Memory deficits for implicit contextual information in amnesic subjects with hippocampal damage

Marvin M. Chun[1,2] and Elizabeth A. Phelps[1,3]

[1] Department of Psychology, Yale University, PO Box 208205, New Haven, Connecticut 06520-8205, USA

[2] Present address: Department of Psychology, Vanderbilt University, 531 Wilson Hall, Nashville, Tennessee 37240, USA

[3] Present address: Department of Psychology, New York University, 6 Washington Place, New York, New York, 10003, USA

Correspondence should be addressed to M.M.C. (marvin.chun@vanderbilt.edu)

The role of the hippocampus and adjacent medial temporal lobe structures in memory systems has long been debated. Here we show in humans that these neural structures are important for encoding implicit contextual information from the environment. We used a contextual cuing task in which repeated visual context facilitates visual search for embedded target objects. An important feature of our task is that memory traces for contextual information were not accessible to conscious awareness, and hence could be classified as implicit. Amnesic patients with medial temporal system damage showed normal implicit perceptual/skill learning but were impaired on implicit contextual learning. Our results demonstrate that the human medial temporal memory system is important for learning contextual information, which requires the binding of multiple cues.

The hippocampus and adjacent medial temporal lobe (entorhinal, perirhinal and parahippocampal cortex) are critical for encoding and retrieving information[1]. In humans, the integrity of these medial temporal lobe structures (termed the hippocampal system) enables conscious recollection or recognition of facts and events, known as explicit or declarative memory[2–4]. Thus, damage to the medial temporal lobe system produces striking explicit-memory impairments, as in the well-known amnesic patient, HM[5]. Such explicit-memory deficits can be contrasted with intact memory capacity for information that does not require such conscious access, termed implicit, nondeclarative or procedural memory[2,3]. Amnesic patients typically show preserved learning performance for a variety of perceptual, motor or cognitive skills[6–8]. These functional dissociations provide strong evidence that our ability to benefit from past experience is subserved by multiple memory systems within the brain, each specialized for different task and information demands[9,10].

Although the notion of multiple memory systems is widely supported, it can be difficult to reliably identify a particular memory process or task as 'conscious' or 'explicit' or to apply such distinctions to animals. Eschewing memory distinctions based on accessibility to awareness, researchers have proposed that the hippocampus and medial temporal lobe structures are important for encoding what has been variously described as contextual[11,12], configural[13], spatio-configural[14] or relational[15] information. Although differences exist among these characterizations of medial temporal lobe function, a common theme is that the hippocampus and its neighboring structures are important for binding configurations of multiple cues in memory, necessary for encoding contextual information from the environment[16]. In animals, such contextual encoding subserves various learning capacities such as spatial navigation and context-dependent learning. In humans, contextual (relational) encoding is proposed to mediate conscious retrieval of memories of past facts and events[15,17].

Memory performance on contextual tasks (and episodic tasks that depend on relational information) is typically accompanied by awareness of memory traces. Accordingly, it is unclear whether the key feature of hippocampus-dependent tasks is that they are context dependent or that they are accessible to awareness. That is, can a contextual task be hippocampus dependent but inaccessible to awareness? Amnesic patients are impaired in learning novel context associations that prime (facilitate) word-stem completion tasks[18,19]. However, 'implicit' retention of contextual associations was often correlated with some degree of explicit awareness in normal controls in these tasks. Hence, any impairment in amnesics may be attributed to the task's dependence on conscious, explicit memory processes[20,21]. In another protocol, indirect eye movement measures show that amnesic patients have deficits in remembering relational information (S.D. Whitlow *et al.*, *Soc. Neurosci. Abstr.* **21**, 754, 1995), but the use of an indirect measure *per se* does not rule out the possibility that performance was mediated by conscious memory retrieval.

To circumvent these limitations, we examined human amnesics' performance in a task that requires intact memory for contextual information, which can be characterized as implicit. Our contextual cuing protocol illustrates how implicit memory for visuospatial context information facilitates perceptual processes such as visual search[22]. Subjects searched visual displays for a rotated T target presented among rotated L distractors (**Fig. 1**), a classic visual task that requires effortful scrutiny (focused spatial attention) of the visual array[23]. In each session, a set of arbitrary, new visual contexts was generated by manipulating the spatial configurations of the items in the search display (**Fig. 1**). To examine contextual learning, we repeated a set of spatial contexts across blocks of trials throughout the session (old condition). In old displays, targets appeared in consistent locations within their invariant contexts so that visual context predicted target location. Search performance was compared
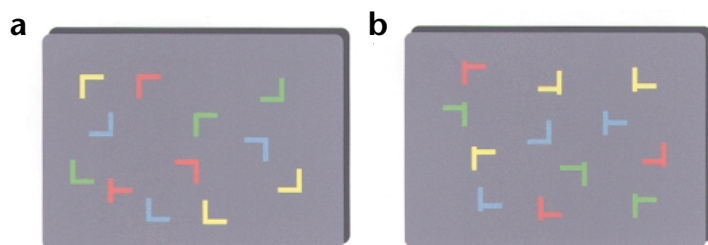
Fig. 1. Two sample displays from our contextual cuing visual search protocol. The task was to search for a T, rotated to the right or to the left and presented among rotated L distractors. The spatial configuration and colors of these distractor items defined the visual context of the target. **(a)** Sample search display for the task tested on the amnesic and first control group. **(b)** Sample search display for the more difficult search task tested on a second control group, in which the L distractors were made to look more similar to the T target.

between targets appearing in old displays and those appearing in new displays, randomly generated in each block as a baseline.

This contextual cuing protocol reveals two learning components. The first, context-independent component is standard perceptual/skill learning, a facilitation in search reaction time (RT)[24]. The second, context-dependent learning component is revealed as faster performance for detecting targets in old displays relative to new baseline displays. This contextual cuing benefit represents learning of visual context information, which guides spatial attention to the target location, facilitating search for targets in old displays[22]. Importantly for present purposes, the memory for context was implicit. Normal subjects were at chance for explicitly discriminating old displays from new displays in recognition tests presented at the end of each experimental session.

Thus, we can decouple conscious, explicit learning from contextual, relational learning. If conscious accessibility and awareness determines whether the hippocampal system participates in a memory task, then amnesic subjects with explicit memory deficits should show preserved implicit contextual cuing, that is, faster search performance for old displays. Alternatively, if the hippocampal system is important for encoding contextual information, whether memory traces are consciously accessible or not, then amnesic patients should not demonstrate a contextual cuing benefit for targets in old contexts.

RESULTS

Each block of 24 trials contained a randomly mixed set of 12 old displays and 12 new displays. Subjects performed 20 blocks of search. Importantly, subjects were simply instructed to perform the search task; we gave no instructions whatsoever to learn the displays. In all experiments, accuracy averaged above 98% correct and did not differ between groups ($p > 0.10$) or between old and new conditions ($p > 0.10$).

As expected[22], the search performance of ten control subjects showed two learning components (**Fig. 2**). Overall search RT decreased over time ($p < 0.001$) by perceptual/skill learning, independent of context information. In addition, two statistical analyses revealed faster performance for detecting targets in old displays relative to new displays, indicating context-dependent learning. This benefit for search in old displays emerged only with experience (**Fig. 2**; epoch (1–4) × condition (old, new), $p < 0.05$). Following a previous convention[22], we defined the magnitude of contextual learning as the difference in performance between the old and new conditions over the latter half of the experimental session only (epochs 3 and 4). This analysis confirmed faster performance in the old condition (48 ms difference, $p < 0.002$). Thus, control subjects encoded the visual contexts of targets as they performed the search task, and this contextual information benefitted search performance as learning progressed.

An important feature of this learning protocol is that the memory representations for context were implicit. After the search task,

subjects were given a test of explicit recognition and awareness. Control subjects performed at chance in discriminating old displays from new displays (hit rate, 0.37 ± 0.09 s.e.; false-positive rate, 0.32 ± 0.08, $p > 0.10$). In addition, although 6 of 10 subjects reported noting that repetitions had occurred, they did not differ from the remaining subjects in recognition test performance (aware group, mean proportion correct, 0.54; unaware group, 0.49, $p > 0.10$), and the magnitude of contextual cuing was indistinguishable between the two groups (aware group, 52 ms; unaware group, 43 ms, $F < 1$). This replicates previous studies with more subjects, in which report of awareness never correlated with recognition performance or magnitude of contextual cuing[22]. Moreover, in a separate study (M.M. Chun & Y. Jiang, unpublished data), subjects could not guess which quadrant of the display was most likely to contain the target in either old or new displays. In sum, contextual representations were implicit, but they nevertheless facilitated search performance.

Returning to our predictions, if the hippocampal system is important for encoding contextual, relational information, independent of whether it is consciously accessible or not, then amnesic patients should not demonstrate contextual cuing. Indeed, contextual cuing was absent in the amnesic subjects. Search perfor-
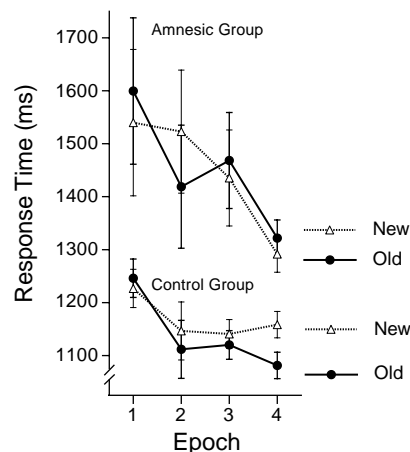

Fig. 2. Mean correct response time to localize and discriminate targets in old versus new configurations as a function of epoch (groups of five blocks), plotted separately for the control group ($n = 10$) and the amnesic group ($n = 4$). For the control group, implicit learning of spatial configurations (context) and their associated target locations facilitated search performance in the old condition, as shown by the difference between the old and new conditions with increasing epoch. The amnesic patients showed standard perceptual/skill learning (performance improvements over time) but no contextual cuing, suggesting a selective impairment for learning contextual information. Error bars indicate within-subject 95% confidence intervals[34], calculated separately for each epoch.

mance for targets appearing in old versus new contexts was nearly identical throughout the session (**Fig. 2**). Amnesic patients showed no contextual cuing in the second half of the experiment, collapsed across epochs 3 and 4 ($p > 0.10$), and old versus new condition performance was constant throughout the session (epoch × condition, $p > 0.10$). Thus, in comparison to the control group, amnesic patients did not show contextual cuing for search performance in the second half of each session (group × condition, $p < 0.005$; across all 4 epochs, group × condition × epoch, $p < 0.05$).

The absence of contextual learning did not reflect a general learning impairment, as search performance improved with increasing epoch, demonstrating intact perceptual/skill learning ($p < 0.01$). Thus in the same task, our amnesic subjects produced the standard signature of preserved implicit memory or perceptual/habit learning. Only contextual cuing was abolished, suggesting selective impairment for encoding contextual information. The amnesic group also performed at chance in the recognition test ($p > 0.10$). Although their hit rate was higher than their false positive rate (0.64 versus 0.42), this was mainly driven by one amnesic patient who had a hit rate of 0.83 and a false positive rate of 0.33. This patient did not show contextual cuing in the reaction time task and did not report awareness of the repetition manipulation. Thus, hippocampus and neighboring medial temporal lobe damage impaired contextual learning in a task that can be defined as implicit.

As in other studies, our amnesic group performed the search task more slowly than the control group ($p < 0.05$). To rule out the possibility that the absence of contextual cuing may have been caused by general perceptual/cognitive slowing, we tested a separate group of control subjects ($n = 5$) on a more difficult version of our task (see Methods; **Fig. 1b**). Significantly more contextual cuing was obtained in this control group relative to the amnesic group (**Fig. 3**; group × condition for epochs 3 and 4, $p < 0.05$), even though search RT was slowed down relative to the amnesic subjects. Hence, the lack of contextual cuing in our amnesic group was not due to slow search performance.

DISCUSSION

This study introduced a new protocol for studying the neural substrate of contextual encoding in humans. We showed that such contextual learning depended on the hippocampus and neighboring medial temporal lobe structures. An important feature of our task was that memory traces for novel spatial context were implicit. Thus, our study demonstrates that the hippocampal system mediates contextual (relational) encoding in humans, without having to evoke conscious memory processes.

An alternative view is that our amnesic patients successfully encoded spatial context information but were impaired at learning the novel associations between spatial contexts and embedded target locations. As noted earlier, this seems unlikely for two reasons. Previous demonstrations of novel association learning deficits[18,19] have used tasks that may require explicit memory to perform, as normal control subjects show explicit awareness of stimulus contingencies[20,21]. More importantly, amnesic patients can learn novel single associations in more sensitive tasks that rely on perceptual identification, rather than stem completion, especially when the information is presented over multiple trials[21,25,26] as in the present contextual cuing task. These considerations indicate that our patients were impaired at learning novel spatial configurations (which involves binding several relational associations between objects), rather than novel simple associations between global context and target locations.

Whether accessible to awareness or not, contextual information is clearly important for a variety of perceptual and cognitive oper-
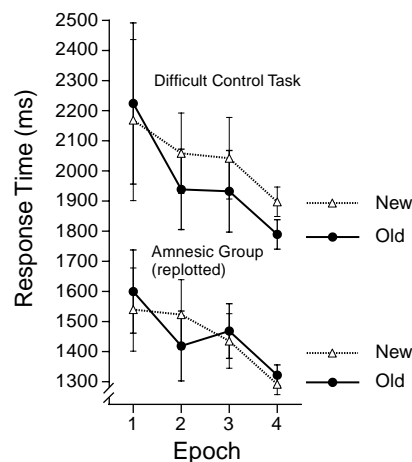

Fig. 3. Mean correct response time for a second group of controls ($n = 5$) on a more difficult version of the search task (**Fig. 1b**). Although this version slowed search performance, control subjects still showed significant contextual cuing. Data from amnesic patients are replotted from Fig. 2 for comparison. Error bars indicate within-subject 95% confidence intervals[34], calculated separately for each epoch.

ations such as object identification, scene processing, navigation and episodic memory[27,28]. Our findings are consistent with demonstrations that lesions to medial temporal lobe structures produce deficits for object-in-place learning and context-dependent object learning in non-human primates[29,30]. Our new results also support evidence that the hippocampal system may be important for some forms of priming. For example, voice-specific priming in identification tasks of low-pass filtered auditory stimuli may require binding of word-specific phonological information and speaker-specific acoustic information, thus perhaps explaining why it is impaired in amnesia[31]. More broadly, our work supports theoretical views of medial temporal lobe function based on its role in binding contextual cues in the environment[11–17,32]. Such computational capacities for contextual (relational, declarative, configural) encoding may support explicit, episodic memory in humans[15,17].

METHODS

Five amnesic patients were tested. Data from one patient were excluded due to an excessively high error rate. Amnesia resulted from an anoxic episode in two patients and from encephalitis in the other two. Hippocampal damage was confirmed by MRI for the two encephalitic patients, both of whom also showed some additional atrophy of the surrounding temporal lobe consistent with this etiology. A CAT scan revealed bilateral hippocampal damage in one of the anoxic patients. The other anoxic patient is suspected to have hippocampal damage on the basis of etiology. The four patients averaged 48 years of age (range, 41 to 55 years) with an average of 15 years of education. Their mean full scale IQ was 99 on the Wechsler Adult Intelligence Scale. Three of the four patients scored below 50 and one patient scored 57 on the Wechsler Memory-Scale Delay subtest. All patients scored normally on the Wisconsin card sort task of frontal lobe functioning. The 15 control subjects averaged 47 years of age and 16 years of education. Ten control subjects were tested in the first experiment, and five were tested in the second experiment. Informed consent was obtained after the nature and possible consequences of the studies were explained. The experimental protocol was approved by the Yale University Faculty of Arts and Sciences Human Subjects Committee.

The experiment was conducted on a Macintosh Powerbook 5300 with active matrix LCD screen. Unrestrained viewing distance was approximately 50 cm. Each search display contained 12 items, which could appear

within a grid of 8 × 6 locations. The background was set at gray. In generating the visual search arrays, the position of each item was jittered in a random location within its cell in the rectangular array to prevent colinearities with other stimuli. (See ref. 22 for details.) Each display contained an equal number of red, green, blue and yellow colored items. The color configurations were preserved across repetitions.

Each trial started with a small dot appearing in the middle of a computer screen for fixation. After a brief pause of 500 ms, the array of stimuli (**Fig. 1**) appeared on the screen. The subjects were asked to search for a rotated 'T' target as quickly and accurately as possible. Every trial contained a target, which was either rotated 90 degrees in the clockwise direction so that the base pointed left (left-pointing target) or rotated 90 degrees in the counter-clockwise direction (right-pointing target). Upon detection of the target, subjects were instructed to press one of two labeled response keys corresponding to the orientation of the localized target. The 'z' and '/' keys were to be pressed for the left-pointing and right-pointing targets, respectively. The response cleared the display with a blank screen, and auditory feedback was given for errors. A mandatory 10-s break was given at the end of each block. ANOVA was used for statistical analyses of RT, based on trials performed correctly within 6 s.

Target identities (pointing left or right) were fully randomized across trials and repetitions of old displays to ensure correct localization and to eliminate any context–response contingencies. Hence, any learning effects cannot be attributed to motor response learning, distinguishing contextual cuing from serial reaction time tasks of skill learning[33].

Each subject performed 20 blocks of the search task. Each block contained 24 intermixed trials of 12 old and 12 new displays. Thus, a total of 12 old and 240 new search arrays were used. To rule out location probability effects, the target appeared equally often in each of 24 possible locations throughout the experiment: 12 locations were used in repeated old configurations, and the other 12 were used in unrepeated new configurations. Hence, any difference in performance between old and new locations must be attributed to learning of invariant contextual information rather than target location *per se*. In addition, we equated the eccentricity of targets between the old and new conditions. The experimental session was preceded by a practice block of 24 trials.

Immediately after block 20 of the search task, we administered an explicit recognition test to assess awareness of the contextual displays. The interval between the recognition test and the last search block was comparable to the interval between successive blocks of the search task. The explicit recognition test procedure was identical to that used in a prior contextual cuing study[22]. Subjects were first asked "Did you notice whether certain configurations (spatial layout) of the stimuli were being repeated from block to block (press 'y' or 'n')?" If they answered yes, they were further asked to estimate when (during which block of trials, 1–20) they think they began to notice the repetition manipulation. They were also asked if they explicitly tried to memorize any of the configurations (none did). Regardless of whether they reported awareness of the repetition manipulation, all subjects were given one block of trials containing 12 old displays from the search task, and 12 new displays constructed in an identical manner. Subjects were asked to press 'y' if they recognized a particular display as having been repeated across blocks throughout the experiment, and 'n' if they did not. They were encouraged to make their best guess, and they were assured that they were under no time pressure to respond quickly. Due to computer error, the recognition test data from one control and one amnesic subject (tested on the same day) were not included in this analysis.

In the more difficult version of our task, tested in five control subjects, we changed the shape of the distractor items to be more visually similar to the T targets (**Fig. 1b**). This makes search less efficient, producing longer reaction times. Essentially all other aspects of the experiment (stimulus sequences, configurations, target locations and so forth) were identical to those used in the first experiment.

ACKNOWLEDGEMENTS

1. Squire, L. R. & Zola-Morgan, S. The medial temporal lobe memory system. *Science* **253**, 1380–1386 (1991).
2. Cohen, N. J. & Squire, L. R. Preserved learning and retention of pattern-analyzing skill in amnesia: dissociation of knowing how and knowing that. *Science* **210**, 207–210 (1980).
3. Schacter, D. L. Implicit memory: History and current status. *J. Exp. Psychol. Learn. Mem. Cogn.* **13**, 501–518 (1987).
4. Clark, R. E. & Squire, L. R. Classical conditioning and brain systems: The role of awareness. *Science* **280**, 77–81 (1998).
5. Scoville, W. B. & Milner, B. Loss of recent memory after bilateral hippocampal lesions. *J. Neurol. Neurosurg. Psychiatry* **20**, 11–21 (1957).
6. Warrington, E. K. & Weiskrantz, L. New method of testing long-term retention with special reference to amnesic patients. *Nature* **217**, 972–974 (1968).
7. Corkin, S. Acquisition of motor skill after bilateral medial temporal-lobe excision. *Neuropsychologia* **6**, 255–265 (1968).
8. Knowlton, B. J., Ramus, S. J. & Squire, L. R. Intact artificial grammar learning in amnesia: dissociation of classification learning and explicit memory for specific instances. *Psychol. Sci.* **3**, 172–179 (1992).
9. Tulving, E. & Schacter, D. L. Priming and human memory systems. *Science* **247**, 301–306 (1990).
10. Squire, L. R., Knowlton, B. & Musen, G. The structure and organization of memory. *Annu. Rev. Psychol.* **44**, 453–495 (1993).
11. Hirsh, R. The hippocampus and contextual retrieval of information from memory: a theory. *Behav. Biol.* **12**, 421–444 (1974).
12. Kim, J. J. & Fanselow, M. S. Modality-specific retrograde amnesia of fear. *Science* **256**, 675–677 (1992).
13. Sutherland, R. J. & Rudy, J. W. Configural association theory: The role of the hippocampal formation in learning, memory, and amnesia. *Psychobiology* **17**, 129–144 (1989).
14. O'Keefe, J. & Nadel, L. *The Hippocampus as a Cognitive Map* (Clarendon, Oxford, 1978).
15. Cohen, N. J. & Eichenbaum, H. *Memory, Amnesia, and the Hippocampal System* (MIT Press, Cambridge, Massachusetts, 1993).
16. Johnson, M. K. & Chalfonte, B. L. in *Memory Systems 1994* (eds. Schacter, D. L. & Tulving, E.) 311–350 (MIT Press, Cambridge, Massachusetts, 1994).
17. Squire, L.R. Memory and the hippocampus: A synthesis from findings with rats, monkeys, and humans. *Psychol. Rev.* **99**, 195–231 (1992).
18. Graf, P. & Schacter, D. L. Implicit and explicit memory for new associations in normal and amnesic subjects. *J. Exp. Psychol. Learn. Mem. Cogn.* **11**, 501–518 (1985).
19. Shimamura, A. P. & Squire, L. R. Impaired priming of new associations in amnesia. *J. Exp. Psychol. Learn. Mem. Cogn.* **15**, 721–728 (1989).
20. Gabrieli, J. D. Cognitive neuroscience of human memory. *Annu. Rev. Psychol.* **49**, 87–115 (1998).
21. Gabrieli, J. D., Keane, M. M., Zarella, M. M. & Poldrack, R. A. Preservation of implicit memory for new associations in global amnesia. *Psychol. Sci.* **8**, 326–329 (1997).
22. Chun, M. M. & Jiang, Y. Contextual cueing: Implicit learning and memory of visual context guides spatial attention. *Cognit. Psychol.* **36**, 28–71 (1998).
23. Wolfe, J. M., Cave, K. R. & Franzel, S. L. Guided search: An alternative to the feature integration model for visual search. *J. Exp. Psychol. Hum. Percept. Perform.* **15**, 419–433 (1989).
24. Treisman, A., Vieira, A. & Hayes, A. Automaticity and preattentive processing. *Am. J. Psychol.* **105**, 341–362 (1992).
25. Musen, G. & Squire, L. R. Implicit learning of color–word associations using a Stroop paradigm. *J. Exp. Psychol. Learn. Mem. Cogn.* **19**, 789–798 (1993).
26. Musen, G. & Squire, L. R. On the implicit learning of novel associations by amnesic patients and normal subjects. *Neuropsychology* **7**, 119–135 (1993).
27. Biederman, I. Perceiving real-world scenes. *Science* **177**, 77–80 (1972).
28. McClelland, J. L. & Rumelhart, D. E. An interactive activation model of context effects in letter perception: Part I. An account of basic findings. *Psychol. Rev.* **88**, 375–407 (1981).
29. Gaffan, D. Scene-specific memory for objects—A model of episodic memory impairment in monkeys with fornix transection. *J. Cognit. Neurosci.* **6**, 305–320 (1994).
30. Doré, F. Y., Thornton, J. A., White, N. M. & Murray, E. A. Selective hippocampal lesions yield nonspatial memory impairments in rhesus monkeys. *Hippocampus* **8**, 323–329 (1998).
31. Schacter, D. L., Church, B. & Bolton, E. Implicit memory in amnesic patients: Impairment of voice-specific priming. *Psychol. Sci.* **6**, 20–25 (1995).
32. Mayes, A. R. Memory and amnesia. *Behav. Brain. Res.* **66**, 29–36 (1995).
33. Nissen, M. J. & Bullemer, P. Attentional requirements of learning: Evidence from performance measures. *Cognit. Psychol.* **19**, 1–32 (1987).
34. Loftus, G. R. & Masson, M. E. Using confidence intervals in within-subject designs. *Psychonom. Bull. Rev.* **1**, 476–490 (1994).