
[60] Smith ML, Milner B. Differential effects of frontal-lobe lesions on cognitive estimation and spatial memory. Neuropsychologia 1984;22:697–705.
[61] Smith ML, Milner B. Right hippocampal impairment in the recall of spatial location: Encoding deficit or rapid forgetting? Neuropsychologia 1989;27:71–81.
[62] Suzuki WA, Miller EK, Desimone R. Object and place memory in the macaque entorhinal cortex. Journal of Neurophysiology 1997;78:1062–81.
[63] Talairach J, Tournoux P. Co-planar Stereotaxic Atlas of the Human Brain: Three-dimensional Proportional System: An Approach to Cerebral Imaging. Stuttgart: Thieme, 1988.
[64] Tulving E, Kapur S, Craik FIM, Moscovitch M, Houle S. Hemispheric encoding/retrieval asymmetry in episodic memory: Positron emission tomography findings. Proceedings of the National Academy of Sciences of the United States of America 1994;91:2016–20.
[65] Tulving E, Markowitsch H, Kapur S, Habib R, Houle S. Novelty encoding networks in the human brain: Positron emission tomography data. NeuroReport 1994;5:2525–8.
[66] Ungerleider LG, Haxby JV. 'What' and 'where' in the human brain. Current Opinion in Neurobiology 1994;4:157–65.
[67] Ungerleider LG, Mishkin M. Two cortical visual systems. In: Engle DJ, Goodale MA, Mansfield RJW, editors. Analysis of Visual Behavior. Cambridge, MA: MIT Press, 1982. p. 549–86.
[68] Wiener SI, Korshunov VA, Garcia R, Berthoz A. Inertial, substratal and landmark cue control of hippocampal CA1 place cell activity. European Journal of Neuroscience 1995;7:2206–19.
[69] Worsley KJ, Evans AC, Marrett S, Neelin P. A three-dimensional statistical analysis for CBF activation studies in human brain. Journal of Cerebral Blood Flow and Metabolism 1992;12:900–18.