

# Visual Working Memory Is Impaired when the Medial Temporal Lobe Is Damaged

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## Abstract

■ The canonical description of the role of the medial temporal lobes (MTLs) in memory is that short-term forms of memory (e.g., working memory [WM]) are spared when the MTL is damaged, but longer term forms of memory are impaired. Tests used to assess this have typically had a heavy verbal component, potentially allowing explicit rehearsal strategies to maintain the WM trace over the memory delay period.

Here we test the hypothesis that the MTL is necessary for visual WM when verbal rehearsal strategies are difficult to implement. In three patients with MTL damage we found impairments in spatial, face, and color WM, at delays as short as 4 sec. Impaired memory could not be attributed to memory load or perceptual problems. These findings suggest that the MTLs are critical for accurate visual WM. ■

## INTRODUCTION

Bilateral damage to the hippocampus and related medial temporal lobe (MTL) structures (entorhinal, perirhinal, and parahippocampal cortex) causes severe memory impairments. This impairment is characterized by profound explicit long-term memory (LTM) deficits, but preservation of many types of procedural and implicit LTM and working memory (WM). The findings from patients with MTL amnesia were consistent with the multistore view of memory (Atkinson & Shiffrin, 1971) that short-term and LTM were separate psychological entities with separate underlying neural systems (Baddeley & Hitch, 1974), and thus these findings became the linchpin evidence for the psychological distinction between short-term (henceforth termed working memory [WM]) and LTM.

The evidence that is most frequently cited for intact WM after MTL damage comes from studies of verbal or phonological memory. For instance, WM for digits (Cave & Squire, 1992; Wickelgren, 1968) and words (Baddeley & Warrington, 1970) appears to be spared in MTL amnesia, whereas LTM for these types of stimuli is impaired (Cohen & Eichenbaum, 1993). These findings helped create one of the central dogmas of memory research: that short-term forms of memory do not rely on the MTL.

In contrast, evidence for intact visual WM with MTL damage is often overlooked because fewer studies have been conducted and those that exist provide a confusing mixture of results. For instance, Cave and Squire (1992)

showed that MTL amnesics could accurately remember the location of a single dot or the shape of a single angle for up to 12 sec. In contrast, other studies by Levy and Squire (2005) have shown that MTL amnesics can accurately remember a single novel shape for up to 25 sec but cannot accurately remember several novel shapes for more than 5 sec (Buffalo, Reber, & Squire, 1998). Levy and Squire also reported that WM for a single face was intact in patients with damage restricted to the hippocampus but impaired at 7-sec delays in patients with large MTL lesions. However, both normal controls and patients with hippocampal damage were at ceiling performance, raising the question of whether hippocampal damage can cause face WM impairments when a more difficult (e.g., more sensitive) task is used. Milner and colleagues tested patients with MTL amnesia on incidental memory for objects or the location of objects and found intact object memory, but impaired location memory with right but not left MTL damage, when there was no delay interval (Smith & Milner, 1989). Interpretation of this finding in regard to spatial WM is complicated by the fact that the encoding manipulation was incidental and the task design encouraged encoding of object-location conjunctions.

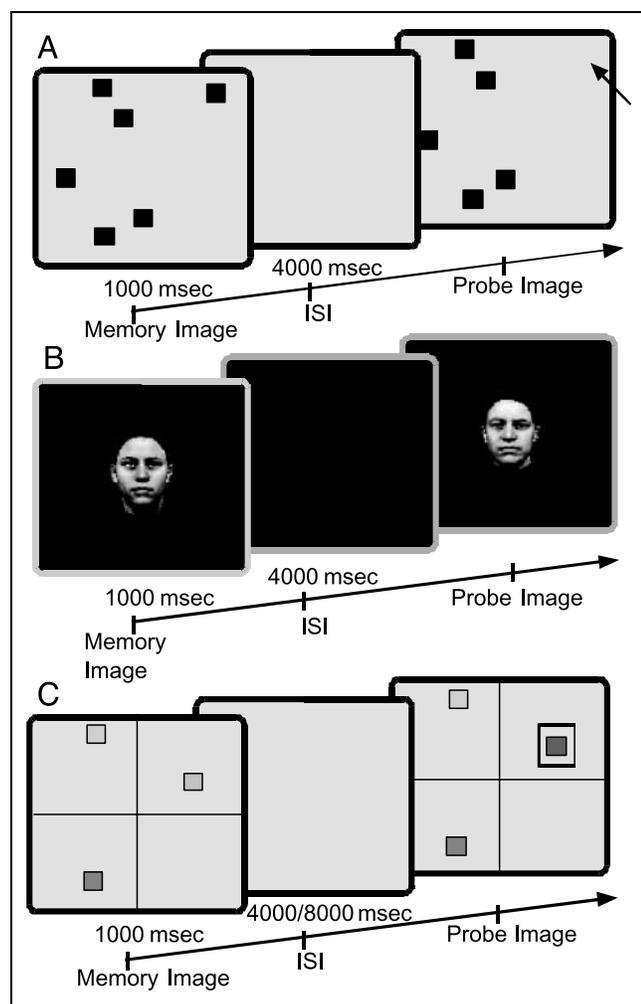
What accounts for the discrepant visual WM results? We hypothesize that visual WM computations typically rely on an intact MTL, but this neural route can be circumvented and accurate performance achieved on easy visual WM tasks by using a variety of strategies. For instance, if the task requires you to remember the visual location of a single dot (Cave & Squire, 1992) rather than holding the location in mind, you could choose instead to covertly orient the eyes, hand, or body

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toward the dot location, or you could simply rehearse a verbal description of the dot location (e.g., 1 in. from left, 2 in. down). In contrast, more difficult visual WM tasks, such as remembering several simultaneously presented locations, can only be mastered by holding in mind a visual representation of the stimuli.

Here we test MTL amnesics and age-matched controls in three experiments that require subjects to remember several locations (Experiment 1), a single face (Experiment 2), or several colors (Experiment 3) over 4 or 8 sec (see Figure 1 for stimuli). Critical features of the present study include the use of tasks and stimuli that were difficult enough to avoid ceiling effects and that minimized the possibility that verbal strategies could be used to perform the task. If the MTL is necessary for accurate visual WM, patients should be impaired in all tasks. Alternatively, if the MTL is critical only for long-term forms of memory (Alvarez, Zola-Morgan, & Squire, 1994; Cave & Squire, 1992) then no deficits should be observed.



**Figure 1.** A schematic diagram of the tasks used in (A) Experiment 1; (B) Experiment 2; and (C) Experiment 3. In all experiments, the actual stimuli were colored (see Methods for description).

## EXPERIMENT 1

We began by testing patients and controls in a spatial WM task. Subjects were required to remember a 2-D representation of several locations over a 4-sec delay, a task that bears some similarity to that tested by Cave and Squire (1992). Our task deviates from their task in that subjects were required to remember either three or six locations, forcing them to use a visual strategy to remember locations.

## Methods

### Participants

All participants were cooperative and attentive and had normal or corrected-to-normal visual acuity. All participants signed an informed consent form prior to taking part in the experiment. Control participants were seven older healthy adults (three men, four women, 45–71 years,  $M = 60$  years) with an average of 13 years of education. Average verbal IQ as measured by the Wechsler Adult Intelligence Scale—Third Edition (Wechsler, 1997a) was 108.

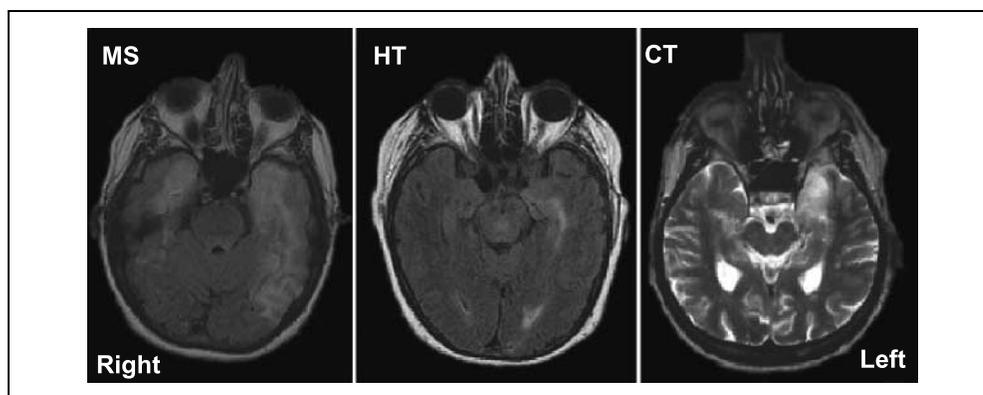
The lesion group consisted of three patients with bilateral MTL damage (one man, two women, 62–68 years,  $M = 65$  years; see Figure 2) who had an average of 12 years of education. Average verbal IQ was 92. General Memory score on the WMS-Third Edition (Wechsler, 1997b) was 60 and the Visual Delayed Memory score was 62. There was no difference between the MTL group and their control group in terms of age ( $p = .34$ ), education ( $p = .27$ ), or verbal IQ ( $p = .065$ ). Detailed information about each patient is listed below.

### Patient MS

Patient MS (age 62 years) has bilateral MTL damage as a result of herpes encephalitis in 1999. Damage extends into the amygdala, perirhinal, and hippocampal cortex on the left and entorhinal and hippocampal cortex on the right, as assessed by magnetic resonance imaging (MRI). Damage on the left extends slightly into posterior temporal regions. MS's chief complaint is anomia, which has steadily lessened over time. When shown Snodgrass line drawings in year 2002, she only named 16 of 65 correct. Her anomia is most likely the result of left temporal pole damage (Lezak, 1995). Because the experiments reported in this article test visual memory, her naming difficulties were not a matter of concern. She did not self-report any visual problems nor was there any evidence of vision problems when asked to match nonsense shapes on the Mattis Dementia Rating Scale (Mattis, 1988). When asked to copy nonsense designs, she made only one small error. Her line cancellation performance was errorless.

Due to her amygdala damage, several emotion tests were administered, including the Beck Depression In-

**Figure 2.** Axial MRI scans from the three patients, MS, HT, and CT, shown in radiological convention (e.g., left on the right). Images for MS and HT are fluid-attenuated inversion recovery (FLAIR) and for CT are T2 weighted.



ventory (BDI). Her score (9) was in the normal range, corroborating her self-report that she is generally in a neutral to happy mood. She also participated in a mood-induction task that involved watching movie clips from sad movies. Her reactions were normal.

#### *Patient HT*

Patient HT (age 64 years) has focal bilateral hippocampal damage as evidenced by hyperintensities in the hippocampus on T2-weighted MR scans (left greater than right), as well as hyperintensity in the left parietal lobe. Damage was caused in the setting of a basilar meningitis and CNS vasculitis. Her family reports that her behavior is unchanged from the past except for a radical decline in her memory. She self-reports that she can no longer read novels or watch television because she cannot follow the story line. In addition, she sometimes gets confused when having a conversation, due to an inability to remember the topic of conversation. She has difficulty navigating and is not allowed to drive. Because her MRI showed a small left inferior parietal hyperintensity, her naming abilities were assessed with selected items from the Boston Naming Test that consists of the presentation of line drawings that vary from high to low frequency. No deficit was found (7/8). Her reading was assessed by requiring her to read aloud 16 printed words. No deficit was found (15/16).

#### *Patient CT*

Patient CT (age 68 years) has MTL damage as a result of encephalitis in 2001. His MR scans show damage to the left anterior hippocampus and portions of the entorhinal cortex and more limited damage to the right anterior hippocampus. He self-reports that he can no longer navigate and that he gets lost in his own neighborhood. His wife drives him to his neurology appointments. His naming abilities are intact as shown by his Boston naming score of 58/60. Although he is officially retired, he continues to work part-time as a skilled cabinetmaker. This ability has not declined since his neurological in-

sult, but he now must write everything down, being unable to commit details about style and size to memory.

#### *Equipment*

Participants were tested individually on either a laptop or a desktop computer. They sat at an unrestricted viewing distance of about 57 cm, at which distance 1 cm corresponds to 1° viewing angle. The experiment was programmed in MATLAB (Math Works, Natick, MA) with Psychtoolbox (Brainard, 1997) for Macintosh.

#### *Materials*

On each memory image several green (RGB 0 255 0) squares ( $1.1^\circ \times 1.1^\circ$ ) were presented on a uniformly gray background (RGB 127). The items were presented at randomly selected locations in a  $10 \times 10$  invisible matrix that subtended  $17.7^\circ \times 17.7^\circ$ . The stimuli were designed so that squares could not touch one another.

#### *Procedure*

Each trial started with a memory image containing  $n$ , 3 or 6, filled locations denoted by green squares lasting 1000 msec (Figure 1A). After a blank interval of 4000 msec, a probe array containing  $n - 1$  green squares was presented. The task was to recall which locations had been filled on the memory image and then decide which filled location was missing from the array on the probe image. Responses were made by unsped mouse click on the missing location. The probe display was cleared and accuracy feedback in the form of a high-pitched tone was given if the mouse click was within 5 mm of the outside edges of the green square (Keefe, Lees-Roitman, & Dupre, 1997; Dale, 1973). If the mouse click was beyond this limit, no tone was played. The next trial commenced after a 500-msec interval. The testing session began with 10 practice trials and was followed by 50 test trials, 25 of set size 3, 25 of set size 6. The dependent measure was mouse click distance, measured in

millimeters away from the center of the missing green square.

### Perceptual Control Task

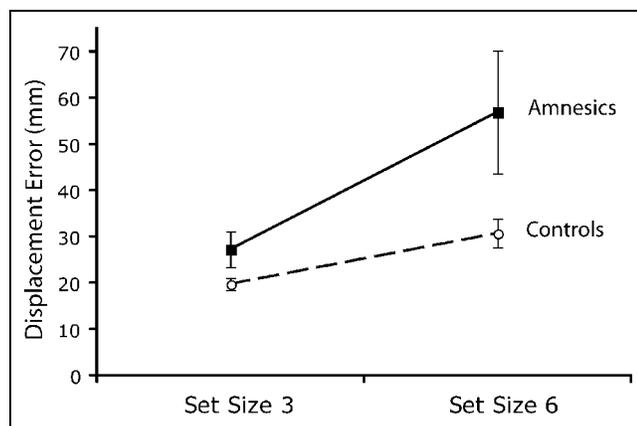
The computer screen was divided into halves, and a memory image appeared on the left half and a probe image appeared on the right half. Images were the same as used in the memory task, but smaller. The task was to look at the two images and to make an unspeeded mouse click on the missing square in the right image. The entry of the response cleared the screen, auditory feedback was given, and the next trial commenced after a 500-msec interval. There were 14 trials.

### Statistical Analyses

The dependent measure in Experiment 1 was displacement error in millimeters. For each experiment we report both parametric and nonparametric tests. The latter tests were performed because the sample size was small. The spatial memory (Experiment 1) and color memory (Experiment 3) tasks involve a mixed two-factor within-subject design for which a standard nonparametric test is not available. For these data, we first computed the  $F$  statistic under the standard mixed two-factor ANOVA model. Then the observed values were randomly permuted across the subjects and for the treatment (set size or delay interval) within each subject. The  $F$  statistics were recomputed for the permuted data set and a one-tailed count over 30000 replicates was used to compute the significance values (Manly, 1997; Legendre, Oden, Sokal, Vaudor, & Kim, 1990).

## Results and Discussion

Figure 3 shows the results of our analysis. A repeated measures ANOVA found a main effect of set size,



**Figure 3.** Results from the location WM task (Experiment 1). Spatial displacement (error) in millimeters as a function of set size. Error bars represent standard error of the mean.

$F(1,1) = 16.06, p < .004$ , due to worse performance with higher memory loads (21.9 vs. 38.6 mm off) and a main effect of group,  $F(1,8) = 12.44, p < .008$ , due to worse performance by the amnesics. The control group deviated an average of 25.2 mm from the correct location, whereas the amnesics deviated an average of 42.1 mm from the correct location. The interaction of group and set size did not provide evidence of differentially poor performance at higher memory loads,  $F(1,8) = 3.40, p = .10$ . The more stringent nonparametric test found an effect of group that approached significance ( $p = .067$ ), a main effect of set size ( $p = .0003$ ), and a nonsignificant interaction of group and set size ( $p = .092$ ). The difference between groups is somewhat less significant in the nonparametric test because one amnesic performed so poorly at Set Size 6 that the within-error term was inflated in the permutation test.

These results show that MTL amnesics have impaired visual WM for locations. This impairment was observed at both easy (Set Size 3,  $p < .04$ ) and difficult (Set Size 6,  $p < .02$ ) memory loads, discounting the explanation that the poorer performance by the amnesics was due to supraspan taxing of WM (Drachman & Arbit, 1966). However, there is a trend, albeit one that is not significant, toward an interaction between set size and group. It is possible that with more power, the interaction would become significant. The presence of an interaction does not undermine our main point—that amnesics are worse than controls at both set sizes; however, it does suggest that they may be additionally impaired by high memory load.

In the perceptual control task, average displacement error in the patient group was 6.6 mm, whereas in the control group it was 5.7 mm. This difference was not significant ( $p = .34$ ), showing that perceptual differences cannot account for the pattern of results exhibited on the visual WM task. Response times (RTs) were also examined and no difference was found ( $p = .45$ ).

## EXPERIMENT 2

Experiment 2 was designed to address two questions elicited by the findings of Experiment 1. First, are MTL amnesic's WM deficits limited to spatial WM? The hippocampus is intimately tied to spatial memory in rodents (O'Keefe & Nadel, 1978), and humans (Spiers, Burgess, Hartley, Vargha-Khadem, & O'Keefe, 2001; Holdstock, Mayes, et al., 2000; Bohbot et al., 1998; Nunn, Polkey, & Morris, 1998; Maguire, Burke, Phillips, & Staunton, 1996; Smith & Milner, 1989), so it is possible that the deficits found in Experiment 1 are specific to spatial forms of memory. A second question raised by the results of Experiment 1 is whether the results generalize to recognition tasks. Many prior studies have shown that MTL damage impairs recall more than

recognition (Yonelinas, 2002) so it is possible that WM deficits will only be observed in recall tasks. Given that visual WM is commonly studied with recognition tasks (Jiang, Olson, & Chun, 2000), it is important to test whether WM deficits exist for both recall and recognition tasks. Thus, Experiment 2 tested whether the WM deficit observed in Experiment 1 generalizes to nonspatial stimuli and to a recognition task. On each trial, participants were required to remember a single face. Memory load was kept low because prior studies have shown that face WM is difficult, with memory capacity in college students calculated to be about 1.5 faces (Eng, Chen, & Jiang, 2005). After a 4000-msec delay, a probe array containing either the same face or a different face was presented. The task was to indicate by keypress whether the face on the probe image matched the face held in memory.

## Methods

### Materials

Each face was presented on a uniformly black background at central fixation. The faces were drawn from a pool of 200 forward-facing male and female faces provided by the Max-Planck Institute ([faces.kyb.tuebingen.mpg.de/index.php](http://faces.kyb.tuebingen.mpg.de/index.php)). Faces were standardized to be of similar size, age, and race. Faces were Caucasian, in color, had neutral expressions, and were devoid of hair, glasses, or other nonface features. Each face subtended 3.8° of visual angle (37.5 mm).

### Procedure

Each trial started with an orienting cue consisting of the words "Get Ready to Remember" for 500 msec in the middle of the screen followed by a blank screen for 500 msec (see Figure 1B). This was followed by a memory image containing one face for 1000 msec, a retention interval consisting of a blank screen for 4000 msec, and then a probe image containing one face, lasting until a response was made. One half of the time the face matched the face from the memory image (= match trial), the other half of the time the face was different from the face on the memory image (= mismatch trial). Trial types were randomly interleaved. Responses were made by unspeeded keypress. Immediately after the response was made, the probe image was cleared and accuracy feedback was provided. The next trial commenced after a 500-msec interval. The testing session began with 12 practice trials and was followed by 96 trials.

### Perceptual Control Task

Two faces, drawn from a reserved portion of the face database that was tested in the memory task, were

presented side by side, and the task was simply to indicate by unspeeded keypress whether the faces were the same or different. Response entry cleared the screen and the next trial commenced after a 500-msec interval. There were 14 trials.

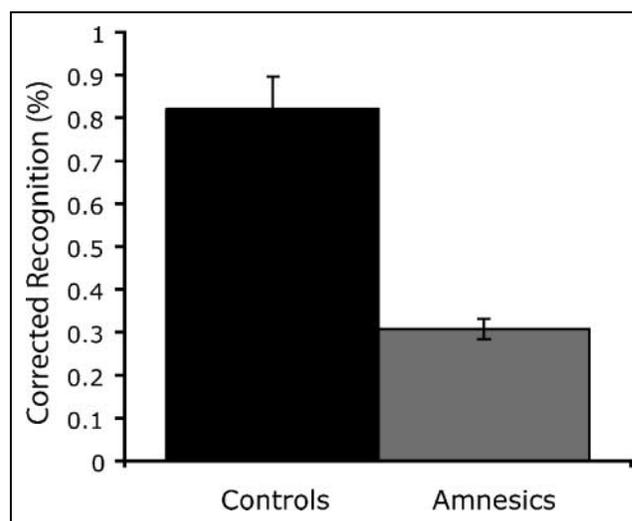
### Statistical Analyses

The dependent measure was corrected recognition (e.g., hit rate, responding "yes" on a match trial, minus false alarm rate, responding "yes" on a mismatch trial). As in Experiment 1, data were analyzed with both parametric and nonparametric tests. Unlike Experiment 1, the Mann-Whitney test was used to test the hypothesis of equality of the two groups.

## Results and Discussion

Figure 4 shows the results of our analysis. Corrected recognition for the control group was .82, whereas for the patients it was .31. This difference was significant, by both parametric ( $p < .003$ ) and nonparametric tests ( $p = .022$ ). These results show that MTL amnesics can barely remember a single face. These results extend the results reported in Experiment 1 to nonspatial stimuli and to a recognition task and suggest that the MTL may have a general role in visual WM.

Were the visual WM results actually due to a face perception deficit? The perceptual analogue to the memory task showed that accuracy was high in the amnesics (1.0) and controls (.99). This difference was not significant ( $p = .57$ ). In addition, RTs were examined and no difference was found ( $p = .91$ ).



**Figure 4.** Results from the face WM task (Experiment 2). Corrected recognition (hit rate – false alarm rate) as a function of epoch. Error bars represent standard error of the mean.

### EXPERIMENT 3

In this last experiment, we again assessed the generality of the WM deficits in amnesics by testing visual WM for color, using a task similar to that used by Jiang et al. (2000). In addition, we asked whether group differences in WM changed at lengthier delay intervals to assess the importance of memory decay. To test this, participants were asked to remember three colored squares over a delay of either 4000 or 8000 msec. Because we were interested in testing visual, not verbal WM, colors were chosen that were difficult to verbalize.<sup>1</sup> If MTL amnesics have impaired color WM, performance should be lower at both delays. If their WM impairment is due to accelerated memory decay, their performance should be worse at the 8000-msec delay.

### Methods

#### Materials

The stimuli consisted of three color patches presented on a gray background separated into quadrants by black crosshairs (see Figure 1C). Colors were defined using the RGB system. The stimulus colors tested were: orange-red [255, 90, 0], peach [238, 198, 0], chartreuse [150, 255, 0], aqua [71, 177, 153], cobalt [0, 114, 255], indigo [130, 0, 201], magenta [255, 0, 255], and burgundy [171, 11, 67]. Colors were pilot tested to ensure difficulty of applying verbal labels. Stimulus size was  $1.5 \times 1.5$  cm. Stimuli were randomly located in an invisible  $8 \times 8$  matrix with the constraint that each item occupy a unique quadrant. The memory image subtended  $15^\circ$  ( $15 \times 15$  cm). The crosshairs remained on the screen between trials and stimulus presentations to serve as a reference frame.

#### Procedure

Each trial started with an orienting cue consisting of the words “Get Ready to Remember” for 500 msec in the middle of the screen followed by a blank screen for 500 msec. This was followed by the memory image containing three colors, which lasted for 1000 msec. This was followed by a blank retention interval of 4000 or 8000 msec, and then a probe image containing three colors, one of which was cued by a surround box, which lasted until a response was made. The task was to report by keypress whether the cued color was the same as the color that had occupied that location on the memory image. Responses were made by unspeeeded keypress. The probe image was cleared and accuracy feedback was provided immediately after the response was made. The next trial commenced after a 500-msec interval. The testing session began with 12 practice trials and was followed by 72 test trials.

#### Perceptual Control Task

Two color memory images, each  $5 \times 5$  cm in size, were presented side by side, and the task was simply to indicate by unspeeeded keypress whether all colors were the same in both memory images or one was different. Response entry cleared the screen and the next trial commenced after a 500-msec interval. There were 14 trials.

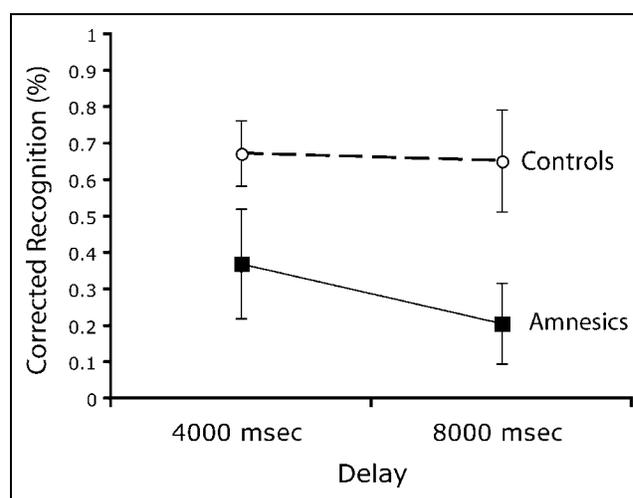
#### Statistical Analyses

The dependent measure was corrected recognition (e.g., hit rate, responding “yes” on a match trial, minus false alarm rate, responding “yes” on a mismatch trial). As in Experiment 1, data were analyzed with standard parametric tests and nonparametric permutation tests.

### Results and Discussion

Figure 5 shows the results of our analysis. The parametric tests showed that there was a main effect of group,  $F(1,8) = 5.4, p < .05$ , due to lower overall performance by the amnesics ( $M = .29$  vs.  $.66$ ). However, increased delay did not affect the performance of either group, as shown by the nonsignificant effect of delay, and Delay  $\times$  Group (all  $F$ s  $< 1, ns$ ). The nonparametric test results were similar: Significant differences were found between groups ( $p < .001$ ), but no effect was found of delay ( $p = .565$ ) or Delay  $\times$  Group ( $p = .816$ ).

Were the visual WM results actually due to a color perception deficit? In the perceptual analogue to the memory task, accuracy was high in the patient group (.98) and the control group (1.0) and did not differ ( $p = .42$ ). RTs were examined and no difference was found ( $p = .21$ ), showing that perceptual differences cannot



**Figure 5.** Results from the color WM task (Experiment 3). Corrected recognition (hit rate – false alarm rate) as a function of epoch. Error bars represent standard error of the mean.

account for the pattern of results exhibited on the color WM task.

## GENERAL DISCUSSION

In this article we asked the simple question of whether visual WM is reliant on the MTL. The results of three experiments suggest that the MTL must be intact to have accurate visual WM. In Experiment 1, patients with MTL amnesia had larger displacement errors when recalling spatial locations that had been seen just 4 sec earlier. There was a trend toward larger memory impairment when more information had to be retained; however, the interaction of group and delay did not reach significance.

In Experiment 2, amnesics had disproportionately poor recognition memory for a single face. This finding extends those reported by Levy and Squire (2005) by showing large face memory deficits at delays as short as 4 sec. Our stimuli had high inter-item similarity, potentially contributing to the large memory impairment observed in our patients.

In Experiment 3, amnesics had disproportionately poor WM for three colors and performance did not change with a lengthier (8000 msec) delay. We have replicated these results in a different group of MTL amnesics (Olson, Page, Chatterjee, & Verfaillie, 2005), adding validity to our findings.<sup>2</sup>

### Interpreting Memory Deficits at Short Delays

There are a number of ways to interpret the findings reported in this article. First, it is possible that MTL amnesics have problems encoding visual stimuli into memory due to some sort of perceptual problem. This idea seems unlikely given that our amnesics demonstrated intact perception of the stimuli used in the memory tasks—locations, faces, and colors (see Experiments 1, 2, and 3). One patient, patient MS, had extensive damage to anterior portions of the MTL, a typical result of herpes encephalitis. Of interest here is whether her perirhinal damage led to perceptual problems that impinged upon her WM performance. Monkeys with perirhinal damage exhibit object discrimination problems when large set sizes, different stimulus orientations, or multiple distracting stimuli are present at testing (Buckley, Charles, Browning, & Gaffan, 2004; Buckley & Gaffan, 1998). There is emerging evidence that damage to this area in humans can result in visual discrimination problems for certain classes of stimuli such as scenes (Lee, Buckley, et al., 2005; Lee, Bussey, et al., 2005). Patient MS did not show impaired perception of the stimuli tested in Experiments 1–3. In addition, she does not exhibit perception problems in everyday life and her performance on a number of visual perception tasks (e.g., DRS, line cancellation)

was very high. Taken together, these findings suggest that she, like the other two patients, has accurate visual perception.

A second possible explanation is that the amnesic's visual WM deficits were due to problems dealing with memory load. This hypothesis is implausible because in all experiments, memory load was lower than the upper bounds of visual WM capacity. Most people can accurately remember about seven locations (Jiang et al., 2000), four colors (Luck & Vogel, 1997), or 1.5 faces (Eng et al., 2005), suggesting that our results are not due to memory load.

A third explanation is that memory deficits at short delays are actually due to a damaged LTM system. This is because amnesia is typically defined as an impairment in LTM; thus, any memory impairment, regardless of delay, can be interpreted as an LTM impairment. For instance, Ryan and Cohen (2004) tested a mixed group of patients with amnesia (amnesia was due to basal forebrain or hippocampal damage) on a scene change detection task that had a short (1–2 sec) delay. The dependent measure was a variety of different eye movement measures. Although patients and controls did not differ on most eye-movement measures, on one measure, overall visual sampling of the scene (e.g., number of fixations, number of regions sampled, and number of transitions when shown a new scene), amnesics showed no change when shown old versus new scenes (Ryan & Cohen, 2004). The authors attributed this eye movement deficit to the influence of impaired LTM on WM. This argument is credible only if WM is viewed as the activated contents of LTM (Cowan, 1995; Ericsson & Kintsch, 1995). However, two of our experiments required subjects to remember novel information over short delays, so it is difficult to see how LTM could have significantly influenced WM in either normal subjects or patients with MTL damage.

The interpretation that is most parsimonious and the most difficult to refute is that portions of the MTL, possibly the hippocampus, are critical for accurate visual WM, refuting the hypothesis that the MTL is only involved in LTM (Alvarez et al., 1994; Cave & Squire, 1992). Because the stimuli used in our experiments were so different from one another, it must be assumed that the WM deficit is not particular to a class of stimuli but rather, is a general visual WM deficit. Our findings are consistent with recent neuroimaging findings that report activations of the hippocampus during visual WM tasks (Ranganath & D'Esposito, 2005). Some investigators interpreted these activations as establishment of an LTM trace for novel stimuli (Ranganath, Cohen, & Brozinsky, 2005; Ranganath & D'Esposito, 2005; Schon, Hasselmo, LoPresti, Tricarico, & Stern, 2004; Stern, Sherman, Kirchoff, & Hasselmo, 2001), whereas others suggest that they reflected WM maintenance for certain classes of stimuli (Mitchell, Johnson, Raye, & D'Esposito, 2000). It is difficult to give a strong interpretation to

these findings given that the majority of functional magnetic resonance imaging (fMRI) studies have not reported MTL activations during WM tasks (Postle, Stern, Rosen, & Corkin, 2000; Stern, Owen, et al., 2000; Cohen et al., 1997; Owen, Sahakian, Semple, Polkey, & Robbins, 1995). In addition, the inferential power of neuroimaging evidence is weak—it cannot tell us whether any given region is necessary for the cognitive process of interest.

Interpretive confusion has also plagued the amnesia literature with some investigators finding unexpected deficits in visual WM but interpreting such deficits as reflecting the beginning of LTM formation (Buffalo et al., 1998) or memory decline due to a change in context between study and test (Crane & Milner, 2005). The few studies that have reported visual WM deficits in patients with amnesia have suffered from shortcomings such as failure to rule out perceptual deficits as a causative factor (Holdstock, Shaw, & Aggleton, 1995; Owen et al., 1995) and grouping together patients with diencephalic and MTL amnesia (Ryan & Cohen, 2004; Holdstock, Shaw, & Aggleton, 1995) thereby precluding inferences to be drawn about the relationship of anatomy to behavior.

### **The Parietal Lobe and Visual Working Memory**

Patient HT had a small amount of left inferior parietal lobe damage and patient MS had damage to anterior portions of the temporal lobe, including the amygdala (see Figure 2). Were visual WM deficits due to damage to these other regions? Although the neural region most closely associated with spatial WM is the parietal lobe (Carlesimo, Perri, Turriziani, Tomaiuolo, & Caltagirone, 2001), there are several reasons why we do not believe HT's parietal damage accounted for her poor WM performance. First, deficits in spatial WM are associated with right, not left parietal damage. Patients with contralesional neglect due to varied right parietal lobe lesions fail to attend to the left side of space and have recently been shown to have impaired spatial memory spans (Malhotra et al., 2005; Pisella, Berberovic, & Mattingley, 2004). Second, HT's parietal lesion was very small; patients with right parietal damage leading to spatial WM deficits tend to have very large lesions (Malhotra et al., 2005; Pisella et al., 2004; Carlesimo et al., 2001). Third, HT had impaired location, face, and color WM, whereas previous reports suggest that parietal damage only affects spatial forms of WM (Pisella et al., 2004). Last, the other two patients tested in these experiments did not have damage to the parietal lobe yet exhibited a similar pattern of WM deficits as patient HT.

### **The Role of the Medial Temporal Lobe in Working Memory: How General Is the Effect?**

How general are the findings reported in this article? There are two senses in which this question should be

approached: generality in regard to other MTL amnesics and generality to other WM tasks. In regard to the former sense, the findings reported here were robust and consistent within our patient group, suggesting that the findings can be generalized to other patients with MTL amnesia. Future studies will need to test whether these results generalize to patients with diencephalic amnesia. In regard to the second sense, we speculate that our findings may be limited to certain classes of stimuli. First, it is likely that verbal WM does not rely on the MTL (Cave & Squire, 1992; Baddeley & Warrington, 1970; Wickelgren, 1968). Verbal information can be overtly rehearsed and various strategies enable one to easily remember verbal information. In addition, verbal information tends to be semantically rich, allowing for the creation of a multifaceted memory representation. In contrast, visual information is difficult to rehearse overtly and when the stimuli are unfamiliar, the representation is semantically sparse. Although there has been at least one fMRI study reporting hippocampal activations to verbal memory encoding, it is thought that these activations reflected relational binding of word triplets rather than verbal memory per se (Davachi & Wagner, 2002).

Second, it is unlikely that all types of visual WM rely on the MTL. We have observed (Olson et al., 2005) that visual WM for common objects is intact in MTL amnesia, replicating findings from the developmental amnesic, "Jon," who has impaired visual LTM for visual topography but intact memory for objects (Spiers et al., 2001). Common objects possess a rich set of attributes, such as being familiar, verbalizable, semantically rich, and highly differentiated. Various computational models have proposed that the hippocampus acts as a pattern separator, amplifying differences between stimuli and events. If true, this would predict that hippocampal damage would cause larger WM deficits for stimuli with subtle differentiation, such as faces, as compared to stimuli with high levels of differentiation, such as common objects.

Other researchers have proposed that the MTL is only critical for remembering novel, as compared to familiar, stimuli (Ranganath & D'Esposito, 2005; Schon et al., 2004; Stern, Sherman, et al., 2001). The results of Experiment 3 do not support this proposal, as colors are a familiar class of stimuli. Most color exemplars, however unusual, have been seen before. Alternatively, it is possible that the MTL is most necessary when novel information must be retained in memory because novel information is relatively undifferentiated. In contrast, familiar stimuli are more differentiated and thus can be categorized and recognized with the help of preexisting cortical representations. As such, the MTL may be necessary for maintaining and differentiating novel information in WM, whereas some combination of cortical structures and the MTL can be used to maintain familiar stimuli in WM (Ranganath et al., 2005; Schon et al., 2004).

Our working hypothesis is that the MTL always participates in WM encoding but that it is critical in only some circumstances, one being when verbal rehearsal or semantic memory cannot be used to support WM maintenance. Verbal rehearsal circumvents the need to maintain an active memory representation; instead, one must simply remember to keep the verbal loop active. It is well known that symbolic recoding of arbitrary stimuli can increase WM performance (Chase & Ericsson, 1981). Thus, semantic memory does not circumvent WM, but rather enriches the representation, affording numerous retrieval strategies.

### Distinguishing Memory Systems

The results presented in this article prompt consideration of whether visual WM can be clearly distinguished from visual LTM. The distinction between these entities is somewhat hazy (Crowder, 1982). Visual representations are tightly linked to information about orientation and the structural relationship between object parts, regardless of delay interval (Hollingworth, 2004). Moreover, visual representations are insensitive to information about absolute size and precise object contours, again, regardless of delay interval (Hollingworth, 2004). The most satisfying evidence for the independence of short- and long-term forms of visual memory comes from studies showing differences in capacity and a different group of studies showing differences in relevant neural structures.

The capacity of visual WM is quite small (Irwin, 1992), whereas the capacity of visual LTM is very large (Nickerson, 1968). However, the testing format of visual WM requires great precision, perhaps at a cost to capacity, because one is required to compare two images that differ in some small way. In comparison, tests of visual LTM typically use old/new recognition paradigms in which one can rely on familiarity, rather than direct comparison of stored visual memories.

The second piece of evidence used to argue for their independence—differences in neural structures—is called into question by the data presented in this article. Although prior studies have reported that MTL amnesics have intact visual WM (Levy & Squire, 2005; Alvarez et al., 1994; Cave & Squire, 1992), interpretation of these findings is clouded by ceiling effects (Ringo, 1991) and the use of stimuli that encourage verbal encoding and rehearsal. Our failure to find intact WM performance at short delays suggests that WM and LTM are not completely independent.

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### Notes

1. Other investigators have used concurrent verbal memory loads to minimize the possibility that colors are remembered by their verbal labels (Olson & Jiang, 2002; Luck & Vogel, 1997). This type of task design is difficult to implement in older and patient populations and introduces additional variables that may confound the effect of interest. Because of this, we chose to limit verbal encoding by instructing study participants to remember the stimuli visually, by presenting stimuli quickly, and by using colors with low namability.
2. Because subjects were required to remember colors plus the quadrant in which they appeared, Experiment 3 can be considered a test of memory for color-location conjunctions. However, because we did not directly compare performance in the color memory task to one in which conjunctions were manipulated or absent, the data from this experiment do not readily enlighten the topic of the MTL involvement in conjunction memory.

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