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Working memory and amnesia: The role of stimulus novelty

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ABSTRACT

Despite the traditional view that damage to the hippocampus and/or surrounding areas of the medial temporal lobe (MTL) does not impair short-term or working memory (WM), recent research has shown MTL amnesics to be impaired on WM tasks that require maintaining a small amount of information over brief retention intervals (e.g., maintenance of a single face for one second). However, the types of tasks that have demonstrated WM impairments in amnesia tend to have involved novel stimuli. We hypothesized that WM may be impaired in amnesia for tasks that require maintaining novel information, but may be preserved for more familiar material, particularly if the material can be easily rehearsed. To test this hypothesis, patient HC, a 22-year-old developmental amnesic with relatively preserved semantic memory and 20 age and education matched controls performed a delayed match-to-sample task that required maintaining a single famous or non-famous face for 1–8 s, digit span and reading span tasks, and a modified Brown–Peterson task that required maintaining a single high- or low-frequency word or a non-word for 4–8 s. HC's performance was impaired for non-famous faces but preserved for famous faces, impaired for the reading span task but preserved for digit span, and it was impaired for non-words and unfamiliar low-frequency words but preserved for familiar words. These results support the hypothesis that an intact hippocampus is necessary for maintaining a single *novel* stimulus in WM. However, stimulus familiarity and rehearsal support WM via cortical regions independent of the MTL.

Patients with amnesia as a result of damage to their hippocampus and/or surrounding structures of the medial temporal lobe (MTL) have impaired long-term memory (LTM), but are traditionally thought to have *preserved* short-term memory (STM; e.g., Baddeley & Warrington, 1970), or what many would now call working memory (WM). This dissociation has provided one of the strongest pieces of support for the notion that there are distinct brain systems devoted to memory over the short-term and long-term. Despite the long-held belief that WM is preserved in amnesia, but LTM is impaired, a surprising number of studies have shown that, under certain circumstances, people with amnesia are impaired at maintaining small amounts of information over short delays (for reviews, see Jonides et al., 2008; Ranganath & Blumenfeld, 2005). Findings of WM task impairments in MTL amnesics have strong implications for how researchers should conceptualize the distinction between WM and LTM. If amnesics cannot reliably maintain a single item for just four seconds, then this suggests that the MTL is necessary to perform both WM and LTM tasks, which casts doubt upon the independence between WM and LTM "systems."

Several studies have shown that amnesics are impaired on various WM tasks that involve maintaining material such as a single face, abstract shapes/patterns, or a scene over delays of just a few seconds (Buffalo, Reber, & Squire, 1998; Ezzyat & Olson, 2008; Hannula, Tranel, & Cohen, 2006; Holdstock, Shaw, & Aggleton, 1995; Olson, Moore, Stark, & Chatterjee, 2006; Owen, Sahakian, Semple, Polkey, & Robbins, 1995; Warrington & Taylor, 1973). For example, Olson et al. (2006) conducted an experiment in which three amnesics with bilateral MTL damage and matched controls performed a task that required maintaining the image of a single face for four seconds before being presented a recognition probe on each trial. The amnesics demonstrated a striking deficit: corrected recognition was 86% for the controls and 31% for the amnesics. These studies suggest a processing-based approach, whereby MTL involvement in a task (regardless of whether it is categorized by researchers as an STM, WM, or LTM task) likely depends on various factors. One common aspect among many of the tasks that have demonstrated STM or WM impairments in amnesia is that they required short-term retention of novel types of visuospatial information. In contrast, the classic studies that

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showed dissociations between STM and LTM required short-term retention of familiar verbal information, such as words or digits (e.g., Baddeley & Warrington, 1970). Whereas verbal information can be maintained over short delays via articulatory rehearsal, fewer mechanisms exist for continuous maintenance of visuospatial information (Ezzyat & Olson, 2008). In addition, representing and maintaining *novel* stimuli may be critically dependent upon the MTL (Jonides et al., 2008), whereas holding items in WM that already have representations in long-term (semantic) memory may be accomplished via cortical regions outside of the MTL (Stern, Sherman, Kirchhoff, & Hasselmo, 2001).

Jonides et al. (2008) suggested that the MTL is particularly important for binding novel relations and that amnesics should be impaired on STM or WM tasks when they involve novel information. In addition, neuroimaging studies which compared activation in the MTL during WM maintenance of novel versus familiar materials indicate that the MTL might be especially critical for maintaining novel information in WM (Ranganath & D'Esposito, 2001; Stern et al., 2001). For example, Stern et al. (2001) had participants perform a two-back WM task with either novel or familiar scenes. They found that the hippocampus was activated only for the task with novel scenes; it was not activated in the task with familiar scenes. In the present study, we show that a developmental amnesic, patient HC, was impaired at maintaining a single face or a single word over delays of 1–8 s when the stimulus was novel (an unfamiliar face or a non-word), but was relatively preserved when the face or word was more familiar (a famous face, e.g., Arnold Schwarzenegger, or a common word, e.g., language).

It is well known that stimulus familiarity can support one's ability to maintain information in WM tasks. For example, the maximum number of letters that an average, healthy adult can immediately recall is reliably near 7 (±2) units (Miller, 1956). However, the number of letters (e.g., *m – p – o – u – p – s – o – a – h – t – p – i*) that can be immediately recalled grows remarkably if the letters are embedded in familiar stimuli (e.g., the word *hippopotamus*). Such an example demonstrates a contribution of long-term (semantic) memory to WM performance. That LTM can support WM is another piece of evidence that argues against a strict distinction between WM and LTM "systems" (cf. Thorn & Page, 2008). Demonstrations of stimulus familiarity supporting WM performance are abundant. For example, WM capacity is greater for words than non-words (Hulme, Maughan, & Brown, 1991), words in sentences than a series of unrelated words (Craik & Masani, 1967), items that can be grouped or chunked than items that are not chunked (Rose, Myerson, Sommers, & Hale, 2009), and for experts in their domain of expertise than for novices (Ericsson & Kintsch, 1995). Additionally, such demonstrations are not specific to verbal WM. For example, normal adults can recall a maximum of 3–4 objects on an 8 × 8 grid following brief exposure (Chase & Simon, 1973), but, if the subject is a chess grand master and the objects are chess pieces on a chess board, then recall of all 32 pieces is nearly perfect (de Groot, 1946/1978). The difference between experts and novices is a particularly telling example of the way stimulus familiarity can support either verbal or visuospatial WM performance. By relying on representations and associations already in semantic memory, the need to establish novel relations among the features of a stimulus is greatly reduced (Stern et al., 2001). Therefore, we expected that an amnesic such as HC would demonstrate relatively preserved WM performance for familiar stimuli, but, based on recent research (e.g., Ezzyat & Olson, 2008), we expected HC's WM to be impaired for novel stimuli.

Case description. HC is a woman with developmental amnesia who was 22 years old at the time of testing. She was born prematurely and suffered a hypoxic episode, which resulted in a 50% bilateral reduction in the volume of her hippocampus with no obvious pathology found in parahippocampal regions, including entorhinal, perirhinal, and parahippocampal cortices (see Rosenbaum et al., 2011, for a detailed neuropsychological profile). She never developed the ability to fully recollect the past; nonetheless, she is capable of semantic learning. For example, she was a flower girl in a cousin's wedding, but upon reflection of the episode she said, "I don't know if I actually remember that, or if I've been told that a bunch of times." HC successfully graduated from high school and completed one year of technical college and one year of a post-secondary culinary program. She is an avid fan of film and is familiar with many actors and celebrities, a point that was relevant for Experiment 1. She is a native English speaker and her vocabulary is about average for her age, a point that was relevant for Experiment 2. For example, she accurately identified synonyms for 14 of the 20 words on the Mill Hill Vocabulary test, including the words *temerity* and *libertine*.

Control participants. Twenty healthy undergraduate students (13 female; mean age = 19.9 years) from the University of Toronto served as control participants. The controls had similar levels of education (mean of 13.8 years) and vocabulary (mean Mill Hill Vocabulary test score of 14.0). Each participant performed a delayed match-to-sample (DMS) task with famous and non-famous faces for Experiment 1, and a digit span and reading span task, and a Brown–Peterson task with words and non-words for Experiment 2. All participants performed the tasks in the same order. HC was tested at the Rotman Research Institute of Baycrest Centre and the control participants were recruited and tested at the University of Toronto. All participants were compensated $12 per hour of participation.

1. Experiment 1

Experiment 1 was conducted to examine the impact of stimulus novelty on HC and controls' performance on a visuospatial WM task. Similar to Ezzyat and Olson (2008), in Experiment 1 we administered a delayed match-to-sample (DMS) task that required maintaining the image of a single face in WM for 1000 or 8000 ms, and then selecting the matching face on a two-alternative forced-choice recognition test. Critically, the face was either of a famous person or a non-famous person.

1.1. Method

DMS with faces. For each trial of the DMS task with faces, an image of a single face was presented for 1500 ms, followed by a mask for 500 ms, then a blank screen for either 1000 or 8000 ms, and finally a two-alternative forced choice test. For the test, two faces were presented – the studied face and a 50% morph of the studied face with a non-studied face – until the participant made a response to indicate which one was the exact match of the studied face (see Fig. 1). On half of the trials the matching face was presented on the left hand side of the screen and on half of the trials it was presented on the right. To assess the role of familiarity, 40 of the faces were famous and the other 40 were non-famous. We selected images of faces with a neutral expression from publicly available photographs and constructed the images using FaceGenModeller software in order to standardize the faces in terms of head position and size. The images were cropped to exclude the hair of each face, and edited to exclude salient features such as facial hair and glasses. Similar to Ezzyat and Olson (2008), lures were made by creating perceptual morphs between the studied face and a different, non-studied face. The faces were counterbalanced across delay and whether the morph was the target or not.

1.2. Results and discussion

Statistical analysis of single case studies is controversial (cf. Corballis, 2009; Crawford, Garthwaite, & Howell, 2009). For this reason, we present multiple techniques. Because we were testing the hypothesis that HC would demonstrate deficits, one-tailed *p*-values are reported.

The proportion correct on the two-alternative forced choice test as a function of fame and delay are presented in Table 1. Following Corballis (2009), we first compared HC's performance to the control

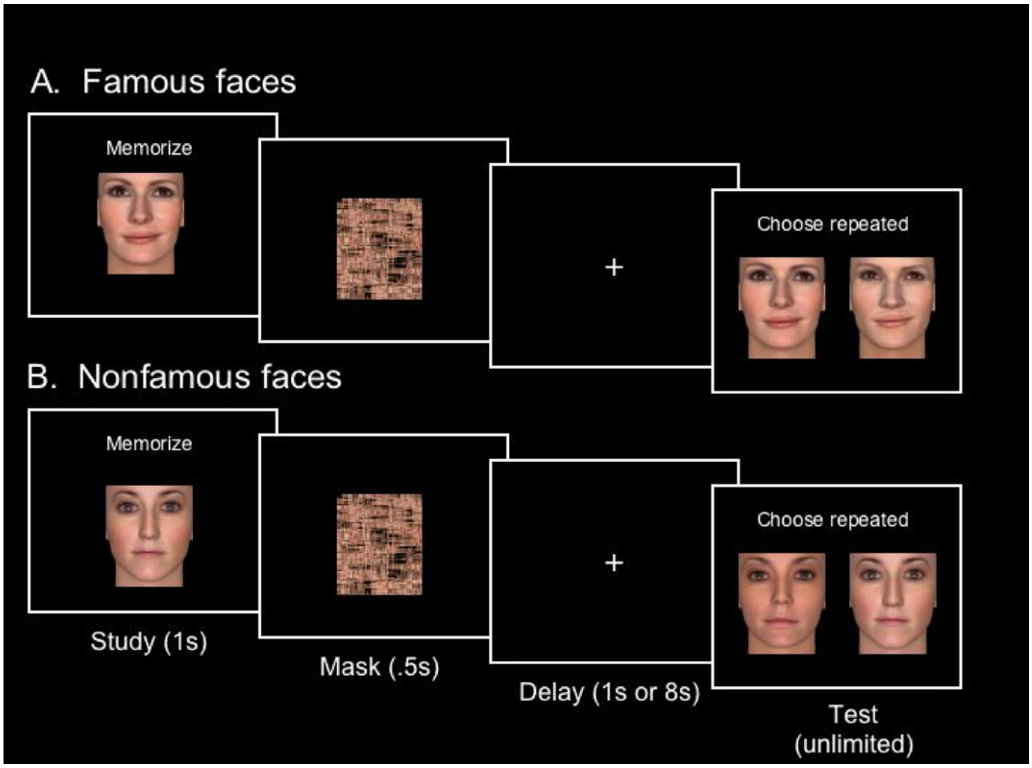

Fig. 1. Example of the delayed match to sample task with famous (*Julia Roberts*) and non-famous faces.

group with a mixed, repeated-measures ANOVA. This analysis revealed a main effect of fame, indicating that performance was better for the famous faces than for the non-famous faces overall, $F(1,18) = 4.3$, $p = .05$. This effect did not interact with delay, and so the mean proportions correct for HC and the control participants were compared, collapsed across delay. As can be seen in Fig. 2, HC's performance for the non-famous faces (70%) appeared to be impaired relative to that of the control participants (81%), similar to previous findings (Ezzyat & Olson, 2008). Expressing HC's score for non-famous faces as a z-score of the control sample revealed a significant difference, $z = -1.631$, $p = .05$. HC's score in comparison to the t-distribution of the control sample approached significance using both Corballis's (2009) method, $t(19) = -1.53$, $p = .07$, and Crawford and Howell's (1998) method, $t(19) = -1.592$, $p = .06$. In contrast, HC's performance for the famous faces (85%) was unimpaired relative to that of the control participants (85%), $t(19) = 0.02$, $p > .10$. Thus, HC's WM was impaired for non-famous famous, but was preserved for famous faces.

After the DMS task, we administered a post-test in which all of the faces were re-presented. We wanted to see if HC's reduced WM performance could be attributed to a perceptual deficit. We administered a perceptual-comparison control task to verify that all participants could accurately select the matching face when the target was presented simultaneously with the probe and the lure. HC accurately selected 96% of the faces on this perceptual comparison task; the control participants accurately selected 95.9% of the faces. Thus, HC's deficit on the DMS task was not attributable to a deficit in perceptual processing.

We also wanted to gauge each participant's personal familiarity with the famous faces used in the DMS task. During the post-test we asked the participants if they thought each face was famous or non-famous. Then, if they thought a face was famous, we asked them to name the person or provide any other details about the person they could think of. Overall, HC accurately classified 97.5% (controls = 79.9%) of the faces as famous or non-famous, and she could accurately name the person for 70% of the famous faces (controls = 74%). Therefore, HC was familiar with most of the famous faces.

Table 1
Proportion correct on the DMS task with faces as a function of fame and delay.

	HC	Controls
Famous faces 1000 ms	.90	.85 (.02)
Famous faces 8000 ms	.80	.85 (.02)
Non-famous faces 1000 ms	.75	.83 (.02)
Non-famous faces 8000 ms	.65	.80 (.02)

Note. Standard error of the mean is in parentheses.

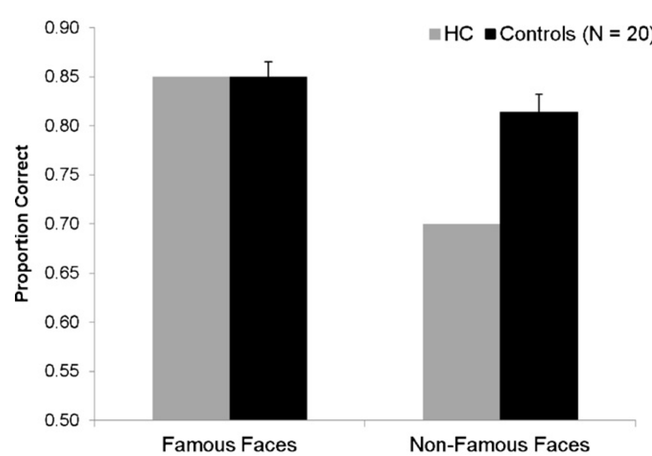

Fig. 2. Mean proportion correct on the two-alternative forced choice test of the DMS task with famous and non-famous faces by HC and the control participants ($N = 20$). *Note*: chance = .50, error bars represent the standard error of the mean.

Table 2
Proportion correct on the DMS task for known and unknown famous faces (as indicated on the post-test familiarity assessment), and non-famous faces for HC and the control participants. The examples are faces which HC did or did not know.

	HC	Controls
Known famous faces (e.g., Paris Hilton)	.89	.86 (.02)
Unknown famous faces (e.g., Hillary Clinton)	.77	.83 (.04)
Non-famous faces	.70	.81 (.02)

Note. Standard error of the mean is in parentheses.

If stimulus familiarity was the source of HC's intact performance for the famous faces, then her performance should have been poorer for the famous faces that she did not know (e.g., Hillary Clinton), relative to the ones she knew (e.g., Paris Hilton). If a famous face was unknown to HC, then that face was essentially a non-famous face to her, and thus, her WM performance for unfamiliar famous faces should be similar to that of the non-famous faces. We rescored accuracy on the DMS task for each participant for famous faces that the participant knew versus those that were unknown, as revealed by the post-test familiarity judgments. Table 2 presents the mean accuracy on the DMS task for famous faces that participants knew versus those that were unknown, and for the non-famous faces as well. As predicted, HC's WM performance was much better for the famous faces with which she was more familiar (89%), whereas her performance for the unfamiliar famous faces (77%) was more similar to that of the non-famous faces (70%). In contrast, the control participants' performance was not as affected by the familiarity of the faces. That is, the control participants did not have as much difficulty as HC with encoding and maintaining unfamiliar faces. Taken together, these findings support the hypothesis that an intact MTL is important for encoding and retrieving novel information, even in the context of a STM task.

2. Experiment 2

Experiment 2 was conducted to examine the impact of rehearsal and stimulus novelty on HC and controls' performance on verbal WM tasks. To this end, we administered a simple WM span task (digit span) and a complex WM span task (reading span) to illustrate the importance of rehearsal in supporting verbal WM. If to-be-remembered items can be continuously rehearsed in mind all the while, then, at the time of recall, the items can simply be reported directly from the focus of attention (Cowan, 2001). In contrast, complex WM tasks, such as the reading span task (Daneman & Carpenter, 1980) or the Brown–Peterson task (Brown, 1958; Peterson & Peterson, 1959), include a secondary distractor task that distracts attention away from maintaining the to-be-remembered items in the focus of attention. Thus, at the time of recall, at least some of the items must be retrieved from LTM (cf. Rose & Craik, in press; Unsworth & Engle, 2007). Therefore, HC should be preserved for simple span tasks like digit span, but impaired for complex WM tasks like reading span and the Brown–Peterson task.

We also wanted to show that the same principle – that an intact MTL is more important for representing and maintaining a novel stimulus in WM than a familiar stimulus – that was observed in visuospatial WM in Experiment 1 applies to verbal WM as well. To this end, we administered a Brown–Peterson task, which required maintaining a single familiar word (high-frequency word), a less-familiar word (low-frequency word), or a novel word (non-word) over a filled delay of 4000 or 8000 ms. Because the distractor task disrupts rehearsal, we hypothesized that HC would be impaired overall, but that the degree of impairment would be larger for non-words than familiar words.

Table 3
The proportion of digits correctly recalled for the digit span and reading span tasks for patient HC and the control participants.

	HC	Controls
Digit span	.78	.82 (.02)
Reading span	.54	.76 (.03)

Note. Standard error of the mean is in parentheses.

2.1. Method

Digit span and reading span. For the digit span task, lists of 2–9 digits were presented visually (1500 ms each) for immediate serial recall. The reading span task was the same except that there were lists of 2–6 digits and a sentence was read aloud and verified for its sensibility prior to the presentation of each digit (for further details, see Hale et al., 2011). There were 2 trials for each list length; lists were presented in the same random order for all participants. For both tasks, the proportion of items recalled in the correct position was calculated and recorded.

Brown–Peterson task with words and non-words. For the Brown–Peterson task, a single high-frequency word (e.g., *direction*), low-frequency word (e.g., *concierge*), or "word-like" non-word (e.g., *glerning*) was presented visually for 1000 ms (the stimuli are presented in Appendix A). Sixty eight- or nine-letter words, and non-words with appropriate lexical characteristics were selected from the English Lexicon Project database (www.elexicon.wustl.edu; Balota et al., 2007). The mean Kucera-Francis and log-HAL word frequencies were 127.3 (SD = 74.8) and 10.4 (SD = .9) for the 20 high-frequency words and 2.6 (SD = 1.9) and 5.5 (SD = 1.8) for the 20 low-frequency words. Importantly, the mean bigram frequency for the 20 non-words was not significantly different from the real words (both $ts < 1.59$, $ps > .10$). Following the presentation of each word or non-word, a random number between 50 and 150 was presented. The participant was to say the number aloud and count backwards by three until "*Recall???*" appeared on the screen, following a delay of either 4000 or 8000 ms. Of course, letters in familiar words were likely encoded as bound chunks whereas the non-words (and perhaps many of the low-frequency words) could have appeared as unfamiliar strings of letters. Therefore, participants were instructed to type in the exact string of letters that was presented and, if they could not recall all of the letters, they were to type in as many letters as possible. We scored the proportion of letters correctly recalled so as to give partial credit for partially recalled words. Following Baddeley, Allen, & Vargha-Khadem (2010), a letter was considered correct if it was recalled in the correct position relative to an adjacent letter and/or correctly recalled in the first or last position.

2.2. Results and discussion

As predicted, HC's performance was preserved on digit span, but was impaired on the reading span task. The proportion of digits correctly recalled for the two WM span tasks are presented in Table 3. On the digit span task, HC's performance was similar to that of the control participants, $z = -0.47$, $t(19) = -0.46$, $p > .10$. However, her performance was significantly worse on the reading span task, $z = -2.11$, $t(19) = -2.15$, $p < .05$. Thus, HC was preserved on the simple, digit span task, but was impaired on the complex, reading span task. This pattern supports our hypothesis that amnesia does not impair verbal WM for tasks in which familiar verbal material can be rehearsed during the retention interval, but performance is more likely to be impaired if rehearsal is disrupted by the performance of other secondary task operations (i.e., reading and verifying the sensibility of sentences).

As predicted, HC was also impaired on the Brown–Peterson task overall, but the degree of impairment was larger for non-words than for familiar words. The proportion of letters recalled as a function of stimulus type and delay are presented in Table 4. Following Corballis (2009), these data were analyzed with a mixed, repeated-measures ANOVA. There were main effects of stimulus type, $F(2, 38) = 13.37$, $p < .001$, and delay, $F(1, 19) = 6.70$, $p < .05$. However, these two factors did not interact, so the data were collapsed across delay. HC's performance was impaired overall, $F(1, 19) = 16.47$, $p < .001$, but this deficit interacted with stimulus familiarity, $F(2, 38) = 2.57$, $p < .05$. Relative to the low-frequency words and non-words, HC could recall the high-frequency words reasonably well: the mean difference between HC and controls was larger for non-words (46.3%) and low-frequency words (45.8%)

Table 4
Mean proportion correct as a function of stimulus type and delay for HC and the control participants.

Stimulus type and delay	HC	Controls
High-frequency words 4000 ms	.67	.92 (.02)
High-frequency words 8000 ms	.50	.80 (.02)
Low-frequency words 4000 ms	.33	.88 (.02)
Low-frequency words 8000 ms	.46	.81 (.03)
Non-words 4000 ms	.32	.79 (.03)
Non-words 8000 ms	.18	.64 (.04)

Note. Standard error of the mean is in parentheses.

Table 5
Mean proportion of letters correctly recalled on the Brown–Peterson task for high-frequency words, low-frequency words that participants did or did not recognize as real, English words on the vocabulary post-test, and non-words. The examples are low frequency words which HC did or did not know.

Stimulus type	HC	Controls
High-frequency words	.82	.92 (.02)
Known low-frequency words (e.g., fledgling)	.66	.92 (.02)
Unknown low-frequency words (e.g., scrivener)	.32	.77 (.03)
Non-words	.28	.74 (.03)

Note. Standard error of the mean is in parentheses.

than for high-frequency words (26.9%). No other interactions were significant. Expressed as *z*-scores, HC's score was −3.36 ($p<.001$) for high frequency words, −5.06 ($p<.001$) for low-frequency words, and −3.56 ($p<.001$) for non-words. Using Crawford and Howell's (1998) test to test for deficits in single cases, the difference between HC and controls was significant for high-frequency words, $t(19)=-3.28$, $p<.05$, low-frequency words, $t(19)=-4.93$, $p<.005$, and non-words, $t(19)=-3.48$, $p<.005$. Using Crawford and Garthwaite's (2005) difference test to test for differences between the differences in multiple conditions revealed that, relative to HC's deficit for high frequency words, her deficit was significantly larger for both low-frequency words, $t(19)=2.82$, $p<.01$, and non-words, $t(19)=1.95$, $p<.05$. This pattern of performance fulfils the criteria for a strong dissociation. Thus, the control participants did not have as much difficulty as HC with encoding and maintaining unfamiliar words, which suggests that an intact MTL is important for encoding and retrieving novel stimuli on the Brown–Peterson task.

Additionally, HC committed a rather large number of intrusion errors. For example, on one trial the to-be-remembered word was 'research'. HC correctly recalled this word; then, on the very next trial when the to-be-remembered word was 'direction', she again recalled 'research'. There were 12 such instances, out of 60 total trials. In comparison, controls had an average of 3.0 intrusion errors. For the interested reader, all of HC's responses on the Brown–Peterson task are presented alongside the stimuli in Appendix A. Moreover, HC committed more intrusion errors for high-frequency words (6) than for low-frequency words (4) and non-words (2), which biased the data differently across the conditions. Therefore, we re-scored the data for all participants, excluding intrusion errors from analysis. Doing so excluded 5.6% of the total trials from analysis. The data for the three types of stimuli are presented in Fig. 3. As can be seen, HC was unimpaired for recall of high-frequency words, $z=-1.38$ ($p>.05$), $t(19)=-1.35$,

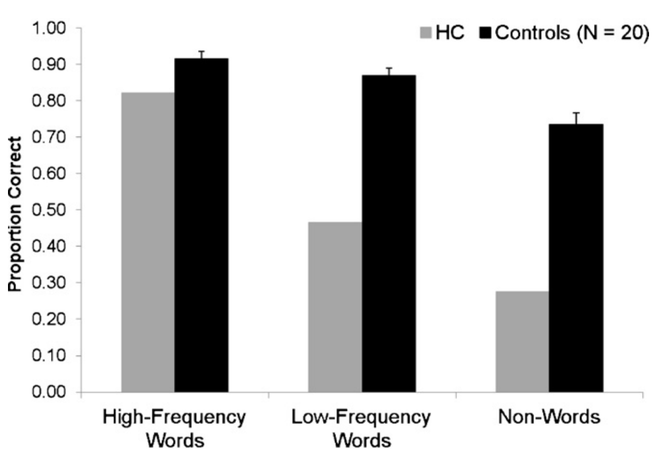

Fig. 3. Mean proportion of letters correctly recalled on the Brown–Peterson task for high-frequency words, low-frequency words, and non-words by HC and the control participants ($N=20$). Error bars represent the standard error of the mean.

$p>.05$, but her deficit remained for recall of low-frequency words, $z=-3.11$ ($p<.01$), $t(19)=-3.98$, $p<.01$, and non-words, $z=-3.37$ ($p<.001$), $t(19)=-3.29$, $p=.001$.

If stimulus familiarity was the source of HC's relatively preserved performance for the high-frequency words, then her performance should have been better for low-frequency words that she did know (e.g., fledgling) than the low-frequency words that she did not know (e.g., scrivener). After all the participants completed the Brown–Peterson task, we gave them a sheet of paper with all of the stimuli on it and asked them to circle only the words that they knew were real, English words. Participants did not know that many of the low-frequency words were in fact real English words. We re-analyzed the low-frequency words that each participant did not know separately from those that the participant did know because the words that were not recognized as real English words were essentially non-words to the participant. Therefore, performance for the low frequency words that HC did recognize as real words should be similar to that of the high frequency words, whereas performance for the low-frequency words that she did not recognize as real words should be similar to that of the non-words. The proportion of letters recalled for the different types of stimuli by HC and the controls are presented in Table 5. Indeed, the proportion of letters recalled for low-frequency words that HC did recognize was similar to the high-frequency words whereas the proportion of letters recalled for the low-frequency words that she did not recognize was similar to the non-words. Moreover, HC's deficit relative to the controls was greatest for the words and non-words that she was not familiar with (mean difference = 45%), but this deficit was reduced for the familiar words (mean difference = 15%). This interaction was significant using both Corballis's (2009) method, $F(1, 19)=7.26$, $p<.05$, and Crawford and Garthwaite's (2005) difference test, $t(19)=2.69$, $p<.01$, and fulfils the criteria for a strong dissociation. Thus, HC's WM was relatively preserved for words that were known, but was impaired for words and non-words that were unknown. In contrast, the control participants did not have as much difficulty with encoding and maintaining unknown strings of letters over the 4000–8000 ms delay. These findings support the hypothesis that an intact MTL is important for encoding and retrieving novel information, even in the context of a WM task.

3. General discussion

We found that HC was impaired at maintaining a single face in WM for 1–8 s, but only if it was a novel (non-famous) face; her performance was unimpaired for famous faces. The result concerning novel faces is similar to previous findings of Olson and colleagues (Ezzyat & Olson, 2008; Olson et al., 2006). The novel result is that, using the same testing procedure as Ezzyat and Olson (2008), the amnesic we tested was unimpaired when the face that was to be maintained was familiar. This finding is consistent with the prediction made by Stern et al. (2001) and Jonides et al. (2008), but, to our knowledge, no study has directly tested this hypothesis in an amnesic person until now. We also found converging evidence in verbal WM. HC was impaired at recalling a single word after just a few seconds of distraction, but only for non-words and less familiar (low-frequency) words; her performance was unimpaired for high-frequency words. Thus, on both visuospatial and verbal WM tasks, HC's performance was impaired for novel stimuli, but was preserved for familiar stimuli.

Many factors can influence maintenance of information over the short term. Familiar material, such as digits, that can be represented in a rather superficial phonological code may be easily maintained via articulatory rehearsal, as long as such rehearsal is not disrupted by other cognitive operations. In this case, the material may be maintained via cortical regions independent of the MTL (Buchsbaum, Olsen, Koch, & Berman, 2005). In contrast, if the material is novel (i.e., is not already represented in semantic memory) and it is difficult to rehearse, as is the case for complex visuospatial stimuli or because rehearsal is disrupted by other cognitive operations, then the features of the stimulus must be quickly bound together in order to be accurately maintained over a delay. In this case, an intact MTL is likely to be important for successful performance, even at very short retention intervals.

The reason it is commonly believed that MTL amnesics have preserved STM or WM may be because the classic studies showing preserved STM in MTL amnesics (e.g., Baddeley & Warrington, 1970) used tasks that required short-term retention of familiar verbal information, such as words or digits that can be easily maintained via articulatory rehearsal. It is now clear that the extent to which amnesics demonstrate preserved or impaired performance on STM or WM tasks depends on certain features of the task. In the present study, we showed that a developmental amnesic, patient HC, was impaired at maintaining a single novel stimulus for 1–8 s, but was preserved when the stimulus was more familiar. These findings have important implications for the way in which researchers should conceptualize the distinction between WM and LTM. They argue against a strict distinction between WM and LTM "systems." We prefer a processing-based approach to the WM/LTM distinction whereby the processes (namely, active maintenance of perceptual codes) and brain regions associated with short-term retention typically differ from those associated with memory over the long-term. However, if the task demands it, the processes and brain regions that support effective LTM (namely, encoding and retrieval of conceptual codes via the MTL) can be necessary to support WM as well (Rose & Craik, in press).

3.1. Relation to prior work

Recently, Baddeley et al. (2010) also examined WM in a developmental amnesic, patient Jon. They assessed Jon's ability to maintain a series of words in WM. In one condition, the series of words formed a coherent sentence, whereas in another condition, the same set of possible words was used, but the series of words itself did not form a coherent sentence. Jon's performance was better when the series of words formed a sentence than when the words did not, but his performance was similar to that of controls. In comparison, HC's performance on the verbal WM tasks that involved distraction was markedly impaired relative to controls. The reason verbal WM was unimpaired for Jon, but was impaired for HC is likely due to differences between the tasks. The task that Baddeley and colleagues administered included highly familiar words that were repeatedly used across the different trials of the task. Had this study used novel words, as in the present study, perhaps Jon's WM performance would have been impaired.

Several studies now have shown that WM is impaired in various amnesics, particularly when the task requires relational binding (Finke et al., 2008; Hannula et al., 2006). It is believed that a critical function of the MTL is to establish lasting representations that involve relations (e.g., Ryan et al., 2000). As Jonides et al. (2008) noted, such relations may be among items in a series or among features of items or between items and their context. In Experiment 1 of the current study, the task likely required binding the relations among novel features for the non-famous faces (eyes, nose, and mouth). Similarly, in Experiment 2, the tasks likely involved binding novel sequences of digits or letters into chunks.

Some researchers believe that the MTL is only involved with particular types of binding. For example, Baddeley et al. (2010) suggested that WM should only be impaired in amnesia when the task requires *spatial* binding. Whereas research has shown MTL amnesics to be impaired at binding a color to a spatial location in WM (Finke et al., 2008), Baddeley et al. (2010) showed that patient Jon's ability to bind a color and a shape in WM (a non-spatial form of binding) was unimpaired. The proposal that the MTL is especially important for spatial binding is consistent with numerous findings of impaired performance by amnesics on a variety of visuospatial WM tasks (Buffalo et al., 1998; Crane & Milner, 2005; Ezzyat & Olson, 2008; Hannula et al., 2006; Holdstock et al., 1995; Olson et al., 2006; Owen et al., 1995; Shrager, Levy, Hopkins, & Squire, 2008; Warrington & Taylor, 1973). Although it is true that many of the WM tasks showing impairments in amnesia required spatial binding, we would also note that many of them involved *novel* stimuli, such as abstract patterns resembling images from a kaleidoscope (Buffalo et al., 1998), or abstract shapes resembling snowflakes (Holdstock et al., 1995) or letters of a foreign language (Owen et al., 1995). Therefore, it is likely that the hippocampus is important for WM tasks that require binding features among novel stimuli, not solely tasks that require spatial binding (see Experiment 2).

Furthermore, the current study sheds light on previous neuroimaging studies that have shown the MTL to be more active during maintenance of novel information than familiar information over brief retention intervals (Stern et al., 2001; Ranganath & D'Esposito, 2001). Of course, the fact that the MTL is active during the delay period of WM tasks is not strong enough evidence alone to prove that this structure is crucial for WM performance. Thus, the pattern of results presented here is precisely the kind of converging evidence needed to bolster the interpretation that the MTL is critically involved in the service of WM for novel information.

3.2. Limitations and future studies

The findings of the current study are clearly limited by the fact that only one developmental amnesic was tested. It is unclear whether other (particularly non-developmental) amnesics would show a similar pattern. However, we find it reassuring that several studies over the past 40 years have shown a variety of amnesics to be impaired on similar WM tasks (e.g., Butters & Cermank, 1974; Ezzyat & Olson, 2008; Olson et al., 2006). For example, in Experiment 1 we used a task similar to that used by Ezzyat and Olson (2008). They showed that three adult-onset amnesics were also impaired at maintaining a single novel face over delays of 1–8 s. As compared to the patients' performance reported in Ezzyat and Olson (2008), HC performed reasonably well on the DMS task, even for the novel faces. This is likely due to differences between the patients: Ezzyat and Olson's patients were older adults between the ages of 64 and 70 with brain damage acquired in adulthood, whereas HC is a developmental amnesic who was 22 years old at the time of testing. As noted, developmental amnesics such as HC demonstrate relatively intact semantic learning, perhaps due to either preserved hippocampal or parahippocampal tissue or because some reorganization of learning abilities has occurred.

It is also interesting that HC recalled a larger number of intrusions than controls. This pattern is consistent with Vargha-Khadem, Salmond, Watkins, Friston, Gadian & Mishkin, 2003 finding that developmental amnesics committed an abnormal number of intrusion errors on a verbal learning test. This finding is interesting given that intrusion errors are typically associated with damage to areas of frontal cortex, yet HC and the other developmental amnesics reported by Vargha-Khadem et al. have no apparent damage to frontal regions. One possibility is that, as suggested by Rosenbaum et al. (2011), developmental amnesia may be associated with a functional disconnect between frontal and medial temporal regions. Another possibility is that HC has a very liberal report criterion. This may be one way she tries to compensate for her memory deficit. That is, she may report anything that comes to mind in order to recall something at all, which would then come at the expense of an exaggerated number of intrusions. Future studies would do well to investigate these possibilities, and to examine whether this behavioral manifestation is unique to developmental amnesia. Clearly, further research is needed to fully understand the nature of WM impairments in amnesia, particularly developmental amnesia. However, these cases are very rare, and the pattern of preserved and impaired function that they exhibit contributes in a meaningful way to the growing consensus about the relation between WM and LTM.

4. Conclusion

In summary, the findings of the present study show that whether a task requires representing and maintaining novel (or familiar) stimuli in WM is an important factor that impacts the extent to which the MTL is necessary to perform the task (see also, Jonides et al., 2008; Stern et al., 2001). Thus, it may be better to conceptualize memory over the short-term and long-term as relying on similar or different processes and brain regions depending on particular aspects of the task (i.e., rehearsal, stimulus novelty) rather than relying on distinct “systems.”

Appendix A. Stimuli and raw data for patient HC from the Brown–Peterson task

Trial #	Delay	StimType	Target	HC recalled	Trial #	Delay	StimType	Target	HC recalled
1	8000	Low-freq	Delusion	Watermelon	31	4000	Nonword	Tariagge	Carriage
2	8000	Low-freq	Scrivener	t	32	8000	Nonword	Pinioned	Tirrage
3	8000	Low-freq	Scrimmage	Teapot	33	4000	High-freq	Reference	Teriage
4	8000	Low-freq	Diaphragm	Diaphram	34	8000	Low-freq	Labyrinth	Labynth
5	8000	Nonword	Hilghful	Hilful	35	8000	High-freq	Knowledge	Knowledge
6	8000	Low-freq	Pedestal	Skilful	36	8000	Low-freq	Nuisance	Nussience
7	4000	Low-freq	Ellipsoid	Tsle	37	8000	High-freq	Committee	Nusience
8	8000	High-freq	Entrance	Entrance	38	4000	High-freq	Decision	Presence
9	4000	High-freq	Research	Research	39	4000	Low-freq	Affluence	Affiliate
10	8000	High-freq	Direction	Research	40	4000	High-freq	Language	Language
11	8000	Low-freq	Cessation	Sucession	41	4000	High-freq	President	President
12	4000	Nonword	Lenerated	Reltsion	42	4000	Low-freq	Vignette	Viniger
13	4000	Low-freq	Fledgling	Fledgling	43	4000	Nonword	Glerning	Glerning
14	8000	High-freq	Existence	Existance	44	8000	Nonword	Duoloque	Glatn
15	4000	High-freq	Judgment	Existance	45	8000	Nonword	Ubiquoty	Gonrn
16	8000	Nonword	Ehuiwocal	Susewod	46	4000	Nonword	Lanjints	Tfomd
17	4000	Nonword	Iphetness	Sltwoeh	47	8000	Nonword	Ceglonged	Gunrts
18	4000	Nonword	Vitriouf	Stilwod	48	4000	High-freq	Commerce	Commerce
19	8000	Nonword	Effluelt	Eftowld	49	8000	Low-freq	Shrapnel	Shrapnel
20	4000	Low-freq	Concierge	Eflitated	50	8000	High-freq	Technique	Shrapnel
21	8000	Low-freq	Tincture	Eltis	51	4000	Low-freq	Flautist	Flunct
22	4000	Nonword	Actrodome	Tien	52	8000	High-freq	Instance	Teacup
23	4000	Nonword	Ecymology	Etyphim	53	8000	Nonword	Isinerant	Irtelce
24	4000	Low-freq	Ambuscade	Esoplt	54	8000	High-freq	Marriage	Marriage
25	4000	Nonword	Firpking	Ferpking	55	4000	Nonword	Harlequil	Herqiul
26	4000	High-freq	Religion	Religion	56	4000	Low-freq	Lethargy	Herquil
27	8000	High-freq	Material	Kingdom	57	8000	Nonword	Foprulate	Herquilate
28	4000	High-freq	Situation	Situation	58	4000	Low-freq	Limerick	Lymrick
29	4000	High-freq	Presence	Persistance	59	8000	Nonword	Thagrazer	Herquils
30	8000	High-freq	Equipment	Equiptment	60	4000	Low-freq	Cartridge	Hertilage

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