



Research Report

Remote spatial and autobiographical memory in cases of episodic amnesia and topographical disorientation

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ABSTRACT

A number of theories have postulated that there is a strong relationship between episodic memory and spatial processes mediated by the hippocampus. Evidence for episodic amnesia following damage to the medial temporal lobes is extensive, but less is known about the types of spatial memory affected by damage to these regions. In this study, we compared episodic memory with detailed scene memory, landmark recognition and schematic (map-based) spatial memory in a group of individuals with amnesia related to damage to the medial temporal lobes (MTL) including the hippocampus. We compared their performance to matched controls, and to an individual with topographical disorientation, a selective spatial memory deficit relating to more posterior temporal and occipital lobe damage. For individuals with MTL lesions, impairments to scene memory were comparable to those in episodic memory. Landmark recognition was impaired only for less familiar landmarks, and schematic spatial memory was not impaired compared to controls. Despite the absence of hippocampal damage, the individual with topographical disorientation, like the MTL amnesic patients, demonstrated impairments to scene memory and recognition of less familiar landmarks, and intact schematic spatial memory, but with less severe episodic memory loss. These results highlight the similarities between detailed scene memory and episodic memory, including their reliance on the medial temporal lobe, and suggest that more schematic forms of spatial memory may be unaffected by medial temporal damage. In addition, the results suggest that damage to more posterior temporal or occipital regions that leads to spatial memory deficits may entail some impairment to episodic memory even if the hippocampus is spared.

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1. Introduction

One of the earliest and most fundamental discoveries in the study of the cognitive neuroscience of memory is that damage to the hippocampus results in profound amnesia: an impairment in the ability to encode and retrieve events from one's life, with a sparing of semantic memory (Scoville & Milner, 1957). In parallel, research in rodents revealed that the hippocampus contains 'place cells', which track the location of an animal in space and are thought to underlie spatial memory (O'Keefe & Dostrovsky, 1971; O'Keefe & Nadel, 1978). Decades later, other major discoveries highlighted the preservation of some forms of memory in individuals with amnesia relating to hippocampal damage. In patient H.M., and in other amnesic patients, while very remote episodic memory was impaired, semantic memory was spared (Corkin, 2002; Moscovitch, Nadel, Winocur, Gilboa, & Rosenbaum, 2006; Steinworth, Levine, & Corkin, 2005; but see Squire and Wixted, 2011). Similarly, in the case of spatial memory it appeared that at least some forms of remote representations could be preserved in cases of hippocampal damage (Rosenbaum et al., 2000; Teng & Squire, 1999). In these studies, participants were able to correctly make navigational decisions about remotely known spatial locations, despite not being able to encode new spatial memories.

While some interpreted these findings as evidence that remote memories are spared by hippocampal damage, as predicted by the standard consolidation theory (Squire & Bayley, 2007; Squire & Zola-Morgan, 1991; Teng & Squire, 1999; Zola-Morgan, Squire, & Amaral, 1986), other evidence suggests a more nuanced interpretation. In light of research indicating that in some cases of hippocampal damage even very remote autobiographical memories lack specificity and detail-richness but semantic memories remain intact (Corkin, 2002; Rosenbaum et al., 2008, 2000; Rosenbaum, McKinnon, Levine, & Moscovitch, 2004; St-Laurent, Moscovitch, Jadd, & McAndrews, 2014; St-Laurent, Moscovitch, Levine, & McAndrews, 2009), it has been proposed that the types of spatial memory that are preserved following hippocampal damage are similarly schematic in nature, while highly detailed spatial memories are impaired (Moscovitch, Cabeza, Winocur, & Nadel, 2016; Nadel & Moscovitch, 1997; Rosenbaum et al., 2008, 2000; Winocur & Moscovitch, 2011; Winocur, Moscovitch, & Bontempi, 2010). This pattern of performance is described by the Trace Transformation Theory (TTT) and the Multiple Trace Theory (MTT; Nadel & Moscovitch, 1997) from which it was derived, which stipulate that all highly detailed memory representations whether recent or remote, are supported by the hippocampus while more schematic or semantic forms of remote memory are supported by neocortical regions and not the hippocampus (Moscovitch et al., 2016; Robin & Moscovitch, 2017a; Winocur et al., 2010; Winocur & Moscovitch, 2011). These theories contrast with standard consolidation theory, which would predict that all remote forms of spatial memory should be intact following hippocampal damage (Teng & Squire, 1999).

Consistent with TTT, the spatial memory tasks that individuals with hippocampal amnesia have been found to be able to perform well tend to be navigational tasks that can be

solved based on general map-like knowledge, such as judging distances or directions "as the crow flies" (i.e., vector mapping), and do not require fine-grained memory representations. This finding has been replicated in a variety of cases of hippocampal damage due to a variety of aetiologies (Herdman, Calarco, Moscovitch, Hirshhorn, & Rosenbaum, 2015; Maguire, Nannery, & Spiers, 2006; Rosenbaum et al., 2000; Rosenbaum, Gao, Richards, Black, & Moscovitch, 2005; Teng & Squire, 1999). Recent studies of individuals with amnesia relating to medial temporal lobe (MTL) damage demonstrated that navigation performance did not differ from controls on coarse measures of accuracy, but was impaired on more fine-grained measures (Kolarik, Baer, Shahlaie, Yonelinas, & Ekstrom, 2017; Kolarik et al., 2016). Consistent with TTT and the studies on which it is based, we predict that in cases of hippocampal damage, schematic map-based spatial memory will be preserved, while detailed memories for spatial scenes will be impaired, much like episodic memories.

Scene Construction (SC) theory also states that the hippocampus is needed to form and maintain complex scenes in memory, which, in turn, form the basis for episodic memory (Bird & Burgess, 2008; Hassabis & Maguire, 2007, 2009; Maguire & Mullally, 2013; O'Keefe & Nadel, 1978; Rubin & Umanath, 2015). Thus, since SC implies that scenes are supported by the hippocampus and provide the foundations of episodes, it also predicts impairments in detailed spatial memory in individuals with hippocampal damage. In the present study, we test predictions based on TTT and SC hypotheses by assessing episodic memory, schematic spatial memory, and detailed spatial memory in individuals with hippocampal damage.

Studies that have tested detailed spatial memory in individuals with hippocampal amnesia have mostly focussed on landmark recognition, and have yielded mixed findings. In the first study to test this hypothesis (Rosenbaum et al., 2000), KC—a man with hippocampal damage—recognized significantly fewer neighborhood landmarks than controls, though was able to recognize and identify a small number of "major" landmarks including a school and a shopping centre in his neighborhood. In subsequent studies, three former taxi drivers who have unique expertise with regard to spatial memory were compared. Two of them with hippocampal damage (L.R. and T.T.) were found to have intact landmark recognition of well-known locations, while one with Alzheimer's disease (S.B.), and evidence of damage to the MTL and inferotemporal cortex, was found to have very impaired performance (Maguire et al., 2006; Rosenbaum et al., 2005). Another study found some evidence for impaired landmark recognition in individuals with hippocampal amnesia: one individual (D.G.) had decreased accuracy and the other (D.A.) had intact accuracy but increased false alarms to lures (Herdman et al., 2015). While all the landmarks tested in these studies were remotely known, an important factor that varied across these studies was whether the landmarks were personally known or "famous" in a more semantic sense. For example, K.C. was tested on pictures of houses from his neighborhood, while T.T. was tested on famous London landmarks, which may have richer semantic associations. In a study of remote spatial memory in older adults, it was found that performance was impaired compared to that of younger

adults on landmark recognition, requiring detailed scene-based recognition of familiar locations, but intact on a variety of spatial memory tasks that could employ more schematic forms of memory (Rosenbaum, Winocur, Binns, & Moscovitch, 2012). Thus, familiarity and experience with the locations may be an important factor to control and consider when testing landmark recognition.

Another important factor when considering the results reviewed above is that all of these studies tested memory based on recognition of landmarks. It is well-known that the demands placed on memory differ substantially between recognition and free recall. In addition, it is difficult to tell which aspects of the scenes are being used to perform landmark recognition tasks (i.e., an overall gist, a single feature, and/or a conjunction of features could cue recognition), thus it is not clear if landmark recognition is adequately testing fine-grained spatial memory representations. In the present study, we aimed at contrasting scene and episodic memories using measures more directly comparable (Robin & Moscovitch, 2014; 2017b). Following procedures used in episodic memory paradigms, we tested free recall of scene memories by eliciting open-ended detailed descriptions of scenes.

While the focus of the present study is on the hippocampus and medial temporal contributions to memory for scenes and episodes, other regions of the brain are known to play important roles in spatial perception and memory. The retrosplenial cortex, the occipital place area, and the precuneus play important roles in scene perception, memory and spatial navigation (Epstein, 2008; Epstein, Higgins, Jablonski, & Feiler, 2007; Epstein & Kanwisher, 1998; Johnson & Johnson, 2014; Park, Brady, Greene, & Oliva, 2011). These areas are known to interact with the hippocampus as parts of the network involved in autobiographical memory (Spreng, Mar, & Kim, 2009; Svoboda, McKinnon, & Levine, 2006). Damage to these structures can result in syndromes such as topographical disorientation and landmark agnosia—the loss of the ability to navigate in familiar environments and recognize familiar buildings, respectively (Aguirre & D'Esposito, 1999; Barrash, 1998; Landis & Cummings, 1986; Rainville et al., 2005; Takahashi & Kawamura, 2002).

Memory impairments other than those for scenes or locations are not usually tested or reported in studies related to spatial navigational skills. Extending the predictions of SC, given the impairments in the ability to perceive and remember scenes in cases of topographical disorientation, deficits in episodic memory may co-exist even without hippocampal damage. Insofar as scene construction provides the foundation of episodic memory, one would expect that episodic memory impairment should be at least as severe as that of scene memory. We hypothesize that such deficits would be due to the degraded scene representations accessible to the hippocampal memory mechanisms (Robin, 2018), but this has yet to be tested in a case of topographical disorientation. Consistent with this hypothesis, amnesia has been reported in patients with reported long-term visual memory loss (Greenberg, Eacott, Brechin, & Rubin, 2005; Greenberg & Knowlton, 2014; Rubin, Deffler, & Umanath, 2019; Rubin & Greenberg, 1998).

In order to test both the effects of hippocampal damage on scene memory and the effects of deficits to scene memory on

episodic memory dependent on the hippocampus, we compare individuals with damage to the hippocampus and medial temporal lobe structures to one individual with topographical disorientation and landmark agnosia relating to posterior ventral temporal, parietal lobe and occipital lobe damage, sparing the hippocampus. In addition, we include a case of MTL damage and amnesia who also has extended damage to the occipital and inferotemporal cortices, demonstrating the combined effects of damage to the MTL and more posterior visual regions. Comparing these cases will allow for a better understanding of the mechanisms of episodic and spatial memory in a broader neural context beyond that of the hippocampus.

Our final question focuses on the role of contextual familiarity in episodic and spatial memory. In healthy young and older adults, more familiar contextual cues are associated with more detailed and vivid episodic and spatial memories (Robin & Moscovitch, 2014, 2017b; Robin, Wynn, & Moscovitch, 2016). The neural mediator of this context effect is not known. If more familiar cues also facilitate performance on memory tasks in individuals with memory impairments due to MTL damage, it would provide evidence that these familiarity effects do not depend exclusively on the hippocampus. In addition, results may help identify what types of memory can benefit from highly familiar semantic or schematic memory cues. For example, if impaired scene or event memory does not benefit from more familiar contexts, but other types of spatial memory, such as landmark location, do benefit from familiar context, then the combination of these results would provide additional evidence scene and event memory are related. Such results would also suggest that the effectiveness of familiarity as a cue depends on the integrity of the underlying memories.

In summary, in the present study, we seek to answer three main questions. First, do individuals with damage to the hippocampus and medial temporal lobes have impaired memory for remotely known scenes, and if so, how do these impairments compare to those in episodic memory? Our scene memory task differs from previous route description tasks in that it focusses on highly detailed spatial representations and does not include a navigational component (Herdman et al., 2015; Hirshhorn, Newman, & Moscovitch, 2011). It also differs from the landmark recognition tasks in that it relies on verbal, rather than pictorial, cues. Both TTT and SC accounts of the hippocampus predict impairments in scene memory, with preserved schematic spatial memory. Standard consolidation theory would predict that remote scene and episodic memories should not be impaired in cases of hippocampal damage. Second, does an individual with spatial memory deficits due to topographical disorientation and landmark agnosia show impairments in episodic memory? Based on SC, impoverished spatial representations should lead to deficits in episodic memory, even without hippocampal damage. Third, do individuals with impairments in spatial and episodic memory benefit from more familiar cues? Previous research has demonstrated that healthy controls do, but it is unclear if cue familiarity effects will be maintained in individuals with damage to the hippocampus and medial temporal lobes. Some previous studies on landmark recognition in MTL amnesia suggest that recognition

may be preserved for highly familiar landmarks but impaired for less familiar landmarks (Rosenbaum et al., 2000). In order to answer these questions, we tested episodic memory and three forms of spatial memory (memory for scenes, landmark recognition and schematic spatial memory) in four individuals with memory impairments relating to damage to the hippocampus and the medial temporal lobes, in one individual with topographical disorientation and landmark agnosia due to ventral temporal, parietal and occipital lobe damage, and in a set of matched control participants with no history of neurological illnesses or injuries.

2. Methods

2.1. Participants

2.1.1. Amnesic cases

2.1.1.1. D.A. D.A. is a right-handed male, 62 years old at the time of testing with 17 years of education. He had lived in the Toronto area for 62 years at the time of testing. D.A. has extensive bilateral MTL damage, including the hippocampus, due to encephalitis caused by the herpes simplex virus, contracted in 1993. Damage is more extensive in the right hemisphere: he shows a 95.7% and 74.2% volume loss of the right and left hippocampus, respectively, and a 79.4% and 47.0% volume loss in the right and left MTL (including perirhinal, entorhinal and parahippocampal cortices), respectively (Rosenbaum et al., 2008). D.A. has volume loss most prominently in the anterior and medial temporal regions. Volume loss was also observed in other right hemisphere regions, including posterior temporal, ventral frontal, and occipital regions, and also in the anterior cingulate cortex. Left hemisphere volume loss was restricted mostly to the MTL region. Small lesions to right posterior thalamus and the left middle temporal gyrus were also observed. Volume loss and lesion extents were characterized by comparing structural scans to those of matched healthy controls, using manual methods (visual inspection by a trained neurologist) and semi-automated brain region extraction techniques (SABRE; Rosenbaum et al., 2008) (see Fig. 1A).

Neuropsychologically, D.A. has been reported to have moderate temporally graded retrograde amnesia, severe anterograde amnesia for autobiographical experiences, and intact semantic memory (Kwan, Craver, Green, Myerson, & Rosenbaum, 2013; Rosenbaum et al., 2008). Notably, D.A. seems to have some preserved autobiographical memories,

perhaps due to frequent retelling and semanticization of the events (Kwan et al., 2013). Previous studies have also documented the strategies that D.A. has employed in order to support performance in hippocampally dependent tasks, on which other amnesic cases demonstrate impaired performance (Ryan et al., 2013, 2016). See previous studies for further details (Herdman et al., 2015; Kwan et al., 2013; Kwan, Kurczek, & Rosenbaum, 2016; Rosenbaum et al., 2008; Rosenbaum, Gilboa, & Moscovitch, 2014; Ryan et al., 2016; Ryan et al., 2013). D.A.'s neuropsychological profile and those of all other amnesic cases in this study are presented in Table 1.

2.1.1.2. L.D. L.D. is a right-handed male, 61 years old at the time of testing with 19 years of education. He had lived in the Toronto area for 17 years at the time of testing. He has a history of epilepsy and complex partial seizures beginning in 2000. An MRI exam showed a left hippocampal lesion and a growth in the left parahippocampal region. As a result, L.D. underwent a left temporal lobectomy and amygdalohippocampectomy in 2011, which involved resection of his left middle temporal gyrus, parahippocampal gyrus, hippocampus, uncus and amygdala (see Fig. 1B). Following the surgery, L.D.'s episodic memory declined relative to pre-surgical levels, especially for verbal material (Kwan, Craver, et al., 2015; Kwan, Kurczek, et al., 2016; Table 1). Previous reports describe L.D. as reporting difficulty with day-to-day memory, such as remembering the content of recent conversations. His memory impairment is selective; his overall intellectual function is average, with the exception of low semantic fluency (Kwan, Craver, et al., 2015; Kwan, Kurczek, et al., 2016).

2.1.1.3. S.P. S.P. is a right-handed male, 58 years old at the time of testing with 12 years of education. He had lived in the Toronto area for 58 years at the time of testing. He has a history of epilepsy and damage to the MTL relating to epileptic seizures. Examination of FLAIR and T1 MPRAGE MRI scans revealed bilateral atrophy to the hippocampus that was more extensive on the left (Romero & Moscovitch, 2012; Sheldon, Romero, & Moscovitch, 2013). A possible additional lesion was found in the right dorsal parietal cortex, but no other lesions were evident. Based on Freesurfer segmentation of the hippocampus and volume comparison with controls, S.P.'s hippocampal volume loss is modest (z-score of $-.80$) (Sheldon et al., 2013). More detailed volumetric analyses were not performed due to the low resolution of the clinical scans. S.P. demonstrates a severe and selective long-term memory

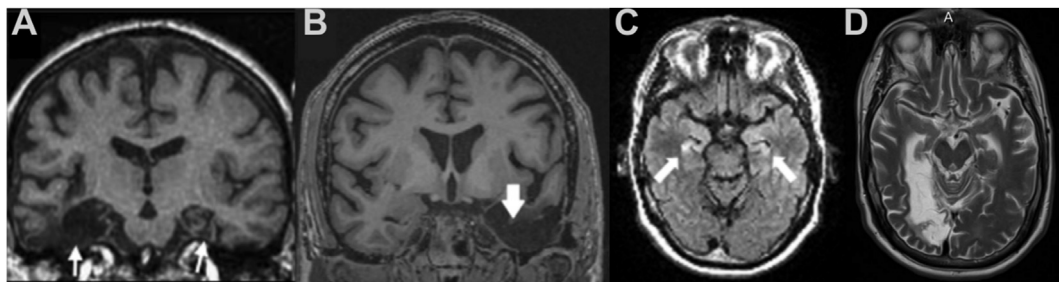


Fig. 1 – Representative structural MRI scans of the four amnesic cases (A: D.A.; B: L.D.; C: S.P.; D: M.H.).

Table 1 – Neuropsychological profiles of amnesic cases.

Case	Age	Ed	IQ	WCST	LF	BNT	WMS-R/III/IV		Verb Learn			ROCF	
							LP/M-I	LP/M-II	AQ	LDFC	R	C	DR
D.A.	62	17	117	6	8	10	7	1	0	0	0	18	0
L.D.	61	19	111	6	8	0	10	2	3	3	0	3	8
S.P.	56	12	99	–	8	–	6	1	–	–	–	–	–
M.H.	56	13	110	6	8	10	8	6	6	4	6	12	5

Notes. Age, age in years at time of neuropsychological testing; Ed, years of formal education; IQ, IQ based on Wechsler Adult Intelligence Scale; WCST, Wisconsin Card Sort Test, number of completed categories/6. The following measures are reported in scaled scores: LF, letter fluency; BNT, Boston Naming Test; WMS-R/III/IV, Wechsler Memory Scale Revised/III/IV, LP/M-I, LP/M-II, Logical Memory I and II; Verb Learn., Verbal learning based on California Verbal Learning Test-II for D.A. and M.H., Hopkins Verbal Learning Test – Revised for L.D., AQ, acquisition; LDFR, long delay free recall; R, recognition; ROCF, Rey Osterrieth Complex Figure, C, copy; DR, delayed recall. Scaled scores (average is 10) are presented for all tests.

deficit, with no deficits in other tests of cognitive abilities including working memory and semantic fluency (Romero & Moscovitch, 2012; Table 1).

2.1.1.4. M.H. M.H. is a right-handed male, 56 years old at the time of testing with 13 years of education. He had lived in the Toronto area for 56 years at the time of testing. M.H. contracted encephalitis as a result of the herpes simplex virus, resulting in atrophy in the bilateral MTL as well as damage along the right medial occipital and inferotemporal cortices (see Fig. 1D; Keven, Kurczek, Rosenbaum, & Craver, 2018).

Neuropsychological testing revealed selective memory deficits, with an average IQ and otherwise intact cognitive functioning (Keven et al., 2018; Table 1). Since M.H. has MTL damage and accompanying memory deficits, but also has more posterior damage to visual regions, his case complements the other amnesic cases by demonstrating the effects of combined MTL and visual cortical damage.

2.1.2. Topographical disorientation case

2.1.2.1. L.H. L.H. is a right-handed male, 69 years old at the time of testing with 21 years of education. He had lived in the Toronto area for 13 years at the time of testing. Four years prior to testing, L.H. developed topographical disorientation following a brain injury sustained during an automobile accident (Rivest, Svoboda, McCarthy, & Moscovitch, 2018; Robin et al., 2017). Immediately following the injury, L.H. was reported to have bilateral posterior circulation infarcts and multiple foci of parenchymal and intracranial hemorrhage secondary to the trauma. He underwent a left fronto-parietal craniotomy with subdural hemorrhage evacuation. An MRI exam showed evidence of a hematoma in the left parietal lobe, as well as a left frontal subdural hematoma and a trace right frontal subdural hematoma. In addition, cortical laminar necrosis was reported in the bilateral posterior and medial occipital lobes, and the left inferomedial parietal lobe. Six months post-injury, imaging found resolution of the hematomas, but sustained damage to the left parietal, left inferior temporal and bilateral occipital lobes, and the right cerebellar hemisphere, sparing the medial temporal lobes (see Fig. 2). An additional follow-up scan conducted 4 years after testing reported no change.

Post-injury, neuropsychological assessments reported that L.H. had strong intellectual abilities with superior IQ,

vocabulary, working memory, conceptual reasoning, and visuo-constructional abilities. In contrast, his performance on measures of memory for prose and word-lists, semantic and phonemic fluency, naming, visual memory and visual object recognition were in the low average or average range (Rivest et al., 2018). Following three months of rehabilitation, he demonstrated improvements in fine motor control, strength, speed of processing and memory, and was discharged from the rehabilitation unit (Rivest et al., 2018).

Despite these improvements, L.H. still demonstrated a profound topographical disorientation, from which he has not recovered. Even in familiar neighborhoods, L.H. is not able to navigate independently and frequently gets lost (Rivest et al., 2018). Further testing revealed that he is impaired at recognizing famous landmarks, locating cardinal directions, at discriminating colors and recognizing faces (Rivest et al., 2018), deficits which frequently co-occur with landmark agnosia relating to topographical disorientation (Aguirre & D'Esposito, 1999). Testing revealed that L.H. has selective deficits in scene perception, especially when focusing on geometric properties of scenes (Robin et al., 2017). In contrast, he is able to recognize objects and distinguish them based on their geometry, read road maps, read text, and performs normally on tests of low-level perceptual abilities. A clinical intervention that trained L.H. to use dynamic maps on a smartphone greatly improved his ability to find his way and travel independently (Rivest et al., 2018).

2.1.3. Control participants

Sixteen healthy older adults, with no known history of psychological or neurological illness or injury were tested. They were matched to the cases in the study: all were male (14 right-handed, 2 left-handed), with a mean age of 65.56 years (SD = 3.03, range: 62–70) and a mean 17 years of education (SD = 3.27, range: 12–27). Years lived in Toronto varied from 25 to 66 years (mean = 45.13, SD = 15.25). All control participants were administered the Montreal Cognitive Assessment (MoCA) as a brief assessment of general cognitive function. All scored 25 or higher (of a possible 30 points), (mean = 28.13, SD = 1.57, range = 25–30), indicative of normal cognitive function (Dong et al., 2012; Larner, 2012; Waldron-Perrine & Axelrod, 2012). Three additional participants were tested but excluded from data analysis. One participant was excluded due to reporting learning disabilities and having a low score

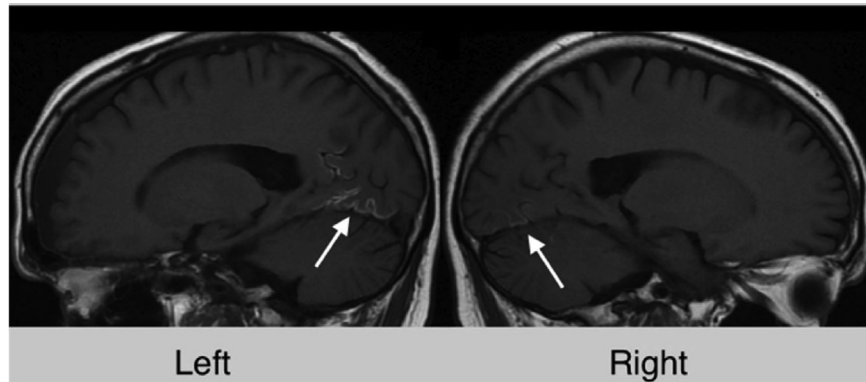


Fig. 2 – Structural MRI scan for the topographical disorientation case, L.H. High signal in the occipital gyri areas as shown by his MRI scan. Cortical laminar necrosis was reported in the bilateral posterior and medial occipital lobes and left inferomedial parietal lobe (Rivest et al., 2018; note: coronal views were not available based on the resolution of this clinical scan).

on the MoCA (score = 22), one participant self-identified as “never having had vivid memories” and had difficulty completing the tasks (see Palombo, Alain, Söderlund, Khuu, & Levine, 2015), and one participant was excluded for not complying with task instructions. All inclusion and exclusion criteria were established prior to data analysis. Control participants were recruited from a database of volunteer research participants from the community. We chose a sample size of 16 control participants to be comparable to the control groups in previous studies of individuals with MTL amnesia (Hassabis, Kumaran, Vann, & Maguire, 2007; Mullally, Intraub, & Maguire, 2012; Palombo, Di Lascio, Howard, & Verfaellie, 2018; Sheldon et al., 2013; Sheldon, McAndrews, & Moscovitch, 2011). In compliance with the Transparency and Openness Promotion (TOP) guidelines, we have reported how we determined our sample size, all data exclusions, all inclusion/exclusion criteria, whether inclusion/exclusion criteria were established prior to data analysis, all manipulations, and all measures in the study.

2.2. Procedure

2.2.1. Pre-study questionnaire

Prior to the study, all landmark stimuli were assessed for personal familiarity for each participant and landmark lists were customized for each participant. Participants were sent names of 120 well-known public places in the city of Toronto and asked to estimate how many times they had visited each location. Since D.A. and L.D. were not familiar with enough locations from this Toronto area inventory, their survey included an additional 50 landmarks from the Greater Toronto Area where they lived. Participants made their best estimate of their total number of visits to each landmark by choosing from the options: ‘Never’, ‘1 to 2 times’, ‘3 to 5 times’, ‘6 to 10 times’ and ‘More than 10 times’. As established in previous studies (Robin et al., 2016; Robin & Moscovitch, 2014, 2017b), landmarks visited between 1 and 5 times were considered ‘low familiarity’ and those visited more than 10 times were classified as ‘high familiarity’. Only those low and high familiarity landmarks were used as stimuli in the study.

Neuropsychological cases completed the survey with a family member, or a family member verified their responses. Interestingly, most of the time, family members corroborated their answers. Despite deficits in long-term memory, amnesic individuals were apparently able to report their familiarity with landmarks quite accurately.

2.2.2. Study procedure

Testing took place in a single session, lasting between 1 and 2 h. All participants were given a general description of the study and provided informed consent before participating. They were remunerated \$16/h. This study was given ethics approval by the Baycrest Hospital Research Ethics Board.

Participants completed four tasks: scene memory, autobiographical memory, landmark location, and landmark recognition, in this order. Due to the small number of cases, we chose to keep their order constant since counterbalancing them could contribute to individual variation in performance. Furthermore, the landmark recognition task had to be completed last as completing it could provide visual memory cues for the landmarks and influence performance on all other tasks. All tasks were included detailed instructions, and two to four practice trials in which participants were given opportunities to ask questions and receive feedback on performance. In an attempt to minimize memory demands of the tasks, explicit instructions were presented on the screen at each trial. Experimental stimuli were displayed and responses were collected using E-Prime 2.0 software (Psychology Software Tools). The experimental paradigms were tailored to each participant in the study, using personally familiar stimuli, and are therefore not available online due to ethical barriers, namely, the potential for identifying participants. The Toronto Landmark Survey, used to assess familiarity with landmarks, and a template experimental paradigm without participant-specific stimuli are available online at the Open Science Framework, DOI: 10.17605/OSF.IO/R73ZN. Participant-specific landmark stimuli and data are available by request, requiring approval of the Baycrest Hospital Research Ethics Board. No part of the study procedures or analyses were pre-registered.

2.2.3. Scene memory

In this task, participants were shown the names of four high and four low familiarity landmarks, as identified with the pre-study questionnaire. Each trial consisted of a 3-sec fixation-cross followed by the name of the landmark. Participants were asked if they could picture the scene including this landmark. They were instructed to say “Yes”, as long as they had even a vague or uncertain image of a scene including the landmark, and “No” if nothing at all came to mind. If they indicated “No”, the trial terminated. If they selected “Yes”, they were next asked to rate how vividly they could picture the scene on a scale of 1–5 (where ‘1’ represented ‘not very vividly’ and 5, ‘extremely vividly’) and to indicate when they last visited the landmark (less than 1 month ago; 1–6 months ago; 6–12 months ago; more than 1 year ago; more than 5 years ago). Next, they were asked to describe the scene including the landmark in as much detail as possible, with the prompt “Describe the scene including [Landmark Name] in as much detail as possible”. This description was recorded, and not time-limited. Participants were free to speak until they felt they had no more details to provide, at which point they pressed a key. Once pressed, they were asked: “Is there anything else you can picture for the scene including [Landmark Name]?” Participants could add additional details or press a key to end the trial.

Scene descriptions were transcribed and coded for details, following the procedure described in studies by Robin and Moscovitch (2014; 2017b). All details pertaining to the visual and/or spatial aspects of the landmark (e.g., height, size, color, signs, appearance of features such as windows or doors, etc.) or its surrounding area (e.g., adjacent buildings, qualities of the street or surrounding area) were counted as ‘spatial details’. Any other details, pertaining to events occurring at the location, memories, non-visual or spatial descriptions of the location (e.g., semantic information) were counted as external details. A second rater coded 25% of descriptions and inter-rater reliability was found to be high ($r = .93$ for visual details; $r = .89$ for external details).

A ratio of spatial to total details was computed for each participant, controlling for verbosity differences across participants. To compare high and low familiarity scenes, the difference in spatial details between conditions was divided by the total spatial details for high and low familiarity scenes. Note that the accuracy of scene memories was not verified in this study, as some locations have changed over the years, making it difficult to verify remote visual details.

2.2.4. Autobiographical memory

The autobiographical memory task followed a similar format to that of scene memory. Participants were shown the names of four high and four low familiarity landmarks (different from those used in the scene task), and were asked to remember specific events occurring at or around the landmark locations shown on the screen (instead of remembering scenes including the landmark). Participants were instructed to choose one unique event that involved themselves and the landmark location, and to recall as many details of that event as possible. The instructions emphasized that even a vague memory of an event should qualify as an event, but general memories of events that had occurred numerous times with no unique details should not qualify.

Each trial consisted of a 3-sec fixation-cross followed by the name of the landmark. Participants were asked if they could remember an event occurring at that location, with the option to answer ‘Yes’ or ‘No’. If they indicated ‘No’, the trial terminated. If they selected ‘Yes’, they were asked to rate how vividly they could remember the event on a scale of 1–5 (where ‘1’ represented ‘not very vividly’ and 5 represented ‘extremely vividly’) and to indicate when the event occurred (less than 1 month ago; 1–6 months ago; 6–12 months ago; more than 1 year ago; more than 5 years ago). Next, they were asked to describe the event memory in as much detail as possible, with the prompt “Describe the memory involving [Landmark Name] in as much detail as possible”. Once again, participants terminated the trial when they felt they had included all details, and were prompted one more time with the instructions “Is there anything else you remembered about the event involving [Landmark Name]?” in order to elicit any additional details.

Descriptions of events were recorded, transcribed and coded, following the guidelines for internal and external details established in the Autobiographical Interview (AI; Levine, Svoboda, Hay, Winocur, & Moscovitch, 2002). The main event being described was identified, and all details pertaining to the specific event were counted as internal details (e.g., actions, events, specific perceptual details, temporal details, thoughts or feelings had at the time of the event). Spatial details about the landmarks were not included in the internal detail totals in order to examine the effects of cue familiarity on non-spatial aspects of the events (but see Figure S2 for internal details including spatial details). All details concerning other events, general or semantic information, reflections on the event, meta-cognitive statements, repetitions or any other unrelated information were counted as external details. A second rater coded 25% of descriptions and inter-rater reliability was found to be high ($r = .84$ for internal details; $r = .96$ for external details).

Performance was assessed by computing a ratio of internal to total details, and the difference between total internal details across the high and low familiarity conditions divided by total internal details, for each participant. The veracity of autobiographical memories could not be verified in this study because events were remote and did not always include other individuals.

2.2.5. Landmark location

In this task, participants were presented with pairs of landmarks, and asked which of the two was farther in a certain cardinal direction (i.e., north, south, east or west). Each trial began with a 3-sec fixation-cross. Then, a screen appeared with the prompt “Which landmark is farther [cardinal direction]?” and displayed two landmark names. Participants pressed a key to indicate which landmark they chose, or had the option to select a third key to indicate ‘Don’t Know’. Participants had unlimited time to make this decision, and completed between 28 and 40 trials, depending on how many familiar landmarks they had identified in the pre-study questionnaire. Landmark pairs consisted of two high familiarity landmarks or two low familiarity landmarks, and equal numbers of high and low familiarity trials were always presented. Each pair was shown twice, once asking

about the north/south axis, and once about the east/west axis, with the specific directions randomly assigned. Some landmarks from the preceding scene and memory tasks in addition to new landmarks were included in this task. Landmarks on the same streets were never paired together, since there would be no correct answer for one of the axes. Accuracy was calculated by determining the proportion of correct trials out of the total trials for each familiarity condition. Trials on which the participant answered incorrectly or selected 'Don't Know' were considered incorrect.

2.2.6. Landmark recognition

In this task, participants were presented with images of landmarks from Google Street View, and asked if they were familiar with the location pictured. Participants completed 40 trials, with two different images of each of 10 high and 10 low familiarity landmarks. Some landmark stimuli were the same as those presented in the previous three tasks, but here the image of each landmark was shown instead of its name. In order to maximize the chance to trigger familiarity, two views of each landmark were presented (participants may have only been familiar with a given location from one angle). On each trial, participants viewed a 3-sec fixation-cross followed by a landmark image. They were asked if they recognized the pictured location, with the option to indicate 'Yes' or 'No.' Participants had unlimited time to make this decision. If they chose 'No', the trial terminated. If they chose 'Yes', they were asked to name the landmark, or, if they did not know its name, give a specific description of it (e.g., the museum with the dinosaurs), or give its exact location (e.g., the intersection where it was located). These answers were recorded for verification and scoring. A landmark was considered correctly identified if participants correctly stated its name, described its details or its precise location on at least one of the two trials featuring its image. Giving a generic label that could be inferred based on the building's characteristics (e.g., a hospital, a school) was not counted as a correct answer. An accuracy score, reflecting the proportion of landmarks correctly identified, was calculated for each familiarity condition.

3. Results

Due to the various aetiologies and case presentations of the amnesic cases, we chose to evaluate each case individually rather than combining them into one averaged sample. We used a descriptive, estimates-based approach to compare each individual's performance to that of controls (see Cumming, 2014). As described in recent studies involving small neuropsychological samples (Kwan et al., 2013; Kwan, Kurczek, et al., 2016), this method is more appropriate for quantifying the performance of individuals when the sample size is small and scores are not normally distributed.

For each task and condition, a z-score is calculated for each individual, reflecting the deviation of his score from the control group, in terms of the number of standard deviations from the control mean. These z-scores can be interpreted using a standard psychometric conversion table based on the Wide Range Achievement Test –Third Edition, Administration Manual (WRAT-III, Wilkinson, 1993), which provides

quantitative (estimated percentile rankings) and qualitative (diagnostic labels) estimates of performance. Level of impairment is determined based on the number of standard deviations (SD) by which each case differs from the control mean (>2 SD below the control mean is considered impaired performance, 1.4–2 SD below the mean is considered borderline, and .7–1.4 is considered low average). This method allows each case to be compared to controls and discussed individually in terms of their level of difficulty, with no need for correction for multiple comparisons since an alpha-threshold is not used. In addition, the standardized z-scores allow for meaningful comparison of the effects across tasks, despite using differing dependent variables. Data and analysis code are available online at the Open Science Framework, DOI: 10.17605/OSF.IO/R73ZN.

3.1. Scene memory

Scene descriptions were coded for spatial details (i.e., those relevant to the visuospatial aspects of the scene in question) and external details (i.e., all other details), and the sum of the details was calculated for the high and low familiarity conditions, separately. In order to control for the variability in verbosity across participants, the ratio of spatial details to total details was calculated, reflecting the proportion of relevant details in each participant's descriptions. Comparisons of the neuropsychological cases to controls (controls: $M_{\text{high}} = .541$, $SD_{\text{high}} = .130$; $M_{\text{low}} = .493$, $SD_{\text{low}} = .135$) revealed that both the topographical disorientation case (L.H.) and the amnesic cases were impaired in terms of the proportion of spatial details produced in the scene memory task (see Table 2; Fig. 3A). This was true for both the high and low familiarity cue conditions, with the exception of one case, D.A., who only showed low average performance in the low familiarity cue condition.

To assess the effect of cue familiarity in controls, a paired t-test comparing the total number of spatial details in the high and low familiarity conditions was conducted, revealing a significantly larger number of details for the high familiarity scenes [$t_{(15)} = 4.52$, $p = .0004$, 95% CI (12.91, 35.96); $M_{\text{high}} = 42.25$, $SD_{\text{high}} = 23.29$; $M_{\text{low}} = 17.81$, $SD_{\text{low}} = 11.21$]. Total internal details were examined instead of ratios in this case since this was a within-subject comparison, which controlled for the intra-individual differences in verbosity, and since the number of internal details, not the ratio of internal to external, was predicted to differ according to familiarity, consistent with previous studies (Robin & Moscovitch, 2014; 2017b). To compare the effect of cue familiarity in neuropsychological cases with the control group, the difference between the number of spatial details in the high and low familiarity conditions was calculated and divided by the total number of spatial details (to control for differences in verbosity), and compared with the mean difference ratio in controls. L.H. and three of the four amnesic cases (S.P., L.D., and M.H.) had a higher number of details in the high than the low familiarity condition, though the size of this effect was borderline compared to controls for L.H. (see Table 2; Fig. 3B). L.D. showed an average familiarity effect, while S.P. and M.H. demonstrated superior effects, possibly due to their very low performance in the low familiarity condition. The familiarity

Table 2 – Spatial details reported in the scene memory task.

Case	Ratio of Spatial Details to Total Details						Difference in Spatial Details		
	High Familiarity			Low Familiarity			z-score	%ile rank	Label
	z-score	%ile rank	Label	z-score	%ile rank	Label			
D.A.	–2.22	2	Impaired	–1.12	13	Low Average	–2.79	0.3	Impaired
L.D.	–3.21	.07	Impaired	–2.24	1	Impaired	.03	50	Average
S.P.	–2.45	0.8	Impaired	–2.97	0.2	Impaired	1.61	94	Superior
M.H.	–3.53	.02	Impaired	–3.23	.06	Impaired	1.71	95	Superior
L.H.	–3.28	.06	Impaired	–2.13	2	Impaired	–1.43	8	Borderline

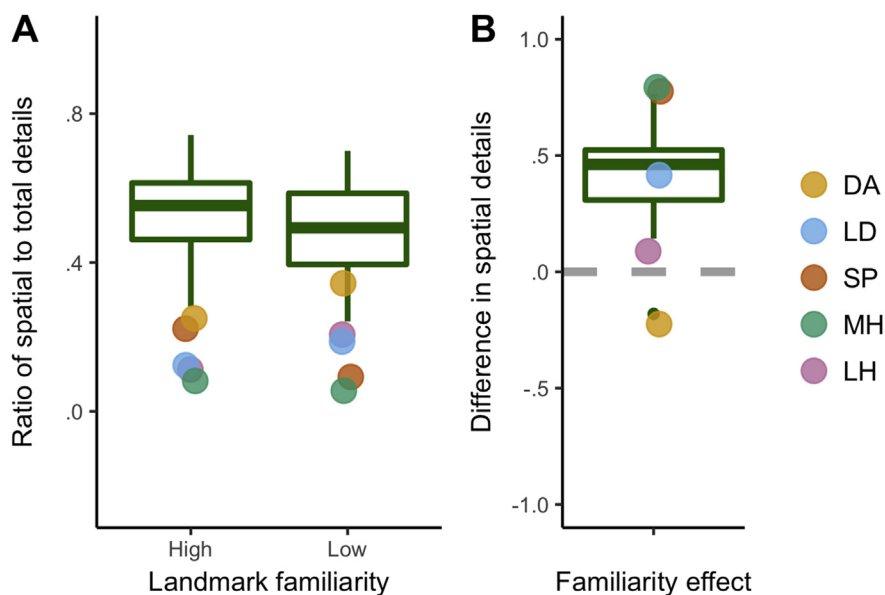


Fig. 3 – A) Ratio of spatial details to total details for high and low familiarity scene memories. Control data are shown in the boxplots, with data for the neuropsychological cases overlaid. B) Difference in spatial details produced for high and low familiarity scenes, divided by total spatial details.

effect was reversed for D.A., who produced more details in the low than in the high familiarity condition, resulting in an impaired effect compared to controls.

In summary, the amnesic cases and the topographical disorientation case all produced few relevant details when describing scenes from remote memory. The number of details recalled was somewhat higher for the more familiar scene cues, like in controls, but this effect was inconsistent (see Table 6 for a summary). Subjective ratings of vividness and recency of visiting the scenes did not vary systematically between controls and neuropsychological cases, see Figure S1.

3.2. Autobiographical memory

Autobiographical memory descriptions were coded according to the number of internal details (i.e., those relevant to the specific memory being described) and external details (i.e., all other details) and details were summed for the high and low familiarity conditions, separately. For these analyses, we omitted spatial details from the internal detail totals, in order to separate the contributions of spatial and episodic memory as much as possible. The results including spatial details show similar patterns, and are included in Figure S2. As in the scene

memory task, the ratio of internal details to total details was calculated, reflecting the proportion of relevant details in each participant's descriptions. In controls, the ratio of internal details to total details in the scene memory task was significantly correlated with the ratio of internal details to total details in the autobiographical memory task [$r(14) = .54, p = .03$]. Due to the small number of clinical cases, it was not meaningful to compute correlations for this group.

Comparisons of the ratio of internal to total details in neuropsychological cases and controls (controls: $M_{\text{high}} = .511, SD_{\text{high}} = .227; M_{\text{low}} = .470, SD_{\text{low}} = .279$) revealed that both the topographical disorientation case (L.H.) and the amnesic individuals performed below controls in terms of the proportion of internal details produced in their autobiographical memories (see Table 3; Fig. 4A). While overall the amnesic cases clearly had lower scores than controls, performance was more varied than in the scene memory task. S.P. had impaired and borderline performance in the high and low familiarity conditions, producing no internal details from specific memories in either condition. L.D. was impaired and low average in the high and low familiarity conditions, respectively. D.A. was low average and borderline for the high and low familiarity conditions, respectively. M.H. was borderline and average in

Table 3 – Internal details reported in the autobiographical memory task.

Case	Ratio of Internal Details to Total Details						Difference in internal details		
	High Familiarity			Low Familiarity			z-score	%ile rank	Label
	z-score	%ile rank	Label	z-score	%ile rank	Label			
D.A.	–1.26	10	Low average	–1.40	8	Borderline	1.46	92	Superior
L.D.	–2.15	2	Impaired	–.90	19	Low average	–5.06	.01	Impaired
S.P.	–2.25	1	Impaired	–1.68	5	Borderline	–1.81	4	Borderline
M.H.	–1.45	8	Borderline	.65	74	Average	–4.14	.01	Impaired
L.H.	–1.48	7	Borderline	–.52	30	Average	–2.28	1	Impaired

the high and low familiarity conditions, respectively. Despite not being classified as an amnesic and performing at average or low average levels on neuropsychological memory measures, L.H. was borderline in the high familiarity condition, and average in the low familiarity condition.

To assess the effect of cue familiarity in controls, a paired *t*-test comparing the total number of internal details in the high and low familiarity conditions in controls was conducted, again revealing a significantly larger number of details in the high familiarity condition [$t_{(15)} = 3.51, p = .003, 95\% \text{ CI } (6.69, 27.44); M_{\text{high}} = 31.94, SD_{\text{high}} = 18.11; M_{\text{low}} = 14.88, SD_{\text{low}} = 11.67$]. To compare the effect of cue familiarity with the control group, the difference between the number of internal details in the high and low familiarity conditions was calculated and divided by the total number of internal details, and this difference ratio was compared with the mean difference ratio in controls. Only one of the amnesic cases, D.A., described more details in the high familiarity condition than the low familiarity condition, showing a superior familiarity effect compared to controls. All other cases had borderline or impaired cue familiarity effects due to describing more details in the low familiarity than the high familiarity condition, or in the case of S.P., describing no internal details in either condition (see Table 3, Fig. 4B).

In summary, the amnesic cases performed below the level of controls in describing episodes from memory, though performance was more varied than in the scene memory task. The topographical disorientation case, L.H., also demonstrated low internal details compared to controls. More familiar cues did not improve performance, except in the case of D.A. (see Table 6 for a summary). Subjective ratings of vividness and recency the memories did not vary systematically between controls and neuropsychological cases, see Figure S3.

3.3. Landmark location

Accuracy on the landmark location task, as measured by percent correct direction judgments, was compared for high

and low familiarity landmark pairs. Notably, the topographical disorientation case L.H. had average performance compared to controls (controls: $M_{\text{high}} = 88.69\%, SD_{\text{high}} = 12.22; M_{\text{low}} = 69.44\%, SD_{\text{low}} = 22.07$) on both the high and low familiarity conditions, despite demonstrating profound navigation deficits in everyday life (see Table 4). In marked contrast to the scene memory task, there was no consistent pattern of impairments in the amnesic group on this task, with most cases performing in the low average to high average range, with the exception of M.H. who had borderline performance on both familiarity conditions (see Table 4; Fig. 5A).

In controls, the high and low familiarity conditions were significantly different in terms of accuracy [$t_{(15)} = 3.36, p = .004, 95\% \text{ CI } (7.05, 31.45)$]. To assess if the familiarity of the landmarks had an effect on accuracy, the difference in accuracy scores between the conditions was calculated, and compared with the mean difference in controls. All cases, except D.A., showed numerically higher accuracy in the high compared to the low familiarity condition (see Table 4; Fig. 5B). These differences between conditions were comparable to those in controls in two cases (S.P. and M.H.) and above average in two cases (L.H. and L.D.) due to lower scores in the low familiarity condition. D.A. showed slightly higher performance (7%) in the low familiarity condition, resulting in a below average familiarity effect.

In summary, performance on the landmark location task, requiring map-like schematic spatial memory, was comparable to that of controls for amnesic and topographical disorientation cases, with the exception of M.H. Accuracy was higher for more familiar landmark pairs in controls and in all cases except D.A (see Table 6 for a summary).

3.4. Landmark recognition

Accuracy on the landmark recognition task, as measured by percent correct landmark identification, was compared for high and low familiarity landmarks (controls: $M_{\text{high}} = 78.12\%$,

Table 4 – Accuracy in the landmark location task.

Case	Accuracy						Difference in accuracy		
	High Familiarity			Low Familiarity			z-score	%ile rank	Label
	z-score	%ile rank	Label	z-score	%ile rank	Label			
D.A.	–.79	22	Low average	.75	78	High average	–1.15	13	Low average
L.D.	–.22	41	Average	–.88	19	Low average	.73	76	High average
S.P.	–1.12	14	Low average	–.65	26	Average	.03	51	Average
M.H.	–1.94	3	Borderline	–1.56	6	Borderline	.47	68	Average
L.H.	.11	54	Average	–.65	26	Average	.69	76	High average

Table 5 – Accuracy in the landmark recognition task.

Case	Accuracy						Difference in accuracy		
	High Familiarity			Low Familiarity			z-score	%ile rank	Label
	z-score	%ile rank	Label	z-score	%ile rank	Label			
D.A.	.12	54	Average	−1.62	6	Borderline	1.53	93	Superior
L.D.	−.54	29	Average	−2.29	1	Impaired	1.53	93	Superior
S.P.	−1.20	11	Low average	−2.29	1	Impaired	.95	83	High average
M.H.	−1.86	4	Borderline	−2.95	.2	Impaired	.95	83	High average
L.H.	−.54	29	Average	−1.62	6	Borderline	.95	83	High average

Table 6 – Summary of predictions and results.

Task	Scene memory		Autobiographical memory		Landmark location		Landmark recognition	
	High	Low	High	Low	High	Low	High	Low
Predictions	x	x	x	x	=	=	=	x
<i>Amnesic cases</i>								
D.A.	x	<	<	x	<	>	=	<
L.D.	x	x	x	<	=	<	=	x
S.P.	x	x	x	x	<	=	<	x
M.H.	x	x	x	=	x	x	x	x
<i>TD case</i>								
L.H.	x	x	x	=	=	=	=	x

Note. Predictions are based on MTT and TTT, which postulate that more detailed forms of spatial and episodic memory are impaired by MTL damage, while more schematic forms remain intact. Predictions apply to MTL amnesic cases, but we additionally report results for M.H., who has more extensive damage to visual cortex and L.H., who is not amnesic but has posterior ventral-temporal damage and topographical disorientation. x indicates borderline or impaired performance; < indicates low average performance; = indicates average performance; > indicates high average performance; + indicates superior performance.

$SD_{high} = 15.15$; $M_{low} = 64.38\%$, $SD_{low} = 15.04$). All cases had accuracy below that of controls for the low familiarity landmarks: three amnesic cases had impaired performance (L.D., S.P. & M.H.), and the topographical disorientation case and

one amnesic case had borderline performance (L.H. & D.A.; see Table 5; Fig. 6A). In contrast, for the high familiarity landmarks, all individuals performed closer to the level of controls with two amnesic cases and the topographical disorientation

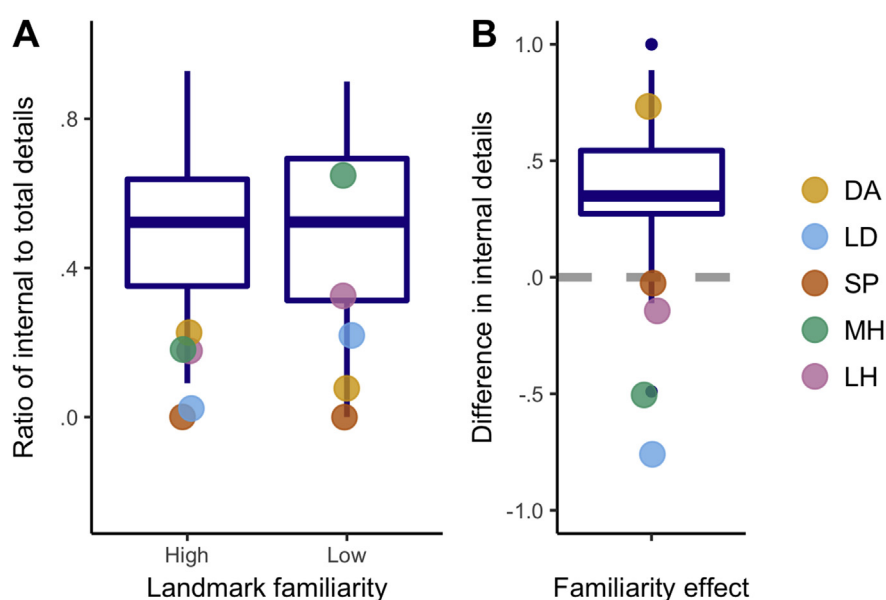


Fig. 4 – A) Ratio of internal details to total details for autobiographical memories cued by high and low familiarity landmarks. Control data are shown in the boxplots, with data for the neuropsychological cases overlaid. **B)** Difference in internal details produced for memories cued by high and low familiarity landmarks, divided by total internal details.

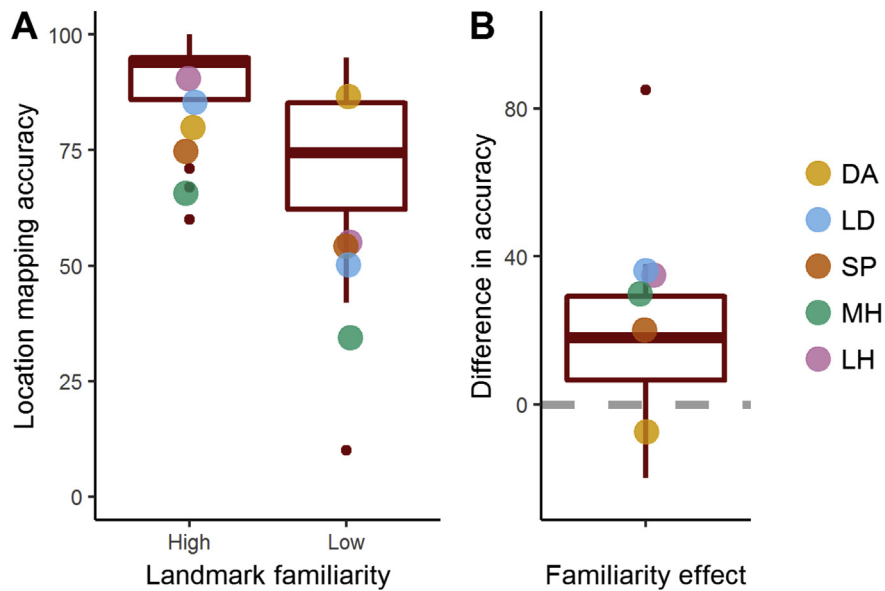


Fig. 5 – A) Percent accuracy on direction judgments for high and low familiarity landmark pairs. Control data are shown in the boxplots, with data for the neuropsychological cases overlaid. B) Difference in accuracy scores for high and low familiarity landmark pairs.

case (L.H., D.A. & L.D.) demonstrating average performance, one amnesic case (S.P.) with low average performance, and one (M.H.) with borderline performance.

In controls, the high and low familiarity conditions were significantly different in terms of accuracy [$t_{(15)} = 3.22$, $p = .005$, 95% CI (4.65, 22.85)]. To assess the presence of familiarity effects, the difference in accuracy scores between the conditions was calculated, and compared with the mean difference in controls. Like controls, all neuropsychological cases had higher accuracy for the more familiar landmarks, as in the control group. The difference between familiarity

conditions was above average in two amnesic cases and the topographical disorientation case (S.P., M.H. & L.H.) and superior in two amnesic cases (D.A. & L.D.). Thus, the familiarity difference in landmark recognition accuracy was more pronounced in all neuropsychological cases (see Table 5; Fig. 6B). This difference resulted from particular impairments in the low familiarity landmark condition compared to controls, as opposed to improved performance in the high familiarity condition.

In summary, performance on landmark recognition was comparable to that of controls for highly familiar landmarks,

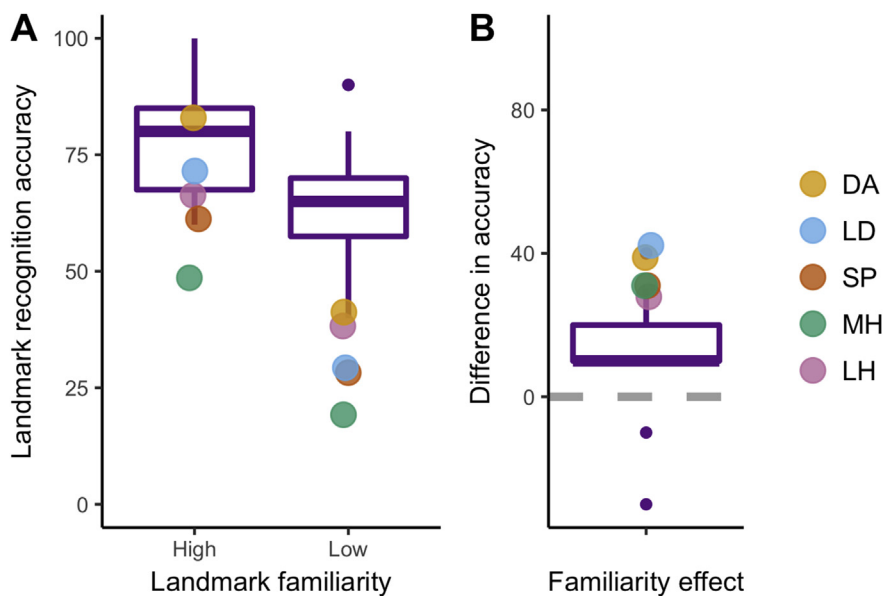


Fig. 6 – A) Percent recognition accuracy for high and low familiarity landmarks. Control data are shown in the boxplots, with data from neuropsychological cases overlaid. B) Difference in recognition accuracy scores for high and low familiarity landmarks.

but impaired for less familiar landmarks for the topographical disorientation case and all amnesic cases, except for M.H. who had low performance in both conditions. As a result, the effect of familiarity was seemingly increased for amnesic and topographical disorientation cases compared to controls (see [Table 6](#) for a summary).

4. Discussion

The present study tested episodic memory and three types of spatial memory, cued by landmarks of varying familiarity, in individuals with amnesia relating to MTL damage and in an individual with topographical disorientation relating to ventral temporal, parietal and occipital lobe damage. All amnesic cases showed low average or impaired performance compared to healthy controls on the scene memory task. Similarly, all amnesic cases had performance ranging from impaired to low average on the episodic memory task, with the exception of one amnesic case, M.H., who had average performance in the low familiarity condition. In contrast, on the landmark location task, amnesic cases performed in the low to high average range as compared to controls, with the exception of M.H. who had borderline performance. Lastly, in the landmark recognition task, amnesic cases performed in the low average to average range for the high familiarity landmarks again with the exception of M.H., who had borderline performance, whereas all had impaired to borderline performance for low familiarity landmarks (for a summary of results see [Table 6](#)). Note that M.H.'s lesions included MTL regions and also extended more posteriorly to infero-temporal and occipital regions, which may have contributed to his more extensive impairments in performance.

L.H., the individual with topographical disorientation relating to more posterior and ventral temporal, parietal, and occipital lobe damage, demonstrated a somewhat similar pattern of results as the amnesic cases (see [Table 6](#)). L.H. was impaired on the scene memory task, and performed at average and borderline levels on the episodic memory task. L.H. performed at average levels on the landmark location task and on recognizing high familiarity landmarks, but at borderline level on recognizing low familiarity landmarks.

Overall, the results are consistent with predictions based on MTT and TTT, which postulate that highly detailed spatial and episodic memories rely on the hippocampus and medial temporal lobes, even when remote. Parallel deficits in scene and episodic memory in the MTL amnesic group are consistent with this view. In addition, spared performance on the landmark location task supports the notion that more schematic forms of spatial memory are intact in cases of MTL damage. The fact that these different forms of spatial memory, elicited by similar spatial cues, show different patterns of impairment supports the prediction that the characteristics of a memory, not its age, determine its reliance on the MTL. This is inconsistent with standard consolidation theory, which would predict that all remote memories would be preserved, while recent memories would be impaired by MTL damage. Finally, the landmark recognition condition provides new evidence that less familiar scenes may require detailed representations for their recognition and identification, while

more familiar scenes may require less detailed representations to support recognition and identification. Thus, familiar scenes can still be recognized following MTL damage owing to non-MTL representations.

These results are also mostly consistent with SC theories, demonstrating that MTL amnesia leads to deficits in scene memory, which appear to be similar or more severe than those in episodic memory. Intact performance in the landmark location task, which presumably does not require scene construction, is also consistent with SC. Intact landmark recognition for more, but not less, familiar scenes is less consistent with SC, which might predict that both conditions would be dependent on the hippocampus since they both involve perceiving and identifying scenes. Results from the topographical disorientation case offer mixed support for SC, demonstrating that spatial memory impairments may entail declines in episodic memory, but linking these patterns to damage outside the MTL. We discuss these results and their theoretical implications in detail in the sections below.

4.1. Impairments to scene memory and episodic memory in cases of MTL amnesia

Our first question was whether scene memory and episodic memory would be equally affected by MTL damage. Notably, the amnesic cases all performed at the same level or worse in the scene memory task compared to the episodic memory task (with the exception of D.A., only for low familiarity cues). These findings are similar to previous reports that detailed route descriptions are impaired in cases of MTL amnesia ([Herdman et al., 2015](#)), but this task focussed on single scene memory as a closer analog for the episodic memory task. This novel comparison of detailed scene memory and episodic memory suggests that impairments to scene memory are equal or more severe than those in episodic memory as result of hippocampal and medial temporal damage. This pattern is consistent with the finding of equivalent reductions in internal details in memory for scenes and episodes in healthy older adults ([Robin & Moscovitch, 2017b](#)) and with declines in detailed descriptions for familiar routes in older adults and amnesic cases ([Herdman et al., 2015](#); [Hirshhorn et al., 2011](#)). These results therefore align with predictions from both TTT and SC, but are inconsistent with standard consolidation predictions that remote episodic and spatial memory are intact following MTL damage. Both TTT and SC predict that the hippocampus is necessary for detailed remote memories of scenes and thus, memory for scenes should be impaired in cases of MTL damage. There is, however, a subtle difference between their predictions: whereas TTT posits that scenes and episodes are both dependent on the hippocampus because they are both highly detailed forms of memory, SC posits that scenes are specifically reliant on the hippocampus, and provide the scaffold on which episodes are built ([Hassabis & Maguire, 2007](#); [Maguire & Mullally, 2013](#); [Moscovitch et al., 2016](#); [Moscovitch et al., 2006](#); [Mullally & Maguire, 2014](#); [Winocur et al., 2010](#); [Winocur & Moscovitch, 2011](#); [Zeidman & Maguire, 2016](#)). The present data cannot arbitrate between TTT and SC. Nevertheless, since scene memory was more consistently impaired than episodic memory, the results suggest that spatial memory impairments are more severe

than episodic memory impairments, which could be viewed as supporting SC.

Based on the finding that impairments in scene memory were consistent across amnesic cases, this study validates scene memory as a measure of medial temporal lobe-related memory impairments and indicates that scene memory is a consistent and reliable index of memory impairment, comparable to standard autobiographical memory measures. This equivalence occurs despite the fact that episodic memory is typically more multi-modal and narrative-based than scene memory, which relies primarily on visuospatial details. It may be that episodic memory is better suited to be supported by schemas or semantic associations when specific episodic details cannot be retrieved (Ghosh & Gilboa, 2014; Gilboa & Marlatte, 2017). Thus, when individuals with memory impairments are asked about a particular autobiographical memory, they may be able to fill in details based on schematic knowledge about the event (i.e., birthday parties typically involve gifts, cake, balloons). Since it is very difficult to verify the accuracy of autobiographical memory, some memory-impaired individuals may be able to mask or attenuate their deficits using strategies such as these. Notably, one individual (D.A.) who showed milder impairments on the episodic memory task, has been known to rely on strategies based on intact semantic memory to compensate for his other memory deficits (Ryan et al., 2013). When remembering particular scenes, some generic details may similarly be deduced from semantic memory (i.e., hospitals are usually large, multi-storey buildings), but the majority of the particular visuospatial details must be retrieved from memory.

One caveat to the conclusions linking scene memory and the MTL is that structures beyond the hippocampus [namely the parahippocampal gyrus, retrosplenial cortex, precuneus and occipital place area (Epstein, 2008; Epstein & Kanwisher, 1998; Johnson & Johnson, 2014)] are known to be involved in the perception and memory of scenes. In the present study, the finding of equivalent deficits in scene memory in L.H., who has topographical disorientation relating to damage to the left parietal, left inferior temporal and bilateral occipital lobes, reinforces the important point that impairments to scene memory may stem from damage to a variety of neural structures. Thus, while damage to the hippocampus and medial temporal lobes appear to impair detailed scene memory and perception, it is also clear that these structures work as part of a larger neural network related to scene processing, and damage to different parts of the network can result in behavioral impairments (Lee, Brodersen, & Rudebeck, 2013; Lee et al., 2005; Lee, Yeung, & Barense, 2012). Importantly, even in the MTL cases in the present study, damage was not confined to the hippocampus, extending into the parahippocampal gyrus in some cases (D.A. and L.D.) and more posterior inferotemporal regions in another (M.H.). Despite differences in lesion location and extent in the amnesic group, all showed deficits on scene and episodic memory tasks, and lesion differences did not appear to relate to the severity of deficits, though this is a small and varied group. In sum, we suggest that MTL damage in the amnesic cases underlies parallel deficits to scene and episodic memory but acknowledge that damage to other structures in the spatial network may also lead to deficits in scene memory. The finding that the topographical disorientation case, L.H.,

showed similar deficits in scene memory as the amnesic group, despite no hippocampal damage, supports this point.

4.2. Mild impairment to episodic memory in a case of topographical disorientation

The second main finding of interest in the present study was that, despite having a different pattern of neural damage and not being amnesic, performing at normal levels of neuropsychological tests of memory, L.H. also showed low average/borderline performance on the autobiographical memory task. Thus, while still being able to retrieve episodes, these were low in detail as compared to control participants, even when non-spatial details were considered. This finding offers mixed support for SC. On one hand, it demonstrates that in an individual with impaired scene memories, episodic memories undergo a decrease in details, perhaps relating to the absent or degraded spatial context on which to construct the memory. This result supports the premise that scenes may underlie episodic memories, and that when scene representations are impaired, there is a decline in episodic memory (Bird & Burgess, 2008; Hassabis & Maguire, 2007, 2009; Maguire & Mullally, 2013; Robin, 2018; Rubin & Umanath, 2015). This result is also consistent with cases of autobiographical amnesia coinciding with visual memory loss (Greenberg et al., 2005; Rubin & Greenberg, 1998). On the other hand, since L.H.'s hippocampus is not thought to be damaged, this finding is not fully consistent with versions of SC that state that the hippocampus, in particular, mediates the link between scenes and episodes (Hassabis & Maguire, 2007; Maguire & Mullally, 2013). In contrast, this result suggests that damage to more posterior scene-related regions is sufficient to impair scene memory and lead to impairments in episodic memory, as some have proposed (Robin, 2018; Rubin & Umanath, 2015).

It is possible, therefore, that in cases such as L.H.'s with more posterior damage, the hippocampus does not receive the necessary input from posterior scene-related areas in the brain, which is enough to cause some decline in episodic memory. Despite this, it may be the case that the hippocampus is still able to retrieve and bind some episodic details represented in other intact neocortical areas. As a result, L.H. has memories that are less detailed, though not as impaired as in the amnesic cases who have damage to the MTL.

More research is required in order to better understand the effects of scene memory deficits on episodic memory, but the findings from L.H. serve as preliminary evidence that episodic memory may at least partially depend on intact scene representation, as predicted by SC. On the other hand, the fact that L.H. is not amnesic and can still retrieve some episodic details demonstrates that impaired scene memory does not lead to a total loss of episodic memory. This suggests that while scenes are a crucial component of episodic memory, they are not its sole basis. Importantly, L.H.'s memory abilities also highlight how damage to more posterior scene-related regions, possibly including the parahippocampal cortex or retrosplenial cortex, may lead to declines in the richness of episodic memory, either directly, or indirectly, by disrupting inputs to the hippocampus.

4.3. Familiar cues provide inconsistent benefits to episodic and scene memory in cases of impairment

A third question in this study was whether more familiar cues lead to memory benefits, as has been previously shown in healthy young and older adults (Arnold, McDermott, & Szpunar, 2011; Robin et al., 2016; Robin & Moscovitch, 2014, 2017b). In the scene memory and autobiographical memory tasks, control participants showed predicted cue familiarity effects, in which more familiar cues led to increased details in both tasks. In control participants, the ratio of internal to total details was positively correlated between the scene and autobiographical memory tasks, suggesting a relationship between these types of memory. SC theories are supported by the findings that performance in the two tasks was related and that more familiar contexts were associated with more detailed episodic memories, even when non-spatial details were considered. The results suggest that a stronger spatial scaffold may support richer episodic memories (Robin, 2018; Robin et al., 2016). They are also consistent with a more spatially agnostic relational memory hypothesis, however, whereby more familiar cues simply have more associations in memory, leading to more detailed episodes (Eichenbaum & Cohen, 1988, 2014; Eichenbaum, Otto, & Cohen, 1994).

In contrast to controls, for both L.H. and the MTL amnesic individuals, cue familiarity effects were inconsistent in the scene and autobiographical memory tasks, with three individuals showing average or even increased familiarity effects in the scene memory task (L.D., S.P., M.H.), while the other two (D.A., L.H.) showed reduced familiarity effects. In the autobiographical memory task, familiarity effects were reduced in all individuals, except for D.A. These results seem to indicate that without the ability to remember detailed scenes, more familiar spatial contextual cues do not reliably improve spatial and episodic memory, though we acknowledge that the findings for scene memory are mixed. The cue familiarity effects on memory observed in previous studies may be dependent on generating internal representations of scenes when remembering their related episodes. A more detailed scene representation may act as a stronger scaffold on which to construct or reconstruct the retrieved memory (Clark & Maguire, 2016; Hassabis & Maguire, 2007; Maguire & Mullally, 2013; Robin, 2018), leading to the increased details generated for memories cued by more familiar contexts. It is possible, however, that more familiar cues also elicit more semantic or schematic details that can help to improve memory for episodes and scenes when specific spatial details are lacking.

4.4. Intact schematic spatial memory in amnesic and topographical disorientation cases

In contrast to the impairments seen in the scene and autobiographical memory tasks, performance was mostly intact in the landmark location task, which required coarse map-based spatial memory rather than detailed scene representations. In the landmark location task, the amnesic cases performed in the low to high average range, with the exception of M.H., who had borderline performance. Since landmark location

judgments rely on more schematic spatial memory and have previously been shown to be intact in individuals with hippocampal and MTL damage (Herdman et al., 2015; Maguire et al., 2006; Rosenbaum et al., 2000, 2005), these findings are consistent with predictions from MTT and TTT and corroborate that remote schematic spatial memory can be supported by regions outside of the MTL. Evidence that individuals with MTL lesions can navigate successfully in familiar environments further supports this conclusion (Rosenbaum et al., 2000; Teng & Squire, 1999), and differentiates these cases from the topographical disorientation case in the present study. M.H.'s more extensive damage to posterior inferotemporal structures and occipital regions may have contributed to his impairments on this task, consistent with neuroimaging results showing activity in these areas during remote spatial memory tasks (Rosenbaum, Ziegler, Winocur, Grady, & Moscovitch, 2004).

Similar to the amnesic cases, L.H. also demonstrated high accuracy on the landmark location task, despite exhibiting major deficits in unassisted real-world navigation (Rivest et al., 2018). Notably, this task provided word cues for navigation decisions rather than visual cues, and did not require mentally constructing a scene. These results provide further evidence that detailed and schematic spatial memory are dissociable, and suggest that L.H.'s impairment stems from a problem with detailed spatial memory, as shown by the scene memory task, while schematic representations remain intact, similar to cases of MTL damage (Herdman et al., 2015; Rosenbaum et al., 2005, 2000; Teng & Squire, 1999). Consequently, the real-world navigation deficits that L.H. experiences may be related to an inability to recognize the details of less familiar landmarks (as we discuss below) and to match scenes to ones in memory, rather than a deficient schematic memory of the layout of the environment. It is of note that despite having damage to posterior inferotemporal regions, like M.H., L.H. has a good memory of layouts. It is possible that the combination of MTL and posterior lesions led to impaired performance for M.H., but damage to only one or the other would not be sufficient to cause such impairments.

Interestingly, while the preservation of schematic spatial memory in conjunction with deficits to detailed spatial memory suggests a dissociation between these two, to our knowledge the reverse pattern of preserved detailed spatial memory with deficits to schematic spatial memory has yet to be shown. It is possible that this relationship is asymmetric, with detailed spatial memory relying on intact schematic memories, and thus detailed memories would not be spared in cases of schematic memory impairments. In contrast, it could be that selective damage to schematic spatial memory leaves detailed representations intact, representing a more complete dissociation between the two (similar to cases of semantic dementia), but it is unknown what regions would have to be damaged to cause such a dissociation. Further research testing various forms of remote spatial memory in individuals with varied patterns of damage and impairments is needed to help resolve this open question (see Dalla Barba & Decaix, 2009; Dalla Barba & La Corte, 2013).

In all cases except D.A., individuals had increased accuracy for more familiar landmark pairs on the landmark location task. The fact that familiarity improved performance on this

task, in the context of the inconsistent cue familiarity effects in the scene and autobiographical memory tasks, suggests that overall performance on a task may determine whether more familiar cues can exert a facilitatory effect. In this case, since individuals were largely unimpaired on the landmark location task, which is thought to depend on schematic spatial memory that does not rely on the medial temporal lobe, more familiar cues appeared to lead to enhanced performance in neuropsychological cases as well as controls, perhaps due to stronger or more accessible memory representations of those cues.

4.5. *Intact landmark recognition for high, but not low, familiarity landmarks in amnesic and topographical disorientation cases*

In the landmark recognition task, for high familiarity landmarks, performance was close to controls for most cases, with L.H. and two amnesic cases in the average range, S.P. below average and M.H. performing at borderline levels. As with the landmark location task, M.H.'s greater impairment compared to other cases may stem from his more extensive damage to both the MTL and more posterior visual cortical regions. In contrast to the high familiarity landmarks, for the low familiarity landmarks, L.H. and D.A. performed at borderline levels, and the three other amnesic cases were impaired. All demonstrated significantly worse performance for the less familiar landmarks, resulting in above average or even superior familiarity effects, as compared to controls. Note that these superior familiarity effects were driven by the larger impairments to the low familiarity landmark condition, and not by an advantage for high familiarity landmarks. As such they do not represent superior performance overall. Combined with the other findings from this study and those from previous studies (Maguire et al., 2006; Rosenbaum et al., 2000, 2005), these results suggest that landmark recognition can be supported by both highly detailed scene memory and more schematic or semantic spatial memory. Thus, participants may have enough experience with very familiar scenes to form schematic representations of these landmarks that rely less on precise representations and therefore can be represented by extra-MTL structures, explaining the intact performance of the amnesic group in the high familiarity condition. For less familiar landmarks, however, schematic representations presumably are not well formed, and highly detailed forms of spatial memory reliant on MTL and posterior temporal structures must be used for accurate memory. Thus, both amnesic and topographical disorientation cases in the present study appear to be disproportionately impaired on recognizing low familiarity landmarks, presumably because they tax highly detailed scene memory more than the high familiarity landmarks.

These differing patterns of results for landmarks that vary in familiarity may explain why previous studies of landmark recognition in amnesic cases have yielded inconsistent findings, owing to the differing nature of the landmarks used as stimuli. For example, T.T. could likely draw on semantic memory to support his intact recognition of famous London landmarks, while K.C. would not have these associations for houses in his neighborhood that were not famous or

particularly visually salient or distinctive, and he would therefore need to rely on specific details to recognize them, which he was unable to do (Maguire et al., 2006; Rosenbaum et al., 2000). Furthermore, these results support the interpretation that L.H.'s navigation deficits may result in part from problems recognizing or identifying his environment. Although his clinical characterization described L.H. as demonstrating difficulty recognizing landmarks, this more sensitive comparison seems to reveal that he can in fact recognize very familiar landmarks but is impaired on less familiar landmarks. Even for familiar landmarks that he can recognize, he may not be able to match them to stored navigational knowledge in order to situate himself and navigate.

A similar dissociation between intact performance on high familiarity cues and impairments on low familiarity cues in the landmark recognition task was not seen in the scene memory task. This difference may be due to the fact that the scene memory task relied on cued recall, in which the scene has to be reconstructed from memory, a task more taxing than recognition, in which the stimulus is present on screen. Following from both the predictions of SC and theories that the hippocampus is needed for binding of features in memory (Eichenbaum & Cohen, 1988, 2014; Eichenbaum et al., 1994; Hassabis & Maguire, 2007, 2009; Maguire, Intraub, & Mullally, 2016; Maguire & Mullally, 2013; Olsen, Moses, Riggs, & Ryan, 2012; Rosenbaum, Gilboa, Levine, Winocur, & Moscovitch, 2009; Ryan, Althoff, Whitlow, & Cohen, 2000; Ryan, Lin, Ketcham, & Nadel, 2010; Zeidman, Mullally, & Maguire, 2015), the scene memory task would be affected since binding or constructive processes are necessary for mentally reconstructing scenes. In contrast, the landmark recognition task would require less binding or mental construction, especially if the landmarks were very familiar and certain features could trigger recognition without needing to be integrated with the other features of the scene.

An alternative, yet related, interpretation focuses on representational content, the hypothesis being that the hippocampus is needed for representing highly detailed information (Robin & Moscovitch, 2017a; Winocur et al., 2010; Winocur & Moscovitch, 2011; Yonelinas, 2013), which is what distinguishes familiar from less familiar scenes and landmarks. As a result, damage to the hippocampus eliminated the familiarity advantage for scenes, and exacerbated the familiarity (dis)advantage for less familiar landmarks whose recognition depends on the hippocampus compared to familiar landmarks whose recognition can be mediated by extra-hippocampal structures.

Familiarity effects are ubiquitous in cognitive psychology, yet we know little about their neural correlates. Recent studies on pictures and names of familiar people (Liu, Grady, & Moscovitch, 2017; Renoult, Davidson, Palombo, Moscovitch, & Levine, 2012; Renoult et al., 2016; Westmacott & Moscovitch, 2003) suggest that in some instances, the familiarity effect depends on activating personally relevant, typically episodic, information, that is associated with the person and is mediated by the hippocampus along with extra-hippocampal knowledge structures, such as the ventromedial prefrontal cortex and anterior temporal lobes. When personal relevance is not a factor, the familiarity effect may be mediated only by “knowledge” structures, such as the anterior

temporal cortex, and ventromedial prefrontal cortex, perhaps along with regions in neocortex specialized in processing the particular stimulus. Our findings are broadly consistent with this framework.

4.6. Limitations

A limitation of the present study is the inability to distinguish between the subregions of the MTL and their individual contributions to the patterns of intact and impaired memories observed in these data. Due to the varied etiologies of the neuropsychological cases, and the fact that damage to the hippocampus often accompanies damage to the perirhinal, entorhinal and parahippocampal cortices, it is difficult to conclude if the memory impairments observed are due to hippocampal damage specifically, or the result of damage to broader MTL areas and disrupted connectivity to other cortical regions. In particular, the parahippocampal cortex is known to be specialized for scene perception and memory, while entorhinal and perirhinal regions have been associated more with object and face processing (Robin, Rai, Valli, & Olsen, 2019). In addition, since many of the cases had additional damage outside the MTL to posterior regions involved in visual and spatial processes, further work is needed to elucidate the contributions of individual structures to these forms of memory. Nonetheless, while not being able to make strong conclusions about specific MTL regions, these results still highlight dissociations in forms of spatial memory and suggest differing neural bases for detailed and schematic memories.

Another limitation is that due to our use of real-world stimuli and open-ended memory cueing in the autobiographical and scene memory conditions, we were not able to precisely control the remoteness of memories or verify their accuracy. Behavioral ratings indicated that most autobiographical memories were remote (occurring at least a year prior to the experiment), and most scene memories were fairly remote (at least a few months old, see [Supplementary Material, Figures S1 and S3](#)). Ratings of recency of memories did not vary systematically between controls and individuals with MTL amnesia or topographical disorientation. Nonetheless, it is possible that memories were from both pre- and post-lesion time periods in the neuropsychological cases. We were not able to systematically examine how the remoteness of memories affected their quality, but this is an important question for future research. Finally, as in most autobiographical memory studies, we were unable to verify the veracity of memories in the present study. Because of this, we focused on the richness of memories rather than their accuracy as our measure of interest.

4.7. Summary

Highly detailed spatial memory, in the form of scene memory, appears to be impaired as much as autobiographical episodic memory in cases of amnesia relating to medial temporal lobe damage. In contrast, more schematic forms of spatial memory, such as map-based location information, remain intact in these cases. These results demonstrate that highly detailed forms of both spatial and episodic memory dissociate from more schematic forms, with detailed spatial and episodic

forms likely reliant on medial temporal lobe structures including the hippocampus. These findings are consistent with ideas from both the Trace Transformation Theory and Scene Construction theory. Second, deficits to scene-based spatial memory in the absence of amnesia coincided with declines in the detail richness of episodic memory. While this finding is only based on a single case and is not causal, it suggests that the ability to remember a scene is a contributing factor to episodic memory, as predicted by Scene Construction accounts. This finding also shows that impairments to scene memory in the absence of hippocampal damage do not lead to total amnesia, indicating that other processes contribute to episodic memory and can partially sustain it in the case of degraded scene representations.

Last, while more familiar contextual cues appear to facilitate detailed and schematic spatial memory and episodic memory in healthy controls, these benefits do not appear to extend to situations when detailed spatial or episodic memory is impaired. These results suggest that the benefits of familiarity in scene and episodic memory are likely mediated by structures, such as the hippocampus, that support such memories. Increased cue familiarity, however, can facilitate forms of memory that are retained in cases of MTL amnesia, such as more schematic spatial memory, since these are not mediated by the hippocampus and related structures. In such cases, increased cue familiarity may even lead to a shift in what type of memory is used for a given task, as may be the case in landmark recognition. Together these findings provide new insight into the interplay between schematic and detailed forms of spatial and episodic memory, and the structures that mediate them. Our results suggest that common neural regions and networks, including the medial temporal lobes and the hippocampus, support detailed episodic and spatial memories.

CRediT authorship contribution statement

Jessica Robin: Conceptualization, Methodology, Formal analysis, Writing - original draft. **Josée Rivest:** Conceptualization, Writing - review & editing. **R. Shayna Rosenbaum:** Conceptualization, Writing - review & editing. **Morris Moscovitch:** Conceptualization, Supervision, Funding acquisition, Writing - review & editing.

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Supplementary data

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