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Medial Temporal Lobe Amnesia Impairs Performance on a Free Association Task

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ABSTRACT: A growing body of evidence suggests that the hippocampus contributes to performance (or is implicated) in non-memory domains from perception to problem solving. In a previous study we found that hippocampal contribution to exemplar generation in a fluency task was determined jointly by the open-endedness of the task and its ability to elicit episodic memories (Sheldon and Moscovitch (2012) Hippocampus 22:1451–1466). In the current study, we extend these observations by exploring the role of the hippocampus in generative, goal-directed open-ended thought in patients with medial temporal lobe (MTL) amnesia on a free association task (think of words as they come to mind). Patients and control participants were asked to associate freely for one minute to cue words that varied in the open-endedness of the responses they elicited (greater for low- than high-frequency words), and in the ease with which episodic memories were evoked (greater for high imageable than low imageable words). As predicted, MTL amnesia patients generated fewer words than control participants when cues were highly imageable and low in frequency, but performed equivalently to them in the other conditions. These results support our prediction that the hippocampus contributes to free association, and possibly more generally to other generative tasks that are open-ended, creative, or that elicit the use of contextual and likely episodic memories in order to derive relevant information. © 2013 Wiley Periodicals, Inc.

KEY WORDS: episodic memory; creativity; open-endedness; imagery

INTRODUCTION

It is acknowledged that the hippocampus plays a key role in recollecting past events (Scoville and Milner, 1957; Eichenbaum, 2004; Moscovitch et al., 2006; Squire et al., 2007). The recombinant nature of hippocampal processes that support recollection likely also support performance on some nonmnemonic tasks such as future thinking, problem solving, and semantic retrieval (Westmacott and Moscovitch, 2003; Westmacott et al., 2004; Addis et al., 2007; Hassabis et al., 2007; Whatmough and Chertkow, 2007; Addis et al., 2008; Ryan et al., 2008; Gerlach et al., 2011; Sheldon and Moscovitch, 2012). This suggests that the hippocampus is involved in integrating or binding information, either retrieved from the past or acquired in the present, to meet current goals and address future needs (Warren et al., 2012).What remains to be known are the precise conditions or task characteristics that recruit the hippocampus?

In this article, we focus on the role of the hippocampus and medial temporal lobe (MTL) in generative tasks. Following the results of a recent neuroimaging study on verbal fluency from our laboratory (Sheldon and Moscovitch, 2012), we explored the prediction that the hippocampus is chiefly involved in generative tasks that jointly require open-ended associative thought, namely information retrieval under ill-defined conditions, and that can elicit episodic or contextual memories easily (Pretz et al., 2003; Schraw et al., 2006; Sheldon et al., 2011). When neither condition is satisfied, when problems are close-ended, and episodic memory is difficult to evoke, the hippocampus will not be implicated.

In our recent article (Sheldon and Moscovitch, 2012), we noted that on nuanced tests of category fluency that could benefit from episodic memory processes (e.g., think of kitchen items), the hippocampus was especially active after the most typical exemplars were generated early in the task and as responses became more idiosyncratic, indicating that the task is more open-ended or ill-defined. Despite similar open-endedness, no hippocampal activation was noted for phonemic fluency, and nor for a more semantic version of category fluency, because these tasks did not evoke or benefit from episodic memories. From these findings, taking a process-based view, we reasoned that the hippocampus is particularly involved in tasks that are open-ended, and thus may elicit episodic memory processes to derive the needed information (Henke, 2010).

To determine the generality of our conclusions, in the current study we employed a free word association task to see whether patients with amnesia resulting from MTL damage would be impaired on this task in a manner that is complementary to the results from our neuroimaging study. Free association conforms to our conception of open-ended thought because it requires generating novel and divergent associative concepts (Gabora, 2010). Also, the role of the hippocampus in free association has been substantiated by neuroimaging findings that report hippocampal activity during single-word free association (Whitney et al., 2009) and during creative writing associative tasks (Shah et al., 2011; Ellamil et al., 2012).

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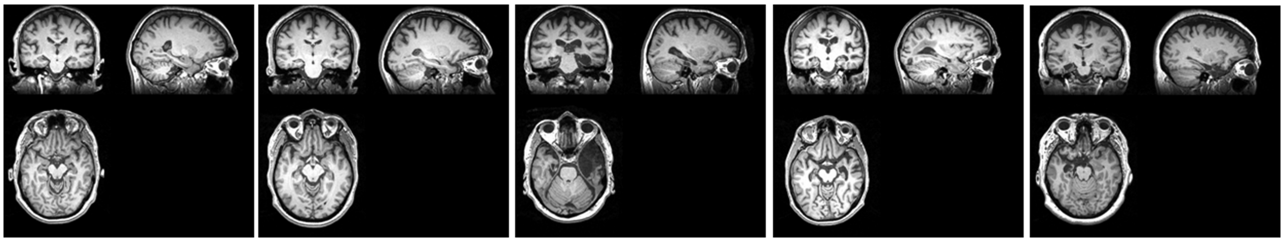

FIGURE 1. Representative structural MRI scans of the five MTL amnesic patients.

To test whether the hippocampus is involved *more* during open-ended tasks that elicit or can benefit from episodic memories as compared to nonepisodic, closed-ended tasks, we varied systematically the type of word cue that was used to generate free associations. To vary *episodic accessibility*, we varied the imageability (i.e., how imageable a word is) of the cue word because there is evidence that visual imagery plays a prominent role in recollection (Greenberg and Rubin, 2003; Greenberg et al., 2005; D'Argembeau and Van der Linden, 2006). Highly imageable (e.g., concrete) words would engage episodic memories more than would low imageable, abstract words. To vary the *open-endedness* of the task, we manipulated the frequency of the cue word, our rationale being that high frequency words have more semantic associates, many of them quite common, in comparison to low frequency words, whose associates tend to be rarer and more idiosyncratic (Hall and Ungelow, 1957). Finding associates to low frequency words, we reasoned, requires more of an open-ended search with ill-defined task characteristics.

Patients with confirmed MTL damage that includes the hippocampus, and healthy control participants, freely associated for 1 min to cue words that varied in frequency and imageability. If the hippocampus is more readily involved in tasks that require an open-ended search and engagement of episodic memory, then patients with MTL amnesia should be impaired to the greatest degree when associating to cue words that are both low in frequency and high in imagery (also referred to as imageability). In this condition, control participants could benefit from the use of episodic memory to generate items to low frequency and highly imageable words given the diminished utility of semantic network, however, patients with MTL amnesia must continue to rely on semantic memory, even though this strategy is no longer useful. If this is the case, the words generated by the amnesic patients should be more representative of semantic memory when compared to the output of the controls participants in this condition, but not in the others.

MATERIALS AND METHODS

Participants

Five patients with confirmed MTL lesions that include the hippocampus and who presented with significant and selective memory impairment were included in this study. Of these patients, four were male, the mean age was 53.8 years (SE = 4.3 years) and the mean years of education was 13.6 (SE = 1.0 years). In two patients damage to the MTL was caused by epileptic seizures, and in one of them the right MTL was resected surgically. Two patients sustained damage due to viral encephalitis and the final patient received a tentative diagnosis of Whipple's encephalopathy. To confirm that damage was localized to the MTL and that the region of overlap across all patients was the hippocampus, T1-weighted structural MRIs were obtained (see Fig. 1 for representative scans and see Table 1 for hippocampal volume measures using automated segmentation methods (free surfer) and *z*-scores calculated by using normative data from a recently published meta-analysis that reported bilateral hippocampal volumes for 5,755 control participants (Stein et al., 2012)). From these volumes, all patients sustained some level of damage to both the left and right hippocampi; this damage was most pronounced in the right for one case and the left in the other four cases. Neuropsychological testing of the patient group confirmed long term memory deficits in all patients, with no other significant cognitive deficits (see Table 2 for both demographics and selected neuropsychological test results). All patients had IQ scores in the average range or higher.

Ten healthy control participants free from neurological or psychiatric disorders and with English as their primary language (6 male) were matched with patients for age (mean age of 52.9

TABLE 1.

Hippocampal Volumes (Left and Right and Average Bilateral Volumes) for the Five Patients with MTL Amnesia

Patient	Right hippocampus	Left hippocampus	Average bilateral hippocampus	Z-score
1	3776	3357	3556.5	−0.80
2	3297	2911	3104	−1.84
3	612	1122	867	−6.91
4	2342	2007	2174.5	−3.95
5	4106	1197	2651.5	−2.87

Measurements were computed from 3D anatomical T1-wieghted magnetic resonance images using Free surfer automated segmentation programs. Volumes are in mm^3. *Z*-scores are calculated by using the mean and standard deviations of bilateral hippocampal volumes (Stein et al., 2012) from a study that collected controlled automatically segmented hippocampal volumes collected 5,755 healthy control participants from various studies [average bilateral hippocampal volume = 3917.4 (SD = 441)].

TABLE 2.

Demographic and Selected Neuropsychological Test Score Results for Patients with MTL Amnesia

Age	Yrs Edu	Est IQ	D.S. Fwd[a] (/14)	D.S. Bwd[a] (/14)	D.S. Tot[a] (/28)	LM 1[b] (/75)	LM 2[b] (/50)	FAS[c]	Animals[c]
56	12	99‡	11	6	17	17	0*	29	16
37	12	average‡	11	8	19	28	8*	29	19
60	16	117†	9	9	18	27	0*	61	23
58	16	high average‡	9	6	15	38	18	47	25
58	12	98‡	7	6	13	20	12	26	18

Asterisk is placed next to the scores that are outside the normal range: scores greater or less than 2 standard deviations from the mean.Yrs Edu, years of education; D. S. Fwd, Digit span forward; D.S. Bwd, Digit span backward; D.S. Tot, Digit Span total; LM 1, Logical memory immediate recall; LM 2, Logical memory delayed recall; FAS, Phonemic fluency; Animals, Semantic fluency.
‡= IQ estimated from Wechsler Abbreviated Scale of Intelligence.
†= IQ estimated from Wechsler Adult Intelligence Scale – Revised.
*= score >2 *SD* below normative mean.
[a]Norms from Wechsler, 1997a.
[b]Norms from Wechsler, 1997b.
[c]Norms from Tombaugh et al., 1999.

years; SE = 3.2 years), education (mean of 14.5 years of education; SE = 0.6 years) and estimated IQ (see Table 3 for demographics and selective neuropsychological test results). The control participants were recruited through on-line advertisements. All participants gave their informed consent in accordance with the research ethics board of the University of Toronto and/or Baycrest Hospital and all received an honorarium for their participation.

Neuropsychological Tests

Scores from standard neuropsychological tests were extracted from the patients' charts or readministered during the experimental sessions (Tables 2 and 3). The control participants were given the National Adult Reading Test to estimate IQ (given time constraints) to match to the estimates extracted from the patients' charts. Control participants were also given measures of memory (California Verbal Learning Test: CVLT) to confirm average memory performance, fluency (FAS and animals) and measures of working memory (digit span forward and backward).

Free Association Test

Sixteen words were selected from a target word list developed for a synonym judgment task by Jefferies et al. (2009, see Appendix 1). Selected words varied along two dimensions, frequency, and imageability. Words were either high or low in frequency (128 (SD = 102) and 4.6 (SD = 4.5) counts per million, respectively, in the Celex database; Baayen et al., 1993), and rated as high or low on an imageability scale (mean imageability of cue words = 276 (17.3) and 622 (14.0), respectively, from the MRC Psycholinguistic Database; Coltheart, 1981). Using each combination of these variables, our wordlist was composed of four words from these four combinations: High imageability + high frequency; High imageability + low frequency; Low imageability + high frequency; Low imageability + low frequency.

Procedure

Participants were instructed that for each word they were to associate freely to that word aloud, meaning that they were to think of associated words in any way and say them as they come to mind. To ensure that they understood what free association meant, examples of free associations were given before the task began. Participants were told that it did not matter how they generated words and that this was not important to the task. They were given 60 s to think of words for each cue. The cues were presented in random order across participants. After each associative task, the majority of the participants were asked to state the word to which they were associating (this

TABLE 3.

Average Demographic and Selected Neuropsychological Test Score Results for MTL Amnesia Patient Participants and Healthy Control Participants (Standard Error are in Parentheses)

	Patients	Controls
Age	53.8 (4.3)	52.9 (3.2)
Yrs Edu	13.6(1.0)	14.5 (0.7)
Est IQ	Average to high average	112 (2.2)
D.S. Fwd (/14)	9.4(0.8)	11 (0.5)
D.S. Bwd (/14)	7.0 (0.6)	8.0 (0.8)
D.S. Total (/28)	16.4 (1.1)	19 (1.0)
CVLT learning (/80)	38.6 (6.2)[a]	50.1(4.1)
LM 1 (/75)	26.0 (3.6)	–
LM 2 (/50)	7/6 (3/5)	–
FAS	38.4 (6.8)	46 (5.5)
Animals	20.2(1.7)	22 (1.7)

Yrs Edu, years of education; Est IQ, estimated IQ from NART; D.S. Fwd, Digit span forward; D.S. Bwd, Digit span backward; CVLT, California Verbal Learning Test; LM 1, logical memory immediate recall; LM 2, logical memory delayed recall; FAS, phonemic fluency; Animals, semantic fluency.[a]Only three patient scores included.

check was added, after two participants had completed the task). If they could not remember the cue word, the scores of that condition were not counted. This was the case only for two of the abstract words for one patient with MTL amnesia. Responses were recorded electronically as well as by hand by the experimenter.

The number of words generated in each category was tallied and the mean number was calculated for each category. Words that were short phrases and proper names were included as one item (e.g., *get ahead* or *Starbuck's*). The items generated were also examined for their semantic similarity to the target cue word using high-dimensional vector representations of the words that were created via a large corpus of text using the latent semantic analysis (LSA; Landauer et al., 1988). LSA is an automated method for determining the semantic similarity between documents, or in this case, terms. It is grounded on the assumption that the meaning of a word, or the underlying semantics, is based on the contextual use of the word as represented in a corpus of text. Words are deemed similar if they appear in similar contexts, that is, if they are surrounded by similar words in a high dimensional space. LSA uses singular value decomposition and multidimensional scaling to represent terms as vectors in a multidimensional semantic space. The pair-wise comparison tool gives a similarity value for a given word-pair, which is mathematically the cosine of the angle between the two word vectors (see http://lsa.colorado.edu/ to learn more about LSA or to extract LSA scores). Practically, a higher LSA value indicates greater similarity between the two words of the pair.

RESULTS

Neuropsychological Tests

Except for memory, there were no apparent differences in scores on the neuropsychological tests between the groups. When we examined the scores for each individual patient participant, we noted that none of their scores on tests besides measures of memory fell outside of the normal range.

Free Association Test

More associations were produced to high than low frequency words and to highly imageable than words with low imageability ratings. The effect of frequency was greater for high imageability words than low imageability words and for controls than for patients: specifically, patients were poorer than controls at producing associations to low frequency words, particularly if they were highly imageable (Table 4). These impressions were confirmed by a three-way mixed ANOVA with group (patient vs. control) as the between-subjects factor and imageability and frequency as within-subject factors. This analysis yielded a main effect of imageability ($F(1,13) = 7.025$, $P = 0.02$) and frequency ($F(1,13) = 109.41$, $P < 0.001$), and significant interactions between imageability and frequency ($F(1,13) = 11.924$, $P = 0.004$), and between frequency and group ($F(1,13) = 6.646$, $P = 0.023$), but not between imageability and group ($F(1,13) = 0.657$, $P = 0.43$). The three-way interaction of imageability, frequency and group was also significant, ($F(1,13) = 7.060$, $P = 0.02$).

TABLE 4.

The Mean Number of Words Produced on the Free Association Task in Each Four Conditions for MTL Amnesia Patient Participants and Healthy Control Participants (Standard Errors are in Parentheses)

Imageability	*Low*	*Low*	*High*	*High*
Frequency	*High*	*Low*	*High*	*Low*
Patients	7.4 (0.8)	7.4 (0.8)	15.0 (1.1)	11.1 (1.3)
Healthy Controls	9.5 (0.6)	9.9 (0.6)	16.8 (0.7)	16.8 (0.8)

Closer inspection of the interactions via planned comparisons revealed a significant difference between patients and controls in the high imageability + low frequency condition ($F(1,14) = 6.518$, $P = .02$; $\eta^2 = 0.34$). The group difference in the low imageability + low frequency condition approached significance ($F(1,14) = 3.893$, $P = 0.07$; $\eta^2 = 0.17$). There was no group difference for the low imageability + high frequency ($F(1,14) = 2.652$, $P = 0.13$; $\eta^2 = 0.23$) or for the high imageability + high frequency ($F(1,14) = 1.245$, $P = .29$; $\eta^2 = 0.00$) conditions. These findings suggest that the advantage controls have over patients with MTL amnesia is determined by word frequency. However, given that there were no significant effects of imageability alone (the group × imageability interaction was not significant), we speculate that the effect of imageability is only present when frequency is taken into account frequency influences the effect of imageability on free association output by controls and patients.

To examine this idea more closely and to remove individual biases in free association production/individual differences, we calculated a ratio that took into account the total number of words produced by each participant using the following formula [(words produced in high frequency condition – words produced in the low frequency condition)/(words produced in high frequency condition + words produced in the low frequency condition)]. This formula was applied to each participant for both the high and low imageability word conditions. We compared these ratios between control and patient participants. As predicted by our hypothesis and visualized in Figure 2, there was a significant interaction between group membership and imageability ($F(1,13) = 10.196$, $P = 0.007$). Planned comparisons revealed a significant difference between patients and controls for the high imageable words ($F(1,14) = 22.898$, $P < 0.001$, $\eta^2 = 0.64$), but not for the low imageable words ($F(1,14) = 0.212$, $P = 0.653$, $\eta^2 = 0.02$). These results should be interpreted with caution as we cannot say how frequency and imageability are interacting *per se* to aid in word production.

Next, the similarity of the generated words to the target words for each category type was compared across group using LSA word-pair similarity values. While a three-way ANOVA

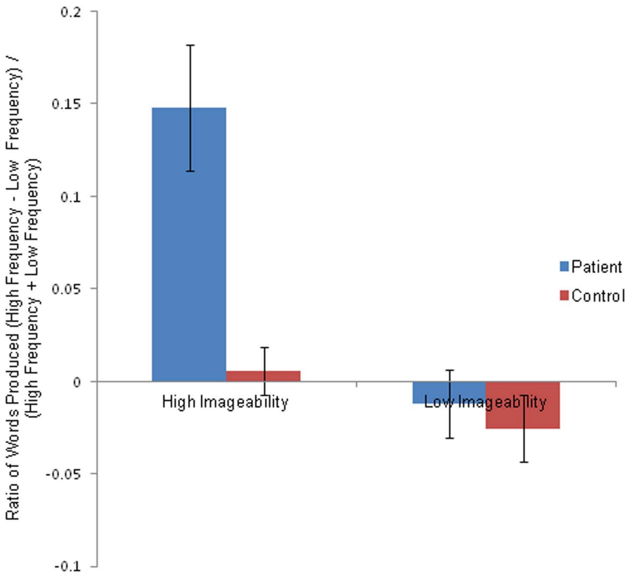

FIGURE 2. The mean ratio of words produced for patients with MTL amnesia and healthy control participants for the high imageability and low imageability word cue conditions. The ratio [(words generated in the high frequency - words generated in the low frequency categories) / (words generated in the high frequency + words generated in the low frequency categories)] controlled for word production differences across participants. Standard error bars are shown. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

did not reveal a significant interaction between imageability, frequency, and group (F(1,3084) = 1.311, P = 0.25), it did reveal main effects of both frequency (F(1,3084)=36.875, P = 0.000) and imageability (F(1,3084) = 84.561, P = 0.000). Given our *a priori* hypothesis that there would only be a group difference in the high imageability + low frequency condition, we compared groups within each condition using pair-wise comparisons. There were no differences between groups in the degree of semantic similarity between the target word and the generated words for the low imageable + high frequency (P = 0.58; η^2 = 0.00), the low imageable + low frequency (P = .10; η^2 = 0.00), and the high imageable + high frequency (P = 0.86; η^2 = 0.00) conditions, but a significant difference in the similarity of the generated words to the target word for the high imageable + low frequency condition (P < 0.001; η^2 = 0.01). Patients with MTL amnesia generated words that were, on average, more semantically similar to the target word as compared to control participants in this condition only (Fig. 3).

We confirmed these findings by looking within each group at the amount of overlap of semantic similarity between high and low frequency within each imageability condition. For low imageable words, the semantic similarity difference generated to high and low frequency words was significant for control participants (F(1,875) = 42.121, P = 0.000, η^2 = 0.05) and patient participants (F(1,270) = 26.777, P = 0.000, η^2 = 0.09); for high imageable words, however, the semantic similarity difference generated to high and low frequency words was significant for control participants (F(1,1411) = 21.276, P = 0.000, η^2 = 0.02), but not for patient participants (F(1,528) = 0.115, P = 0.734, η^2 = 0.00). While there were more common or semantically-related responses for control participants in the high imageable/high frequency condition than in the high imageable/low frequency condition, we did not see this difference for patient participants.

Finally, it is of note that the LSA analysis did not find values for all the words. In total, 63 terms returned without similarity values with the target word; the proportion of these idiosyncratic responses, however, were split equally between patients and control participants (0.039% and 0.035%, respectively). Given that we speculated that high imageable words have higher episodic accessibility than low imageable words, we further tested whether high imageable words would have a greater proportion of idiosyncratic responses than the low imageable words. Indeed, this was the case (Chi-square (1) =29.35, P < 0.001).

DISCUSSION

In a free association task to cue words varying in frequency and imageability, we found that performance in patients with

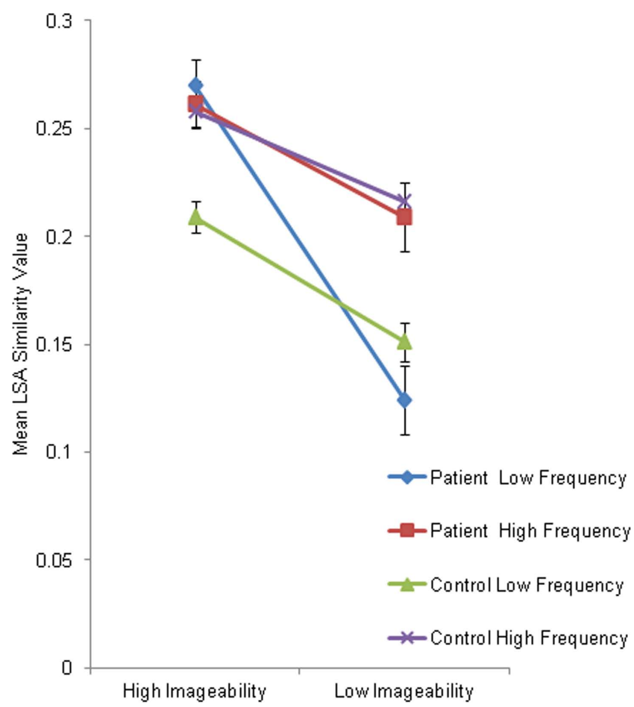

FIGURE 3. The mean LSA ratings of similarity for the words generated for patients with MTL amnesia and control participants in each of the four free association conditions. The x-axis plots the LSA similarity values for the high and low imageability conditions while separate lines are used to illustrate how these values are influenced by frequency (high versus low) and group membership (patient versus control; standard error bars are shown). A higher value indicates greater semantic similarity. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

MTL amnesia and in control participants was influenced positively by both factors. Importantly, we found that although patients performed worse than controls in all conditions, the differences between them were only significant in the high imageability + low frequency condition. If, as postulated, we take frequency as an index of *open-endedness* (low frequency as an index of open-endedness and high frequency as an index of close-endedness) and increased imagery as an index of *episodic accessibility* (the more imageable, the more accessible), our results confirm the hypothesis that MTL amnesia selectively impairs performance on generative tasks, such as free association, only when they are open-ended and can benefit from the processes of episodic memory.

In principle, it is possible that episodic memory can be used to generate associates in all conditions: however, we speculated that it is especially beneficial in the low frequency + high imageable words condition for the following reasons. In the high frequency cue word condition, where semantic neighborhoods are dense, participants can take advantage of semantic memory networks to generate associates. This strategy is less effective in generating items in the low frequency word condition where semantic neighborhoods of the words are sparse, making the search for associates more open-ended. In such cases, participants may adopt alternative strategies for generating responses, such as deriving words associated with episodic memories evoked by the cue. This episodic memory strategy, we predicted, would be most effective when the cue words are imageable (i.e., high in imagery) and can evoke recollections or other episodic-like processes more easily than words that are not as imageable (Paivio et al., 1968; Richardson, 1992; Moulton and Kosslyn, 2009). Control participants could take advantage of the evoked episodic memory by quickly accessing a memory or simulated scene and produce a word associated with it. This episodic process is either not as available to MTL amnesic patients or they are less likely to engage in it because of their deficit in conjuring rich episodic memories (Moscovitch et al., 2006; Winocur and Moscovitch, 2011) scenes (Hassabis et al., 2007), or simulated episodes (Addis and Schacter, 2011). As predicted and noted, MTL amnesic patients performed significantly worse than controls in the high imageable + low frequency condition.

Consistent with our speculations regarding the nature of the underlying associations in each of the conditions, we found that in controls the degree of semantic similarity to the cue word was higher for high frequency than low frequency words in the high imageable condition, suggesting that the latter were more idiosyncratic, and likely relying on non-semantic strategies. By contrast, there was no difference in MTL patients between these conditions who obtained values in both conditions equivalent to those of controls in the high imageable + high frequency condition, suggesting that the MTL amnesia participants were drawing their responses from a common associative semantic network that resembled that of control participants (although the small effect sizes mean we must interpret these results with caution).

We attribute the deficit of the MTL patients to their damaged hippocampus because it was the only region of the brain that was damaged consistently across the tested patients. Fittingly, the patients' neuropsychological performance conformed to the expected pattern for hippocampal amnesia: significant impairment on a test of free recall, (logical memory subtest from the WMS; Weschler, 1997a, b), and normal performance on tests of function other than memory (e.g., phonemic fluency, and digit span). Though not expected, performance on category fluency for the patients with MTL amnesia was also normal. It is possible, as we have argued here and elsewhere (Sheldon and Moscovitch, 2011), that deficits in fluency are more likely to occur under conditions that promote the use of episodic memory and are less likely to be evident when given categories that are well-represented in our semantic networks, as animals likely are. Second, it could be that the deficits we report are subtler in that they are prominent when we compare our patients to matched control participants, but not when we use standardized norms.

Given the limited sample size of our patient group, we comment only briefly on hippocampal laterality effects. We know from previous reports that both left and right hippocampal regions contribute to tasks similar to this free association task, such as on certain tests of semantic fluency (Sheldon and Moscovitch, 2012). Likewise, performance on tests of autobiographical memory and episodic simulation are affected both by right and by left hippocampal damage (Addis et al., 2007; St-Laurent et al., 2009). Thus, we speculate that the left and right hippocampi are both contributing to the free association task. It is likely that other subregions of the MTL also contribute to free association. Given that the entrorhinal cortex and the pararhippocampal cortex interact with the hippocampus to varying degrees during encoding of specific stimuli (i.e., objects, places), retrieval of contexts may implicate these structures as well as the hippocampus in the service of free association (Diana et al., 2008; Litman et al., 2009).

While our study supports the hypothesis that under conditions of open-endedness and episodic accessibility, the hippocampus supports performance on generative tasks, such as free association, word fluency (Sheldon and Moscovitch, 2012), and even problem solving (Sheldon et al, 2011), a number of questions remain that require investigation. To what extent is open-endedness linked to generation, and how does that influence hippocampal involvement? For example, would the hippocampus be similarly engaged if, instead of having the individual generate responses, he or she were required to make decisions as to whether, or to what extent, particular items were associated to the cue word or were good members of a semantic category? Would hippocampal activation under such conditions be absent entirely, or would it be modulated by the prototypicallity of the exemplars for a particular category, or by their imageability and frequency, and semantic similarity to the cue?

Another open question is precisely how does the hippocampus contribute to performance on these open-ended, generative tasks? The general consensus is that the hippocampus supports the recombination and flexible utility of memory components for events details to reconstruct past memories as well as novel events, and can do so quite rapidly (Eichenbaum, 2004; Addis et al., 2007; Hassabis et al., 2007; Moscovitch, 2008; Hoscheidt et al., 2010; Martin et al., 2011; Sheldon et al., 2011). We speculate that these recollections and simulations can be used to derive responses when freely associating (e.g., recollecting details from a past Christmas for the cue word *Winter,* leading to the association "*presents*" or imagining a frightening ride for the cue word *Ambulance,* leading to the association, "*crying*"), thus making this strategy particularly useful for generating responses to low frequency and highly imageable, concrete words. This interpretation suggests that episodic memory processes, mediated by the hippocampus, can be used to stimulate or support creative or divergent thinking which would account for evidence of hippocampal involvement on social problem solving and other creative tasks (Pollert et al., 1969; Luo and Niki, 2003; Duff et al., 2009; Whitney et al., 2009; Shah et al., 2011; Ellamil et al., 2012). More generally, this interpretation posits a function for recollection. As many others have noted, we do not merely recollect details for the sake of recollection, we recollect details to help guide decision-making, problem-solving and general cognition when rules are not available: when situations are open-ended.

More broadly, our findings add to a growing body of evidence that shows that the hippocampus is engaged in a variety of tasks in ostensibly nonmemory domains, from perception (Barense et al., 2010) to working memory (Hannula and Ranganath, 2009; Rose et al., 2012; Warren et al., 2012), from language (Duff et al., 2009, 2011; Park et al., 2011), to problem solving (Gerlach et al., 2011; Sheldon et al., 2011), and from thinking about the past to thinking about the future (Addis and Schacter, 2011; Race et al., 2011) (but see Squire and Wixted, 2011 for alternative views). It remains to be determined whether performance on such tasks are dependent on hippocampally-mediated episodic memories, whether they draw on hippocampal computations and representations that support a variety of functions, of which the formation and retention of episodic memories are only a subset (Eichenbaum, 2004; Eichenbaum and Fortin, 2005; Konkel and Cohen, 2009), or both, as we have suggested with respect to our episodic accessibility hypothesis and reconstructive processes that make flexible use of episodic memories (see also Addis and Schacter, 2011). Regardless of which of these views prevails, by identifying the conditions under which the hippocampus is engaged on generative tasks, our findings extend the domain over which the hippocampus operates and provide important evidence for theory development.

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APPENDIX

APPENDIX A1.

A List of the Cue Words Used in the Four Conditions for the Free Association Task

Abstract high	Abstract low	Concrete high	Concrete low
Advantage	Attribute	Coffee	Ambulance
Consider	Fallacy	Telephone	Kite
Function	Protocol	Window	Lobster
Ordinary	Suffix	Winter	Violin

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