

Remote spatial memory in an amnesic person with extensive bilateral hippocampal lesions

R. Shayna Rosenbaum¹, Sandra Priselac¹, Stefan Köhler², Sandra E. Black³, Fuqiang Gao³, Lynn Nadel⁴ and Morris Moscovitch^{1,5}

¹ Department of Psychology, University of Toronto, 100 St. George St., Toronto, Ontario M5S1A1, Canada

² Montreal Neurological Institute, Cognitive Neuroscience Unit, McGill University, 3801 University St., Montreal, Quebec H3A 2B4, Canada

³ Sunnybrook and Women's College Health Science Centre, 2075 Bayview Ave., Toronto, Ontario M4N 3M5, Canada

⁴ Department of Psychology and Neural Systems, Memory and Aging Division, University of Arizona, Tucson, Arizona 85721, USA

⁵ Rotman Research Institute and Psychology Department, Baycrest Centre for Geriatric Care, 3560 Bathurst St. Toronto, Ontario M6A 2E1, Canada

Correspondence should be addressed to R.S.R. or M.M. (shayna@psych.utoronto.ca; momos@credit.erin.utoronto.ca)

The hippocampus may have a time-limited role in memory, being needed only until information is permanently stored elsewhere, or this region may permanently represent long-term allocentric spatial information or cognitive maps in memory. To test these ideas, we investigated remote spatial memory in K.C., a patient with bilateral hippocampal lesions and amnesia for autobiographical events. In his spatial knowledge, general aspects were preserved, but details were lost, a pattern that resembled his memory loss in other domains. K.C. performed normally on allocentric spatial tests of his neighborhood and the world. He had difficulty, however, in recognizing and identifying non-salient neighborhood landmarks, and in recognizing city locations on world maps. This suggests that the hippocampus is not crucial for maintenance and retrieval of remotely formed spatial representations of major landmarks, routes, distances and directions, but is necessary for specifying location details, regardless of when they were acquired.

A cognitive map is a mental representation of the spatial arrangement of the physical environment used to facilitate movement toward a goal¹. There is considerable evidence that the hippocampus is necessary for acquiring cognitive maps of allocentric space, which includes topographical knowledge of large-scale, natural environments^{1–4}. Far less is known about the role of the hippocampus in recovering remote (as compared to newly acquired) topographical knowledge. If the hippocampus is needed for maintaining and recovering all aspects of cognitive maps as some investigators have suggested, damage to the hippocampus should impair remote memory for cognitive maps much as it impairs acquisition^{5–7}. If, however, remote spatial memory resembles remote memory in other domains, then we would expect that some general knowledge would be retained, whereas specific details would be lost. Recent evidence indicates that some remote spatial representations are preserved after bilateral hippocampal complex lesions¹. Here we examined remote topographical memory in a severely amnesic patient with extensive bilateral hippocampal lesions in more detail to determine what type of spatial information and environmental features were preserved or lost.

K.C., a 49-year-old man, became amnesic because of 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 (Fig. 1). A close examination of K.C.'s hippocampus indicates severely reduced volume compared to age-matched controls (Table 1) and bilateral volume loss in his parahippocampal cortex. However, there are few signs of actual damage in the parahippocampal cortex of the right hemisphere,

which allows for the possibility of normal functioning of this region. Other regions involved in spatial memory and navigation, such as the right parietal lobe and posterior cingulate cortex, are relatively well preserved. Consistent with the extent of his medial temporal lobe damage, K.C. exhibits severe anterograde and 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. His semantic memory, both remote and recently acquired, is relatively preserved^{8,9}. Given this pattern of impaired and preserved memory functions, we were interested in determining whether K.C.'s remote spatial memory would depend on the hippocampus and would be as impaired as his autobiographical memory, or whether it would be spared, like his semantic memory.

Formal testing addressed the question of whether K.C. had an internal, spatial representation of his neighborhood, how detailed the representation was, and whether he was able to manipulate this information to reach a specified goal. To do so, we assessed his knowledge of distances, directions, routes, locations and landmarks in his neighborhood (in which he has lived for almost 40 years), and of the locations of large geographic features and cities on world maps.

RESULTS

Along with K.C., we tested four controls. The first controls—his mother, R.C., and brother, P.C.—have lived in K.C.'s neighborhood for almost 40 years. The second controls were age-matched males, J.S. and S.M., who moved away from the neighborhood approximately 20 years ago. Each subject was tested on the same

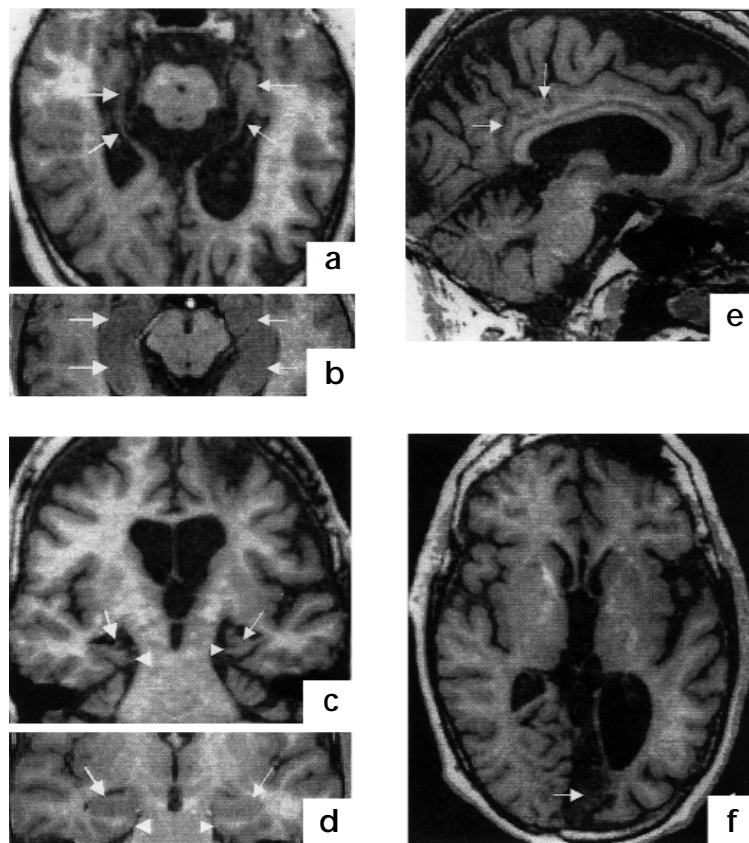


Fig. 1. Magnetic resonance imaging slices showing K.C.'s pathology. (a) Axial view showing severely atrophic right and left hippocampus (arrows). (b) Axial view showing controls' intact right and left hippocampus (arrows). (c) Coronal view showing severe atrophy of the right and left hippocampus (arrows) and atrophy of the right and left parahippocampal gyri (arrowheads). (d) Coronal view showing controls' intact right and left hippocampus (arrows) and right and left parahippocampal gyri (arrowheads). (e) Midsagittal view showing relatively preserved posterior cingulate (arrows). (f) Axial view showing left medial occipital infarction (arrow).

topographical and geographical tasks. Additional spatial acquisition tasks were administered to K.C.

Participants were asked to draw detailed sketch maps of their neighborhood. K.C. retrieved 12 streets and 5 landmarks, compared with R.C. (8 streets and 8 landmarks), P.C. (16 streets and 10 landmarks), J.S. (15 streets and 14 landmarks) and S.M. (11 streets and 13 landmarks). All five maps showed an accurate positioning of landmarks and orientation, although K.C.'s map had fewer landmarks than that of any control.

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 inaccessible; all eight of his descriptions were correct. R.C., P.C. and S.M. also gave eight correct descriptions; J.S. described seven of eight routes correctly.

K.C. was able to navigate between two locations by means of heading vectors. His navigations did not differ significantly from those of controls in terms of the mean deviation from the correct distance in centimeters (K.C., 3.4; R.C., 3.2; P.C., 2.9; J.S., 3.6; S.M., 3.5), or direction (K.C., 11°; R.C., 46°; P.C., 9°; J.S., 13.5°; S.M., 7.8°) as measured on a 10 × 10 cm map of the neighborhood. R.C.'s high direction score reflects errors of confusing right with left; the absolute mean deviation of R.C.'s judged directions from the actual directions in degrees was six. Further analy-

ses revealed correlations that were significant across all participants for actual and judged distances (K.C., 0.87; R.C., 0.94; P.C., 0.96; J.S., 0.80; S.M., 0.99; $p < 0.05$), but only significant for K.C., P.C., J.S. and S.M. for actual and judged directions (0.80, 0.88, 0.95 and 0.91, respectively; $p < 0.01$).

Participants were asked to judge the distances between pairs of landmarks. With regard to the mean deviation from the correct distance in kilometers, K.C. and the controls performed similarly (K.C., 0.35; R.C., 0.39; P.C., 0.26; J.S., 0.26; S.M., 0.40). Actual distances were subsequently fitted against estimated distances and yielded correlation coefficients of 0.74, 0.83, 0.85, 0.99 and 0.97 ($p < 0.01$) for K.C., R.C., P.C., J.S. and S.M., respectively. This demonstrates that K.C. was relatively consistent at representing metric properties of familiar environments.

To assess memory for more basic spatial relationships, we asked participants to decide which of two landmarks was closest in distance to a third landmark. K.C. and the controls performed perfectly on this task (six of six correct), with the exception of S.M., who made one error. Participants were also asked to order landmarks along a route. K.C. was able to order correctly six of the seven landmarks, whereas the controls ordered all correctly.

To assess further K.C.'s mental representation of environmental features and topographical details, he and the other participants were asked to recognize and identify photographs of landmarks in their neighborhood. K.C. had difficulty on this forced-choice recognition test. Of the 48 photographs of landmarks taken in his neighborhood, 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, P.C. correctly recognized and identified the locations of 46 landmarks, J.S. identified 43 of the 44 landmarks that he correctly recognized, and S.M. recognized 47 landmarks, of which he identified 37. A more detailed

analysis of K.C.'s results revealed that all 7 landmarks that K.C. could recognize and whose location he could identify were 'major' ones (for example, a school or shopping center), whereas the 33 photographs of landmarks that K.C. could not recognize or locate correctly were of houses. Moreover, his errors indicated that he had little awareness of the type of building that characterized his neighborhood. He was just as likely to choose buildings different from those in his neighborhood as he was to choose those that were similar. When controls erred, they always chose a house similar to one in the neighborhood. However, K.C. displayed perfect performance on a perceptual-matching task using the same pictures as in the recognition test, and was unimpaired on both the Benton Visual Discrimination test (27 of 32; above 95th percentile) and on the line orientation test (23 of 30; within normal range), matching tasks that measure visual perception of figures and angles, respectively. It is possible, therefore, that K.C.'s poor visual perception, caused by his occipital infarct and developing glaucoma, contributed to his poor performance on the recognition test. However, our results indicate that K.C. has some sense of the locations of salient, major landmarks, but is deficient at recognizing and identifying more specific environmental features that typically are included in one's spatial knowledge of a neighborhood.

The standard version of the Fargo Map Test (FMT-S)¹⁰ was adapted to Canadian geography to determine if intact remote spatial memory extends to world geographical knowledge. Results indicated that K.C. and controls performed equally well at identifying features on the two global maps (world, 7 of 7; North America, 10 of 10). However, K.C.'s performance was poorer than that of controls on maps that required the identification of cities on maps of Canada (K.C., 8 of 18; R.C., 14; P.C., 14; J.S., 18; S.M., 17) and the province of Ontario (K.C., 2 of 11; R.C., 6; P.C., 11; J.S., 11; S.M., 9).

In stark contrast to K.C.'s normal ability to retain and operate on most aspects of a remotely formed spatial representation of his neighborhood, K.C. has been unable to acquire new representations since his injury. In particular, he could not retrieve the spatial layout of the floor plan of a library where he had worked for the last two years, or learn to navigate the corridors in a university building after extensive training. In addition, he had difficulty with a tabletop test of spatial memory³; his scores were comparable to those of H.M., another patient with bilateral hippocampal lesions.

DISCUSSION

There are two major findings in our study, one related to sparing of function and one to its loss, both of which are crucial to understanding the contribution of the hippocampus to maintenance and retrieval of remote spatial memories. Our findings suggest that remote topographical memory is spared in an individual with extensive bilateral damage to his hippocampus, countering the argument that the hippocampus is necessary for both forming and storing all aspects of allocentric cognitive maps¹. Our study showed that, even with severely damaged hippocampi, it is possible to retain a representation of information about routes, absolute and relative distances, the appearance and location of salient landmarks, and directions between identifiable landmarks. Having this representation enables K.C. to navigate easily in his familiar environment, and to find new routes from one location to another when old ones are not usable. K.C.'s performance was normal on tests such as Sketch Mapping, Distance Judgments and Vector Mapping, which do not permit or show ceiling effects even in controls. In this respect, our findings are consistent with other accounts of patients with hippocampal lesions. These patients are able to navigate familiar neighborhoods and reproduce accurate sketch maps of some familiar locations such as floor plans of houses, though they are extremely deficient at acquiring new spatial knowledge¹¹⁻¹³. 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 used extensively, long before the injury.

It is possible that K.C.'s damaged hippocampus may be able to support a cognitive map of a familiar environment. However, it is more likely that remote topographical memory may depend on a network of extra-hippocampal structures involved in spatial representation and memory¹⁴, including the parietal lobe²⁰ and posterior cingulate gyrus^{21,22}, which are relatively spared in K.C. (Table 1). It is less likely that K.C.'s atrophied parahippocampal gyrus¹⁷⁻¹⁹ supports his cognitive map, especially after considering the intact performance of patient E.P. (see below), who has extensive damage in this region¹. Some profound deficits, however, were noted in K.C.'s acquisition of new spatial memories and in retention of some aspects

of remote spatial memory. K.C. failed to recognize houses in his neighborhood and identify their locations, despite often passing them for about 40 years. Similarly, whereas he was able to identify gross geographical features on world maps, he was deficient at identifying the location of cities, which required more detailed knowledge. These deficits indicate that K.C.'s remote spatial memory and his spatial representation of his neighborhood were impaired. Although he remembers necessary information about major landmarks and spatial coordinates needed for navigation, he lacks information about incidental, topographic details and environmental features that make for a rich and individualized spatial representation of a locale. By analogy, his spatial representation can be considered abstract and spatially semanticized, rather than detailed and episodic. Because K.C.'s damage extends beyond the hippocampus proper to encompass adjacent regions of the medial temporal lobe, we attribute this loss to the extended hippocampal system or complex, and possibly the adjacent visual cortex, until there is more evidence to the contrary.

Our results complement and qualify findings in another patient with extensive hippocampal lesions and sparing of remote spatial memory¹. The additional topographical and geographical tasks used in our study contribute more information about the function of the hippocampus. In particular, whereas the previous study¹ relied primarily on verbal descriptions of spatial representations, we used additional nonverbal tests to get information about relative and absolute distances, topographical details of his environment, and world geographical knowledge. Thus, we showed that many varied aspects of spatial memory not tested in ref. 1 were preserved, and, in the case of landmark pointing, our patient was more accurate than theirs. K.C.'s greater accuracy may simply be a function of the areas that were tested, with K.C.'s neighborhood being much smaller than E.P.'s district. Despite a prolonged absence from his district, E.P.'s normal memory for the same aspects of the environment, which were also retained by K.C., suggests that continuous exposure is not needed to maintain those memories. Conversely, even near-daily exposure for 40 years in K.C.'s case was not sufficient to preserve topographical details of the environment after damage to the hippocampal complex. It should be noted that such memories are almost as well-preserved in K.C.'s controls who moved away over 20 years ago as in those who continued to live in the neighborhood. The resilience of such memories may be a function of extensive and prolonged early experience with the environment. Also, though neither of the controls who moved away visited the particular landmarks we tested, one control occasionally visited near the neighborhood, and the other had driven near some of the landmarks, and had possibly been reminded of them. Whatever process is needed to maintain memories of topographical details, our results indicate that the hippocampal complex and perhaps adjacent cortex are involved.

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
Parahippocampal cortex	-4.2	-20.5	-0.6	-3.9
Posterior cingulate cortex	-1.7	-1.3	-1.5	-1.9

Mean volumes corrected for head size 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 of 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.

Although consistent with the assertion that the hippocampus and related medial-temporal structures are not needed for retention of some aspects of cognitive maps¹, our findings counter two stronger claims. The first, developed in the context of traditional consolidation theory, is that all remote memories, spatial or otherwise, are spared after hippocampal complex damage once consolidation is complete. According to this view, the role of the hippocampus in memory is time limited. The second is that normal cognitive maps can exist in a person with extensive hippocampal damage. Our results indicate that the hippocampal complex is needed to retain and retrieve information about details that provide for rich, spatial representations, even of very old, well-rehearsed memories. Thus, very old cognitive maps are compromised following extensive hippocampal complex damage, and perhaps following damage to portions of the inferotemporal cortex. It will be informative to compare K.C.'s performance on the incidental landmark test with that of E.P. and other amnesic people whose damage is more circumscribed than K.C.'s, and thereby learn if lesions restricted to the hippocampal complex, or hippocampus proper are sufficient to produce this loss. As yet, no such data have been reported.

Conceivably, had we tested remote spatial memory for locations visited only once rather than for those that were experienced repeatedly, the deficits may have been even more pronounced, just as episodic memory deficits are greatest for single autobiographical events. We (J. Booker, L.N. and M.M.) are currently in the process of collecting these data on normal people before proceeding to test people with hippocampal complex damage. Even without these data, our results argue against the second of the strong claims, namely that old cognitive maps, in the sense that they are detailed spatial representations, do not depend on the hippocampus and adjacent cortex. Full, rich cognitive maps of the environment cannot be maintained in the face of extensive damage to the hippocampal complex. The specific contributions of different regions of the hippocampal complex remain to be determined, as does how they act in concert with the neocortex and other brain areas to form and retain such detailed representations. As we noted earlier, our results also argue against a version of the hippocampal-cognitive map hypothesis that states that the hippocampus is necessary for representing relational information about salient landmarks, routes, distances and directions. Clearly, such map-like representations can exist in a relatively preserved form even in a person with a badly damaged or absent hippocampal complex. If this version of the cognitive map hypothesis is to remain viable in the face of our evidence and that of ref. 1, it will be necessary to show that performance that is supposedly dependent on cognitive maps can also be supported by fundamentally different types of spatial representations, such as those based on vector headings and landmarks^{24,25}.

The most parsimonious account of evidence on remote spatial memory is that the hippocampus or hippocampal complex is necessary for retention and retrieval of information about topographical details and environmental features, no matter how old the spatial memory. Such information, along with information about the spatial relationships among features, is necessary for constructing a rich, spatial representation of the environment from which a more rudimentary map can be extracted. That map, which can be considered a schematic version of a complex spatial representation, can exist independently of the hippocampus. It may be adequate for navigation but not for conjuring up a rich memory of a particular locale.

The pattern of preserved and impaired spatial abilities in K.C. may correspond to episodic and semantic memory.

Well-rehearsed spatial layouts representing a cognitive map of a familiar neighborhood may resemble other context-independent general facts, which are the hallmark of semantic memory that does not depend on the hippocampus. Likewise, loss of specific topographical details may correspond to the specific, context-dependent events and personal experiences associated with loss of episodic memory, whether recent or remote²⁶. 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^{27,28}.

METHODS

K.C.'s performance on remote spatial memory tests was compared to that of four normal controls: K.C.'s 76-year-old mother (R.C.) and 44-year-old brother (P.C.), who continue to reside in K.C.'s neighborhood, and two males aged 44 and 45 (J.S. and S.M., respectively), who moved away from K.C.'s neighborhood around the time of his injury. All participants were right-handed, had 16 years of education, and had lived in their neighborhood for approximately 20 years before K.C.'s injury. None of the participants had difficulty navigating in their neighborhood as indicated by their ability to roam freely in it on foot or by car. All procedures followed the applicable guidelines on ethical conduct for research with human participants as defined by the University of Toronto and Rotman Research Institute.

Spatial maps. Participants were first asked to reproduce the configuration of spatial elements of their neighborhood (streets, landmarks) in a sketch map. 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.

Blocked-route problem solving. Next, a human analog to Tolman's blocked-route task²⁹ was used to test survey knowledge³⁰. 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.

Vector maps. Vector mapping was tested by asking participants to draw arrows indicating the correct direction and distance between 'major' landmarks (school, shopping center) and their house on 10 sheets of paper with only the northmost and southmost borders defining their neighborhood. Distance, direction and location accuracy were subsequently analyzed. Judged distances and directions were first subtracted from actual distances and directions, respectively, and averaged for each participant separately to yield mean deviation scores. Second, 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 before testing to give the participants an indication of scale. Different actual distances between landmarks were randomly intermixed across trials, and all trials were conducted in the participant's preferred unit of measure. 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. Ten sets of three photographs of major neighborhood landmarks correctly identified by all participants (see below) were presented. The actual distance between randomly ordered sets of landmarks varied from trial to trial.

Landmark sequencing. Participants then received seven randomly ordered photographs of major landmarks that were taken en route between 'start' and 'finish' locations, and were told to order the land-

marks in the sequence that would be passed if the participants were walking along the route.

Landmark recognition and identification. Forty-eight photographs of major and incidental landmarks (salient houses located on corners or next door, belonging to friends) were taken along three routes known to have been frequently traversed by all participants. An additional 48 photographs of landmarks taken in unfamiliar neighborhoods served as distractors; half were taken in a similar-looking neighborhood and the other half were taken in a dissimilar-looking neighborhood. All photographs were taken with a 35 mm automatic camera with color film at average 'eye-level.' First, 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 neighborhood and were asked to indicate which landmarks were familiar. Participants were then required to describe the locations of landmarks identified as familiar by indicating the direction the photographer was facing when the photo was taken, and by providing a brief description of the area surrounding the photographer.

World geographical knowledge. The geographical task, modeled after the Fargo Map Test¹⁰, proceeded from the identification of gross geographical features (continents, countries, oceans) on outline maps of the world and North America to more specific features (cities) on outline maps of Canada and Ontario. Each map contained numbered dots, approximately two-thirds of which corresponded to geographical features listed on a separate sheet of paper. Participants were instructed to match each number with its correct geographical feature on the list.

Acquisition of large and small-scale spatial memory. To assess whether K.C. acquired a cognitive map of a postoperatively learned environment, he was engaged in two large-scale and one small-scale spatial acquisition tasks. He was first 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 position accurately elements that correspond to landmarks (main doors, restrooms, reference desk) and the network of hallways that likely resemble routes.

Next, K.C. was trained across 12 trials to walk along a set route from a lab to a washroom on the ground floor of a university building. The route consisted of eight points at which K.C. was told to turn either right or left. In the test phase, K.C. was asked to retrace a route that he had previously walked with the experimenter.

Smith and Milner's object-location task was used as a tabletop test of recent memory for the spatial layout of common objects³. Two versions (presented one week apart) were administered and scored in the same manner as in a study on the densely amnesic patient H.M.³⁰.

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