



Research report

Impoverished descriptions of familiar routes in three cases of hippocampal/medial temporal lobe amnesia



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ABSTRACT

Recent research has challenged classic theories of hippocampal function in spatial memory with findings that the hippocampus may be necessary for detailed representations of environments learned long ago, but not for remembering the gist or schematic aspects that are sufficient for navigating within those environments (Rosenbaum et al., 2000; Rosenbaum, Winocur, Binns, & Moscovitch, 2012). We aimed to probe further distinctions between detailed and schematic representations of familiar environments in three cases of hippocampal/medial temporal lobe (MTL) amnesia by testing them on a route description task and mental navigation tasks that assess the identity and location of landmarks, and distances and directions between them. The amnesic cases could describe basic directions along known, imagined routes, estimate distance and direction between well-known landmarks, and produce sketch maps with accurate layouts, suggestive of intact schematic representations. However, findings that their route descriptions lack richness of detail, along with impoverished sketch maps and poor landmark recognition, substantiates previous findings that detailed representations are hippocampus-dependent.

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1. Introduction

The hippocampus has long been implicated in learning and memory (Scoville & Milner, 1957), and in spatial memory in particular (O'Keefe & Nadel, 1978). It is well-established that the hippocampus is required for forming new spatial memories in animals (Morris, Garrud, Rawlins, & O'Keefe, 1982;

Olton, Becker, & Handelmann, 1979) and humans (Ekstrom et al., 2003; King, Burgess, Hartley, Vargha-Khadem, & O'Keefe, 2002; Kumaran et al., 2007; Maguire, Nannery, & Spiers, 2006; Rosenbaum et al., 2000; Suthana, Ekstrom, Moshirvaziri, Knowlton, & Bookheimer, 2011; Teng & Squire, 1999; but see Rosenbaum, Cassidy, & Herdman, 2015); less clear is the role of the hippocampus in remote spatial memory

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for places learned long ago. Studies of remote spatial memory in humans suggest that the hippocampus is needed for representing some, but not all, aspects of remote spatial memory. Specifically, individuals with compromised hippocampal function can make accurate decisions about spatial relations contained within remotely learned environments, such as the locations and identity of landmarks, and the distances and routes between them (e.g., [Rosenbaum et al., 2000](#); [Rosenbaum et al., 2012](#); [Teng & Squire, 1999](#)). However, at least some of these individuals appear to have difficulty representing details contained within old environments, such as landmarks ([Rosenbaum et al., 2000, 2005, 2012](#)) and minor roads ([Maguire et al., 2006](#)). The current study further investigates possible dissociations between schematic, gist-like representations of spatial environments and representations of peripheral details that may be necessary for vivid re-experiencing of routes but that are not essential for navigation.

Classic theories of hippocampal function make different predictions about the role of the hippocampus in spatial memory. To account for findings of place cells in the hippocampus of rats freely navigating a newly learned maze, [O'Keefe and Nadel \(1978\)](#) postulated that the hippocampus supports the formation of a “cognitive map”, which contains allocentric spatial representations (flexible, viewer-independent knowledge of spatial relations among landmarks) of an environment. In extending the Cognitive Map Theory (CMT) to humans, they suggested that allocentric representations may provide the context in which episodic memories unfold. However, CMT does not differentiate between recent and remote cognitive maps and, therefore, it is not clear if hippocampal damage would lead to impaired spatial and episodic memory, regardless of when the memory was acquired.

A second influential theory of hippocampal function, the Standard Consolidation Theory (SCT), posits that declarative memories (whether episodic, semantic, or spatial in nature) initially rely on the hippocampus, but gradually become established in the neocortex and thus, over time, no longer require the hippocampus for the maintenance or retrieval of those memories ([Scoville & Milner, 1957](#); [Squire, 1992](#); [Teng & Squire, 1999](#)). Strong support for SCT is found in observations of temporally graded retrograde amnesia in individuals with hippocampal damage, which typically occurs together with anterograde amnesia ([Winocur & Moscovitch, 2011](#)).

Based on studies of amnesic patients with hippocampal damage, remote spatial memory has been added to those memories that are preserved (K.C.: [Rosenbaum et al., 2000, 2005](#); E.P.: [Teng & Squire, 1999](#); T.T.: [Maguire et al., 2006](#)), as compared to additional evidence that episodic memory of events may be lost, even if they were experienced as long ago as childhood (e.g., K.C.: [Rosenbaum, McKinnon, Levine, & Moscovitch, 2004](#); [Rosenbaum et al., 2005](#); S.J.: [Rosenbaum et al., 2008](#); H.M. and W.R.: [Steinvorth, Levine, & Corkin, 2005](#)). Not all aspects of spatial memory, however, are preserved. There is evidence suggesting that although amnesic individuals are able to navigate familiar remote environments, representations of detailed features appear to be lost

in at least some patients ([Maguire et al., 2006](#); [Rosenbaum et al., 2000, 2005](#)). For instance, when [Rosenbaum et al. \(2000\)](#) tested K.C., an amnesic person with bilateral MTL lesions caused by a motor vehicle accident, he retained the ability to negotiate his way in his premorbidly learned home neighbourhood and drew a sketch map of this neighbourhood with the general schematic layout intact; however, his sketch map contained noticeably fewer landmarks and streets compared to controls' sketch maps. In addition, K.C. performed poorly compared to controls on a landmark recognition task as a result of his inability to recognize individual houses and landmarks that were salient but unlikely to be critical for navigation ([Rosenbaum et al., 2000](#)).

Additional findings of impoverished detailed representations are suggested in [Maguire et al.'s \(2006\)](#) report of the case T.T., a former London taxi driver with bilateral hippocampal damage due to viral encephalitis. T.T. performed normally on static mental navigation tests that involved recognition of landmarks from static photos and judgments of spatial relations in imagination, as well as dynamic tests that involved active navigation in a virtual reality rendering of downtown London. Although T.T. could rely on main artery roads to reach a destination, he had difficulty on those dynamic tests that required navigation along non-artery (minor) roads, which may require a more fine-grained, detailed spatial representation. In addition, T.T.'s floor plans of houses that he had lived in before and after the onset of his hippocampal damage were inaccurate relative to his wife's in terms of the placement of several key features, such as the staircase and balconies ([Maguire et al., 2006](#)). T.T.'s errors on this task appear to be consistent with the impoverished sketch maps drawn by K.C.

Findings of what appears to be impoverished detailed representations of large-scale environments may parallel the patients' episodic memory impairment, where narratives of personal events lack contextual details that would otherwise enable them to vividly re-experience their past ([Rosenbaum et al., 2000, 2008](#)). Neither SCT nor CMT predict this pattern of impaired and preserved function. An alternative account, the Multiple Trace Theory (MTT; [Moscovitch, Nadel, Winocur, Gilboa, & Rosenbaum, 2006](#); [Moscovitch et al., 2005](#)), argues that some types of memory can exist independent of the hippocampus. According to MTT, a new trace element is added each time a memory is retrieved, serving to strengthen the memory. Most often only the semantic (gist) information of a memory is reactivated, meaning that over time traces of gist-like representations of the memories become well-represented neocortically and, as a result, are less vulnerable to disruption. This may be contrasted with episodic or detailed information, which is believed to rely always on the hippocampus, regardless of the age of the memory ([Nadel & Moscovitch, 1997](#); [Moscovitch et al., 2006](#)).

More recently, MTT was extended to accommodate findings of dissociations in spatial memory in amnesic patients with hippocampal/MTL damage. A “transformation hypothesis” was proposed to predict that all relational/

declarative memories, including spatial, initially depend on the hippocampus but with time and/or experience can exist independently of the hippocampus within neocortical regions if they lose their detailed, contextual features (Winocur & Moscovitch, 2011; see also Rosenbaum, Winocur, & Moscovitch, 2001). Within spatial memory, this would include coarse, schematic, gist-like information, such as well-known landmarks and the approximate relations between them. Fine, detailed information about an environment, in contrast, would continue to rely on hippocampal function, similar to detailed episodic representations, regardless of how long ago that information was acquired. An important addition to MTT is that the transformed memory is not believed to replace the initial, more detailed memory but, rather, the two representations can coexist and even interact when the situation requires it. The Transformation Hypothesis was built on findings that healthy older individuals and cases of hippocampal amnesia have difficulty representing detailed features of well-known environments that they can otherwise navigate in imagination and in the real world (Hirshhorn, Newman, & Moscovitch, 2011; Maguire et al., 2006; Rosenbaum et al., 2000, 2005, 2012).

The current study aims to determine if finer dissociations might be revealed between impaired and preserved aspects of remote spatial memory in a way that more closely parallels known dissociations between impaired re-experiencing of personal episodes but intact memory for personal facts. One way to do this is to assess participants' ability to describe the route that would be taken between a particular start and end point. Ghaem et al. (1997) found that the hippocampus (along with the insula and precuneus) was activated when healthy younger adults mentally navigated routes. In a study by Hirshhorn et al. (2011), healthy older adults described routes with and without the requirement to provide vivid descriptions of details along the way. Results suggested that the hippocampus is required for vivid re-experiencing of a route, but not for map-like knowledge of it (for related findings, see Ciaramelli, Rosenbaum, Solcz, Levine, & Moscovitch, 2010 and Rosenbaum et al., 2012).

To further elucidate the role of the hippocampus in retrieving schematic and detailed representations of familiar environments, we extended Hirshhorn et al.'s (2011) route description task, along with spatial memory measures of distance, direction, and landmark recognition (Ciaramelli et al., 2010), to amnesic patients with hippocampal/MTL damage and episodic memory impairment. The route description task is unique in that it allows for the assessment of both schematic and detailed representations within a single measure. This task has been used with healthy older adults (Hirshhorn et al., 2011), but this is the first time that it is being administered to cases of hippocampal/MTL amnesia to directly assess the involvement of the hippocampus. Static mental navigation tasks from previous studies of remote spatial memory were administered to the amnesic cases in the current study to validate previous results and relate the findings on established tests to the novel route description task.

If the hippocampus is needed for representing detailed spatial features to enable rich re-experiencing of an environment, but not for schematic representations of spatial relations, then amnesic patients with hippocampal damage would be expected to produce fewer details in sketch maps of well-known neighbourhoods, although the general configuration of the sketch maps would be intact. On the route description task, amnesic participants would be expected to show a similar pattern of fewer details (such as landmarks and sensory descriptions of perceptual features along the route) but intact directions to navigate from the start to end locations in their verbal descriptions of routes. To compensate for less vivid details within the descriptions, amnesic participants might rely to a greater extent than controls on spatial references that may be based on schematic representations. Finally, amnesic individuals would be expected to provide accurate judgments of distance and direction between well-known landmarks on a vector mapping task, which is thought to depend on a context-free survey representation of the environment conducive to allocentric representations. In contrast, recognition of the visual appearance of landmarks located in remotely learned environments, especially those that constitute perceptual details that are not essential to navigation, might be compromised in hippocampal/MTL amnesia.

Findings of impoverished detailed representations of environments and intact schematic representations sufficient for navigation in amnesic individuals with clear evidence of hippocampal/MTL damage would provide more definitive support for alternative theories of hippocampal/MTL function. These include MTT and its derivative, the Transformation Hypothesis, which view the role of the hippocampus as involved in representing and binding vivid details to enable the re-experiencing of routes, which, in turn, might help in planning.

2. Methods

2.1. Participants

2.1.1. Amnesic cases

Three previously studied amnesic individuals with extensive MTL damage (D.G., D.A., and K.C.) participated in the study (see Table A1 for a summary of performance of each case on standard neuropsychological measures). D.G. is a right-handed man with 16 years of education who formerly worked as a civil engineer. His characteristic amnesic pattern of preserved semantic, but impaired episodic memory, is due to anoxia secondary to cardiac arrest that occurred in 2010 (Kwan, Craver, Green, Myerson, & Rosenbaum, 2013). D.G. has a cardioverter-defibrillator implanted, and therefore is unable to undergo magnetic resonance imaging (MRI) scanning, though his neuropsychological profile is suggestive of hippocampal damage (for further characterization, see Kwan et al., 2013).

D.A. is a right-handed man with 17 years of education who has been described in several prior studies (Kwan et al., 2013;

Rosenbaum et al., 2008; Westmacott, Black, Freedman, & Moscovitch, 2003). In 1993, he contracted herpes encephalitis, which resulted in temporally graded retrograde amnesia and extensive anterograde amnesia for personal experiences (Kwan et al., 2013; Rosenbaum et al., 2008). D.A. has volume reductions in the posterior temporal, occipital, ventral frontal regions, anterior cingulate, and posterior thalamus in the right hemisphere (Kwan et al., 2013). He has severe damage to MTL structures, affecting the right side (79.4% volume loss) substantially more than the left (47.0% volume loss). D.A.'s left and right hippocampus is damaged by 74.2% and 95.7%, respectively (Rosenbaum et al., 2008).

K.C. is a right-handed man with 16 years of education who sustained a closed-head injury in 1981 at the age of 30 from a motorcycle accident. His accident left him with severe anterograde and retrograde amnesia (Rosenbaum et al., 2000, 2005). His MRI scans show bilateral atrophy of his parahippocampal gyrus and almost complete bilateral destruction of his hippocampus (Rosenbaum et al., 2005). K.C.'s hippocampal volume was reduced by 81.2% on the left and 86.7% on the right (Rosenbaum et al., 2005). Areas outside of the MTL that were affected include bilateral posterior thalamus, septal area, and caudate nucleus as well as the left mammillary body, amygdala and anterior thalamus (see Rosenbaum et al., 2005 for a thorough neuropsychological and neuroanatomical profile).

At the time of testing, D.G. was 47 years old, D.A. was 61, and K.C. was 62. All three cases were tested on the route description test in the current study. D.G. and D.A. were also administered several static navigation tasks for familiar, premorbidly learned environments, designed to assess remote spatial memory for distance, direction, and landmark appearance. As reviewed in the Introduction, K.C.'s performance on tests of recent and remote spatial memory had been assessed previously at age 49 (13 years prior), and was not tested further in the current study (Rosenbaum et al., 2000; Rosenbaum, Winocur, Grady, Ziegler, & Moscovitch, 2007).

2.1.2. Healthy comparison controls

Thirty-eight healthy comparison controls (26 women), matched for age ($M = 68.13$, $SD = 15.48$) and education ($M = 16.92$, $SD = 2.85$), were tested on the route description task (Hirshhorn et al., 2011). Comparisons in performance on tests of mental navigation were made with a separate group of 6 controls; 2 women and 1 man with extensive experience navigating in the environment familiar to D.G. (City S), matched for age ($M = 46.67$, $SD = .58$) and education ($M = 17$, $SD = 3.61$), and 3 women with extensive experience navigating in the environment familiar to D.A. (Neighbourhood M), also matched for age ($M = 44.67$, $SD = 13.61$) and education ($M = 16.33$, $SD = 2.08$).

Controls were recruited through the patients' family and friends, postings in community centres and at York University, and via online advertisements. Additional control route description transcripts were obtained from Hirshhorn et al.'s (2011) previously collected data set and rescored by the same raters as in the current study. All participants were fluent in English and provided written informed consent in accordance with the Human Research Ethics Committees of Baycrest and

York University. Each participant received monetary compensation for his or her time.

2.2. Materials and procedure

A summary of experimental tasks and how they are believed to relate to schematic and detailed representations is presented in Table A2.

2.2.1. Route description task

All three amnesic cases and matched controls were asked to describe one to two familiar walking routes. Although participants described different routes based on their personal experiences, all participants were asked to describe routes that took approximately 10 min to walk, allowing us to compare performance on this task across participants. At first, participants were asked to provide the basic directions necessary to get from their start point to their end point. Then, they were asked to provide as much detail as possible, describing not only their surroundings but also where visual features of the environment were located in relation to each other and to the participant. Participants were instructed to continue with their descriptions until they came to a natural end. The examiner then probed participants for further details of three landmarks that were mentioned by the participant. Examiners refrained from introducing any new landmarks that had not already been mentioned by the participant.

Each route description was segmented into a set of statements by one of two independent, reliable scorers, blind to group membership, using a modified version of Hassabis, Kumaran, Vann, and Maguire's (2007) scoring procedure. Each segmented statement, or meaningful unit of information, was classified as belonging to one of 3 categories: 'entities', 'sensory descriptions', and 'spatial references'. The entities category included any distinct item mentioned (landmark, person, or object). The sensory descriptions category included any descriptive statement about an entity along the route, regardless of modality. Spatial references referred to statements about the participant's location in space, the relative position of entities along the route, or explicit measurements (see Hassabis et al., 2007 for more detail on scoring). Information provided by participants that fell outside of these categories (such as emotions, thoughts, or actions) was not included in the total output as it was considered extraneous to our primary objective of probing detailed spatial-perceptual representations of routes in remote spatial memory. The number of statements in each category was divided by the participant's total output, allowing us to examine the proportion of each individual's total output that was attributed to spatial references, entities, or sensory descriptions, while controlling for variations in total verbal output among participants.

Independent, blind scorers also provided a quality judgment score for each route, on a scale of 1–10, reflecting how well they could envision a detailed, vivid image of the route and features along the way in their own mind's eye, after reading participants' transcribed route descriptions. Quality

judgment scores were averaged for those participants who provided two familiar route descriptions.

2.2.2. Static mental navigation tasks

Amnesic cases D.G. and D.A., and six control participants were tested on static navigation tasks known to assess memory for familiar, remote environments for distance, direction, and landmark appearance (Ciaramelli et al., 2010; Rosenbaum et al., 2000, 2012).

2.2.2.1. ENVIRONMENTS. At the time of testing, D.A. had lived in Neighbourhood M for 29 years. Neighbourhood M is approximately 2 km², close in size to the one in which K.C. had lived and on which he was tested. Amnesic case D.A. lived in this area for nine years prior to the onset of his amnesia, and continues to reside there. The three age- and education-matched controls also currently reside in the neighbourhood; two controls had lived there for 25 + years, and one control had lived there for 11 years at the time of testing.¹

Case D.G. and matched controls were tested on “City S”, a premorbid environment, approximately 50 km², where D.G. lived for the first 25 years of his life. At the time of testing, D.G. had not lived in City S for 22 years and does not visit it often. Likewise, all controls matched to D.G. had lived in City S for 22–25 years and moved away from their neighbourhood 22 years ago.

2.2.2.2. SKETCH MAPPING. Participants were first asked to reproduce the configuration of spatial elements of their environment in a sketch map. The maps were analyzed for the amount of detailed information provided (number of landmarks and street segments, defined as the total number of named or unnamed streets, roads, walkways and lanes drawn on a map that are bound by segments on at least one side), and accuracy in the placement of those details. The overall gestalt, scale, and relative relationships between landmarks and street segments were commented on qualitatively.

D.G. and matched controls were given the boundaries of smaller regions, measuring approximately 2 km², located within the larger City S, to make the environment comparable to the one on which D.A. and matched controls were tested and to encourage the production of a more detailed map. To control for familiarity, we opted to have all participants draw the 2 km² region with which they were most familiar. D.G. and Control 101 provided a sketch map of an identical region, but controls 103 and 104 drew distinct regions in City S that were similar in size and complexity to D.G.'s region.

2.2.2.3. VECTOR MAPPING. For each of 10 pairs² of landmarks, participants were given an outline map that included only the

¹ While it would have been ideal also to test controls who had moved away from Neighbourhood M at the time of D.A.'s onset of amnesia, attempts to recruit such controls were unsuccessful. Nevertheless, using only controls who currently reside in the neighbourhood would serve to make D.A.'s intact performance on static navigations tasks all the more remarkable.

² One control for D.A.'s Neighbourhood M was tested on 9 pairs of landmarks.

boundary roads of the environment. The position of one of the landmarks from the pair was indicated on the map, and participants were asked to draw a vector representing the distance and direction from that landmark to an unmarked landmark. Deviation in estimates from actual directions in degrees and distances in centimeters was calculated for each trial and averaged to derive absolute error scores. The performance of each patient was independently analyzed using Crawford and Garthwaite's (2002) modified t-test procedure, which allows comparison of single cases to small control samples. All analyses were tested at a significance level of $p < .05$.

2.2.3. Landmark recognition

Participants were shown photographs of landmarks, located within the target environment, as well as photographs of unknown ‘foil’ landmarks, located outside of the target environment. Foils were matched to each target landmark in terms of building category, architectural style, and contextual features. For each photograph, participants were asked whether or not the landmark was within the target environment and, if so, to provide some additional identifying information (name, location, type of building, etc.). The proportion of hits was calculated, with one point given for each landmark correctly recognized and identified, and a half point given for each landmark correctly endorsed as a target but not identified. In addition, the proportion of false alarms (foil landmarks erroneously identified as within the target environment) was calculated. Each individual amnesic case was compared to controls on two dependent variables, hits and false alarms, using Crawford and Garthwaite's (2002) modified t-test procedure.

3. Results

3.1. Route description task

As predicted, all patients were able to provide the basic directions for their route. Analysis of the route description task revealed that the total output for D.G. and K.C. was comprised of significantly fewer sensory description segments ($t = -1.734, p = .046$ and $t = -2.013, p = .026$, respectively; see Fig. 1), whereas the total output for D.A. approached significance ($t = -1.604, p = .059$; see Fig. 1).³ This suggests that patient route descriptions lacked detail about what things looked like along the route compared to controls. Fig. 2 provides sample probe descriptions from patient K.C. and a control, with the scoring overlay. Note that K.C. was unable to provide any sensory descriptions, or detailed information about the appearance of the landmark, even when given an additional (unscored) probe requesting that information specifically.

Surprisingly, none of the patients differed significantly from control participants in terms of the proportion of entities provided (D.G.: $t = -.387, p = .351$; D.A.: $t = -.365, p = .359$; K.C.: $t = -.119, p = .453$; see Fig. 1).³

³ Withholding an outlier did not change the results.

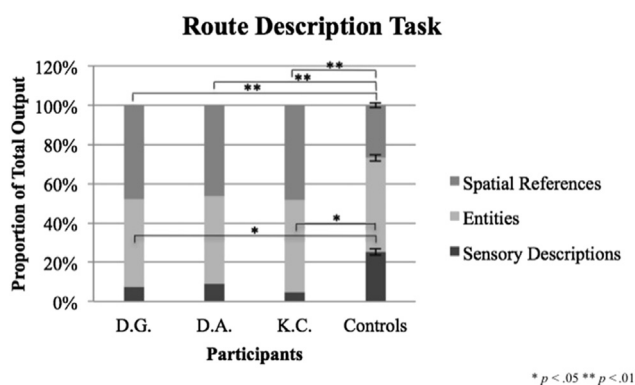


Fig. 1 – Proportion of total output attributed to spatial references, entities and sensory descriptions on the Route Description Task for amnesic cases and controls matched for age and education. All amnesic cases provided a significantly higher proportion of spatial references and approximately equal amount of entities compared to controls. Amnesic cases D.G. and K.C. provided significantly less sensory descriptions compared to controls, while D.A. was trending towards significance on this measure. Standard error is represented in the figure by the error bars attached to each column.

Nonetheless, as predicted, spatial references comprised a significantly larger proportion of amnesic participants' output compared to that of controls (D.G.: $t = 2.703$, $p = .005$; D.A.: $t = 2.512$, $p = .008$; and K.C.: $t = 2.739$, $p = .005$; see Fig. 1). While patients' total output consisted of proportionally more spatial references compared to controls' output, post-hoc analyses using Crawford and Garthwaite's (2002) modified t-test procedure showed that there was no significant difference in the actual number of spatial references (as opposed to proportion) provided by patients compared to controls (D.G.: $t = -.923$, $p = .181$; D.A.: $t = .970$, $p = .169$; K.C.: $t = -.487$, $p = .315$).

In line with our hypotheses, we found that the quality of D.G.'s and K.C.'s route descriptions was rated as significantly lower compared to the quality of controls' descriptions ($t = -2.196$, $p = .017$, and $t = -2.433$, $p = .010$, respectively; see Fig. 3), indicating that scorers had greater difficulty envisioning the visual appearance of routes described by patients than routes described by controls. Contrary to our predictions, the quality of D.A.'s route descriptions was not rated differently from the quality of controls' descriptions ($t = -.537$, $p = .297$; see Fig. 3).

3.2. Static mental navigation tasks

Results of the vector mapping and landmark recognition tasks are presented in Table A3 for D.G. and D.A. K.C.'s data, originally reported in Rosenbaum et al. (2000), are included in the table for comparison. The sketch maps were qualitatively analyzed and described below.

3.2.1. Sketch mapping

Amnesic case D.G. retrieved fewer landmarks and street segments (4 landmarks and 19 street segments; Fig. A1) compared to control 101 (17 landmarks, 21 street segments; see Fig. A1

Sample Patient Probe (K.C.): SPA = Spatial References
EP = Entities
SD = Sensory Descriptions

Brother's House

EP SPA

"I pass my brother's house at the end of the street. It's on [Street Name 2], and it's right opposite of [Street Name 1], and it's a single story building. And there's houses all the way up [Street Name 2] to the South Service Road, on both sides, and the sidewalk's on the left.

Experimenter: So, you described where your brother's house is. Can you tell me anything about what it looks like? You said that it's a single story, is there anything else? (Unscored)

"It's a bungalow, with a garage."

Sample Control Probe:

Splash Pad

EP SD

"The splash pad, uh, a couple of them are poles that are tall. If you press the button there are little spouts on the sides of it, so it just kind of sprays out over them. There are also, they look like pipes, they are arches and water comes down from the top of those ones. And basically it's just a... the arches are white, the poles I think are white. Um, the kids just run in and out all the time. What else can I think about...the walkway, uh, just between it and the boardwalk is now, it's a new kind of like a rubberized interlocking. So there's less chance of them slipping or falling on cement or that. Uh, because the, the ground part of the splash pad is kind of like that rusty reddish colour, it looks gravel-y, so it's got traction for them. But now they've got the other rubbery part from where they come out so that they don't fall."

Fig. 2 – Sample transcript of patient and control probes from the route description task, with scoring overlaid. The sample patient probe (from K.C.'s route description) lacks in detail compared to the control probe, which includes intricate details about the structure being described, including colour and size.

for control comparison), control 103 (18 landmarks, 33 street segments), and control 104 (43 landmarks, 52 street segments).

While D.G.'s sketch map contained considerably fewer streets and landmarks than the sketch maps of controls, landmarks and street segments that were included were properly placed and did not deviate from the scale more than those included by controls. Interestingly, unlike controls, some of the street segments included by D.G. were detached at both ends, which may reflect D.G.'s fine motor difficulties. However, D.G.'s sketch map shows a basic schematic representation of his home environment, limited to major streets and landmarks, and minor streets that would have been pertinent for navigating to his home.

D.A.'s sketch map, presented in Fig. A2, included 7 landmarks and 28 street segments, which, like that of D.G., is impoverished in comparison to control 301 (41 landmarks, 76 street segments; see Fig. A2 for control comparison), control 302 (25 landmarks, 32 street segments), and control 304 (43 landmarks, 42 street segments). Also similar to D.G., D.A. correctly placed landmarks and street segments and produced an accurate overall layout and scale.

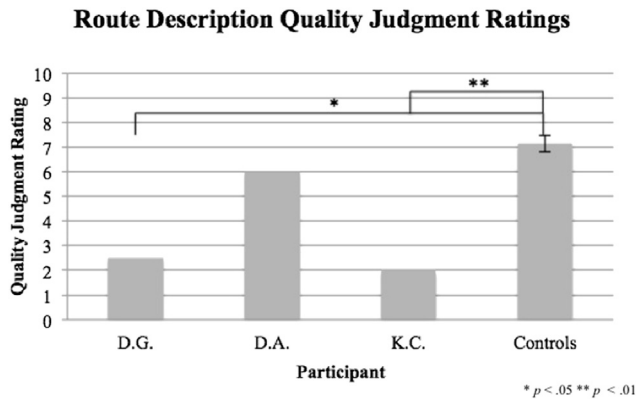


Fig. 3 – Quality judgment ratings representing scorers' judgments about how vivid a mental representation they could conjure based on participants' transcribed route descriptions. Amnesic cases D.G. and K.C. earned significantly lower quality ratings compared to matched controls, indicating that their route descriptions evoked a less vivid and detailed representation of the route and features along the way in scorers. Amnesic case D.A. did not differ significantly from controls on this measure. Standard error is represented in the figure by the error bar attached to the column.

3.2.2. Vector mapping

In line with previous research with K.C. (Rosenbaum et al., 2000), amnesic case D.G. did not differ significantly from controls on the vector mapping task in terms of the mean deviation from the correct direction in degrees ($t = -.178$, $p = .438$) or distance in centimeters ($t = .703$, $p = .277$; see Fig. 4). Amnesic case D.A. performed similarly to controls in terms of distance ($t = 1.197$, $p = .177$, Fig. 4), but showed worse performance than controls for direction, a result that approached statistical significance ($t = 2.443$, $p = .067$). Careful inspection of the results revealed that D.A.'s worse performance was due to a single error in which he confused two gas stations in his neighbourhood, resulting in a deviation of 173° from the correct direction on one trial. When this trial was removed from the analysis, D.A.'s estimates of direction were indistinguishable from controls' estimates ($t = .739$, $p = .269$, Fig. 4).

3.3. Landmark recognition

D.G. recognized 68% of the landmarks from City S, which approaches significant impairment ($t = -2.448$, $p = .065$) compared to controls ($M = 91\%$, $SD = .08\%$; see Fig. 5). The proportion of false alarms produced by D.G. (18%) did not differ significantly from the proportion of false alarms produced by controls ($M = 27\%$, $SD = 16\%$; $t = -.459$, $p = .346$).

D.A. correctly identified 100% of the target landmarks from his neighbourhood and did not differ significantly from controls who recognized an average of 95.6%, $SD = 3.8\%$ ($t = 1.003$, $p = .211$; see Fig. 5). However, D.A. also exhibited a significantly higher proportion of false alarms (93%) compared to controls ($M = 2\%$, $SD = 3.8\%$; $t = 20.494$, $p = .001$), indicating that D.A. mistakenly identified landmarks as located within his home

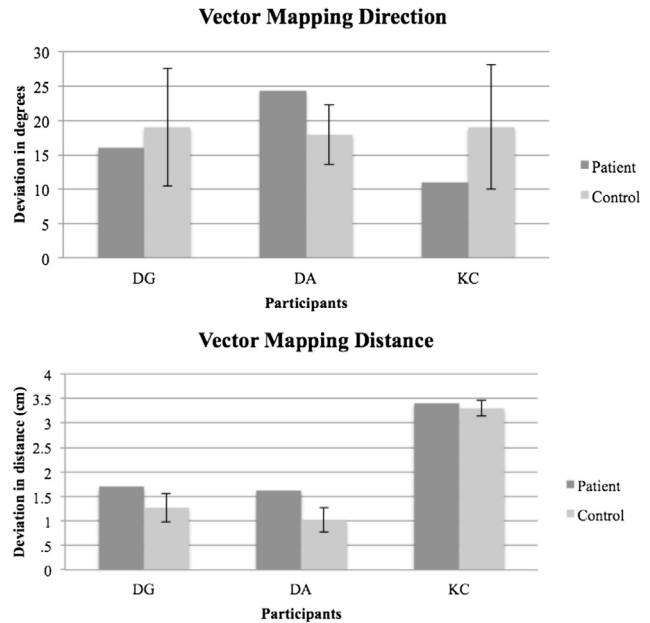


Fig. 4 – Deviation in direction (degrees) and distance (cm) for amnesic cases and their individually matched controls on the Vector Mapping task. Note influential observation withheld from amnesic case D.A.'s overall performance. None of the three amnesic cases differed significantly from their controls, matched for age, education, and environment. Standard error is represented in the figure by the error bars attached to each column. K.C.'s data reproduced with permission from Rosenbaum et al., 2000.

neighbourhood. Although D.G. is much more conservative in his responding than D.A., results indicate that both have difficulty recognizing landmarks.

4. Discussion

Previous research has pointed towards a possible dissociation between schematic and detailed representations of space, with the hippocampus required to support the latter but not the former. The purpose of the current study was to examine the role of the hippocampus in schematic and detailed spatial representations, and possible interactions with episodic re-experiencing, in a more direct way by assessing three cases of hippocampal/MTL amnesia on tests of route descriptions, judgments of spatial relations, and landmark recognition based on remotely learned environments that had been navigated extensively by patients and controls.

4.1. Intact schematic representations of space in hippocampal/MTL amnesia

All three amnesic cases were found to have intact schematic representations of their respective environments, as reported in Rosenbaum et al. (2000) for K.C. and in the current paper for D.A. and D.G. This conclusion is based on the patients' intact

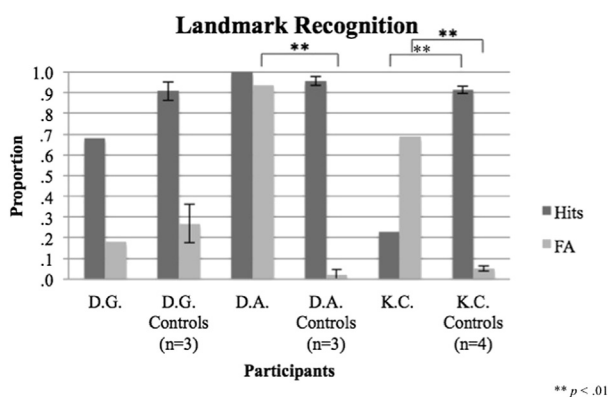


Fig. 5 – Proportion of hits and false alarms (FA) for amnesic cases and matched controls on the landmark recognition task. Amnesic case D.G. recognized fewer target landmarks than controls, but demonstrated a similar number of false alarms. D.A. showed a less conservative response style, identifying every target landmark, but also incorrectly identifying significantly more foil landmarks. Amnesic case K.C. also seems to have difficulty recognizing landmarks, with significantly less hits and more false alarms compared to his matched controls (forced-choice data from Rosenbaum et al., 2000). Standard error is represented in the figure by the error bars attached to each column.

performance on a vector mapping task and correct configuration and layout of familiar home environments on sketch maps. Intact performance on a route description task also speaks to the integrity of the three cases' schematic spatial representations. Further corroborating the claim that the hippocampus is not required for navigating familiar environments, D.G., D.A. and K.C. were able to provide basic directions from the start to end point of premorbidly familiar walking routes. In addition, the total output of the route descriptions provided by each case consisted of a significantly greater proportion of spatial references than perceptual details in comparison to controls. However, post-hoc analyses comparing patients' actual number of spatial references to that of controls suggests that this finding may be more indicative of the patients' paucity of perceptual detail than an over-provision of spatial references.

The current results substantiate previous research claims that at least some aspects of spatial memory that are schematic in nature can be preserved following hippocampal damage (Rosenbaum et al., 2000). The current study only allows for speculation about the brain structures that are required for maintaining schematic representations of environments. It is possible that schematic representations are mediated by residual hippocampal tissue or other brain structures in these patients. A fMRI study of remote spatial memory in K.C. examined hippocampal activity as he performed tests of remote spatial memory to determine if what remained of his hippocampus was functional. K.C. and controls familiar with the neighbourhood in which K.C. lived were tested on static mental navigation tasks, including landmark recognition and navigation tasks used in the current study (Rosenbaum et al., 2007). K.C.'s hippocampus itself was not

activated during any navigational tasks on which he performed well, suggesting that schematic representations are not mediated by residual hippocampal tissue. However, the tasks engaged several common regions, including: middle-superior frontal gyrus, which has been implicated in spatial working memory; medial-superior parietal lobule, known for its role in egocentric processing and imagery; retrosplenial/posterior cingulate cortex, involved in rigid forms of map learning, heading direction, and/or translation between egocentric and allocentric representations; and parahippocampal cortex, required for acquisition of new landmarks (for reviews, see Aguirre & D'Esposito, 1999; Byrne, Becker, & Burgess, 2007; Epstein, 2008; Maguire, 2001; Weniger, Ruhleder, Wolf, Lange, & Irlle, 2009; Wolbers & Büchel, 2005; Zhang & Ekstrom, 2013). K.C. showed activation in these regions in the right hemisphere in relation to intact performance on the various mental navigation tasks, whereas controls recruited these regions in both hemispheres (Rosenbaum et al., 2007). In K.C. and D.A., for whom detailed volumetric data are available, medial-superior frontal gyrus and superior parietal cortex appear to be intact. Posterior cingulate cortex is slightly reduced in volume in D.A. and parahippocampal cortex is structurally compromised in both patients, though activation in these regions in K.C. appears to be functionally relevant (Rosenbaum et al., 2007), and the same may be true of D.A.

4.2. Impaired detailed representations of space in hippocampal/MTL amnesia

As hypothesized, our results implicate the hippocampus as necessary for recollecting detailed representations of space. Similar to K.C. (Rosenbaum et al., 2000), amnesic cases D.G. and D.A. produced sketch maps that, while accurate in their overall configuration and layout, had fewer landmarks and fewer streets than controls, suggestive of an intact schematic representation but difficulty with accessing a detailed representation of neighbourhoods learned long ago.

Performance of the amnesic cases on the route description task may also shed light on the necessity of the hippocampus for retrieving detailed representations of space. The proportion of entities named did not differ between patients and controls, contrary to our hypothesis that control participants would name more entities along the route. In Chan, Baumann, Bellgrove, and Mattingley's (2012) review, they assert that the specific location of objects within an environment can determine how salient they are in verbal route descriptions, with those objects at decision points and involved in navigational decisions being more readily remembered. Our results might reflect a natural inclination for both patients and controls to mention mostly those landmarks or entities along the route that are pertinent to navigation, or those that are especially salient, in that they are useful in differentiating one route from any other. It is possible that entities incidental to navigation may have been accessible to the control participants in our study, but not divulged in this task as expected.

What is of note is that although patients and controls provide a similar proportion of entities, only the controls seem to be able to describe them in detail. As hypothesized, both D.G.'s

and K.C.'s total output was comprised of significantly fewer sensory description segments compared to healthy controls, and D.A. showed a trend towards significance. Even when probed for additional information, the three cases had difficulty describing landmarks. Their descriptions were often vague, whereas control participants would often describe several additional, more detailed, aspects of the probed landmarks, such as colour and size (see Figs. 2 and 6 for sample descriptions from patients and controls in response to probes).

Both D.G. and K.C. received significantly worse quality judgment ratings compared to controls, suggesting that, unlike controls, neither patient was able to evoke vivid images in independent scorers' minds based on the route descriptions that they provided. Unlike D.G. and K.C., D.A. did not differ significantly from controls in terms of quality judgment ratings. It is possible that the high quality judgment score might be a reflection of D.A.'s very particular descriptions of the schematic aspects of space. For example, D.A. would describe the route down to the meter, and was much more specific when describing the distance from one part of the route to the next compared to the majority of controls. It is possible that raters felt this amount of spatial detail evoked a sense of vividness comparable to that achieved by the descriptive details proffered by controls, and may have been factored into his quality judgment score. This may reflect a strategy that D.A. has adopted to compensate for areas of deficit in episodic

re-experiencing and spatial detail memory. Indeed, we have shown previously that D.A. has, at times, demonstrated performance that is indistinguishable from controls or better than them on tasks that otherwise have been shown in amnesic cases and in lesioned animals to depend on hippocampal function (Ryan, Moses, Barense, & Rosenbaum, 2013).

Amnesic cases D.G. and D.A. both had difficulty recognizing landmarks, results that are in line with previous findings in K.C. (Rosenbaum et al., 2000; but see Maguire et al., 2006). Their impaired performance on the landmark recognition task may further implicate the hippocampus in retrieving a detailed visual perceptual representation of space. The results from the current study may reflect other, non-mnemonic, difficulties experienced by hippocampal/MTL amnesics, such as discriminating spatial scenes and binding information into a unified percept (Erez, Lee, & Barense, 2013; Graham, Barense, & Lee, 2010; Lee et al., 2005). The results are also consistent with recent research by Barker and Warburton (2011) showing that the hippocampus plays a role in recognition memory specifically when a stimulus must be remembered to occur in a particular place. Our landmark recognition task explicitly examined this type of memory, as we asked participants to decide whether each landmark presented could be found in their pre-experimentally familiar environment.

Our findings of intact schematic representations and impoverished detailed representations of familiar environments in amnesic patients with confirmed hippocampal damage have theoretical implications. The Standard Consolidation Theory would predict intact representations of remote environments in amnesic patients, as the hippocampus is not thought to be involved in maintaining or retrieving spatial memories learned long ago. However, the Standard Consolidation Theory might not have predicted the impoverished detailed representations of remote environments that were observed in the three amnesic cases presented here, a finding that suggests that the hippocampus is required for at least some aspects of remote spatial memory.

Our findings also have implications for two recently developed theoretical accounts, the Transformation Hypothesis (Winocur, Moscovitch, & Sekeres, 2007; Winocur & Moscovitch, 2011) and Scene Construction Theory (Maguire & Mullally, 2013). Both theories propose that the hippocampus plays a key role in the binding of information from multiple modalities into vivid recollections. As previously described, the Transformation Hypothesis implies a role for the hippocampus in forming contextually bound detailed representations, whether spatial or non-spatial. The Transformation Hypothesis stemmed from K.C.'s difficulty representing detailed features of a well-known environment that he was otherwise able to navigate (Rosenbaum et al., 2000, 2001, 2005). Similar findings in healthy older individuals and other cases of hippocampal amnesia have substantiated these claims (Maguire et al., 2006; Rosenbaum et al., 2012).

The Scene Construction Theory suggests a similar role for the hippocampus that is specific to spatial context (Hassabis & Maguire, 2007). This theory was formed based on findings that individuals with amnesia were significantly impaired in comparison to controls when asked to construct imagined experiences that were independent of time and unrelated to the self (Hassabis et al., 2007). Compared to controls, the

<p>Sample Patient Probe (D.G.):</p> <p>His House</p> <p>"Hmm... we just had our, um, our front walk way in... beside the driveway, we had some of that redone. They put like interlocked bricks along the sides. And across the top, cut it all out, looks pretty nice too."</p> <p>Sample Control Probe:</p> <p>House</p> <p>"It's set back from the road. It doesn't have a fence, which is strange for that area. It's got a driveway which dips down as it's set back and down from the street level. It's stained timber, not quite logs, but it's sort of a log-cabin look about it. It's got a large sort of slanted roof, not like a standard pitched roof like most houses have. And it has a flat roof which is strange as well, because everyone has the pitched tall roofs. You can see that the entire front which is all stained timber which is like an overlapping board. And the windows are very large compared to the other houses, and it's got a timber front door too, and it's all sort of stained the same colour. It's got, I think it's a pine tree out the front, a really large pine tree. And other than that there's no real standout features, other than that the driveway is gravel, and that's about it. Oh, and it's got a brick chimney on the right hand side."</p>
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Fig. 6 – A representative sample transcript of patient (D.G.) and control probes from the route description task. When probed about his house, patient D.G. provided fewer sensory details about what the house looked like compared to the control's description of a house, suggestive of impoverished detailed representations of his familiar home environment.

patients' descriptions were less rich and lacked spatial coherence. One amnesic case who showed intact performance (P01) was subsequently found to engage residual hippocampal tissue during scene construction, providing further evidence of a necessary role for the hippocampus in constructing spatial scenes (Mullally, Hassabis, & Maguire, 2012).

The current study has extended previous findings of scene construction deficits for imagined scenes in amnesic patients with hippocampal damage (Hassabis et al., 2007) to actual memories of frequently traveled places. The amnesic patients with hippocampal/MTL damage in our study were unable to form a scene in their minds' eye of visual details along their familiar routes. A prime example of this is patient K.C.'s inability to elaborate on a house along the route beyond describing it as a “bungalow with a garage” (see Fig. 2).

While our findings of impoverished detailed representations of familiar environments may help to support Scene Construction Theory, our findings of intact mental navigation of such environments are not readily accommodated within that theory. Scene construction might provide an organizing principle, in the way that schematic representations do according to the Transformation hypothesis, serving as an anchor for episodic experiences and other details. However, it is unclear whether or not the theory would have predicted the intact schematic representations found in our study, a finding that would seem to depend on retained coherence. The Transformation Hypothesis, on the other hand, which implicates the hippocampus as necessary for retrieving detailed, but not schematic, representations of space, readily accounts for both the impoverished route descriptions and sketch maps produced by the patients but intact mental navigation along routes and accurate estimation of distance and direction between landmarks (Winocur & Moscovitch, 2011; Winocur et al., 2007).

Perceptually rich representations, both visual (Erez et al., 2013; Graham et al., 2010; Lee et al., 2005) and in visual imagery (as in the current study), are impoverished following hippocampal damage. Findings of impaired landmark recognition in S.B. and house recognition in K.C., two individuals with compromised hippocampi, have been found alongside impaired autobiographical memory for details about personal events (Rosenbaum et al., 2005, 2000), linking episodic memory and perceptual details. It is possible that impoverished detailed representations of environments may not just parallel episodic memory impairment found in hippocampal amnesia, but may interact with or contribute to it. A paucity of perceptual details may contribute to impoverished episodic memory, as context-specific perceptual details are required to form a rich episode and engage in vivid re-experiencing (Robin & Moscovitch, 2014). St-Laurent, Moscovitch, Jadd, and McAndrews (2014) had individuals with unilateral MTL epilepsy and healthy controls describe the perceptual features and story lines for film clips, written narratives, and personal autobiographical memories. They found that patients showed a deficit in perceptual details, especially in the autobiographical memory and film clip conditions, suggesting that a paucity of perceptual episodic memory details may impair re-experiencing of the past (St-Laurent et al., 2014). These findings are consistent with neuroimaging work that shows that the hippocampus seems to be driven by the vividness of episodic memories or future imaginings (Bergouignan, Nyberg, & Ehrsson, 2014; Gilboa,

Winocur, Grady, Hevenor, & Moscovitch, 2004; Rabin, Gilboa, Stuss, Mar, & Rosenbaum, 2010). Findings of impoverished detailed representations that lack perceptual richness suggest that the hippocampus may play an important role in binding details from multiple modalities into vivid recollections, as predicted by the Transformation Hypothesis (Winocur & Moscovitch, 2011; Winocur et al., 2007).

5. Conclusions

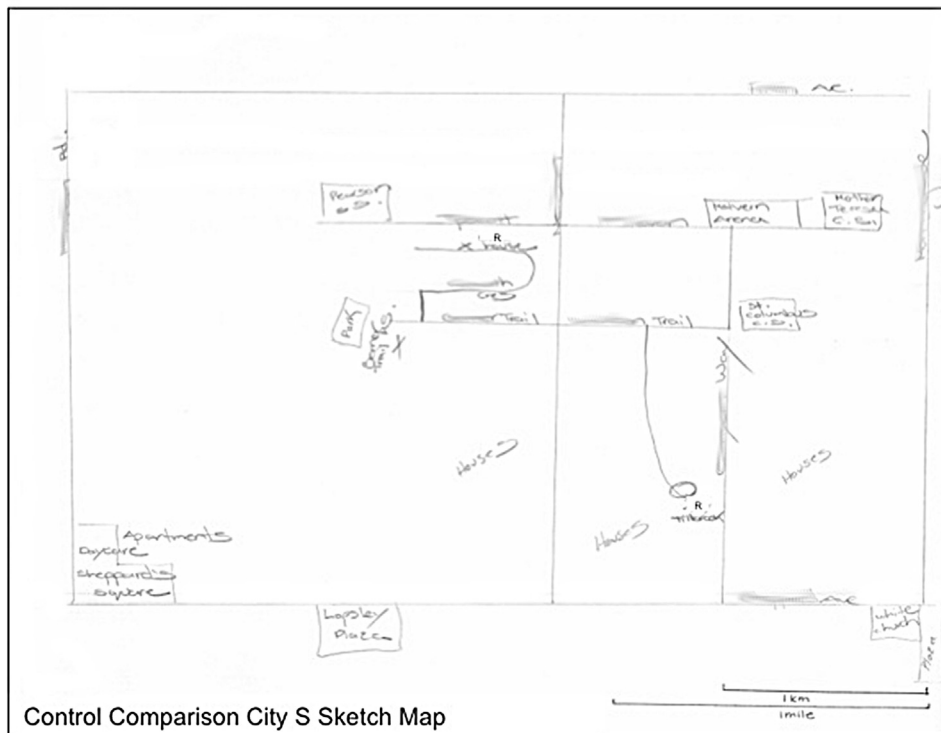
Prior to the current study, conclusions regarding dissociations between detailed and schematic representations of space were largely inferred from performance of amnesic patients on separate tasks. The current study included two measures, a route description task and a sketch mapping task, that allow for both detailed and schematic representations to be assessed within the same measure. Use of the route description task in a previous study by Hirshhorn et al. (2011) demonstrated impoverished perceptual details of routes retrieved by healthy older adults. The authors concluded that age-related changes to hippocampal function likely accounted for these results, but it was not possible to rule out the contribution of other brain structures that also undergo age-related changes as responsible for the poor performance in the older adults.

In the current study, we aimed to extend previous findings of intact schematic representations and hints of impoverished detailed representations by testing three individuals with hippocampal/MTL amnesia on static mental navigation tasks and a route description task. Individuals with amnesia were able to provide basic directions along a route, draw sketch maps that were schematically intact, and perform similarly to controls on a vector mapping task, indicative of intact schematic representations of familiar environments. However, the low proportion of sensory descriptions about features along the route, sketch maps that lacked detail, and poor landmark recognition performance by the patients provides converging evidence that the hippocampus is necessary for representing details of environments. More definitive support comes from dissociations between intact descriptions of the spatial properties of routes but impoverished descriptions of perceptual features along those routes on a single measure. On the surface, the current results accommodate recent theoretical claims by the Transformation Hypothesis that the hippocampus is needed for generating and binding details into vivid representations, but not for recollecting schematic, gist-like representations of environments that are sufficient for navigation.

Acknowledgements

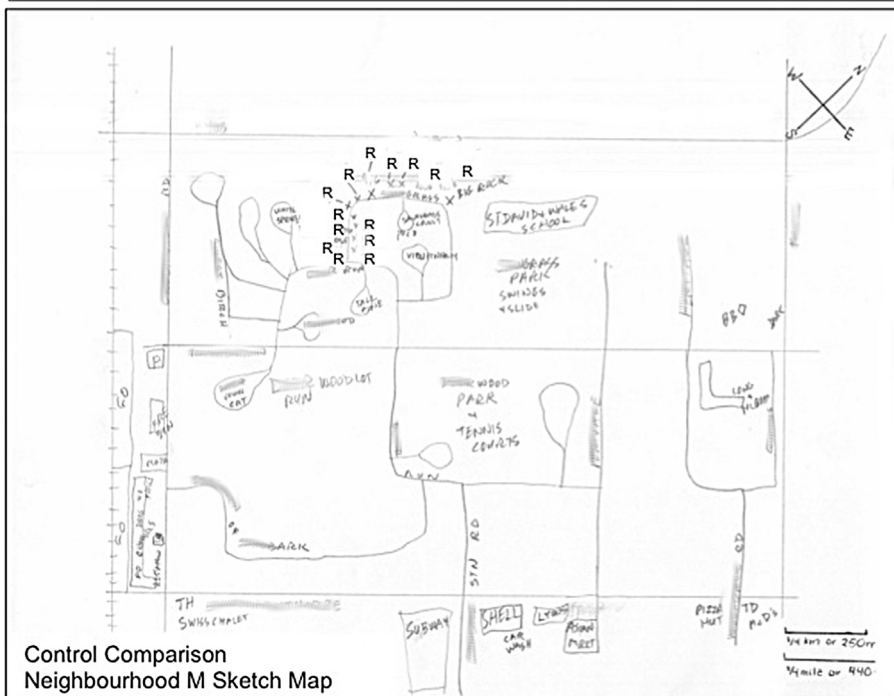
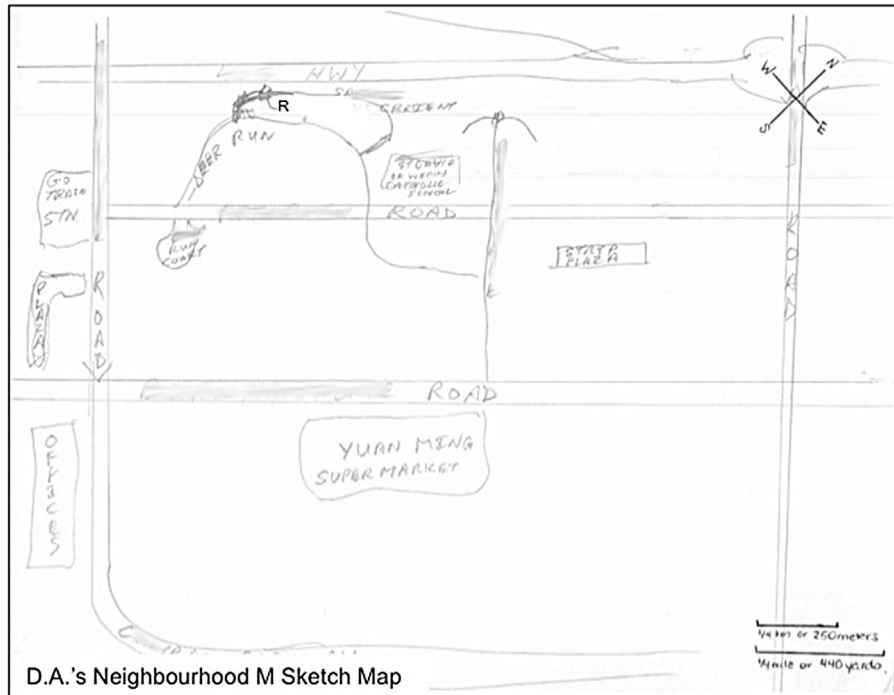
We are grateful to D.G., D.A., the late K.C., and their families for their continued participation in research on memory. This work was supported by a Natural Sciences and Engineering Research Council of Canada (NSERC) (2014-06704) grant awarded to R.S.R. and a Canadian Institutes of Health Research (CIHR) (MGP 6694) grant to R.S.R. and M.M. K.A.H. acknowledges support from a Canadian Institutes of Health Research (CIHR) Master's Award and Queen Elizabeth II Graduate Scholarship in Science and Technology (QEII-GSST).

Appendix



R = redacted

Fig. A1 – Amnesic case D.G.'s sketch map of home neighbourhood in City S, showing an intact basic schematic representation of his home environment, but fewer landmarks compared to controls.



R = redacted

Fig. A2 – Amnesic case D.A.'s sketch map of home neighbourhood M, showing intact layout of the environment, but fewer landmarks and street segments compared to controls.

Table A1 – Neuropsychological profiles of the amnesic cases.

Neuropsychological characteristic	D.G.	D.A.	K.C.
Intellectual function			
WAIS-R ^a			
FSIQ	92	117	99
VIQ	83	121	99
PIQ	104	106	99
Visual perception			
Judgment of line orientation (/30)	–	26	23
Language			
Semantic fluency (scaled score) ^b	5	12	10
Boston naming test (/60)	56	56	57
Anterograde memory			
WMS-R			
LP I (percentile)	–	15th	5th
LP II (percentile)	–	<1st	<1st
ROCF			
Copy (/36)	30	35	36
Immediate recall	<1percentile	–	4
Delayed recall	<1percentile	0	0
CVLT			
Acquisition (t-score)	33	9	12
Short delay free (z-score)	–4	–4	–2
Long delay free (z-score)	–4	–4	–1.5
Recognition discrimination (z-score)	–3	–4	–1
Retrograde Memory			
Adapted AI (Addis, Wong, & Schacter, 2008)			
Average number detail (past)	11.8	17.4	<1
AMI autobiographical (/9)			
Childhood	–	7	2
Early adult life	–	6	3
Recent life	–	3	1
AMI personal semantics (/21)			
Childhood	–	17.5	16
Early adult life	–	21	13.5
Recent life	–	16	8
Executive Function			
WCST			
Categories (/6)	6	6	6
Perseverative responses (z-score)	.33	–.5	–.9
Letter fluency (scaled score) ^c	6	8	6
WAIS-R digits (scaled score)	–	13	12

Note. WAIS-R – Wechsler Adult Intelligence Scale- Revised; FSIQ – Full-scale IQ; VIQ – Verbal IQ; PIQ – Performance IQ; WMS-R – Wechsler Memory Scale- Revised; LP – Logical Passages; VR – Visual Reproduction; ROCF – Rey Osterrieth Complex Figure; CVLT – California Verbal Learning Test; AI – Autobiographical Interview; AMI – Autobiographical Memory Interview; WCST – Wisconsin Card Sorting Test.

^a Scores reflect performance on the Weschler Abbreviated Scale of Intelligence-II.

^b Score is based on the number of animal names produced in 1 min.

^c Score is based on the number of words produced for the letters F, A, and S, given 1 min for each.

Table A2 – Experimental tasks and how they are expected to relate to schematic and detailed representations of space.

Experimental task	Brief description	Specific aspects of task	Expected to provide insight about integrity of _____ representations
Route description	Provide basic directions for walking route and describe walking route in as much detail as possible, providing information about the appearance of landmarks and where they are located in relation to each other and yourself.	Ability to provide basic directions Proportion of spatial references Proportion of entities Proportion of sensory descriptions Quality judgment rating	Schematic Schematic Detailed Detailed Detailed Schematic
Sketch mapping	Draw a map of specified environment, including as many details as possible.	Overall configuration # of landmarks, street segments	Detailed Schematic
Vector mapping	Draw a line indicating distance and direction from marked landmark to unmarked landmark.	Deviation in distance (cm) Deviation in direction (°)	Detailed Schematic
Landmark recognition	Recognize and identify landmarks from target neighbourhood amidst foil landmarks.	Ability to discriminate between hits and false alarms	Schematic Detailed

Note: H, hits; FA, false alarm; NA, not applicable.

Table A3 – Performance of amnesic cases and matched controls on static mental navigation tasks.

Experimental task	Environment					
	City S		Neighbourhood M		Neighbourhood E	
	Control mean (SD)	Modified t-test, one-tailed	D.A. Control mean (SD)	Modified t-test, one-tailed	K.C. Control mean (SD)	Modified t-test, one-tailed
	(n = 3)		(n = 3)		(n = 4)	
Mental navigation						
Vector deviation (km)	1.695	1.273 (.520)	1.620	1.020 (.434)	3.400	3.300 (.316)
Mapping deviation (°)	16.000	19.050 (14.876)	39.250	17.950 (7.552)	11.000	19.075 (18.117)
		t = .703, p = .277	24.390 ^a	17.950 (7.552)		t = .283, p = .398
		t = -.178, p = .438				t = -.399, p = .358
Landmark appearance						
Recognition	.682	.909 (.079)	1.000	.956 (.038)	.229	.914 (.034)
Proportion of H	.182	.268 (.162)	.933	.022 (.038)	.688	.052 (.027)
Proportion of FA		t = -2.488, p = .065				t = -17.808, p < .001
		t = -.459, p = .346				t = 21.127, p < .001

Note: H, hits; FA, false alarm; SD, standard deviation.

Bold text indicates a significant difference in performance.

^a Influential observation withheld.

REFERENCES

- Addis, D. R., Wong, A. T., & Schacter, D. L. (2008). Age-related changes in the episodic simulation of future events. *Psychological Science*, 19, 33–41. <http://dx.doi.org/10.1111/j.1467-9280.2008.02043.x>.
- Aguirre, G. K., & D'Esposito, M. (1999). Topographical disorientation: a synthesis and taxonomy. *Brain*, 122, 1613–1628. <http://dx.doi.org/10.1093/brain/122.9.1613>.
- Barker, G. R. I., & Warburton, E. C. (2011). When is the hippocampus involved in recognition memory? *The Journal of Neuroscience*, 31(29), 10721–10731. <http://dx.doi.org/10.1523/JNEUROSCI.6413-10.2011>.
- Bergouignan, L., Nyberg, L., & Ehrsson, H. H. (2014). Out-of-body-induced hippocampal amnesia. *Proceedings of the National Academy of Sciences*, 111(12), 4421–4426. <http://dx.doi.org/10.1073/pnas.1318801111>.
- Byrne, P., Becker, S., & Burgess, N. (2007). Remembering the past and imagining the future: a neural model of spatial memory and imagery. *Psychological Review*, 114(2), 320–375. <http://dx.doi.org/10.1037/0033-295X.114.2.340>.
- Chan, E., Baumann, O., Bellgrove, M. A., & Mattingley, J. B. (2012). From objects to landmarks: the function of visual location information in spatial navigation. *Frontiers in Psychology*, 3, 304. <http://dx.doi.org/10.3389/fpsyg.2012.000304>.
- Ciaramelli, E., Rosenbaum, R. S., Solcz, S., Levine, B., & Moscovitch, M. (2010). Mental time travel in space: damage to posterior parietal cortex prevents egocentric navigation and re-experiencing of remote spatial memories. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, 36, 619–634. <http://dx.doi.org/10.1037/a0019181>.
- Crawford, J. R., & Garthwaite, P. H. (2002). Investigation of the single case in neuropsychology: confidence limits on the abnormality of test scores and test score differences. *Neuropsychologia*, 40, 1196–1208. [http://dx.doi.org/10.1016/S0028-3932\(01\)00224-X](http://dx.doi.org/10.1016/S0028-3932(01)00224-X).
- Ekstrom, A. D., Kahana, M. J., Caplan, J. B., Fields, T. A., Isham, E. A., Newman, E. L., et al. (2003). Cellular networks underlying human spatial navigation. *Nature*, 425(6954), 184–188.
- Epstein, R. A. (2008). Parahippocampal and retrosplenial contributions to human spatial navigation. *Trends Cognitive Science*, 12(10), 388–396. <http://dx.doi.org/10.1016/j.tics.2008.07.004>.
- Erez, J., Lee, A. C. H., & Barense, M. D. (2013). It does not look odd to me: perceptual impairments and eye movements in amnesic patients with medial temporal lobe damage. *Neuropsychologia*, 51, 168–180. <http://dx.doi.org/10.1016/j.neuropsychologia.2012.11.003>.
- Ghaem, O., Mellet, E., Crivello, F., Tzourio, N., Mazoyer, B., Berthoz, A., et al. (1997). Mental navigation along memorized routes activates the hippocampus, precuneus, and insular. *NeuroReport*, 8(3), 739–744.
- Gilboa, A., Winocur, G., Grady, C. L., Hevenor, S. J., & Moscovitch, M. (2004). Remembering our past: functional neuroanatomy of recollections of recent and very remote personal events. *Cerebral Cortex*, 14, 1214–1225. <http://dx.doi.org/10.1093/cercor/bhh082>.
- Graham, K. S., Barense, M. D., & Lee, A. C. (2010). Going beyond LTM in the MTL: a synthesis of neuropsychological and neuroimaging findings on the role of the medial temporal lobe in memory and perception. *Neuropsychologia*, 48(4), 831–853. <http://dx.doi.org/10.1016/j.neuropsychologia.2010.01.001>.
- Hassabis, D., Kumaran, D., Vann, S. D., & Maguire, E. A. (2007). Patients with hippocampal amnesia cannot imagine new experiences. *Proceedings of the National Academy of Sciences*, 104(5), 1726–1731. <http://dx.doi.org/10.1073/pnas.0610561104>.

- Hassabis, D., & Maguire, E. A. (2007). Deconstructing episodic memory with construction. *Trends in Cognitive Sciences*, 11(7), 299–306. <http://dx.doi.org/10.1016/j.tics.2007.05.001>.
- Hirshhorn, M., Newman, L., & Moscovitch, M. (2011). Detailed descriptions of routes traveled, but not map-like knowledge, correlates with tests of hippocampal function in older adults. *Hippocampus*, 21, 1147–1151. <http://dx.doi.org/10.1002/hipo.20871>.
- King, J. A., Burgess, N., Hartley, T., Vargha-Khadem, F., & O'Keefe, J. (2002). Human hippocampus and viewpoint dependence in spatial memory. *Hippocampus*, 12, 811–820.
- Kumaran, D., Hassabis, D., Spiers, H. J., Vann, S. D., Vargha-Khadem, F., & Maguire, E. A. (2007). Impaired spatial and non-spatial configural learning in patients with hippocampal pathology. *Neuropsychologia*, 45(12), 2699–2711. <http://dx.doi.org/10.1016/j.neuropsychologia.2007.04.007>.
- Kwan, D., Craver, C. F., Green, L., Myerson, J., & Rosenbaum, R. S. (2013). Dissociations in future thinking following hippocampal damage: evidence from discounting and time perspective in episodic amnesia. *Journal of Experimental Psychology: General*, 142, 1355–1369. <http://dx.doi.org/10.1037/a0034001>.
- Lee, A. C., Bussey, T. J., Murray, E. A., Saksida, L. M., Epstein, R. A., Kapur, N., et al. (2005). Perceptual deficits in amnesia: challenging the medial temporal lobe 'mnemonic' view. *Neuropsychologia*, 43(1), 1–11. <http://dx.doi.org/10.1016/j.neuropsychologia.2004.07.017>.
- Maguire, E. A. (2001). The retrosplenial contribution to human navigation: a review of lesion and neuroimaging findings. *Scandinavian Journal of Psychology*, 42, 225–238. <http://dx.doi.org/10.1111/1467-9450.00233>.
- Maguire, E. A., & Mullally, S. L. (2013). The hippocampus: a manifesto for change. *Journal of Experimental Psychology: General*, 142(4), 1180–1189. <http://dx.doi.org/10.1037/a0033650>.
- Maguire, E. A., Nannery, R., & Spiers, H. J. (2006). Navigation around London by a taxi driver with bilateral hippocampal lesions. *Brain*, 129. <http://dx.doi.org/10.1093/brain/awl286>, 2894–2097.
- Morris, R. G. M., Garrud, P., Rawlins, J. N., & O'Keefe, J. (1982). Place navigation impaired in rats with hippocampal lesions. *Nature*, 297(5868), 681–683. <http://dx.doi.org/10.1038/297681a0>.
- Moscovitch, M., Nadel, L., Winocur, G., Gilboa, A., & Rosenbaum, R. S. (2006). The cognitive neuroscience of remote memory: a focus on functional neuroimaging. *Current Opinion in Neurobiology*, 16, 179–190. <http://dx.doi.org/10.1016/j.conb.2006.03.013>.
- Moscovitch, M., Rosenbaum, R. S., Gilboa, A., Addis, D. R., Westmacott, R., Grady, C., et al. (2005). Functional neuroanatomy of remote episodic, semantic and spatial memory: a unified account based on multiple trace theory. *Journal of Anatomy*, 207, 35–66. <http://dx.doi.org/10.1111/j.1469-7580.2005.00421.x>.
- Mullally, S. L., Hassabis, D., & Maguire, E. A. (2012). Scene construction in amnesia: an fMRI study. *The Journal of Neuroscience*, 32(16), 5646–5653. <http://dx.doi.org/10.1523/JNEUROSCI.5522-11.2012>.
- Nadel, L., & Moscovitch, M. (1997). Memory consolidation, retrograde amnesia and the hippocampal complex. *Current Opinion in Neurobiology*, 7, 217–227. [http://dx.doi.org/10.1016/S0959-4388\(97\)80010-4](http://dx.doi.org/10.1016/S0959-4388(97)80010-4).
- Olton, D. S., Becker, J. T., & Handelmann, G. E. (1979). Hippocampus, space, and memory. *Behavioural and Brain Sciences*, 2(3), 313–365. <http://dx.doi.org/10.1017/S0140525X00062713>.
- O'Keefe, J., & Nadel, L. (1978). *The hippocampus as a cognitive map*. Oxford: Clarendon Press.
- Rabin, J. S., Gilboa, A., Stuss, D. T., Mar, R., & Rosenbaum, R. S. (2010). Common and unique neural correlates of autobiographical memory and theory of mind. *Journal of Cognitive Neuroscience*, 22, 1095–1111. <http://dx.doi.org/10.1162/jocn.2009.21344>.
- Robin, J., & Moscovitch, M. (2014). The effects of spatial contextual familiarity on remembered scenes, episodic memories, and imagined future events. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, 40(2), 459–475. <http://dx.doi.org/10.1037/a0034886>.
- Rosenbaum, R. S., Cassidy, B., & Herdman, K. A. (2015). Patterns of preserved and impaired spatial memory in a case of developmental amnesia. *Frontiers in Human Neuroscience*, 9, 196. <http://dx.doi.org/10.3389/fnhum.2015.00196>.
- Rosenbaum, R. S., Köhler, S., Schacter, D. L., Moscovitch, M., Westmacott, R., Black, S. E., et al. (2005). The case of K.C.: contributions of a memory-impaired person to memory theory. *Neuropsychologia*, 43, 989–1021. <http://dx.doi.org/10.1016/j.neuropsychologia.2004.10.007>.
- Rosenbaum, R. S., McKinnon, M. C., Levine, B., & Moscovitch, M. (2004). Visual imagery deficits, impaired strategic retrieval, or memory loss: disentangling the nature of an amnesic person's autobiographical memory deficit. *Neuropsychologia*, 42, 1619–1635. <http://dx.doi.org/10.1016/j.neuropsychologia.2004.04.010>.
- Rosenbaum, R. S., Moscovitch, M., Foster, J. K., Schnyer, D. M., Gao, F. Q., Kovacevic, N., et al. (2008). Patterns of autobiographical memory loss in medial temporal lobe amnesic patients. *Journal of Cognitive Neuroscience*, 20, 1490–1506. <http://dx.doi.org/10.1162/jocn.2008.20105>.
- Rosenbaum, R. S., Priselac, S., Köhler, S., Black, S. E., Gao, F. Q., Nadel, L., et al. (2000). Remote spatial memory in an amnesic person with extensive bilateral hippocampal lesions. *Nature Neuroscience*, 3, 1044–1048. <http://dx.doi.org/10.1038/79867>.
- Rosenbaum, R. S., Winocur, G., Binns, M. A., & Moscovitch, M. (2012). Remote spatial memory in aging: all is not lost. *Frontiers in Aging Neuroscience*, 4, 1–10. <http://dx.doi.org/10.3389/fnagi.2012.00025>.
- Rosenbaum, R. S., Winocur, G., Grady, C. L., Ziegler, M., & Moscovitch, M. (2007). Memory for familiar environments learned in the remote past: fMRI studies of healthy people and an amnesic person with extensive bilateral hippocampal lesions. *Hippocampus*, 17, 1241–1251. <http://dx.doi.org/10.1002/hipo.20354>.
- Rosenbaum, R. S., Winocur, G., & Moscovitch, M. (2001). New views on old memories: re-evaluating the role of the hippocampal complex. *Behavioural Brain Research*, 127, 183–197. [http://dx.doi.org/10.1016/S0166-4328\(01\)00363-1](http://dx.doi.org/10.1016/S0166-4328(01)00363-1).
- Ryan, J. D., Moses, S. N., Barense, M. D., & Rosenbaum, R. S. (2013). Intact learning of new relations in amnesia is achieved through unitization. *Journal of Neuroscience*, 33(23), 9601–9613. <http://dx.doi.org/10.1523/JNEUROSCI.0169-13.2013>.
- Scoville, W. B., & Milner, B. (1957). Loss of recent memory after bilateral hippocampal lesions. *Journal of Neurology, Neurosurgery & Psychiatry*, 20, 11–21. <http://dx.doi.org/10.1136/jnnp.20.1.11>.
- Squire, L. R. (1992). Memory and the hippocampus: a synthesis from findings with rats, monkeys, and humans. *Psychology Review*, 99(2), 195–231. <http://dx.doi.org/10.1037/0033-295X.99.2.195>.
- St-Laurent, M., Moscovitch, M., Jadd, R., & McAndrews, M. P. (2014). The perceptual richness of complex memory episodes is compromised by medial temporal lobe damage. *Hippocampus*, 24(5), 560–576. <http://dx.doi.org/10.1002/hipo.22249>.
- Steinvorh, S., Levine, B., & Corkin, S. (2005). Medial temporal lobe structures are needed to re-experience remote autobiographical memories: evidence from two MTL amnesic patients, H.M. and W.R. *Neuropsychologia*, 43, 479–496. <http://dx.doi.org/10.1016/j.neuropsychologia.2005.01.001>.

- Suthana, N., Ekstrom, A., Moshirvaziri, S., Knowlton, B., & Bookheimer, S. (2011). Dissociations within human hippocampal subregions during encoding and retrieval of spatial information. *Hippocampus*, 21(7), 694–701. <http://dx.doi.org/10.1002/hipo.20833>.
- Teng, E., & Squire, L. (1999). Memory for places learned long ago is intact after hippocampal damage. *Nature*, 400, 675–677. <http://dx.doi.org/10.1038/23276>.
- Weniger, G., Ruhleder, M., Wolf, S., Lange, C., & Irle, E. (2009). Egocentric memory impaired and allocentric memory intact as assessed by virtual reality in subjects with unilateral parietal cortex lesions. *Neuropsychologia*, 47(1), 59–69. <http://dx.doi.org/10.1016/j.neuropsychologia.2008.08.01>.
- Westmacott, R., Black, S. E., Freedman, M., & Moscovitch, M. (2003). The contribution of autobiographical significance to semantic memory: evidence from Alzheimer's disease, semantic dementia, and amnesia. *Neuropsychologia*, 42, 25–48. [http://dx.doi.org/10.1016/S0028-3932\(03\)00147-7](http://dx.doi.org/10.1016/S0028-3932(03)00147-7).
- Winocur, G., & Moscovitch, M. (2011). Memory transformation and systems consolidation. *Journal of the International Neuropsychological Society*, 17, 766–780. <http://dx.doi.org/10.1017/S1355617711000683>.
- Winocur, G., Moscovitch, M., & Sekeres, M. (2007). Memory consolidation or transformation: context manipulation and hippocampal representations of memory. *Nature Neuroscience*, 10, 555–557. <http://dx.doi.org/10.1038/nn1880>.
- Wolbers, T., & Büchel, C. (2005). Dissociable retrosplenial and hippocampal contributions to successful formation of survey representations. *The Journal of Neuroscience*, 25(13), 3333–3340. <http://dx.doi.org/10.1523/JNEUROSCI.4705-04.2005>.
- Zhang, H., & Ekstrom, A. (2013). Human neural systems underlying rigid and flexible forms of allocentric spatial representation. *Human Brain Mapping*, 34(5), 1070–1087. <http://dx.doi.org/10.1002/hbm.21494>.