

The Hippocampus Is Required for Short-Term Topographical Memory in Humans

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ABSTRACT: The hippocampus plays a crucial role within the neural systems for long-term memory, but little if any role in the short-term retention of some types of stimuli. Nonetheless, the hippocampus may be specialized for allocentric topographical processing, which impacts on short-term memory or even perception. To investigate this we developed performance-matched tests of perception (match-to-sample) and short-term memory (2 s delayed-match-to-sample) for the topography and for the nonspatial aspects of visual scenes. Four patients with focal hippocampal damage and one with more extensive damage, including right parahippocampal gyrus, were tested. All five patients showed impaired topographical memory and spared nonspatial processing in both memory and perception. Topographical perception was profoundly impaired in the patient with parahippocampal damage, mildly impaired in two of the hippocampal cases, and clearly preserved in the other two hippocampal cases (including one with dense amnesia). Our results suggest that the hippocampus supports allocentric topographical processing that is indispensable when appropriately tested after even very short delays, while the presence of the sample scene can allow successful topographical perception without it, possibly via a less flexible parahippocampal representation. © 2006 Wiley-Liss, Inc.

KEY WORDS: amnesia; short-term memory; long-term memory; perception; spatial; allocentric; cognitive map; aging

INTRODUCTION

Since the case of HM was first described (Scoville and Milner, 1957), the human medial temporal lobe (MTL) has been implicated in the formation of new long-term memories. All forms of consciously accessible long-term memory are at risk from MTL damage (Squire and Zola-Morgan, 1991). Where this includes extensive bilateral damage to the hippocampus, memory deficits are invariably marked by anterograde amnesia for personally experienced events (Spiers et al., 2001c).

Short-term memory (STM) is traditionally assumed to rely on distinct processes from long-term memory (LTM, e.g., James, 1890; Atkinson and Shiffrin, 1971). In terms of neural systems, some neuropsychological patients show spared LTM and impaired STM (Shallice and Warrington, 1970; Warrington et al., 1971; Saffran and Marin, 1975) and others show impaired LTM but spared STM (Drachman and Arbit, 1966; e.g., Baddeley and Warrington, 1970; Milner, 1971; Cave and Squire, 1992; Baddeley and Wilson, 2002). However, these dissociations do not necessarily imply separate neural substrates specialized for short- and LTM per se. In particular, STM performance in different tasks relies on different neural substrates, often reflecting strategic rehearsal or reactivation of domain-specific sensory and motor resources (Baddeley and Hitch, 1974; Baddeley, 1986). Thus, the multiple neural systems supporting STM overlap with those supporting online processing of specific types of stimuli (e.g., speech perception/production or visuospatial sensorimotor control). Similarly, although declarative LTM depends on the MTL (Squire and Zola-Morgan, 1991), the exact role of the hippocampus within this remains the subject of much debate and may not be restricted to LTM. Here we examine the hippocampal contribution to perception and STM, using stimuli explicitly designed to require hippocampal processing on theoretical grounds described below.

Many argue that the unique anatomy of the hippocampus enables the rapid formation of cross-modal associations (Marr, 1971; Teyler and DiScenna, 1986; Damasio, 1989; McClelland et al., 1995), and that this gives it a crucial role in encoding personally experienced events and their context (“episodic memory,” see e.g., Kinsbourne and Wood, 1975; O’Keefe and Nadel, 1978; Gaffan and Hornak, 1997; Vargha-Khadem et al., 1997; Aggleton and Brown, 1999; Yonelinas et al., 2002; Mayes et al., 2004; but see also Squire and Zola, 1998). Related proposals for hippocampal function seek to further constrain the nature of hippocampal processing as encompassing the formation of configural associations between otherwise independent elements (Rudy and Sutherland, 1989, 1995), or of flexible relations between discontinuous stimuli (Wallenstein et al., 1998; Eichenbaum and Cohen, 2001). Here we focus on another such proposal, namely that the hippocampal role in episodic memory evolved out of an ability to support a flexible allocentric representation of environmental spatial relationships or “cognitive map”

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Grant sponsors: MRC, Wellcome Trust, UK.

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Accepted for publication 14 September 2006

DOI 10.1002/hipo.20240

Published online 1 December 2006 in Wiley InterScience (www.interscience.wiley.com).

(O'Keefe and Nadel, 1978), a specifically spatial form of flexible relational processing (Eichenbaum et al., 1999; Eichenbaum and Cohen, 2001). Although this type of representation would be well suited to LTM, for instance, permitting a place to be recognized when later encountered from a novel perspective (Milner et al., 1999; Burgess et al., 2001) or contributing to memory for the spatial context of an event (O'Keefe and Nadel, 1978), it would also imply a role in on-line processing of location and orientation relative to the environment.

Evidence for the concept of an allocentric representation of space in the hippocampus and its inputs comes from neurophysiological experiments showing striking spatial correlates of neuronal firing in freely moving rats. "Place cells" in the hippocampus fire whenever the rat is at a particular location (O'Keefe and Dostrovsky, 1971), as determined by the geometry of the environment (O'Keefe and Burgess, 1996) and regardless of the presence or absence of particular subsets of cues (O'Keefe, 1976; Muller, 1996) or the animal's orientation (at least in open environments, Muller et al., 1994). "Head-direction cells," with a compass-like representation of heading (Taube et al., 1990), and very recently "grid cells," whose firing shows a remarkably regular grid-like spatial pattern (Hafting et al., 2005), have been found in the regions providing input to the rat hippocampal formation. Neurons with similar properties to place cells have now been found in primates (Ono et al., 1991; Rolls et al., 1997; Hori et al., 2003) and in humans (Ekstrom et al., 2003). Neuropsychological experiments have also shown the hippocampus to be specifically required when a flexible or allocentric representation of spatial layout is required. For instance in recognizing object locations when tested from a new viewpoint (Abrahams et al., 1997; Holdstock et al., 2000; King et al., 2002) and in large-scale navigation (Spiers et al., 2001a,b). In addition, functional neuroimaging studies indicate the specific involvement of the hippocampus in accurate navigation (Maguire et al., 1998; Hartley et al., 2003) and allocentric spatial processing (Iaria et al., 2003; Wolbers et al., 2004), while the posterior parahippocampus is involved in perceptual processing of spatial scenes (Epstein and Kanwisher, 1998; Epstein et al., 2003) and landmark recognition (Aguirre and D'Esposito, 1999). Finally, some lateralization of function is indicated by studies of unilateral temporal lobectomy, with right-sided damage specifically impairing spatial tasks such as object-location memory, navigation, and map drawing (Smith and Milner, 1981; Cave and Squire, 1991; Pigott and Milner, 1993; Abrahams et al., 1997; Bohbot et al., 1998; Nunn et al., 1999; Spiers et al., 2001b; see Burgess et al., 2002, for a review). Thus, environmental spatial relationships (or "topography") at the very least provide a particularly clear cut example of stimuli that require processing by the hippocampus.

The hippocampal contribution to processing over short timescales has been investigated previously (see Ranganath and Blumenfeld, 2005 for a brief review). Cave and Squire (1992) examined immediate memory performance on spatial and nonspatial tasks, finding no impairment. Ryan and colleagues (Ryan et al., 2000; Ryan and Cohen, 2004a) investigated the effects of hippocampal damage on implicit memory by monitoring eye movements as participants looked at spatial scenes. Healthy partici-

pants sampled repeated scenes less thoroughly than novel scenes, while showing more intensive sampling of locations in repeated but modified scenes where elements had been added, deleted, or moved. Hippocampal patients showed similar effects after short delays but did not show the increased sampling of modified locations after long delays, indicating impaired implicit LTM (but not STM) for the composition of scenes. However, the stimuli used in these experiments (2D designs and scenes presented from a single point of view) may have allowed successful performance on the basis of visuospatial STM, without requiring access to an allocentric topographical representation in the hippocampus.

Some recent studies have shown impairments in hippocampal patients' memory after brief delays (King et al., 2002, 2004; Holdstock, 2005; Lee et al., 2005a,b; Hannula et al., 2006; Olson et al., 2006). It is notable that the vast majority of these tasks involve the retention of 3D spatial information or of spatial–nonspatial conjunctions. For example, Olson et al. show a deficit in recognition memory for object–location conjunctions but not for either element (object, 2D screen location) tested in isolation. Others show STM deficits in nonspatial tasks (Buffalo et al., 1998; Holdstock, 2005; Olson et al., 2006) in the context of damage to extrahippocampal areas such as perirhinal cortex. A rare exception of a short-term nonspatial impairment in hippocampal patients is provided by Hannula et al. (2006, experiment 2) who show a deficit in face–scene associations. Interestingly, this type of cross-modal context-dependent memory test is thought to be characteristic of episodic recollection, and of longer-term deficits following mild hippocampal damage (Vargha-Khadem et al., 1997; Mayes et al., 2002), and is also an example of relational memory. We return to the possible relationship between topographical, relational, and episodic memory in the discussion.

The nature of the deficit in spatial processing associated with hippocampal damage has also been recently investigated in more detail. Using topographical stimuli (irregularly shaped rooms seen from shifted viewpoints), Lee et al. (2005a) suggest that the human hippocampus plays a specific role in allocentric processing and/or storage over short timescales. They used four-alternative odd-one-out tasks to test perceptual processing for different types of material, finding patients with focal hippocampal damage to be specifically impaired on spatial scene oddity, whereas patients with larger MTL lesions were also impaired on similar tasks using faces and objects. Nonetheless, the proposed specificity of the spatial impairment is compromised by a ceiling effect in the nonspatial conditions, and the proposed role in perception is compromised by the possibility of a memory load in odd-one-out paradigms (in which a large number of pairwise comparisons must be borne in mind). Lee et al. (2005b) also used a learning paradigm to show the need for the hippocampus in processing spatial scenes over short timescales, without conclusively demonstrating an involvement in perception. However, a subsequent study (Shrager et al., 2006) used very similar methods, creating a range of visually similar stimuli (including faces, objects, and scenes) which must be discriminated or matched, but found no evidence of perceptual impairment in patients with focal hippocampal lesions or more extensive MTL lesions.

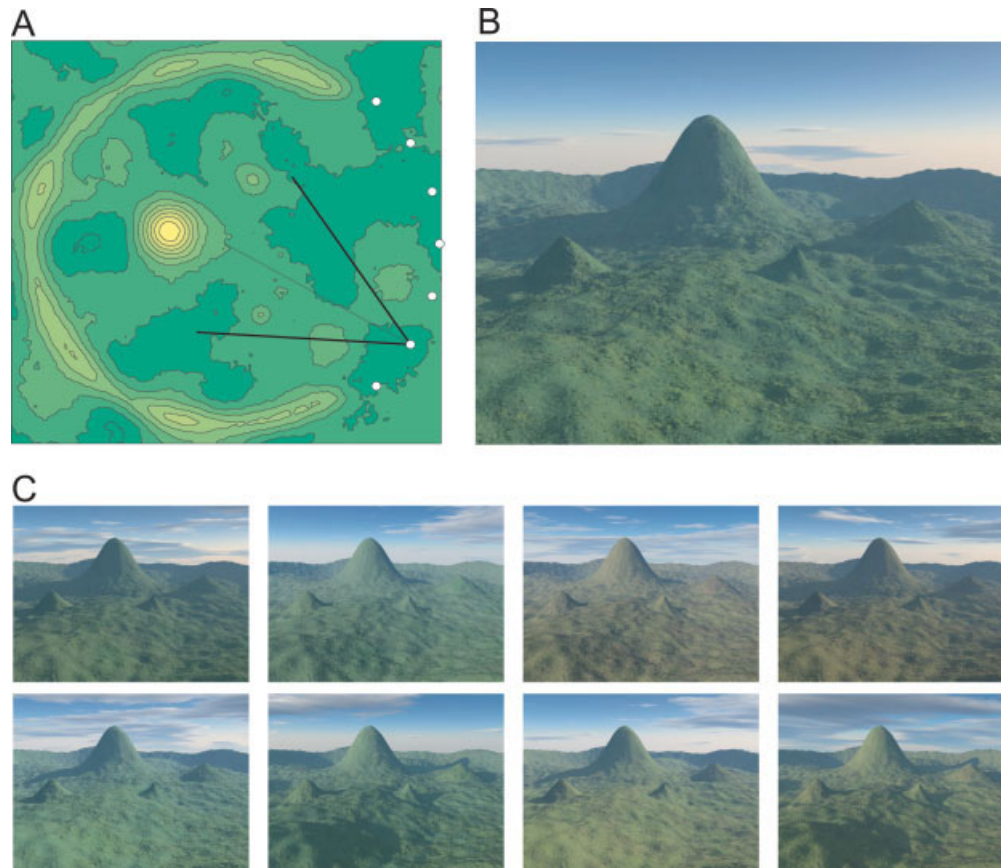


FIGURE 1. Stimuli used for the 4 Mountains Test. **A:** Each landscape is comprised of four scattered hills of varying shape and size within a semicircular range of hills. Each stimulus used in the experiment used a unique configuration of hills. Smoothed interpolated 2D noise was also added to the heightfield to produce unique, naturalistic variations between landscapes. The scenes are rendered as through a virtual camera sited at one of seven points (shown by white circles) equidistant from the center of the heightfield. **B:** Typical example of a rendered stimulus image based on topography

shown in (A) **C:** Topography shown in (A) rendered under the eight different combinations of nonspatial parameters used in the experiment (see text). These combinations vary cloud cover, lighting (apparent elevation of sun), texture, and color of vegetation: properties that combine to create an overall impression of the distinctive prevailing conditions at a particular time. For each combination, lighting direction (apparent azimuth of sun) could come from either due “north” or “south” relative to camera locations shown in (A).

A subsequent study (Shrager et al., 2006) using closely related tasks and stimuli (a range of visually similar stimuli including faces, objects and scenes which must be discriminated or matched) found no evidence of perceptual impairment in patients with focal hippocampal lesions or more extensive MTL lesions. Such concerns and discrepancies indicate that further investigation of the timecourse of the involvement of MTL structures in spatial perception and memory is warranted.

In the current study, we examined the hippocampal contribution to perception and STM for the topographical and nonspatial information in spatial scenes. Inspired by Piaget and Inhelder (1967), we used computer-generated landscapes containing four mountains in which the topography of the landscape (i.e., the geometry of the surface) and its nonspatial visual features could be independently varied (Figs. 1 and 2). Perception was tested by four-alternative match to sample, to minimize any memory load (cf. odd-one-out procedures), while memory was tested by four-alternative delayed match to sample (delay = 2 s). In topographi-

cal tasks, participants matched a sample scene to the target (the same place from a different viewpoint) rather than three foil scenes with different topography. In nonspatial tasks, participants matched global nonspatial properties of the scene reflecting the “prevailing conditions” when the picture was taken (i.e., weather, time-of-day, and time-of-year as reflected by the conjunction of parameters such as lighting, cloud cover, and vegetation color). In both types of task, the nontested (spatial/nonspatial) attributes were the same for the four choices but different from the sample. The changes in both the viewpoint and the nonspatial properties between sample and target serve to make the topographical tasks dependent on matching the allocentric topographical information in the scenes and less susceptible to solution by visual pattern matching. The similarity of the targets and foils was varied to ensure that the performance of healthy young participants did not differ significantly across the four tasks (place perception, place memory, nonspatial perception, nonspatial memory) to avoid any nonspecific effects of difficulty.

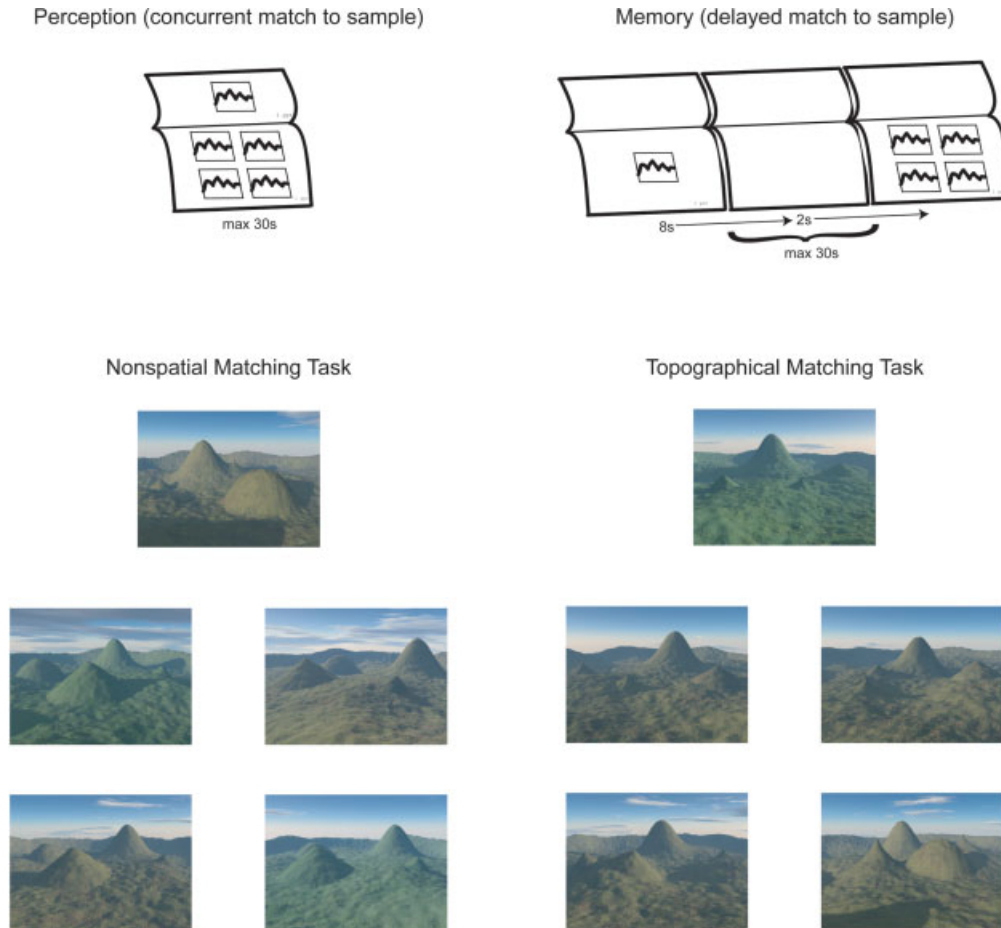


FIGURE 2. Top: Timing and layout of test items. Perceptual tests used a concurrent match to sample task. Participants had a maximum of 30 s to choose one picture from four alternatives (on the lower page of the test booklet) that matched the sample image (upper page). Memory tests used a delayed match to sample task, interposing a 2-s delay (during which a blank page was shown) between sample and test images. Bottom: Examples of nonspatial and topographical items. In nonspatial tests, participants had to match images based solely on the nonspatial features in the scene; cloud cover, lighting,

texture, and color of vegetation. The target is shown at the bottom left of the four choices. Topographical features were varied between sample and test images. In topographical tasks, subjects had to match images based solely on the topographical features; viewpoint and nonspatial features were varied between sample and test images. The target is shown at the top left of the four choices. The spatial foil is at the top right, the configural foil at the bottom left, and the elemental foil at the bottom right (2 hills changed as in the topographical memory test), see Experimental Procedures.

EXPERIMENTAL PROCEDURES

Participants

Four patients with focal hippocampal damage (3 bilateral, 1 right-sided), and one with more extensive damage, including right parahippocampal gyrus were tested, see Figure 3, along with matching control groups, see Table 1.

Case 1: KC3

KC3 (Chan et al., in preparation) is a 57-year-old male. Six months prior to the present investigation, KC3 began to experience “panic attacks” manifested as episodes of anxiety, with no obvious triggers. The following month he continued to experience frequent daily panic attacks and began to notice some problems with epi-

sodic memory that rapidly became more severe. In addition, KC3 began to get lost when driving along a route from home to work upon which he had traveled three times a week for over 20 years. General neurological examination was normal, although discussions relating to his symptoms would often precipitate a “panic attack”. A magnetic resonance imaging (MRI) scan revealed abnormal high signal restricted to the hippocampi and amygdalae with no abnormality elsewhere in the temporal lobe (Fig. 3).

A neuropsychological assessment was carried out two months prior to the present investigation. Verbal and performance IQ was in the average range, which was considered to represent some degree of intellectual underfunctioning in view of his estimated high average premorbid IQ based upon educational level. Anterograde memory was found to be intact on most tests, although retrograde memory was impaired (Chan et al., in preparation). He performed poorly on a verbal fluency test of executive function-

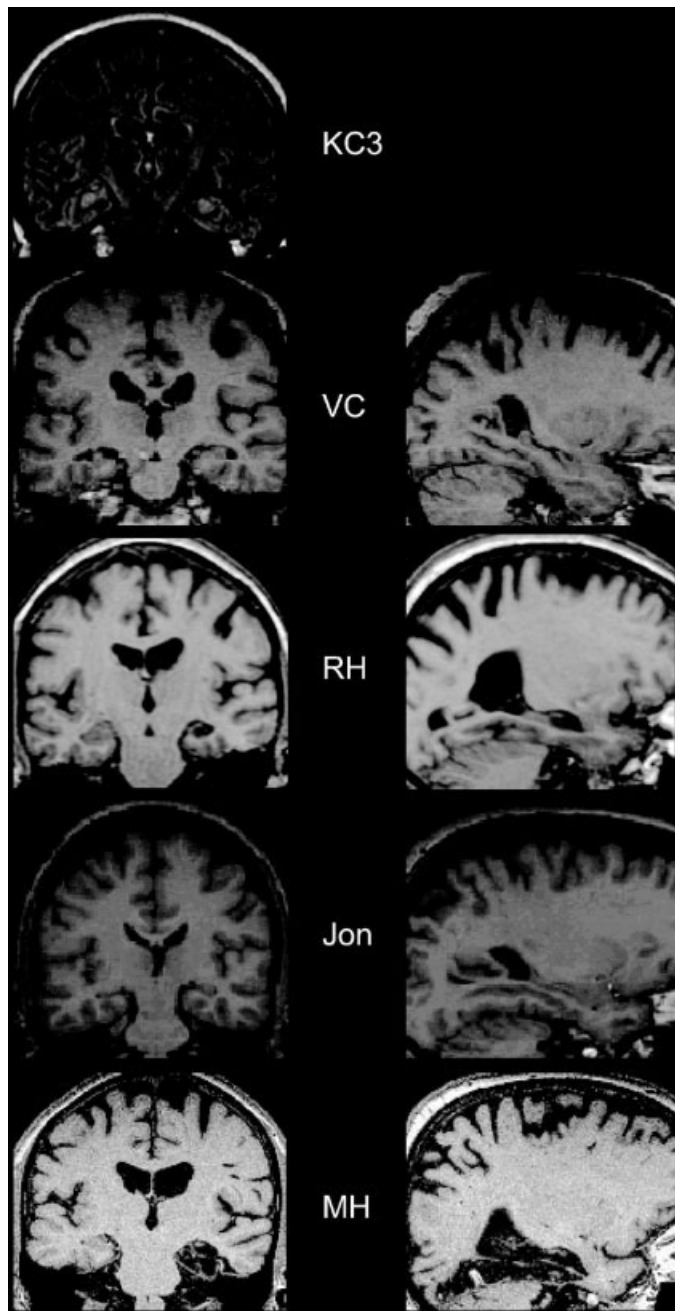


FIGURE 3. MRI images showing the location and extent of lesions in each patient. The left column shows a coronal section through the hippocampi, and the right column shows a sagittal section through the right hippocampus. Patient KC3's scan is a FLAIR T2 weighted image showing abnormal high signal in the hippocampus prior to treatment. No corresponding sagittal scan is available for KC3. The other scans are T1 weighted structural images. Brief lesion descriptions: KC3, bilateral hippocampal damage; VC, bilateral hippocampal damage; RH, right hippocampal damage; Jon, bilateral hippocampal damage; MH, right-sided lesion including hippocampus, medial-ventral parts of occipital and temporal cortices. See Experimental Procedures for further details of the lesions and etiology for each patient involved in the study, and Tables 1 and 2 for further information on patient age, sex, and cognitive profile.

ing, although this may be confounded by the fact that English is his second language. See Table 2 for more detailed results.

A diagnosis of autoimmune encephalitis associated with anti-voltage gated potassium channel (anti-VGKC) antibodies was made and subsequently confirmed (the anti-VGKC antibody titer was markedly raised, see Vincent et al., 2004). Video EEG telemetry revealed that the "panic attacks" were partial seizures arising from the right temporal lobe. KC3 received immunomodulatory therapy in the form of plasma exchange and subsequent oral corticosteroids, and he was also started on antiepileptic therapy, with complete cessation of his "panic attacks." After treatment there was subjective recovery of episodic memory function, although he continued to experience topographical disorientation.

Case 2: VC

VC is a 78-year-old male. His medical history and detailed investigation of his retrograde and anterograde amnesia have been reported elsewhere (Cipolotti et al., 2001, 2006). He suffered cerebral ischemia at the age of 67, following which he became densely amnesic. Extensive neuroradiological investigations have confirmed extensive bilateral hippocampal damage in this patient (Fig. 3). The hippocampi were reduced in volume by 47% on the left and 44% on the right. There is no evidence that the remaining tissue is functional (Maguire et al., 2005). The only other finding of note is a reduction in volume of the left parahippocampal gyrus by 31%, which lies between 2 and 3 standard deviations below controls. This has been argued to reflect white matter loss consequent to atrophy in the hippocampus (Cipolotti et al., 2001).

Neuropsychological assessments have revealed a fairly static profile over several years. Verbal IQ is in the average range, while performance IQ has risen from over repeated assessments. Language, visual perception, and executive functions are all unimpaired. VC is profoundly impaired on all tests of verbal and visual memory recall and recognition memory (Table 2).

Case 3: RH

RH is a 58-year-old female. In 1996, she developed sudden onset tingling and weakness in the left arm. Subsequent to this event, she noticed impairment in remembering events, appointments, and conversations. She also began to notice a difficulty with her sense of direction particularly when walking in unfamiliar places. Neurological examination was entirely normal. At the time of the present study, RH claimed that her memory has improved, although her husband still noted a mild topographical disorientation that is more pronounced in unfamiliar environments. Two recent MRI brain scans have identified atrophy involving the right hippocampus only, with normal appearance of the fusiform and parahippocampal gyri and the remainder of the temporal lobes (Fig. 3).

Neuropsychological assessments have revealed a static profile over the last two years (Bird et al., in preparation). Verbal and performance IQ are both in the average range, consistent with estimates of premorbid ability. Language, visual perception, and executive functions are all unimpaired. Verbal memory is also unimpaired. However, she performed poorly on tests of visual

TABLE 1.

Control Group Demographics and Comparison of Control Participant and Patient Scores on Measures of IQ, Mental Rotation, and Scene Recognition Memory

Subject/group	Sex	Age		Matrices ^a		Flags test ^b		Topographical RMT ^c	
		Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range
Young controls	♂8:0♀	28.4 (2.9)	24–33	10.9 (1.5)	8–12	9.8 (0.5)	9–10	26.6 (4.2)	18–30
Jon	♂	26		11		10		25	(normal)
Old controls	♂11:9♀	65.2 (6.9)	51–80	8.9 (1.7)	6–12	9.7 (0.5) ^d	9–10	28.5 (1.4) ^e	24–30
KC3	♂	57		7		10		22	(normal)
VC	♂	78		8		10		12	(<5%ile)
RH	♀	58		6		8		16	(5%ile)
MH	♂	70		n.t. ^f		10		27	(normal)

Results of additional testing carried out with the patients are presented in Table 2.

^aRaven's Advanced Progressive Matrices Set I (Raven, 1976) a nonverbal test of general intelligence.

^bA simple 10-item test of planar mental rotation using flags, based on Thurstone and Jeffreys (1956).

^cWarrington's (1996) a test of scene recognition memory.

^dOne participant's data missing.

^eTwo participants' data missing.

^fMHs intelligence is average (VIQ = 106, PIQ = 93) see Table 2.

recall and a test of visual recognition (Table 2). Given the sudden onset of her symptoms and her static neuropsychological profile, a vascular etiology is suspected (ischemia).

Case 4: Jon

Jon is a 26-year-old male, whose medical and neuropsychological history are described extensively elsewhere (Vargha-Khadem et al., 1997; Gadian et al., 2000; Maguire et al., 2001). He was born prematurely after 26 weeks of gestation. He initially suffered apnoeic attacks and at the age of 3 years 10 months, he had an unconfirmed convulsive episode. No hard neurological signs were apparent, but at the age of about 5 years his parents first noticed he had memory difficulties. Despite considerable problems with episodic memory, he attended mainstream school and achieved near-normal levels of general knowledge. Several neuroradiological investigations have found Jon's hippocampi to be reduced in volume by 50% along the length of both, while the surrounding tissue was found to be normal. There is evidence from Maguire et al. (2001) that the remaining tissue within his hippocampi may be functional.

Neuropsychological assessments have found Jon's verbal IQ to be in the average range, while his performance IQ has risen over serial assessments. At the age of 19, he had a performance IQ of 120. Jon performs poorly on tests of recall memory, while his performance on tests of recognition memory is usually in the normal range (Table 2).

Case 5: MH

MH is a 70-year-old male. In August 2000, he had a sudden onset of dizziness and mild weakness in his left arm. Subsequently he was disorientated and had difficulty walking as he started bumping into objects. A neurological examination revealed a left homonymous upper quadrantanopia. The only

other neurological sign was a mild postural tremor. An MRI brain scan showed right sided occipital and temporal lobe infarction in the territory of the posterior cerebral artery (Fig. 3). This affected the lingual and parahippocampal cortices and extended into posterior portions of the hippocampus.

Following discharge, MH complained of difficulty in recognizing famous people's faces on television, although friends and family never presented a problem. He has experienced several episodes of topographical disorientation, although he is able to live independently. He was also concerned that his quadrantanopia was expanding although this was found not to be the case. A formal neuropsychological investigation found his verbal and performance IQ's to be in the average range, which is broadly in keeping with premorbid estimates. High level visual perceptual deficits were also detected.

Healthy adult controls

Twenty-eight healthy adults were recruited to serve as a control group. Twenty of these were older adults selected to be representative of the older patients in the study (RH, VC, KC3, and MH). Eight of these were young adults selected to match patient Jon. The demographics of each control group are shown in Table 1. The relatively large size of the control groups meant that this was a more sensitive analysis than choosing matched controls for each participant.

Materials

Landscape stimuli were based on a heightfield (a 2D array of altitudes) constructed using MATLAB 6.1 (Mathworks Inc.). Each stimulus heightfield (Fig. 1A) was built by summing six 256 × 256 height fields: four hills of varying shapes and sizes (Fig. 1B), placed at different locations around the center, a semicircular range (in the background of the stimulus images)

TABLE 2.

Patients' Score on a Range of Cognitive Tests

		VC	KC3	RH	MH	Jon
Intelligence	VIQ ^a	107 (Average)	99 (Average)	109 (Average)	106 (Average)	108 (Average)
	PIQ ^a	138 (Very superior)	92 (Average)	101 (Average)	293 (Average)	120 (Superior)
	Matrices ^b	8/12 (>75%ile)	7/12 (50–75%ile)	6/12 (50–75%ile)	n.t.	11/12 (>75%ile)
Semantic memory	Graded naming test ^c	24/30 (75%ile)	4/10 ^d (<5%ile)	27/30 (>75%ile)	17/30 (25–50%ile)	n.t.
Object perception	Object decision ^e	18/20 (>5% cutoff)	17/20 (>5% cutoff)	19/20 (>5% cutoff)	12/20 (<5%ile)	n.t.
Spatial perception	Number location ^f	n.t.	8/10 (>5% cutoff)	9/10 (>5% cutoff)	10/10 (>5% cutoff)	n.t.
	Cube analysis ^g	10/10 (>5% cutoff)	10/10 (>5% cutoff)	10/10 (>5% cutoff)	8/10 (>5% cutoff)	n.t.
Mental rotation	Flags test ^h	10/10 (w.n.l.)	10/10 (w.n.l.)	8/10 (w.n.l.)	10/10 (w.n.l.)	10/10 (w.n.l.)
Memory	RMT words ⁱ	35/50 (5%ile)	46/50 (75%ile)	44/50 (50–75%ile)	47/50 (>75%ile)	45/50 (25%ile)
	RMT faces ⁱ	39/50 (25%ile)	44/50 (50–75%ile)	41/50 (25–50%ile)	30/50 (>1%ile)	41/50 (25%ile)
	Topographical RMT ^j	12/30 (<5%ile)	22/30 (25–50%ile)	16/30 (5%ile)	27/30 (>75%ile)	25/30 (25–50 %ile)
	Doors and people ^k					
	Verbal recall	7/36 (<1%ile)	21/36 (10–25%ile)	30/36 (75%ile)	28/36 (75%ile)	6/36 (<5%ile)
	Verbal recognition	7/24 (<1%ile)	16/24 (25%ile)	21/24	17/24 (50–75%ile)	19/24 (50%ile)
	Visual recall	12/36 (<1%ile)	33/36 (50–75%ile)	10/36 (<1%ile)	18/24 (50–75%ile)	6/36 (<1%ile)
	Visual recognition	10/24 (<1%ile)	18/24 (50%ile)	17/24 (10–25%ile)	24/36 (10–25%ile)	20/24 (50–75%ile)
Executive functioning	Verbal fluency (s) ^l	17	8	18	n.t.	n.t.

n.t., not tested; w.n.l., within normal limits; %ile, percentile.

^aVerbal IQ (VIQ) and Performance IQ (PIQ) scores are based on a 7-subtest version of the Wechsler Adult Intelligence Scale—Revised (Wechsler, 1981).

^bThe Advanced Progressive Matrices (Raven, 1976) is an untimed nonverbal test of abstract problem solving. There are 12 eight-alternative forced-choice (AFC) problems.

^cA stringent test of object naming (McKenna and Warrington, 1983). Stimuli are 30 black and white pictures of low frequency objects that must be named orally.

^dFirst ten items.

^eA 4AFC test of visual object perception from the Visual Object and Space Perception Battery (Warrington and James, 1991). For each of the 20 items, the participant must select the silhouette of a real object from three nonsense shapes.

^fA stringent test of visuospatial perception from the Visual Object and Space Perception Battery (Warrington and James, 1991). The participant is presented with 10 stimuli comprising two separate squares containing either a single dot or a multiple number array. He/she must identify which number corresponds to the position of the single dot.

^gA test of complex spatial relationships from the Visual Object and Space Perception Battery (Warrington and James, 1991). The 10 stimuli are black outline representations of a 3D arrangement of square bricks. Participants must report how many square bricks are in the drawing.

^hA 2AFC test of mental rotation based on Thurstone & Jeffreys' (Thurstone and Jefferys, 1956) Flags Test. The 10 stimuli comprise a single "flag" which must be matched to an identical flag rotated by a variable amount. The lure item has one of the internal features of the flag misplaced.

ⁱThe Recognition Memory Test for Words and Faces (Warrington, 1984) comprises two subtests. Both involve a 50-item study phase followed by a 2AFC test phase. Stimuli are high frequency 4–6 letter words and unfamiliar male faces.

^jA test of scene recognition memory taken from the Camden Memory Test Battery (Warrington, 1996). There is a 30-item study phase followed by a 3AFC test phase. Stimuli are color photographs of outdoor scenes.

^kThe Doors and People Test battery comprises two verbal and two visual recall and recognition subtests which are matched for difficulty (Baddeley et al., 1994). The verbal recall subtest requires the learning of four forename and surname pairs. The verbal recognition subtest is a 4AFC recognition test of 24 forename and surname pairs. The visual recall subtest requires the learning of four simple geometric shapes. The visual recall subtest is a 4AFC recognition test of colour photographs of external doors.

^lInstructions were taken from Lezak (1995). Participants had to generate as many words as possible in 1 min, starting with the letter "S", excluding proper nouns.

and a smoothed interpolated 2D noise field. The noise served to add realism and additional unique small scale topographical features.

The heightfields were rendered with realistic lighting and texture (Terragen v0.9 Planetside Software). Parameters supplied to the rendering software could be used to determine the location and orientation of a virtual camera. In addition, sunlight direction (elevation), cloud cover, atmospheric conditions, and surface texture parameters were varied. Eight different combinations of these parameters were used to produce eight distinct sets of “prevailing conditions” under which each height field could be rendered (Fig. 1C).

Each scene was rendered from a virtual camera facing the origin and placed at one of seven predefined viewpoints, at an altitude of 30 units and spaced at 15° intervals around the origin at a radius of 128 units (as indicated in Fig. 1A).

Stimuli were systematically generated to fit the constraints described below, while ensuring that the peaks of all four hills were clearly visible in each rendered scene. There were 15 items in each task, each item being composed from five images. No image was repeated. Hills varied in shape, size, and relative location to create unique landscapes for each item. All landscapes included one larger, rounded hill. This was necessary to avoid any ambiguity about the viewpoint used across different images of the same landscape. The four experimental tasks detailed below were pilot tested in a group of elderly women. This, and other pilot data from younger volunteers, was used to select the final set of stimulus items from a larger set generated at random, and to modify items where necessary, with the objective of matching performance across the four experimental tasks.

Experimental Tasks

The four experimental tasks are summarized in Figure 2: a topographical perception task, a topographical memory task, a nonspatial perception task, and a nonspatial memory task. All participants completed the tasks in this order; it was not possible to counterbalance task order for the individual patients, and the order was preserved for the control group in order to match the procedure used for the patients.

Participants were seated in a quiet room and gave informed consent in accordance with UCL or UCLH Ethics Committee requirements. Each task was presented in a separate A4 booklet, with the experimenter turning the pages to control the timing of the stimulus presentation and responses.

Prior to each task, participants read through the instructions. Because the variation in prevailing conditions used in the nonspatial tasks corresponded to environmental features that normally vary over time these tasks were framed in terms of matching the “time of day and time of year”—a description that we found participants readily understood in pilot work. The instructions for tasks involving memory or perception of the topography of the scene were framed in terms of matching the “place.” For example, in the topographical memory task, participants were told “Your task is to identify which of the four pictures shows the same place as the previous picture. Focus on the

layout of the scene (the shape and arrangement of mountains and other geographical features).”

Participants then completed three practice items, with verbal feedback from the experimenter which, where necessary, drew their attention to relevant features of the stimuli. Participants were told to ask for clarification (which reiterated relevant information in the written instructions) if they were unsure of what to do.

Topographical perception

In this task the participant was presented with a “sample” image, and simultaneously a four-alternative choice of scenes arranged randomly in a 2 × 2 grid on the facing page of the A4 test booklet.

All four alternative responses were rendered under the same prevailing conditions as each other, but with different prevailing conditions and viewpoint from the sample image. The task was to identify the target image that matched the topography of the sample image. Each of the landscapes depicted in the three foil images were constructed so as to resemble the target in different ways with the objective of exposing the nature of any retained spatial information in the pattern of erroneous responses. The four alternative responses thus comprised:

1. *Target*: the correct response, all topographical information is preserved.
2. *Spatial foil*: a scene in which the spatial layout is varied (i.e., some of the hills are moved), but the order of distinctively shaped hills about the central origin is preserved.
3. *Configural foil*: the order of the hills about the origin is altered (by exchanging the locations of two or more distinctively shaped hills) but the layout is otherwise very similar to the target scene.
4. *Elemental foil*: the shape and/or size of one hill is changed, while the spatial layout is otherwise very similar to the target scene's.

To prevent participants being misled by local matches with small scale features, each of the four alternatives was rendered from a different camera position (Figs. 1 and 2) For the same reason and to ensure that each of the foil landscapes was unambiguously different from any point of view (as any two real landscapes would be) each foil used a unique pattern of 2D noise, and the spatial layout (polar coordinates of hill locations) was also jittered slightly for configural and elemental foils. However, the most obvious differences from the target topography were those resulting from the deliberate manipulation of spatial layout, configuration, and elemental shape and size as described above.

Topographical memory

The topographical memory task was essentially the same as the place perception task, except that the sample image was presented in isolation for approximately 8 s. The page of the booklet was turned and participants then saw a blank page for approximately 2 s before being presented with the four way choice on the next page.

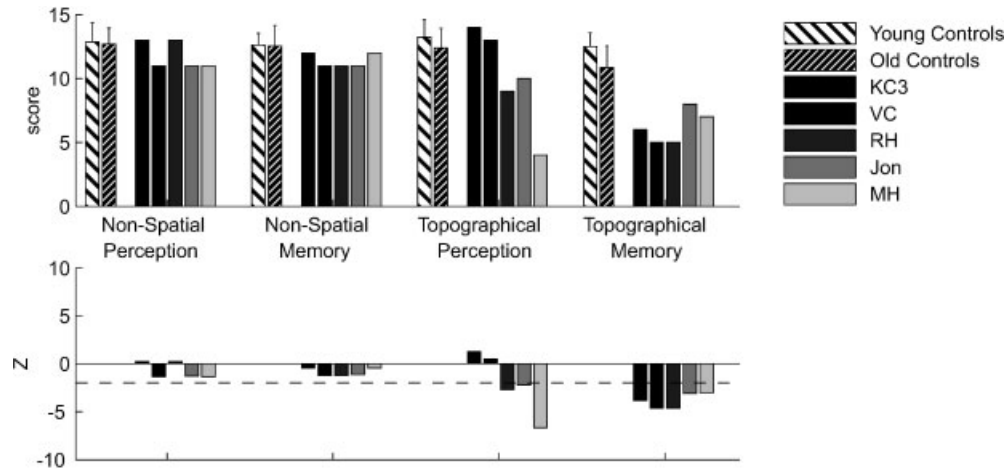


FIGURE 4. Top: Raw scores for each patient on each of the four tests (maximum 15). For control group the mean score is shown by the bar, and error bars indicate the standard deviation (SD). Patient MH has damage to medial and ventral parts temporal and occipital neocortex, including parahippocampal gyrus, as well as damage to the hippocampus; the other patients have focal damage to

the hippocampus (refer to text and Fig. 1 for further details). Bottom: Corresponding z -scores derived by comparing each patient to the relevant control group. Patient Jon is compared with the young control group, while the other patients are compared with the older control group. The dashed line shows 1.96 standard deviations below the mean.

The four alternative responses were generated for each sample landscape in the same way as the perceptual task, but in order to match difficulty with the perceptual version of the task, it was necessary to make the elemental foils more distinctive by changing the shape and size of two of the hills.

Nonspatial perception

In this task, participants had to match the prevailing conditions in the sample image to one of the four alternatives presented simultaneously in a 2×2 grid on the facing page of the booklet. Each of the four alternative scenes depicted the same place seen from different viewpoints and under a different set of prevailing conditions. Only the combination of texture/color, lighting, and cloud cover was unique to target and sample images—individual elements might also match in foil scenes. Rendered landscapes based on each set are shown in Figure 1C.

Nonspatial memory

Items in the nonspatial memory task took the same form of stimuli as the nonspatial perception task, and participants had the same aim, identifying the scene in which prevailing conditions matched those in the sample image, but in this case after a very brief delay. As in the place memory task, participants were given approximately 8 s to study the sample image, before the stimulus was obscured and replaced after approximately 2 s with the four alternatives arranged in a 2×2 grid. As in the nonspatial perception task, the three foil images were generated by randomly rendering the same landscape with a mismatched set of prevailing conditions selected at random.

RESULTS

The mean scores for each of the control groups, and raw scores for each patient are shown in Figure 4 (top). Figure 4 (bottom) shows the corresponding z -scores for each patient.

None of the patients was impaired on either nonspatial task.

All five patients were significantly impaired on the topographical memory task. The level of impairment was roughly equal in all five patients (scores ranged from 5/15 to 8/15), with scores that would place them all below the 3rd percentile of the normal population (Crawford and Garthwaite, 2002), with all four focal hippocampal cases (RH, KC3, Jon, VC) being below the 1st percentile. All patients performed well on a simple test of planar mental rotation (Table 1), suggesting that the topographical impairment did not arise from a failure to manipulate spatial information *per se*, but rather from disruption of processes required for establishing and retrieving a representation that could support such operations for complex 3D scenes.

As expected, MH, the patient with a large right MTL lesion including much of the parahippocampal and entorhinal cortex (EC) as well as hippocampus, was grossly impaired on the place perception task (well below what would be expected of the 1st percentile of the normal population). Of the focal hippocampal patients, RH and Jon were impaired on place perception. Their impairments were less profound than MH's, placing them between the 2nd and 4th percentiles (z -scores between -2 and -3). However, the other two focal hippocampal patients, KC3 and VC, were not only unimpaired, but in fact scored above than the mean of the elderly control group. VC's score on this task is of particular interest because he is densely amnesic (Cipolotti et al., 2001), and at age 78, he is one of the oldest participants we tested.

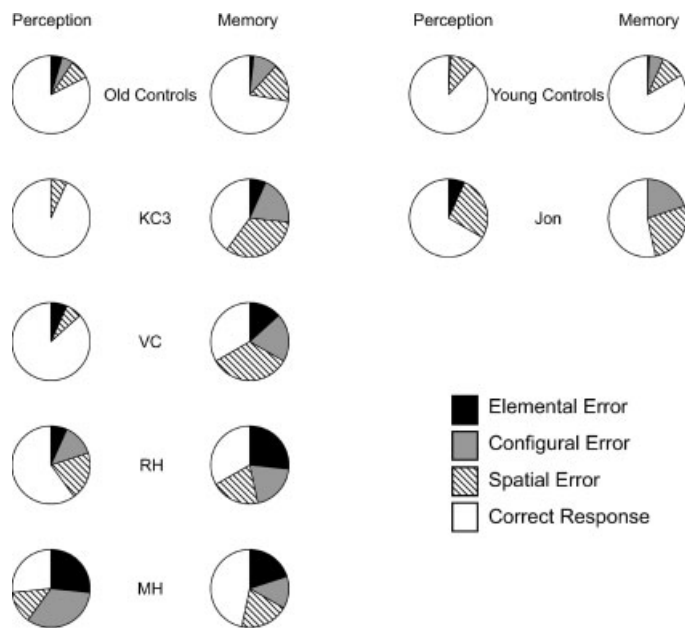


FIGURE 5. Pie charts showing qualitative breakdown of responses to topographical tests. Each response in the topographical tests could take one of four forms: In correct responses (white segments) the selected image shows the same topography as the sample image (albeit from a different viewpoint). In spatial errors (stripes) the selected foil retains the same combination of distinctive hills arranged in the same order around the origin, but with the locations of the hills disrupted. In configural errors (gray) the selected foil retains the same combination of distinctive hills arranged in a different order around the origin. In elemental errors (black) the shape and size of one (perception) or two (memory) hills is changed. The figure shows the breakdown of responses for each patient both perception (left column) and memory (right column) tasks. Patient Jon (who is substantially younger than the other patients) is shown on the right of the figure, beneath the overall results for the young control group. The other patients are shown on the left of the figure beneath the overall results for the old control group.

The four possible responses to each topographical question included three different types of foil—spatial, configural, and elemental, each differing from the target scene in different ways (see Experimental Procedures and Fig. 2 for further details). Spatial and configural foils were constructed using the same elements (distinctive hills) as the target scene, but arranged in a different configuration, whereas elemental foils included elements not present in the target/sample scenes. This was intended to expose the nature of any retained spatial information in the pattern of erroneous responses. For instance, if patients had been able to retain information about the order, but not the precise locations of the hills within the scene, they might be expected to make a preponderance of spatial errors (spatial foils preserved the order but not the locations of the distinctive hills) but be able to correctly reject configural foils (in which the order was varied). The patterns of error made by each patient and the two control groups in the topographical tasks are shown in Figure 5. Although they do not bear formal analysis, some interesting qualitative features are evident. Spatial and configural errors are

made in similar proportions in patient and controls. There is little sign that the relative proportions of spatial and configural errors differ between patients and controls; patients on the whole make more errors of all types. However, the proportion of elemental foils seems to vary somewhat between patients. For example, although impaired on both tasks, patient Jon appears not to guess randomly, making mostly spatial errors in perception and spatial and configural errors in memory. Thus, Jon's performance may show some preservation of function, despite his severe overall deficit which allows him to reject elemental foils, e.g., remembering something of the shapes of individual hills. It is notable that MH uniquely shows a high proportion of elemental errors in both perception and memory (very close to the 25% that would be expected by chance). This suggests that the on-line processing of local topographical cues may be dependent on the ventral neocortical regions damaged in this subject. However, as noted earlier, these data do not support strong conclusions, for example RH's level of elemental errors in the memory condition complicates this simple picture.

The performance of the young control group showed no significant effect of task ($F_{(3,21)} = 0.75$; $P > 0.05$). The performance of the older control group did show an effect of task ($F_{(3,57)} = 6.50$; $P = 0.001$), reflecting a weak correlation between age and topographical memory performance ($r = 0.38$, $P = 0.045$, $n = 28$; all controls), consistent with a previous finding (Inagaki et al., 2002).

DISCUSSION

Our results indicate a specific hippocampal role in topographical memory, even over very brief delays (2 s). In addition, hippocampal damage led to impairment in topographical perception in some, but not all, cases. More extensive damage, including the right MTL, caused clear perceptual as well as memory problems. We discuss the implications of these findings below.

Is the Hippocampus Specialized to Process the Topographical Information in Visual Scenes?

Our results support the idea that the hippocampus is specialized for topographical information, in that we tested both topographical and nonspatial information in approximately difficulty matched tasks and found focal hippocampal damage to be associated solely with topographical deficits. The recent paper by Hannula et al. (2006, experiment 2) provides an example of nonspatial relational processing (face-scene associations) which shows a short-term impairment in hippocampal patients, supporting the idea that the hippocampus contributes to more than just spatial processing even at short delays. As noted in the Introduction, it is generally agreed that the hippocampus is vital for long-term context-dependent episodic memory. What is at issue is whether this deficit arises from a more fundamental role, detectable even at short delays, in cross-modal association (Marr, 1971; Teyler and DiScenna, 1986; e.g., Damasio, 1989; McClell-

land et al., 1995; Vargha-Khadem et al., 1997; Mayes et al., 2004), provision of spatial context (O'Keefe and Nadel, 1978), or relational (Eichenbaum and Cohen, 2001) or declarative (Squire and Zola, 1998) processing. The data presented here, and in other recent studies (King et al., 2002, 2004; Lee et al., 2005a,b; Hannula et al., 2006, experiment 1; Olson et al., 2006) strongly support a spatial role. The data from Hannula et al. (2006, experiment 2) also supports a role in cross-modal association. Nonetheless, both of these types of memory are also relational and declarative.

Can we narrow the field of explanatory theories by considering the preserved processing of nonspatial information in our patients? Both spatial and nonspatial tasks appear to be equally good examples of declarative memory, and so our data do not appear to be well-described by this theory. Are both tasks equally good examples of relational memory? Although spatial and nonspatial information are inherently qualitatively different, we attempted to restrict these differences. So for instance, our nonspatial tasks depend on combining information from multiple global, parametrically varying features, rather than unitary, local, or categorical features. On the face of it, this would appear to indicate that nonspatial conjunctions are being processed and stored normally in the hippocampal patients. However, it could be argued that the nonspatial task might benefit from memory or perception of unitary features to a greater extent than the spatial task (in which only the elemental foil can be ruled out by unitary features). It is also true that the topographical task depends on metric relationships between elements, while the nonspatial task depends on simple conjunctions of stimulus elements. Thus, we cannot rule out the possibility that the topographical deficit reflects a more general deficit in relational processing.

What is the Hippocampal Role in Topographical Processing for Perception and Memory?

Two of the four focal hippocampal patients (RH, Jon) showed deficits in both topographical memory and topographical perception, as consistent with a role for the hippocampus in on-line processing of topographical information (see also Lee et al., 2005a). However, the preserved performance of the other two focal hippocampal patients (VC and KC3) show that an intact hippocampus is not critical for the topographical tasks until a brief delay is introduced, in which case all of the hippocampal patients are impaired. Importantly, and by contrast to the traditional association of the hippocampus with long-term declarative memory, the delay used in the topographical memory task was only 2 s. Consistent with the traditional view, amnesiacs such as VC are often able to maintain working memory in a range of other tasks involving brief delays such as digit span or Corsi's block span (Milner, 1971; Cave and Squire, 1992). As we argued in the Introduction, memory for many kinds of visuospatial stimulus *can* be supported by STM systems in the absence of the hippocampus. The key difference with our task is that the stimuli were explicitly designed to tax flexible allocentric topographical processing (matching the relative location/shapes of the hills despite changes in viewpoint and surface features), and it seems that

such processing requires the hippocampus for retention over even very brief delays.

It is possible that the stored hippocampal representation of a spatial scene is allocentric in that the effects of movement of viewpoint can be calculated within it (Gaffan, 1998; Robertson et al., 1998; Burgess, 2002; King et al., 2002), allowing both topographical memory and perception tasks to be performed. By comparison, the posterior parahippocampal cortex, having been consistently implicated in the perceptual processing of topographical landscapes and scenes in neuroimaging studies (e.g., Epstein and Kanwisher, 1998; Epstein et al., 2003; Hasson et al., 2003), appears less flexible. This has been investigated using fMRI adaptation, in which repeated presentation of the same scene (with varying viewpoints) can be compared with presentation of different scenes. The earliest studies using this paradigm showed no difference, suggesting that the region treats different views of the same place as entirely distinct (i.e., it is a viewpoint dependent representation; Epstein et al., 2003). More recent studies have pointed to a refinement of this position, with adaptation effects seen, where the viewpoint changes incrementally over successive presentations (Ewbank et al., 2005). Such incremental changes correspond with the way scenes are normally encountered over the timescale of perception and STM (though not in our tasks). Over the longer term, an environment is more likely to be encountered from different viewpoints on different occasions, necessitating a viewpoint invariant representation, perhaps dependent on hippocampal processing.

Interestingly, from the point of view of the current study, short-term adaptation effects in the posterior parahippocampal cortex increase with exposure to a scene (Epstein et al., 2005), so that initially the representation appears highly sensitive to changes of viewpoint, becoming less so over time, while the same region increasingly shows an adaptation to new views of the same place relative to different places. However, even after several exposures and a long delay, the parahippocampal representation remains sensitive to changes in viewpoint.

While the likely viewpoint specificity of the parahippocampal representation might make it insufficient to support the topographical memory task, it could still support alternative processes sufficient for the perceptual matching task. Distinct processes seem to support imagined movement of viewpoint relative to an array of objects, compared to an equivalent mental rotation of objects relative to the viewpoint (Wraga et al., 2000). An advantage is observed for the mental manipulation of viewpoint, except where the array contains a single object, in which case mental rotation of the object is equally efficient. We have previously argued that accurate mental manipulation of viewpoint within a complex 3D scene necessitates the involvement of the (viewpoint independent) hippocampal representation (Burgess, 2002; King et al., 2002), but it seems reasonable to suppose that the (putatively viewpoint-dependent) parahippocampal representation is capable of supporting mental rotation of isolated objects or topographical features relative to a static viewpoint. In the current study, the parahippocampal representation might thus allow a piecemeal mental rotation of individual scene elements and their comparison with those in the sample image. By contrast, the memory task would demand mental manipulation of the entire

scene (or imagined viewpoint) rather than individual elements within it, there being no sample scene to support piecewise matching. Under this interpretation, we would also expect parahippocampal representations to be sufficient for processing and STM of scenes that are tested from the same point of view (Smith and Milner, 1989; Ryan et al., 2000; Ryan and Cohen, 2004a,b; Shrager et al., 2006), or where only a single object location need be remembered (King et al., 2002). Extrahippocampal representations may also be sufficient for the mental rotation of 2D stimuli (Cave and Squire, 1992), since all patients in the current study were able to successfully complete a simple 2D mental rotation task (Table 1).

The representation of environmental topography by the hippocampus is consistent with the idea that it provides a cognitive map or spatial-relational representation, and with the way in which environmental geometry is encoded by hippocampal place cells in rats (O'Keefe and Burgess, 1996). It is also possible that the hippocampal role in supporting viewpoint independence relates to the ability of the place cell representation of location to perform pattern completion from partial cues (Nakazawa et al., 2002), to accommodate the effects of self-motion (McNaughton et al., 1996) and to generalize across representations of environmental geometry (Wills et al., 2005). All of these properties are thought to result from the presence in hippocampal region CA3 of an extensive and recurrent collateral system that is capable of long-term potentiation (LTP) (Marr, 1971; McClelland et al., 1995; Nakazawa et al., 2002). It has long been proposed that this distinctive anatomical feature of the hippocampus makes it particularly suited to the rapid acquisition and long-term storage of information. Equally, and as mentioned in the Introduction, the flexible allocentric nature of the spatial representations in the hippocampus are also well suited for LTM, allowing scenes to be recognized from new viewpoints after long delays. Nonetheless, we have shown that for tasks specifically designed to tap this type of representation, the hippocampus is required even over very brief delays. Indeed, our results indicate that hippocampal damage can even lead to perceptual impairments in some cases, although performance is preserved in other cases. We have argued above that the perceptual task may be solvable on the basis of less flexible parahippocampal representations, given the continued availability of the sample.

What Explains the Individual Differences in Hippocampal Patients' Topographical Perception?

One potential explanation for the topographical perceptual impairment shown by RH and Jon, but not by VC and KC3, would be additional nonspecific memory problems in RH and Jon. However, this seems unlikely given VC's generally much denser amnesia than Jon or RH. Another possibility of additional covert damage to the medial temporal neocortex of RH and Jon (making their performance more similar to that of MH) also seems unlikely given their relatively preserved performance in other tests (e.g., the Topographical RMT, see Table 2) compared to VC. It might be argued that feedback from an intact hippo-

campus is required for the normal development of scene processing in the parahippocampus, even where it is anatomically intact. Though this might account for Jon's deficit, it would not explain RH's. We note that a fourth possibility, of additional hippocampal damage in RH and Jon, is unlikely given VC's virtually complete hippocampal lesion. A fifth potential explanation is that, for hippocampal patients, successful performance of the perceptual task is possible, but depends on strategy. For instance it might be argued that VC and KC3 adopted viable nonhippocampal dependent strategies that were somehow unavailable to the other patients. However, this would be hard to square with VC's profound amnesia. A more likely, if speculative, explanation is that the patients (RH and Jon) with impaired topographical perception have learned to use compensatory strategies for scene processing, which fail in the particular circumstances of our test. For example, patients with poor topographical memory but relatively preserved recognition memory are likely to become reliant on the familiarity of local visual cues to identify places. In everyday life, such a strategy would be useful because unique or unusual local features of a scene are often available. However, it will fail in our topographical tasks, since similar local topographical cues are present in all the test images, while the nonspatial cues and viewpoint are explicitly varied between sample and test images. Thus, these patients' normally reliable approach may be counterproductive. On the other hand, these counterproductive strategies might not be available to VC due to his more strongly impaired recognition memory (Tables 1 and 2), or to KC3 who had only recently begun to experience memory problems.

Topographical Processing Beyond the Hippocampus

MH's striking impairment on the topographical perception task is fascinating, because it comes in the context of other test results (Tables 1 and 2) which indicate a good degree of preserved function in spatial perception and memory tasks, including the Topographical Recognition Memory Test (Warrington, 1996). Some of this preserved function may be due to dorsal stream processing, to ventral stream processing involving the spared tissue in the left MTL, or else to the more lateral tissue spared bilaterally. In contrast with our topographical tasks, the Topographical RMT, on which MH performs very well, depends on recognizing identical images containing unique local features not shared by the foil items. Our interpretation is that even where there is no delay, strictly topographical processing (i.e., where the task cannot be solved with reference to local features alone) is critically dependent on the right medial temporal cortex. Indeed, given the severity of MH's impairment compared with the other patients, and the unusually high proportion of elemental errors he makes in the perceptual task, online processing of topography can probably be supported by the right parahippocampal or entorhinal cortices without the hippocampus (but note the difficulty in drawing strong conclusions from the error data and RH's commission of elemental errors in the memory condition).

In this interpretation, MH's impaired topographical memory is likely to result from his impaired ability to perceive the scene's topography, although additional effects of right hippocampal damage cannot be ruled out. The degree of functional lateralization is not clear from the current study (since we have no patients with left-sided lesions). It may be that damage to the left MTL alone would produce a similar deficit, although this seems unlikely in the context of previous studies involving unilateral patients which show a consistent tendency for topographical processing to be somewhat right-lateralized (Burgess et al., 2002).

CONCLUSIONS

We have presented a new test of perception and memory for topographical and nonspatial aspects of naturalistic landscapes, designed so that topographical information cannot contribute to the nonspatial task and nonspatial visual information cannot contribute to the topographical task. The four conditions show matched performance in healthy young participants, while older participants have slightly worse topographical memory reflecting a weak aging effect (see also Inagaki et al., 2002).

Hippocampal damage selectively impairs topographical memory at a delay of 2 s, while two out of four hippocampal patients are also impaired on the topographical perception task. One patient (MH) with additional MTL and occipital damage, including the right parahippocampal gyrus, showed a very severe impairment in topographical perception.

Our results suggest that the hippocampus forms a viewpoint-independent representation of environmental topography which is also insensitive to changes in nonspatial features that are typically transient in the real world. This type of representation would clearly be particularly useful for LTM, but may also be useful over shorter timescales when alternative representations or STM systems are not available. However, the presence of the sample scene in the perceptual task can allow for successful alternative strategies, possibly based on less flexible parahippocampal representations (see also Shrager et al., 2006).

The proposed role of the hippocampus in specifically supporting a flexible or allocentric (viewpoint-independent) topographical representation is consistent with the cognitive map (O'Keefe and Nadel, 1978) and flexible-relational (Eichenbaum and Cohen, 2001) theories of hippocampal function. Nonetheless, our results also indicate a predominantly mnemonic role for the hippocampus, arguing against the most general interpretation of these theories (see also Fortin et al., 2002). It is notable that no deficit was found on nonspatial tasks involving perceptual processing and storage of combinations of parametric nonspatial visual features, suggesting that spatial relations are more readily disrupted by hippocampal damage than nonspatial information, at least in this ecologically realistic task. Our results are consistent with suggestions that a defining characteristic of hippocampal spatial representations is their "flexibility," in that they can support manipulations of viewpoint (Gaffan, 1998; Robertson et al., 1998; Burgess, 2002; King et al., 2002). More surpris-

ingly, these results argue against the generality of the long-held dissociation between the neural bases of long-term and STM. Although this dissociation holds for many types of traditionally used memoranda, for which STM systems exist, it appears that the hippocampus, while crucial to LTM, is also required for specific forms of spatial processing even over very short timescales.

Acknowledgments

We thank Joanna Adams for help with pilot studies and assistance with testing, and Martin Rossor and the Dementia Research Centre for their support.

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