

**STUDIES OF REMOTE SPATIAL MEMORY IN AN AMNESIC
PERSON WITH EXTENSIVE BILATERAL HIPPOCAMPAL LESIONS**

by

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**A thesis submitted in conformity with the requirements
for the degree of Masters of Arts
Graduate Department of Psychology
University of Toronto**

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Abstract

Remote spatial memory was investigated in K.C., a patient with extensive bilateral hippocampal lesions. Despite his severe amnesia for autobiographical knowledge, K.C. performed normally on a wide range of spatial tests of his neighbourhood and the world which included: 1. natural navigation in his neighbourhood, 2. sketch mapping, 3. verbal mapping, 4. vector mapping, 5. blocked-route problem-solving, 6. distance judgments, 7. proximity judgments, 8. sequencing landmarks along routes, and 9. locating gross features on world maps (i.e., continents, countries, oceans). He was severely impaired, however, in recognizing and identifying all but the most salient neighbourhood landmarks and locating specific features on world maps (i.e., cities). The results suggest that the hippocampus does not appear critical for the maintenance and retrieval of remotely-formed cognitive maps but may be necessary for specifying details of different locations within a map. This deficit may be similar to K.C.'s episodic memory deficit where he remembers remote general knowledge but not specific autobiographical details.

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Studies of Remote Spatial Memory in an Amnesic Person with Extensive Bilateral Hippocampal Lesions

The ability to capitalize on a rich and varied environment is dependent on the propensity to attend to, perceive, and remember geographical information. These components are involved in the formation of a cognitive map, a mental representation of the spatial arrangement of the physical environment (O'Keefe & Nadel, 1978). This term was coined by Tolman when he observed that rats initially trained to take a particular path in a maze to reach a food reward were able to devise an alternate route that they had never traveled along if the initial path was blocked. This finding suggests that the rats learned the location of the reward relative to the starting position, rather than just learning a series of turns and responses.

A primary use of these mental representations is to facilitate the ability to move efficiently through an environment towards a goal (e.g., Downs & Stea, 1977). This navigational ability is common across species and often referred to as way-finding or topographical orientation. The fundamental nature of this cognitive capacity is most readily apparent in various reports in the literature of individuals who display navigational difficulties as a result of memory disturbances. Whiteley and Warrington (1978) have described a patient with unimpaired visual, perceptual, and attentional faculties who was unable to recognize novel landmarks. Conversely, there are cases of individuals whose general cognitive functioning, including memory for landmarks, is intact, yet they do not appear to remember the location of, and spatial relationships between landmarks (De Renzi, Faglioni, & Villa, 1977; Bottini, Cappa, & Sterzi, 1990). However, it is important to distinguish loss of topographical memory from perceptual disorders (e.g., prosopagnosia) that prevent an individual from recognizing landmarks (Landis, Cummings, Benson, & Palmer, 1986).

Amnesia and Memory Subtypes

Memory is not a unitary process. Rather, it is dependent upon the operation of several component systems highlighted in cases of patients with amnesia produced by selective damage to the medial temporal regions (i.e., hippocampal formation) of the brain. There is usually a retrograde amnesia for information learned during a period of time prior to the onset of damage. However, the cardinal feature of amnesia is a severe impairment in the acquisition of explicit factual information encountered after the damage (anterograde amnesia) that contrasts with relatively preserved immediate, remote, and implicit memory functioning (Moscovitch, 1982; Squire & Cohen, 1984; Schacter, Chiu, & Ochsner, 1993). For instance, amnesics are unable to learn and recall unrelated paired associates and contents of short stories (e.g., Cutting, 1978 and Squire & Shimamura, 1986, respectively). H.M., the well-studied patient who was amnesic following bilateral medial temporal ablations to treat epilepsy, was also found not to have learned any words that had been introduced into the English language since his bilateral hippocampal lobectomy (Gabrieli, Cohen, & Corkin, 1988). However, there is growing evidence that amnesics are capable of learning new semantic information in the absence of the spatiotemporal context in which the information was learned (e.g., Shimamura & Squire, 1988; Glisky & Schacter, 1989; Vargha-Khadem et al., 1997). This illustrates a further division of memory into episodic, which is memory for autobiographical events organized in time and identified by particular contexts, and semantic, which is general knowledge about the world not associated with specific learning situations (Tulving, 1983). These distinctions reflect the global involvement of the hippocampal system in memory.

The Hippocampus and Recent Spatial Memory

Animal models. The disruption of recent memory characteristic of damage to the human hippocampal system also includes memory for spatial information. Evidence for the spatial role of the hippocampus derives primarily from single-unit recording in freely-moving rats and from lesion studies showing a performance impairment in hippocampally-damaged rats on spatial tasks. Seminal work on this topic was conducted by O'Keefe and Dostrovsky (1971) who recorded the activity of individual pyramidal cells in the hippocampus of rats as they moved about in their environments. Different neurons in the hippocampus were found to have different spatial receptive fields and responded only when a rat was in a particular location. These 'place cells' appear to be guided by visual stimuli, because their receptive fields are altered when objects outside an environment are relocated. It is notable that O'Keefe and Nadel (1978) proposed that the locations of landmarks are not remembered absolutely. Rather, memory for locations is processed either in reference to the organism (i.e., egocentric processing) or relative to objects in other locations (i.e., allocentric processing); the hippocampus appears to govern the latter. Finally, Thompson and Best (1990) obtained data that cognitive maps within the hippocampus are stable, as they found that the receptive fields of place cells remain unchanged for lengthy periods of time.

Studies of rats with hippocampal damage also indicate that this structure is important in the ability to learn spatial relations. The Morris Water Maze, a circular pool of milky water with a hidden platform, requires rats to find a particular location in space solely by means of visual cues external to the apparatus (Morris, Garrud, Rawlins, & O'Keefe, 1982). Following

several trials, normal rats learn to swim directly to the hidden platform regardless of the location from which they are released. However, rats with hippocampal lesions appear to swim in a random fashion until the platform is encountered. In addition, rats permitted to explore a radial arm maze, eight arms that radiate from a central platform with a reward at the end of each arm, learn to retrieve the food efficiently, entering each arm once (Olton & Samuelson, 1976). By contrast, Olton, Becker, and Handelman (1979) have described how lesions to the hippocampus severely disrupt the ability of rats to visit the arms of a radial maze efficiently. Also, bilateral hippocampectomy in the monkey has been found to disrupt the acquisition and retention of associations between object and place (Parkinson, Murray, & Mishkin, 1988). The place cell and lesion studies in rats and monkeys are consistent with reports that the hippocampal formation of cache-storing birds and rodents is significantly larger than that of animals without this ability (see Sherry, Jacobs, & Gaulin, 1992). Taken together, animal research supports the proposition that cognitive maps are established in the hippocampus in the form of neural networks, and the firing pattern of place cells seems to guide animals to goals in familiar environments.

Human models. Animal research on the hippocampus accords well with findings in humans. For example, Smith and Milner (1981) studied patients following unilateral brain operations to relieve epilepsy and found that only patients with extensive excision to the right hippocampus were unable to recall the location of objects in spatial arrays after a 4-minute delay. In another study of patients with unilateral damage to the hippocampus, Abrahams, Pickering, Polkey, and Morris (1996) investigated performance on the Nine-box Maze, the human analog of the radial arm maze. Participants were instructed to learn the location of common objects hidden

in cylindrical containers fixed around a board. Following a shift in viewpoint to ensure allocentric processing, participants were asked to locate the hidden objects, relying only on cues external to the apparatus. The researchers found a selective spatial memory deficit on the maze in patients with right hippocampal damage, but intact performance in patients with corresponding damage to the left side. Moreover, recognition for spatial elements in complex visual scenes appears to be compromised in patients with right temporal lesions (Pigott & Milner, 1993). Right hippocampal damage has also been associated with impairments on spatial block tapping sequences (Corsi, 1972) and on visual and tactual stylus maze learning (Milner, 1965, and Corkin, 1965, respectively). However, unilateral lesions to the left medial temporal lobe have also been found to compromise certain aspects of spatial memory (see Maguire, Burke, Phillips, & Staunton, 1996a).

Extra-hippocampal structures. Although there is a large body of evidence implicating the hippocampal formation in spatial memory, the inability to identify place cells within the monkey hippocampus (Rolls, 1991) and the observation that unilateral hippocampal lesions do not necessarily selectively impair topographic behavior in humans suggest that alternate regions may subserve this function in humans. Indeed, damage in the patients with spatial memory loss described by Habib and Sirigu (1987) was confined to the parahippocampus and subiculum. A neuroimaging study conducted recently by Milner, Johnsrude, and Crane (1997) revealed that memory for item location on a panel activated both the hippocampus and the parahippocampus. In a separate neuroimaging study, Aguirre presented his participants with a large-scale virtual maze of an environment and found that medial-temporal activity was restricted to the

parahippocampus during the learning and recall of topographic information. These findings counter the belief that it is primarily the hippocampus that houses cognitive maps (O'Keefe & Nadel, 1978).

Real-world tasks. It is clear that the cognitive mapping theory has gained a large amount of support from investigations across species, but one restriction in discerning the neural substrates of spatial representations in humans has been the almost exclusive reliance on small-scale, table-top tests which do not account for changes in viewpoint typical of navigation in real-world environments (Maguire, Burke, Phillips, & Staunton, 1996a). Changes in the optic array during active exploration of environments commonly navigated by organisms provide powerful information about movement, location, depth, and the orientation of surfaces. Functionally meaningful stimuli encountered from differing perspectives are internalized and constantly referenced to solve everyday problems involving environmental contexts. In fact, there are reports of patients who show a dissociation between performance on table-top tests of spatial ability and topographical functioning. For instance, Incisa della Rochetta, Cipolotti, and Warrington (1996) described a patient with selective episodic and semantic memory deficits who was unable to provide a description of routes in a familiar environment but showed no deficit in identifying countries and cities on an outline map. A patient described by Maguire, Frackowiak, and Frith (1996) was found to be severely deficient at acquiring spatial information for navigation in a novel environment following a right temporal lobe resection. However, he displayed average or above average performance on such visuospatial memory tests as the Corsi Block Tapping task, Rey-Osterrieth Complex Figure, design learning, and maze learning. On the

other hand, Zola-Morgan, Squire, and Amaral (1986) identified a patient who showed signs of intact topographical orientation but was deficient on smaller-scale measures of spatial memory. Thus, although laboratory studies of simple stimuli offer a useful foundation, they do not adequately capture the day-to-day challenges of life in the complex environments of the real world.

Cognitive Maps: An Environmental Cognition Perspective

Spatial features within cognitive maps. An understanding of topographical orientation in real-world environments has been further delayed by widespread disagreement in the environmental psychology literature over the ways in which people mentally structure the physical urban environment. In the exemplary work of Lynch (1960), urban elements were organized into five categories: paths (routes), nodes, landmarks, districts, and edges. Although there is experimental support for this scheme (Aragones & Arredondo, 1985), researchers have since reduced these categories to landmarks and routes (Norberg-Schulz, 1971; Siegal & White, 1975). In general, landmarks refer to salient environmental features which serve as reference points and signal navigational decisions (Sadalla, Burroughs, & Staplin, 1980), whereas routes refer to the sequencing of landmarks (Siegal & White, 1975). Another controversy concerns which features of a new environment are learned first. Although this controversy exists (Evans, 1980), it is argued that the maintenance of geographical orientation necessarily relies on memory for landmarks (Lynch, 1960; Siegel & White, 1975).

Synthesis of spatial features into cognitive maps. Debate also surrounds the exact processes underlying the integration of these urban elements into a cognitive map of large-scale

space. However, many researchers in the environmental domain seem to promote a stage-model of cognitive maps which is envisioned to advance from the simple encoding of landmarks in relation to the organism (i.e., undifferentiated egocentric) to a more complex mental representation of the spatial relationships between landmarks (i.e., differentiated allocentric and abstractly coordinated; see Piaget & Inhelder, 1967 and Hart & Moore, 1973). The five-stage model proposed by Siegal and White (1975) is especially significant, as it shows a strong parallel between a child's acquisition of spatial competence and an adult's acquisition of the spatial structure of a new environment. The initial stage of spatial mapping involves the memory of isolated points of reference in environmental space, analogous to a type of 'photographic' knowledge. The second stage is identified by the rudimentary organization of routes around the single points of reference. Third, a number of distinct spatial clusters become cognitively integrated. Orientation ability appears in the fourth stage, signaling the development of a more objective reference system. Finally, additional routes within the environmental space are coordinated in relation to the system of reference formed in the former stages. Similarly, the three interrelated components of a cognitive map posited by Garling et al. (1984) include: information regarding units constituting environmental space, the egocentric and allocentric spatial relations which can be established between them in terms of direction-distance or proximity, and indications about the ways individuals can reach a determined point in the environment.

Role of familiarity. Interestingly, these models presuppose some degree of familiarity with the environment in question (Garling et al., 1984). Other studies have noted the existence

of links between the degree of familiarity individuals have with their own urban environments and the characteristics of their cognitive maps. In particular, detail and accuracy of the maps tend to increase as a function of an increase in the length of residence in the urban vicinity (Moore, 1974), and there is a tendency to overestimate the size of familiar areas (Milgrim & Jodelet, 1976). A study of sketch maps of a university campus drawn six months apart by new students showed significant increases not only in the amount of information, but in the integration of that information (Schouela, Steinberg, Levelton, & Wapner, 1980). Also, Sadalla et al. (1980) have suggested that familiarity is the best predictor of the transformation of landmarks into reference points. They found distance judgments between reference and nonreference points to be asymmetrical; the estimated distance from a familiar to an unfamiliar landmark is not necessarily the same as the distance from an unfamiliar to a familiar landmark.

Extracting spatial information. The various methodologies employed for the analysis of cognitive maps differentially accommodate the stages of acquisition. Landmark recognition tasks are commonly used to test the reliability of other methods. For example, Lynch (1960) asked participants to report whether they recognized photographs of landmarks which were interspersed with photographs of unfamiliar locations and compared these responses with more descriptive methods. Passini (1984) believes that recognition tasks more closely approximate navigation within familiar environments, because it is often the case that an individual need not recall a landmark prior to encountering it within an environment. More importantly, the ability to identify photographs of isolated spatial elements indicates the most basic level of egocentric processing. The second stage involves memory for spatial relations between landmarks in terms

of proximity and direction-distance relations. Participants are typically instructed to decide whether a pair of landmarks are closer together than another pair during proximity judgment tasks (Evans & Pezdek, 1980). Yet, a more advanced method for inquiring about spatial relationships requires numerical judgments of distance between pairs of landmarks. Actual distances are subsequently fitted against estimated distances to yield a correlation coefficient. In fact, numerous experiments have demonstrated that humans are remarkably consistent at representing metric properties of familiar environments (e.g., Golledge & Zannaras, 1973; Baird, Merrill, & Tannenbaum, 1979). For instance, distance estimations between landmarks on a university campus were found to be highly correlated with the actual distances (Baum & Jonides, 1979). Route knowledge could then be assessed by studying the sequencing of landmarks along a specified path. An even more sophisticated navigation system would allow a person to arrive at the same location via a number of different routes that were not necessarily traversed beforehand. Such spatial problem-solving is generally regarded as evidence that a person has graduated from route understanding to survey knowledge (Golledge et al., 1985). However, the most widely-used procedure for the empirical study of spatial cognition popularized by Lynch (1960) assigns individuals the task of reproducing the configuration of spatial elements of a specific environmental setting in a sketch map. This represents the most advanced stage of allocentric processing. Nonetheless, although fractionation of spatial ability is strongly promoted in the environmental cognition literature, very few cognitive neuropsychology studies of topographical disorientation have taken the specific components of cognitive maps into account (e.g., Milner, Corkin, & Teuber, 1968; Zola-Morgan et al., 1986; Beatty, Salmon, Bernstein, & Butters, 1987).

This oversight makes testing of patients less precise than it should be, and may not prove sensitive enough to detect subtle deficits.

Application of environmental methods to neuropsychology. Maguire, Frackowiak, and Frith (1996b) adopted some of these methods when they addressed the issue of navigation in novel, natural environments. Patients who underwent unilateral temporal lobe surgery viewed a film containing footage of two routes taken in a small town in order to test their capacity to encode new environments. Measures to assess memory for spatial relationships ranged from simple proximity and distance judgments to more complex sketch map and locational accuracy tasks. Both right and left temporal lobe patients exhibited difficulty on all measures, with the exception of intact performance on the proximity task by the left temporal group. These findings suggest that acquisition of allocentric spatial mapping during real-world navigation relies on the integrity of both temporal lobes. Encoding of new environments also seemed to activate the hippocampus in a positron emission tomography (PET) study conducted by Maguire et al. (1996a). Participants were scanned as they learned to navigate through a video-taped small town. This navigation condition was contrasted with a static condition that also included film footage of a similar urban district, but the camera was stationary. Although construction of a cognitive map was not permissible in the second condition, both conditions involved comparable episodic memory demands. Subtraction of the static condition from the navigation condition revealed activity localized in the medial parietal region, right hippocampus, and bilateral parahippocampi, whereas the static condition alone produced patterns of activation that did not include the medial temporal lobes. In a separate study, Ghaem et al. (1996) imaged subjects as they imagined

themselves navigating through a large-scale environment. While being scanned, participants imagined that they were retracing a path that they had walked along the day before as they were scanned. This group reported activation of the posterior cingulate, precuneus, and bilateral hippocampal and parahippocampal regions during retrieval of recent spatial knowledge. Based on the congruence between this behavioural and neuroimaging data, it can be concluded that topographical learning and recall broadly share the same neural network.

The Hippocampus and Remote Spatial Memory

Although the studies mentioned above appear to confirm the importance of the hippocampus and parahippocampus in short-term spatial memory acquisition and retrieval, they do not consider retrieval of well-rehearsed environmental information learned many years prior to the experiment. Indeed, active encoding might continue to occur during the retrieval of recently-formed memories. But, more importantly, most human behaviour takes place in familiar environments, and this long-standing knowledge exists in the semantic memory store of general facts. To date, the only attempt to acknowledge the retrieval of remote spatial information was in a follow-up PET study conducted by Maguire, Frackowiak, and Frith (1997). These researchers recruited London taxi drivers of many years experience and presented them with various tasks that were either topographical or nontopographical and involved either a sequencing component or not. More specifically, in the topographical conditions with a sequencing or static component, participants were asked either to construct the shortest possible route between several locations in London from their remote knowledge of this geography or to provide a description of famous landmarks that had never been visited by participants, respectively. The latter condition

prevented the confound of location information. In order to fulfill the two nontopographical conditions, participants were either required to recall and describe plots or static frames, both from famous films. This factorial design permitted the researchers to establish whether common brain regions subserve semantic memory notwithstanding memory type. The most relevant findings were that both topographical conditions showed increased activation of the parahippocampal gyri relative to the nontopographical conditions and the right hippocampus was only active during the route-recall task in comparison to the other three conditions. The finding of parahippocampal activity during the route-recall and landmark tasks provides further evidence that this structure responds to the location of objects in space. Of equal importance, it now seems quite clear that the hippocampus is engaged during processing of recent as well as of remote memory for spatial layouts.

Amnesia and Remote Memory Preservation

Amnesia, however, can also be defined by the kinds of memory that are commonly spared. As briefly mentioned above, studies have found amnesics to be able to learn new information or skills normally even when they are unable to recall explicitly the circumstances of learning, indicating preserved implicit memory (Tulving, Hayman, & Macdonald, 1991; Schacter et al., 1993). Likewise, there is evidence in many studies of patients with damage to the medial temporal lobe of a temporal gradient in memory impairment (i.e., Ribot's Law) with significantly better performance on tests of memory for remote events as compared to memory for more recent events. Consolidation refers to the conversion of short-term memories into long-term memories and is viewed as the basis for the resistance of remote memories to disruption over time. Graham

and Hodges (1997) explain that memories from the distant past are consolidated and stored in the neocortex and do not require retrieval by the medial temporal area of the brain. Measures of memory for remote events include recognition tests of famous faces and recall and recognition tests of famous names and events. The former test, developed by Butters and Albert (1982), involves presenting participants with pictures of famous individuals from the distant to the more recent past. Amnesic patients exhibited little difficulty remembering famous faces from the distant past compared to those from more recent time periods. Findings also indicate that the ability to locate either gross or specific geographical features on the Fargo Map Test (FMT) of remote memory for visuospatial information was preserved in patient J. N. who underwent a right temporal lobectomy (Beatty, MacInnes, Porphyris, Troster, & Cermack, 1988). On the premise that established geographical knowledge of regions of former residence is widely shared by others and persists for at least 30 years after one has moved to a new region (Beatty, 1988; Beatty & Spangenberg, 1988), the FMT serves as a reliable test of semantic memory for remote spatial information. However, as mentioned previously, sound performance on table-top stimuli does not necessarily predict topographical functioning in real-world settings. In fact, the patient documented by Zola-Morgan et al. (1986) had sustained selective hippocampal damage resulting in anterograde amnesia and did not present topographical disorientation in a familiar neighbourhood. Another instance of such sparing was found in patient K.C. who was described as unable to remember recent events for more than a few seconds following extensive bilateral hippocampal and possible parahippocampal damage (Tulving et al., 1991), yet appeared to exhibit few, if any difficulties in navigating his own neighbourhood (TV Ontario, 1988). Thus, it

appears plausible that preserved remote memory in amnesia might extend to topographical memory in large-scale, natural environments.

The Extent of Hippocampal Involvement in Remote Spatial Memory

Consistent with the degree of his medial-temporal-lobe damage, K.C. exhibits severe anterograde and extensive retrograde amnesia on explicit tests of episodic and autobiographical memory. However, his performance on implicit tests of memory, whether perceptual, conceptual, or procedural, is normal, and his semantic memory, both remote and recently-acquired, is relatively preserved (Tulving et al., 1988 & 1991). Given this pattern of impaired and preserved memory functions, we were interested in knowing whether remote spatial memory would be dependent on the hippocampus and be as impaired as K.C.'s autobiographical memory or whether it would be spared like his semantic memory.

In addition, it is difficult to reconcile the navigational ability of the amnesic patients mentioned above with Maguire et al.'s (1997) finding that the medial-temporal region is activated during the retrieval of familiar routes from remote memory. A city that offers abundant landmarks and complex routes differs fundamentally from the simple infrastructure of a neighbourhood. In addition, the hippocampal activation in the neuroimaging study might have been peculiar to the task administered to participants. Specifically, judging the shortest route to a destination point is a form of problem-solving which may involve the recruitment of brain areas not normally activated during simple recall of the location of landmarks along routes. In general, little is known about the role of the hippocampus in recovering remote topographical knowledge. If the hippocampus is needed for maintaining and recovering cognitive maps as these

investigators have suggested, damage to the hippocampus should impair remote memory for cognitive maps much as it impairs acquisition.

The goal of the present study is to use a variety of environmental tests to determine whether K.C. has a representation of his neighbourhood in the form of a cognitive map and whether he is able to manipulate this information to reach a specified goal. K.C.'s navigational performance will be compared with that of neurologically-intact controls on a series of tasks ranging from standard, small-scale to naturalistic, large-scale in an attempt to discover how the patient's unimpaired remote memory influences his spatial ability in a familiar setting. The real-world topographical tasks were adopted from the field of Environmental Cognition (discussed above) to simulate some of the demands on memory posed by environmental circumstances in the natural world. It is notable that there is no published systematic study of spatial memory for familiar environments in patients with bilateral medial-temporal damage; such a demonstration would suggest a temporal gradient for spatial memory in amnesia and counter the well-established argument that the hippocampal formation is the seat of all spatial memories.

Method

Participants

The Patient

K.C., a 47-year-old man, became amnesic following a closed-head injury from a motorcycle accident in 1981. High-resolution magnetic resonance images (MRI) reveal that K.C.'s brain damage is widespread (see Figure 1), and damage is more prominent in the left than in the right hemisphere. Of most relevance, a close examination of K.C.'s hippocampus indicates

that it is severely reduced in volume bilaterally compared to age-matched controls (see Table 1). With respect to his parahippocampal gyri, there is clear bilateral atrophy with few signs of actual damage, making it difficult to judge whether this region functions normally (see Table 1). Other damage includes a large left white-matter lesion in dorsal frontal-parietal cortex and an additional large lesion in left occipital-temporal cortex. Damage is also found in the medial occipital-temporal-parietal and occipital regions. It is notable that K.C.'s left posterior occipital-temporal lesion extends into retrosplenial cortex, as it may also contribute to his memory deficits. Other limbic structures such as the mammillary bodies, the septal area, and the fornices also show clear signs of atrophy. Given that the damage exhibited by K.C. is rather wide-spread, demonstration of preserved remote spatial memory would be all-the-more remarkable.

Patient K.C. has been extensively studied by many researchers (e.g., Tulving, Schacter, McLachlan, & Moscovitch, 1988; Tulving et al., 1991; Köhler, Black, Levine, & Tulving, 1994) because his amnesia is relatively pure. His intellectual ability as measured by the Wechsler Adult Intelligence Scale-Revised (Wechsler, 1981) is 88 (VIQ = 96; PIQ = 79; Köhler et al., 1994) and his immediate verbal memory are normal (Tulving et al., 1988, 1991). He is able to repeat 8 numbers forwards and 5 backwards and recall 9 items both forwards and backwards on the visual memory span subset of the Wechsler Memory Scale-Revised (WMS-R; Wechsler, 1987). He shows normal language comprehension on the Token Test and near-normal frontal lobe functioning as assessed by the Wisconsin Card Sorting Test. Also, it has been demonstrated that implicit conceptual and perceptual memory, as well as semantic learning is relatively preserved in K.C. With regards to visual perception, K.C. is able to perform the Benton Visual

Discrimination test at an unimpaired level of 27/32 (above 95th percentile) and the line orientation test at 23/30 (within normal range; Köhler et al., 1994). In general, K.C. can carry on conversations and is polite, well-mannered, and eager to participate in all tasks presented to him.

In contrast to these spared abilities, K.C. has an anterograde and retrograde amnesia for experiences and events. This total loss of episodic memory is quite atypical of individuals with bilateral hippocampal damage, but it appears to be particularly pronounced in K.C. Although K.C. is able to maintain information in immediate memory so long as he is not distracted, rehearsal does not appear to have any long-term effects. Indeed, most of his scores on the WMS-R reveal his impoverished long-term memory: Attention and Concentration, 99; Verbal Memory, 70; Visual Memory, 76; and General Memory, 67. Notably, K. C. performs below the scores of typical amnesics on the Warrington Recognition Test (26/50; Warrington, 1984) and the WMS-R Delayed Recall test (< 50 ; Tulving et al., 1991). With particular significance to the present study, K.C. appears unable to acquire new spatial memories. He was unable to reproduce the various paths taught to him on Milner's (1965) visually-guided stylus maze or the series of turns required to successfully navigate a large-scale route from a classroom to a washroom on the ground floor of a university building (Hayman, personal communication). K.C. can recall older semantic memories quite well, but he has a retrograde amnesia for semantic information attained during the several years preceding his brain damage. Also, he did not perform normally on perceptual tests such as the Hooper Visual Organization Test of perceptual integration of fragmented objects (13/30, $t = 79$) and copying of the Rey-Osterrieth Complex Figure (17/36; for a description of these tests, see Lezak, 1983). He also had deficits on the Benton Face Recognition test, where he

obtained 31/54 (within the 1st percentile). Finally, K.C. displayed visual impairments in color perception on the City University Color Vision Test (classification: borderline tritan) and on the Farnsworth-Munsell 100-hue test (Köhler et al., 1994). A more detailed description of the case history and results of the general neuropsychological testing for K.C. is provided in two separate case studies conducted by Tulving et al. (1988, 1991).

Controls

K.C.'s performance on remote spatial memory tests was compared to that of two neurologically-intact controls: K.C.'s 76-year-old mother (R.C.) and 44-year-old brother (P.C.).

All participants were right-handed and had 16 years of education. None of the participants had difficulty navigating in their neighbourhood as indicated by their ability to roam freely in it on foot or by car.

Materials

Topographical Orientation Tasks

For the vector map task, there were seven pieces of 8.5 X 11 paper on which lines were drawn representing two parallel streets running from East to West in the participants's neighbourhood. Both streets were drawn in their correct positions on the top and bottom of the page, representing North and South, respectively.

For the forced-choice recognition and identification task, forty-eight photographs of familiar landmarks and salient houses (e.g., located on corners or next-door, belonging to friends) were taken along three routes known to have been frequently traversed by all participants (Figure 2). Landmarks were operationally defined as distinct objects within a particular environment that

might serve as organizing features. An additional 48 photographs of landmarks taken in unfamiliar neighbourhoods served as distractors; half were taken in a similar-looking neighbourhood and the other half were taken in a dissimilar-looking neighbourhood. All photographs were taken with a 35-mm automatic camera with colour film at average "eye-level."

Standard Spatial Task

The standard version of the Fargo Map Test (FMT-S; Beatty, 1988) was adapted to Canadian geography. Specifically, five high-resolution outline maps (i.e., inclusion of external boundaries only) were generated on the computer. The Continent Location Task was a world map with a small blank space located on each of 7 continents along with a list naming the 7 continents printed on a separate sheet of paper. The stimuli for the Gross Feature Location Task was similar in construction to the Continent Task: a map of North America with small blank spaces corresponding to certain gross localizations (e.g., Atlantic Ocean, Alaska) and a separate list of the names of each location to be identified on the map. Next, two outline maps of Canada containing 28 numbered dots served as the Canadian Cities Tasks. 18 of the dots represented cities printed on an adjacent list and the remaining 10 dots were distractors. Only capital and major cities (e.g., Victoria, Vancouver) were chosen to prevent the inclusion of items requiring finer discriminations and to ensure approximately equal spacing between numbered dots. The two Canadian maps were identical with the exception that only one contained borders separating the provinces. For the final Regional Task, 17 numbered dots were printed onto a regional map of Ontario-Quebec with a corresponding list of 11 major cities within that vicinity printed on a separate page.

Spatial Acquisition Tasks

An 8.5 X 11 blank piece of paper was allotted for the sketch map. Also, Smith and Milner's object location task (1981) required a 60 X 60 cm board on which 16 unique toys had been placed in a distinct configuration.

Procedure

Participants were tested individually in one session that lasted approximately 90 minutes. Prior to experimentation, descriptive methods for assessing topographical orientation were administered to the patient and controls. In particular, participants were asked to report any difficulties with way-finding in novel and familiar environments, to describe routes that they were most familiar with, and to rate their general way-finding ability. As well, in order to elicit information about familiar routes, the patient sat in the passenger seat of a car and verbally directed the driver to various destination points in the patient's neighbourhood. Topographical and standard spatial tasks were administered to each individual in a fixed order. Administration of topographical tasks progressed from those posited to involve more global aspects of an environment to those posited to involve more specific aspects and were followed by standard spatial tasks. Additional spatial acquisition and visual perception tasks were administered only to K.C. following the standard spatial tasks. No time limit was imposed for any of the tasks.

Topographical Orientation Tasks

Sketch map. On a blank piece of paper, participants were asked to draw a map of their neighbourhood bounded by four street names told to them by the examiner. Participants were asked to include the street network and any salient houses, buildings, or landmarks

circumscribed within the four boundaries. Maps were subsequently analyzed by two independent examiners blind to group membership for the number and positioning of streets and landmarks and for the general orientation of the map (scored on a scale from 1 to 5).

Verbal map. There is a probability that participants will not include certain routes or landmarks in their sketch maps for reasons other than lack of memory (see Downs & Stea, 1973). Thus, to supplement the sketch map, participants were required to describe verbally directions from one landmark to another told to them by the examiner as though they were giving instructions to a stranger who was unfamiliar with the neighbourhood. Verbal reports were recorded verbatim by the examiner and were assessed in a manner similar to the sketch map analysis; the number and order of landmarks and streets, as well as the overall accuracy of directions described by participants were considered across 5 trials.

Blocked-route problem-solving. Next, a human analog to Tolman's blocked route task (Tolman, 1948) was used to test survey knowledge (Golledge et al., 1985). This in-depth measure of route knowledge was assessed across 10 route problem-solving trials. Participants were asked to describe the most efficient route from one specified landmark to another given that the street vital to taking the most direct route was inaccessible. The number of deviations from the most efficient route was subtracted from the total score.

Vector map. The ability to navigate between two locations by means of heading vectors was tested next. Participants were presented with the 11 identical sheets of paper with only the North- and South-most borders defining their neighbourhood. On the first sheet, participants were asked to mark the location of their house with a dot relative to the two major streets

presented to them. The examiner then traced the exact dot drawn by participants on the ensuing five pages and asked the participants to indicate with an arrow the direction and distance to a specified major landmark (e.g., school, shopping mall). On the remaining five pages, the examiner traced the location of each landmark from the prior five trials, one per page, and participants were required to draw an arrow representing the direction and distance to their house. Distance, direction, and location accuracy were subsequently analyzed. Scoring proceeded as follows: 1. judged distances and directions were subtracted from actual distances and directions, respectively, and averaged for each participant separately to yield mean deviation scores, and 2. distance and direction judgments of each participant were correlated with the actual distances and directions, respectively.

Distance judgments. Another method for inquiring about spatial relationships required participants to provide numerical judgments of distance between each of 10 pairs of major landmarks. A sample trial was administered prior to testing in order to give the participants an indication of scale. Varying actual distances between landmarks were randomly intermixed across trials. All trials were conducted in the participant's preferred unit of measure and the examiner recorded each distance judgment verbatim. The mean deviation of the judged distances from the actual distances and the correlation between judged and actual distances were calculated separately for each participant.

Proximity judgments. To assess memory for more basic spatial relationships, participants were asked to decide which of two landmarks was closest in distance to a third landmark. Ten sets of three photographs of major neighbourhood landmarks correctly identified by all

participants (see below) were presented. The actual distance between each set of landmarks varied from trial to trial and the target landmarks ranged from more familiar (i.e., visited more often, more perceptually salient) to less familiar across trials. Trials were randomly ordered and the number of correct responses was recorded by the examiner.

Landmark sequencing. A landmark sequencing task ensued. Participants received 7 randomly-ordered photographs of major landmarks that were taken en route between "start" and "finish" locations and were told to order the landmarks in the sequence that would be passed if the participants were walking along the route. The number of landmarks ordered correctly served as the dependent measure.

Forced-choice recognition and identification. To assess further K.C.'s mental representation of landmarks in his cognitive map, a landmark recognition and identification task was administered. Participants viewed 12 sets of 8 photographs of landmarks, half target and half distractor, that were randomly ordered within each set. Participants were told that only four of the eight landmarks were taken in their neighbourhood and were asked to indicate which landmarks were familiar. Participants were then required to describe the locations of landmarks identified as familiar in relation to where the photographer took the photograph. Hence, not only did this task serve as a test of landmark recognition, but it also provided a measure of memory for place of familiar landmarks in space. "Yes" responses and their respective locations were recorded verbatim.

Standard Spatial Task

The FMT-S was administered to determine if intact remote spatial memory extends to

world geographical knowledge. Following the standard technique described by Beatty (1988), the task proceeded from the identification of gross geographical features (i.e., continents, countries, oceans) to more specific features (i.e., cities) on outline maps of the world, North America, Canada, and Ontario-Quebec. Maps were presented individually along with their respective lists of geographical names. Prior to administration of the FMT-S, participants were told to be prepared to encounter some unfamiliar items and were encouraged to guess if they did not know the exact location of a feature. First, participants were asked to write down the code numbers of seven continents in their appropriate locations on the world map. The second subtest required participants to locate gross geographical features on the map of North America by writing the code number that identified each item in its appropriate location. Next, two outline maps of Canada were presented separately to participants who were instructed to locate 18 cities from 28 numbered dots printed on the map. Finally, participants were shown the map of Ontario-Quebec and their task was to locate 11 cities by writing the number that corresponded to the location of the city in the space after the printed name of the city. Responses were scored as full credit (1 point), partial credit (.5 point), or no credit (0 points), and a percentage of correct and partially-correct localizations was calculated. Targets located closer to borders were weighted less heavily than targets located closer to the centre of a map.

Spatial Acquisition Tasks

Sketch map. In order to assess whether K. C. acquired a cognitive map of a postoperatively-learned environment, he was asked to draw as precisely as possible the general floor plan of the first floor of a library where he has worked from 1997 to the present. He was

instructed to accurately position elements that likely resemble landmarks, such as the main doors, washrooms, reference desk, and bookshelves, and the network of hallways that likely resemble routes.

Spatial location memory. Smith and Milner's (1981) episodic memory task for the spatial location of visually-presented common objects was used to probe memory for the spatial layout of an array of easily identifiable objects (Köhler et al., 1994). The task has been shown to be sensitive to unilateral right-sided and bilateral medial-temporal-lobe damage (Smith and Milner, 1981; Smith, 1988). Two versions (presented one week apart) were administered to K.C. in the same manner as in Smith's study on the densely amnesic patient H.M. (Smith, 1988). At encoding, K.C. was presented with an array of 16 objects and was asked to name each object (which he could do flawlessly) and estimate the price of the real object represented by each toy to ensure that every object was attended to and identified. Immediately following presentation, K.C. was seated in another position, given the empty board and the set of toys, and instructed to place the toys in their original locations on the board. Practice trials which included arrays with 3 objects were administered prior to actual testing to establish that K.C. understood the task requirements. The accuracy of recall of spatial location was assessed by measuring the mean displacement between the assigned location of each object at encoding and the location where it was repositioned by K.C. from memory.

Perceptual Tasks

Given that K.C. is impaired on tests of complex visual perception, it could be argued that any deficit described on the forced-choice recognition memory test for landmarks (see below) is

secondary to perceptual discrimination deficits. To test for this possibility, we also tested K.C. on perceptual matching of landmark photographs and identification of features contained within each photograph. For the matching task, K.C. was presented with a target photograph of a landmark (either major landmark or house) and a set of 4 additional photographs, only one of which was identical to the target. K.C. was asked to place the target with its duplicate in each of 10 trials. Two of trials consisted of matching a pair of the same landmark taken at different orientations. For the feature identification task, K.C. was asked to provide a detailed description of the elements (e.g., objects, colours) in each of 10 landmark photographs.

Results

Topographical orientation tasks

Sketch Maps

Participants were successful at reproducing the configuration of spatial elements (e.g., streets, landmarks) of their neighbourhood in a sketch map. K.C. retrieved 12 streets and 5 landmarks (Figure 3) as compared to R.C. who included 8 streets and 8 landmarks (Figure 4) and P.C. who included 16 streets and 10 landmarks (Figure 5). All 3 maps showed an accurate positioning of landmarks and general orientation (5/5).

Verbal Maps

All three participants provided detailed, precise directions from one specified landmark to another across five trials.

Blocked-Route Problem-Solving

K.C. was able to provide a detailed description of the most efficient route from one

specified landmark to another given that the most direct route was blocked (8/8 correct) relative to the controls (8/8 correct).

Vector Mapping

K.C. performed normally on this task. Specifically, K.C. did not differ from controls in terms of the mean deviation from the correct distance in cm (K.C. = 3.4, R.C. = 3.2, and P.C. = 2.9) or direction in degrees (K.C. = 11, R.C. = 46, and P.C. = 9) as measured on a 10 X 10 cm map of the neighbourhood (see Figures 6 and 7 for an example). It is notable that R.C.'s high distance score reflects errors in confusing right with left; the absolute mean deviation of R.C.'s judged directions from the actual directions in degrees is 6. Further analyses revealed correlations that were significant across all participants (K.C. = 0.87, R.C. = 0.94, and P.C. = 0.96; $p < 0.01$) for actual and judged distances but only significant for K.C. and P.C. (0.80 and 0.88, respectively; $p < 0.01$) for actual and judged directions.

Distance Judgments

With regards to the mean deviation from the correct distance in km, K.C. and the controls performed similarly (K.C. = 0.35, R.C. = 0.39, and P.C. = 0.26). Actual distances were subsequently fitted against estimated distances and yielded correlation coefficients of 0.74, 0.83, and 0.85 ($p < 0.01$) for K.C., R.C., and P.C., respectively. This demonstrates that K.C. is relatively consistent at representing metric properties of familiar environments.

Proximity Judgments

The analysis revealed that K.C. and the controls performed perfectly on this task (6/6). This indicates that K.C. has a strong mental representation of basic spatial relations within his

cognitive map relative to controls.

Landmark Sequencing

K.C. was able to order correctly 6 of the 7 landmarks, whereas the controls displayed perfect performance (7/7).

Forced-Choice Recognition and Identification

Figure 8 demonstrates K.C.'s profound impairment on the forced-choice recognition test relative to the controls. Of the 48 photographs of landmarks taken in his neighbourhood, he chose correctly only 15 items, and of these he was able to identify the exact locations of only 7. In contrast, R.C. identified the locations of 43 of the 45 landmarks that she correctly recognized, and P.C. correctly recognized and identified the locations of 46 landmarks. A more detailed analysis of K.C.'s results revealed that the 7 landmarks correctly identified consisted only of major landmarks, whereas the 33 photographs of landmarks that K.C. could not recognize or identify were of houses. These results indicate that K.C. has some sense of the locations of salient, major landmarks, but is deficient at recognizing and identifying more specific details contained within his cognitive map.

Standard Spatial Task

Figure 9 shows the participants's separate scores for each of the five maps. Results indicated that K.C. and controls performed equally-well at identifying gross features on the two global maps (world = 7/7; North America = 10/10). However, K.C.'s performance was inferior to that of controls on maps that required the identification of cities on maps of Canada (K.C. = 8/18, R.C. = 14/ 18, and P.C. = 14/18) and Ontario (K.C. = 2/11, R.C. = 6/11, and P.C. = 11/11).

Spatial Memory Acquisition Tasks

Sketch Map and Route Learning

In stark contrast to K.C.'s normal ability to retain and operate on a remotely-formed cognitive map of his neighbourhood, K.C. has been unable to acquire new maps since his injury. In particular, he could not retrieve the spatial layout of the floor plan of a library where he has worked for the last two years in addition to his inability to navigate the paths within a university building after extensive training.

Spatial Location Memory

K.C. was severely impaired on a table-top test of spatial memory. Specifically, K.C.'s mean displacement score averaged across both testing sessions was 23 cm. This score was comparable to the one reported by Smith (1988) for H.M., another patient with bilateral hippocampal lesions, who showed severe deficits as compared to normal control subjects (H.M. = 26.5 cm; controls = 7.4 cm). K.C.'s and H.M.'s performance on this task was also inferior to that of patients who underwent right-sided unilateral temporal lobectomy with radical excision of the medial-temporal-lobe region and who showed no deficit immediately after learning but only after a delay (Smith & Milner, 1989).

Perceptual Tasks

K.C. was able to match correctly identical landmarks regardless of orientation and provide accurate, detailed descriptions of the features contained within each photograph presented to him.

Discussion

The objective of the present study was to assess the effect of bilateral damage to the hippocampus on aspects of remote spatial memory that relate to a real-world environment. Remote topographical memory appears to be maintained in an individual with extensive bilateral damage to his hippocampus, countering the early argument that the hippocampus is necessary for both forming and storing allocentric cognitive maps (O'Keefe & Nadel, 1978). Despite his severe amnesia for autobiographical knowledge, K.C. performed normally on spatial tests of his neighbourhood and the world such as natural navigation in his neighbourhood, sketch mapping, vector mapping, blocked-route problem-solving, distance judgments, proximity judgments, sequencing landmarks along routes, and locating gross features on world maps (i.e., continents, countries, oceans). However, he was extremely deficient at house recognition and identification and at locating specific features (i.e., cities) on an outline map of Ontario. He also seemed to experience great difficulty at finding his way around novel environments and learning the locations of objects in an array.

Coherence with Other Cases

Our findings of remote spatial memory preservation are consistent with other, more cursory accounts in the literature of patients with hippocampal lesions who are able to navigate familiar neighbourhoods and reproduce accurate sketch maps of them, though they are extremely deficient at acquiring new spatial knowledge (Milner, Corkin, & Teuber, 1968; Zola-Morgan et al., 1986; Beatty, Salmon, Bernstein, & Butters, 1987). These studies indicate that the hippocampus is crucial for the acquisition of cognitive maps but not for their maintenance and retrieval if the maps had been acquired and extensively used long before injury.

Resilience of Spatial Memories to Partial Hippocampal Lesions

It is conceivable that whatever remains of K.C.'s severely-damaged hippocampus may be sufficient to support a cognitive map of a familiar environment. The literature on ischemia in rats shows that spatial memory acquisition survives even if only a minimal section of the hippocampus remains intact (Auer, Jensen, & Whishaw, 1989; Whishaw, Rod, & Auer, 1994). Rats with damage to the septal half of the CA1 sector of the hippocampus were found to be unimpaired on amphetamine-induced locomotion and negative patterning and only mildly impaired on other tests known to be sensitive to hippocampal damage. However, recent research has demonstrated that spatial memory retrieval in preoperatively-trained rats requires the entire dorsal 70% of the hippocampus (Moser & Moser, 1998). This study revealed that although damage to a select portion of the dorsal hippocampus did not affect new learning, it produced a spatial navigation deficit on the Morris Water Maze in rats that received training prior to experimentally-induced lesions. This finding suggests that, unlike acquisition which can be supported by less than a quarter of total hippocampal volume, retrieval involves a distributed ensemble of neurons within the hippocampus rather than a localized neural network.

Alternate Neural Regions Subservicing Remote Spatial Memory

A more likely alternative is that remote topographical memory may be dependent, instead, on a network of extra-hippocampal structures in the medial-temporal lobe, such as the parahippocampal gyrus (Habib & Sirigu, 1987; Bohbot et al., 1998; Epstein & Kanwisher, 1998), and in the neocortex, such as the parietal lobe (Suzuki, Yamadori, Hayakawa, & Fujii, 1998) and posterior cingulate gyrus (Cammalleri et al., 1996; Katayama, Takahashi, Ogawara, & Hattori,

1999) which is spared in K.C. (see Table 1), but which have been implicated in spatial representation and memory (De Renzi, 1985; Maguire et al., 1997). In fact, these structures have strong, reciprocal anatomical connections. The entorhinal cortex, which serves as the primary source of input to the hippocampal formation, receives its inputs from the cingulate cortex either directly or indirectly via the perirhinal and parahippocampal cortex and relays output from the hippocampal formation back to the same regions that provide inputs (Suzuki & Amaral, 1994a, 1994b). The posterior cingulate cortex strategically links the parahippocampal with the parietal associative (area 7a) cortices (Cammalleri et al., 1996; Van Hoesen, Morecraft, & Vogt, 1993). Finally, the parietal lobe is reciprocally connected to the hippocampus via the parahippocampus (Suzuki & Amaral, 1994a; Rockland & Van Hoesen, 1999).

Parahippocampal gyrus. As a result of its intricate direct connections with the hippocampus, deficits resulting from parahippocampal lesions may reflect inadequate input to the hippocampus rather than exclusive parahippocampal dysfunction (Bohbot et al., 1997). As in K.C., patients with parahippocampal damage often exhibit difficulties in finding their way around new environments (Habib & Sirigu, 1987; Bohbot et al., 1998), but this may partly reflect an inability to process the geometry of new spatial layouts (Epstein & Kanwisher, 1998) and mentally retain the positioning of objects in space (Milner et al., 1997). Nonetheless, whether this region offsets any topographical dysfunction relating to K.C.'s hippocampal lesions remains uncertain, as the extent to which this region functions normally is unknown.

Parietal lobe. Researchers have differentiated between dorsal and ventral streams in visual processing, the former being concerned with 'what' objects are and the latter with 'where'

objects are (Ungerleider & Mishkin, 1982). Rather than representing objects within an allocentric framework, the parietal lobe, which is part of the dorsal stream, has been implicated in the coding for spatial location of objects within an egocentric framework. This theory partially derives from the observation that individuals with right parietal damage experience a neglect of the contralateral half of space that travels with their body movements (e.g., Farah, Brunn, Wong, Wallace, & Carpenter, 1990; Karnath, 1994) disabling them from representing locations of objects in reference to the body. The animal literature describes how visual and saccadic signals of parietal neurons respond strongly to head position, and these 'heading-vector' cells specify the direction and distance of the goal from body-centred coordinates (Brotchie, Andersen, Snyder, & Goodman, 1995). Maguire et al.'s (1997) imaging study goes further to suggest that this region is involved in the sequencing component of topographical memory; both the medial and inferior parietal cortex were active during comparisons between the sequencing of film plots (non-topographical) and landmarks (topographical).

Accordingly, the compensatory support provided by K.C.'s posterior parietal cortex is most readily apparent in his intact vector mapping and landmark sequencing, but this region is probably less involved in K.C.'s sketch mapping and landmark recognition. A patient recently documented in the literature manifested topographical disorientation following right medial parietal damage in the absence of an afflicted cognitive map as evidenced by her ability to draw sketch maps, describe routes, and recognize landmarks (Suzuki et al., 1998). Instead, her inability to navigate in the real world and in a novel environment with the aid of a map appeared to be associated with an inability to identify the viewpoint of a landmark or building, a deficit of

the viewpoint-dependent, egocentric processing system (Milner & Goodale, 1995). That is, landmarks no longer conveyed directional information to this patient.

Posterior cingulate gyrus. Actually, the posterior cingulate, which is strategically situated beside the medial parietal lobe, was hypothesized to contribute to this patient's viewpoint-identification deficit (Suzuki et al., 1998). However, another patient with a right posterior cingulate lesion (BA 29) that did not extend into parietal or temporal cortex was described as unable to learn new routes although she was able to orient in environments that were familiar before her injury (Katayama et al., 1999). Sutherland and Hoising (1993) found that rats with damage to the same region performed similarly to hippocampectomized rats and concluded that both structures are involved in spatial mapping. Even so, Katayama et al.'s investigation was too casual to compare to the present case of preserved and impaired aspects of spatial memory.

Insufficiency of Functional Neuroimaging Studies

The pattern of preservation found in the present study argues against Maguire et al.'s (1997) conclusion that episodic and semantic spatial memory, alike, are subserved by the hippocampal complex. These researchers defined a spatial memory task as semantic if it concerned retrieval from long-standing topographical knowledge as opposed to retrieval of newly-acquired environmental information where memory for the learning episode is still accessible. Nonetheless, this definition does not rule out the possibility that well-established spatial memories are not enmeshed in a consciously-accessible spatiotemporal context.

Historically, knowledge of the neural correlates of human behaviour was derived from the study of impaired and unimpaired functioning displayed by lesion patients. There is no doubt

that lesions often extend outside the region of interest, a dilemma that is somewhat evaded by functional neuroimaging, as it provides the resolution sufficient to visualize those regions engaged during memory processing. Nevertheless, the present study indicates that the critical activation obtained by Maguire et al. (1997) during the retrieval of remote spatial information occurred in the brain region that was severely damaged in K.C., yet this fact had little bearing on his global topographical memory for a well-rehearsed neighbourhood. This opposing finding is open to many possible interpretations. As mentioned earlier, tasks may differ across the two studies in terms of the size and structure of the environment that must be operated on and the demands it poses on participants's cognitive processing. In addition, the subtraction method used in Maguire et al.'s (1997) study necessarily assumes fractionation of memory processes, and hippocampal activation may represent correlated memory processes that are not specific to remote spatial memory. Also, when using this subtraction method, these researchers employed a great deal of subjective interpretation; they had reported activation as arising from the difference between tasks which varied according to their topographical and sequencing requirements, but these comparisons may have been confounded by task difficulty and duration.

The Hippocampus and Non-Salient Feature Recognition and Identification

Relation of house recognition to episodic memory. The hippocampus may still be essential for the retention of detailed, incidental knowledge of non-salient landmarks associated with a cognitive map as indicated by K.C.'s failure to recognize and identify the locations of houses in his familiar neighbourhood. These specific topographical details may correspond to the specific, context-dependent events and personal experiences associated with episodic

memory. Likewise, well-rehearsed spatial layouts representing a cognitive map of a familiar neighbourhood may resemble other context-independent general facts that are the hallmark of semantic memory. If so, K.C.'s impaired memory for non-salient landmarks but spared cognitive map may parallel his profound episodic memory failure for details of personally-relevant information but relatively intact remote memory for semantic information and for the gist of personal experiences. This demonstration of a behavioral dissociation is crucial to our argument and can be considered independently of the histology controversy discussed above.

Interestingly, left lateral prefrontal activation was related to landmark recall, but not route recall, in Maguire et al.'s (1997) PET study of remote spatial memory in London taxi drivers. Functional neuroimaging studies assert that the left prefrontal cortex is preferentially involved in episodic memory encoding, particularly of verbal material, whereas enhanced activity in the right prefrontal cortex is associated with episodic memory retrieval (Tulving, Kapur, Craik, Moscovitch, & Houle, 1994; Shallice et al., 1994; Nyberg, Cabeza, & Tulving, 1996). In a study of imagery and semantic relatedness on cued retrieval of word pairs (Fletcher et al., 1996), recall of non-imageable words was accompanied by left dorsolateral prefrontal activity. These researchers believed that subjects created additional semantic connections between cues and responses for words that were non-imageable. Perhaps such is the case with recognition of less salient landmarks when they are presented as photographs which lack contextual information (e.g., their position relative to other structures in a neighbourhood), making them less imageable. This interpretation is notable since the controls's house recognition appeared to be related to their verbal descriptions of the families residing in each house, whereas more major landmarks and

spatial layout did not seem to involve such extended networks of associative information.

Whether similar neural activity would be found during recognition of familiar houses but not major landmarks is unclear, but a functional neuroimaging study investigating the anatomical relationship between episodic memory and house recognition would be informative.

Multiple Trace Theory. If, in fact, memory for details within a remotely-formed cognitive map is a form of episodic memory, remote spatial memory would conform better to a multiple trace model of hippocampal memory processing (Nadel & Moscovitch, 1997) rather than to a standard consolidation model (e.g., Squire & Amaral, 1995; Squire & Zola Morgan, 1996). In particular, the former acknowledges the continuous contribution of the hippocampus to the retrieval of episodic memories across the entire life span, accounting for the relatively flat temporal gradient in episodic memory loss displayed by patients with selective medial-temporal lobe pathology. Episodic memory traces are represented as spatially-distributed interactions between the hippocampus and neocortex, and the number of traces is positively related to the frequency of recalling the episode in question. Accordingly, partial hippocampal damage would lead to a temporally-graded memory loss (i.e., better memory for remote events relative to more recent events) similar to that accounted for by the standard model. However, unlike the standard model, complete damage to the hippocampus would lead to both a retrograde amnesia (RA) and anterograde amnesia (AA) for episodic information. In the present case, the sparse amount of hippocampal tissue that remains is insufficient to support any memory trace of specific details within K. C.'s cognitive map, yet inconsequential to his neocortically-stored remote memory for more general spatial information.

Animal models of RA gradients for spatial information. The multiple trace theory has received modest support from models of human behaviour derived from studies with hippocampectomized rats (Nadel & Moscovitch, 1997). Indeed, relatively flat gradients have been found on those spatial tasks in which good performance is critically dependent on hippocampal functioning (e.g., water maze, radial arm maze) in rats that were trained at various time intervals prior to experimentally-induced lesions (e.g., Bolhuis, Stewart, & Forrest, 1994; Weisand, Astur, & Sutherland, 1996; Bohbot, Liu, Thurm, Nadel, & Bures, 1996). These findings oppose those obtained in the present study which showed a temporal gradient for spatial memory. It must be acknowledged, however, that the success of any animal model depends on how closely it resembles human function. Retention intervals of 30 days prior to surgery in rats may not meet the criteria for a definition of remote memory in humans, especially in comparison to an individual who had experienced an environment for close to 20 years prior to neural insult. Also, a remote spatial memory deficit in humans similar to that observed in rats might require a less sophisticated neural network of subcortical and cortical structures, environment in which to navigate, and intrinsic goals directing navigation. Moreover, episodic and semantic memory are human constructs that may not have animal counterparts.

In addition, the animal RA literature is not entirely consistent. Other studies of rats receiving hippocampal lesions following long retention intervals have found a temporally-graded RA for spatial information on tasks for which the hippocampus is essential (e.g., Cho, Beracochea, & Jaffard, 1993; Cho, Kesner, & Brodale, 1995; Kubie, Sutherland, & Muller, in press). However, close examination of these results has revealed subtle defects in the

performance of rats that had received training in the 'remote' past. These rats might have employed a less-than-optimal strategy governed by the neocortex (Kubie et al., in press). This interpretation is applicable to the behavioural dissociation exhibited by K.C. in the present study. The hippocampus and neocortex might normally engage in simultaneous processing of spatial information and cooperate on a given spatial task in the sense that they promote similar behaviours, but each structure would be specialized to address different aspects of the task. The task may be accomplished by either structure alone, but the elements of the task may correspond more closely to the processing style of the hippocampus, thereby leading to suboptimal performance if the hippocampus was disabled and the neocortex took over. In the present case, the elements necessary to achieve the tasks for which there was no observable effect on performance might have been equally-represented by K.C.'s neocortex. However, the house recognition task may be relatively pure in the sense that its elements only correspond to the processing style of the hippocampus.

Visual-perception deficits. It is unlikely that K.C.'s spatial memory impairment is an artifact of the his changing cognitive states, as he was monitored for fatigue, and critical comparisons of performance on tasks were made in the same session and examined by several means. It is possible, however, that K.C.'s poor vision caused by his occipital infarct and developing glaucoma contributed to this house-recognition deficit. Though he displayed perfect performance on perceptual-matching and feature-identification tasks using the same stimuli and was able to perform the Benton Visual Discrimination and line orientation tests at unimpaired levels, he performed poorly on some tests of complex vision. This pattern suggests that he

performs well on tasks that require basic visual feature analysis but exhibits deficits on more complex visual tasks that require the synthesis of multiple visual features.

Specific geographical feature identification. Another deficit revealed by K.C.'s performance that may or may not relate to his difficulty with specific neighbourhood details is his inability to identify specific features on world maps administered in the Fargo Map Test. This finding contrasts with the amnesic patient J.N.'s preserved ability to locate both gross and specific features on the map (Beatty et al., 1988). J.N., however, only exhibited right hippocampal damage and may have adopted compensatory verbal strategies. Beatty et al. also noted that J.N.'s preservation may have been atypical of other amnesics with right hippocampal lesions. In fact, her performance was superior to that of controls which probably resulted from her extensive traveling, but not from any sex differences. Nonetheless, K.C.'s pattern of spared and impaired abilities on this task seems to mirror the performance of patients with Korsakoff's amnesia and Huntington's disease who were found able to locate gross but not specific features on outline maps (Beatty et al., 1988; Beatty, 1989). This may suggest that extra-hippocampal lesions were partially responsible for K.C.'s deficit.

Methodological Considerations

An issue that pervades this study is the use of family members as controls. In addition to constituting an unrepresentative sample, K.C.'s mother and brother both continue to reside in the neighbourhood from which the topographical memory tasks were taken. Perhaps impaired memory for specific neighbourhood details is a feature of normal spatial memory loss when one is removed from an environment for a sufficient amount of time. In fact, it is possible that K.C.'s

impaired cognitive map acquisition of new neighbourhoods extends to an inability to update remotely-encoded details such as houses within an environment. In contrast, R.C. and P.C.'s daily exposure to their neighbourhood may account for their unhindered ability to recognize houses. Thus, future studies of house and major landmark recognition in neurologically-intact individuals who had moved away from a former residence at least twenty years prior to testing might further elucidate the relationship between house recognition and updating. In any case, age-matched individuals who had lived in the same neighbourhood as K.C. but moved from the neighbourhood around the time that K.C. had incurred his injury would serve as better controls.

Conclusion

The present study represents a detailed report of preservation on real-world tasks of remote spatial memory in a patient with bilateral hippocampal lesions. These results both complement and qualify in important ways the findings reported recently by Teng and Squire (1999) on another patient with extensive hippocampal lesions and sparing of remote spatial memory. The additional topographical and geographical tasks employed in the present investigation contribute substantially more information about the function of the hippocampus. In particular, whereas Teng and Squire relied primarily on verbal descriptions of cognitive maps, we used additional nonverbal tests. In doing so, we managed to show that many, varied aspects of spatial memory not tested by Teng and Squire were preserved and, in the case of landmark pointing, that performance exceeded their patient's. More importantly, we discovered that some aspects of spatial memory were compromised, notably recognition of non-salient landmarks.

This suggests that the hippocampus may still be essential for the retention of detailed, incidental knowledge of non-salient landmarks associated with a cognitive map. Nonetheless, neither study attempted to delineate the extra-hippocampal structures responsible for residual spatial functions in amnesia and, hence, do not permit conclusions regarding other patient populations who experience topographical disorientation. Further research is also required to clarify the exact role of the hippocampus in remote spatial memory for details.

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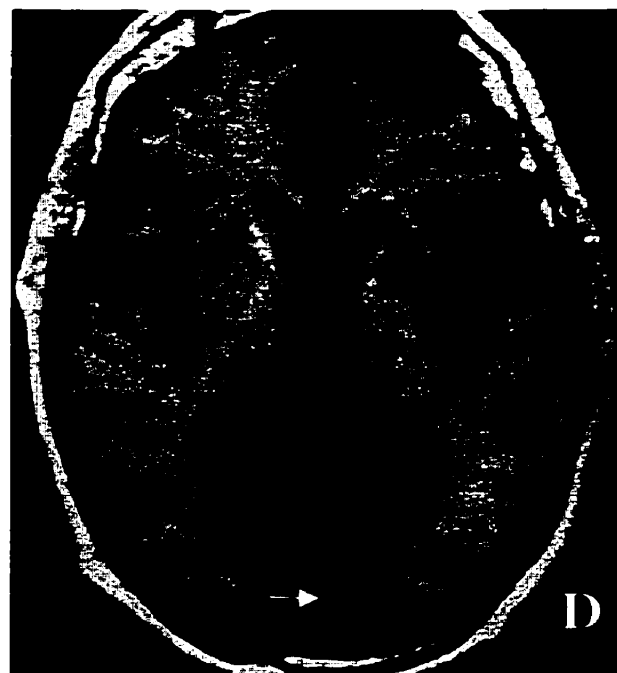
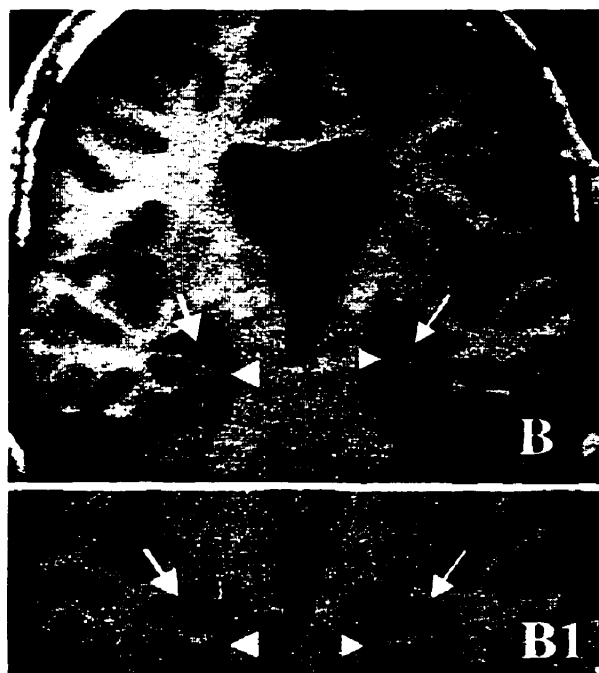
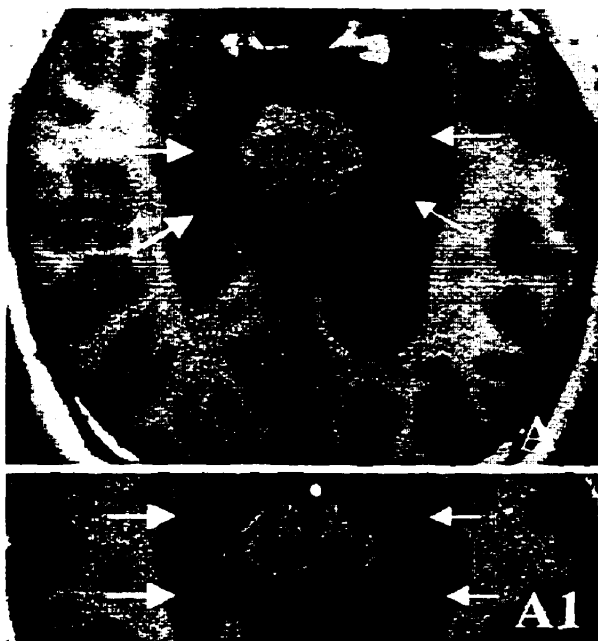
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Table 1

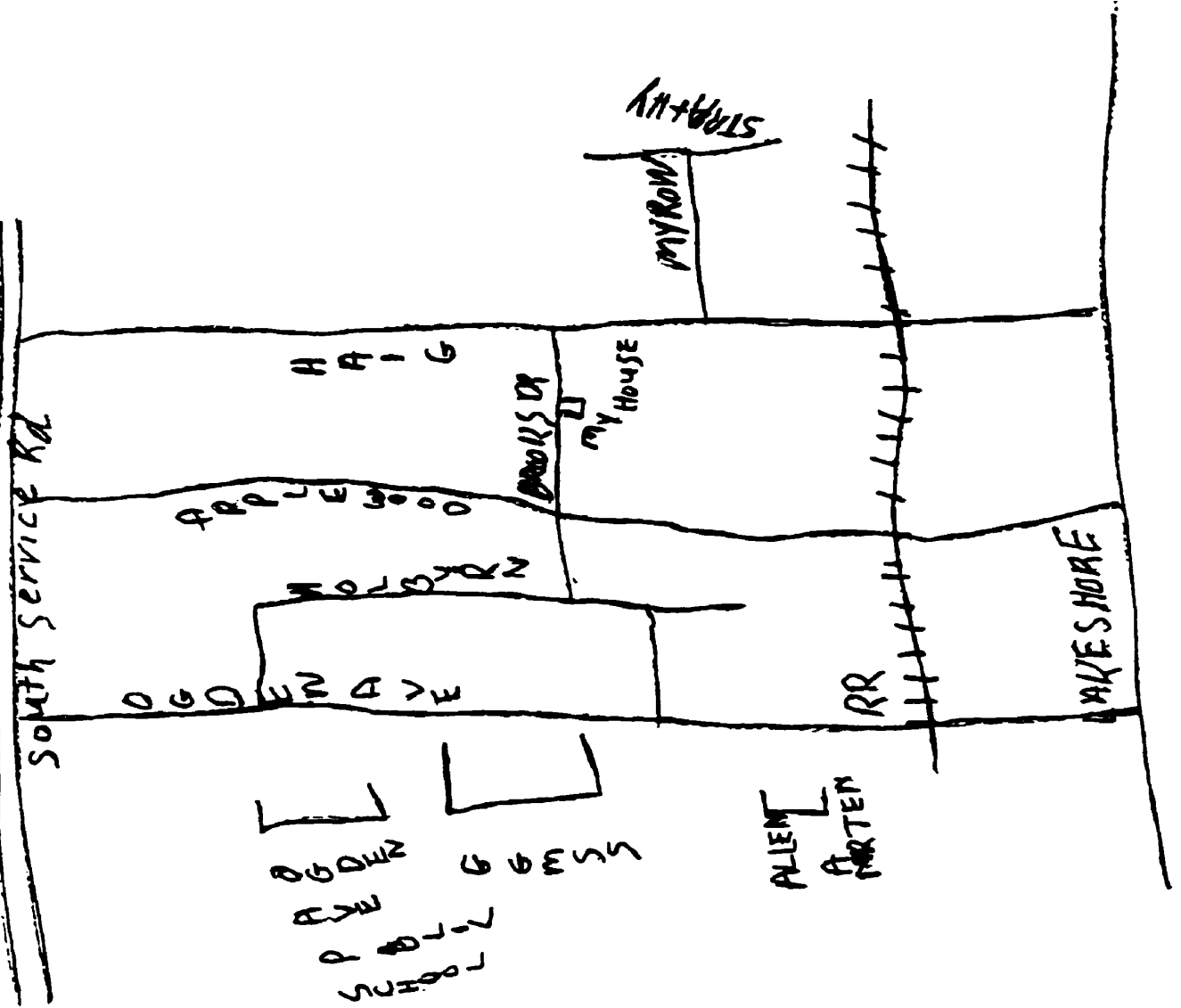
Z-Scores for Medial Temporal and Posterior Cingulate Volumes

	K.C. Z-Score		AD Z-score	
	Right	Left	Right	Left
Hippocampus	-8.6	-7.6	-4.0	-3.1
Parahippocampal Gyrus and Amygdala	-8.7	-6.1	-4.2	-2.4
Posterior Cingulate Cortex	-1.7	-1.3	-1.5	-1.9

Note. The mean head-size corrected volumes for 4 control subjects (mean age = 56) were used to calculate Z-scores for K.C. and a patient with Alzheimer's Disease (AD; age = 54, Mini Mental State Score = 20/30). The AD patient was included for comparison to indicate the severity of K.C.'s hippocampal and parahippocampal lesions and the relative preservation of posterior cingulate cortex.



Q E W



GEW

S. Service Rd

gas station

DIXIE MALL

DIXIE Rd

MYRON DR

HALG BLVD

BROOKS DR

Hydro fields

Hydro field

*Library.
ATWATER

LAKE SHORE BLVD

note

High School
Kendall

ALAN A MARTEN

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Post Office Service.

DIXIE VAPOR

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(Queen Elizabeth Way)



Lakeshore Rd.

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