

# Comparison of explicit and incidental learning strategies in memory-impaired patients

Christine N. Smith<sup>a,b</sup>, Zhisen J. Urgolites<sup>a,b</sup>, Ramona O. Hopkins<sup>c,d</sup>, and Larry R. Squire<sup>a,b,e,f,1</sup>

<sup>a</sup>Veterans Affairs San Diego Healthcare System, San Diego, CA 92161; <sup>b</sup>Department of Psychiatry, University of California at San Diego, La Jolla, CA 92093; <sup>c</sup>Department of Psychology and Neuroscience Center, Brigham Young University, Provo, UT 84143; <sup>d</sup>Department of Medicine, Pulmonary and Critical Care Division, Intermountain Medical Center, Murray, UT 84143; and Departments of <sup>e</sup>Neurosciences and <sup>f</sup>Psychology, University of California at San Diego, La Jolla, CA 92093

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**Declarative memory for rapidly learned, novel associations is thought to depend on structures in the medial temporal lobe (MTL), whereas associations learned more gradually can sometimes be supported by nondeclarative memory and by structures outside the MTL. A recent study suggested that even rapidly learned associations can be supported by structures outside the MTL when an incidental encoding procedure termed “fast mapping” (FM) is used. We tested six memory-impaired patients with bilateral damage to hippocampus and one patient with large bilateral lesions of the MTL. Participants saw photographs and names of animals, plants, and foods that were previously unfamiliar (e.g., mangosteen). Instead of asking participants to study name–object pairings for a later memory test (as with traditional memory instructions), participants answered questions that allowed them to infer which object corresponded to a particular name. In a second condition, participants learned name–object associations of unfamiliar items by using standard, explicit encoding instructions (e.g., remember the mangosteen). In FM and explicit encoding conditions, patients were impaired (and performed no better than a group that was given the same tests but had not previously studied the material). The same results were obtained in a second experiment that used the same procedures with modifications to allow for more robust learning and more reliable measures of performance. Thus, our results with the FM procedure and memory-impaired patients yielded the same deficits in learning and memory that have been obtained by using other more traditional paradigms.**

amnesia | long-term memory

Damage to the hippocampus, as well as larger medial temporal lobe (MTL) lesions, severely impairs the formation of declarative memory. Declarative memory can be expressed flexibly and is accessible to conscious recollection (1–3). There has been interest in the development of new techniques that might benefit the learning of memory-impaired patients with MTL lesions. Recently, a technique was described that appeared to allow patients to acquire information as readily as healthy individuals (4). The technique is based on a mechanism termed “fast mapping” (FM), which is hypothesized to support the rapid learning of vocabulary in young children (5, 6).

A key feature of FM is that the learning is incidental. In the study by Sharon et al. (4), participants saw photographs and names of animals, plants, and foods that were previously unfamiliar (e.g., mangosteen, tenrec). Instead of asking participants to study the name–object pairings for a later memory test (as with traditional memory instructions), participants answered questions that allowed them to infer which object corresponded to a particular name. Memory-impaired patients readily learned the names of the test items as well as controls, and what they learned exhibited some of the characteristics of declarative memory. For example, the knowledge could be expressed flexibly, and (for controls and the one patient who was tested) confidence ratings were higher for correct answers than for incorrect answers (i.e., participants had conscious access to what had been learned). The authors suggested

that the information had been acquired directly into neocortex, independent of the MTL.

Because the reported findings are exceptional, we have explored the FM technique further in two experiments. We tested seven memory-impaired patients with bilateral lesions limited to the hippocampus or with larger MTL lesions. We first investigated the FM learning procedure in comparison with traditional learning procedures, as in Sharon et al. (4). In a second experiment, we used the same two learning procedures but with modifications to allow for more robust learning and more reliable measures of performance. Neither experiment revealed any benefit of FM learning for the patients.

## Results

**Experiment 1. Recognition.** At 10 min after study, controls in the FM condition (Fig. 1A) performed marginally better than the patient and baseline groups at selecting the correct study item ( $53.1 \pm 4.0\%$  correct vs.  $39.8 \pm 5.6\%$  and  $40.7 \pm 5.0\%$ ; all  $P = 0.06$ ). Patients performed similarly to the baseline group. Thus, controls did learn noticeably in the FM condition, but patients did not. One week later, control performance declined and was not significantly different from patient or baseline performance. In the explicit encoding (EE) condition (Fig. 1B), controls performed better than in the FM condition at both delays (all  $P < 0.05$ ) and also well above the patient and baseline groups at both delays (all  $P < 0.05$ ). Patients performed similarly to the baseline group at both delays. **Categorization.** At the 10-min delay, controls in the FM condition (Fig. 1C) did better than the patients ( $P < 0.05$ ) but similarly to the baseline group at categorizing the study items ( $46.4 \pm 3.1\%$  vs.  $33.7 \pm 4.1\%$  and  $40.9 \pm 3.8\%$ ). One week later, control performance declined and did not differ significantly from patient or baseline performance. Patients performed like the baseline group at both delays. In the EE condition (Fig. 1D), controls did better than in the FM condition (all  $P < 0.05$ ) and better than the

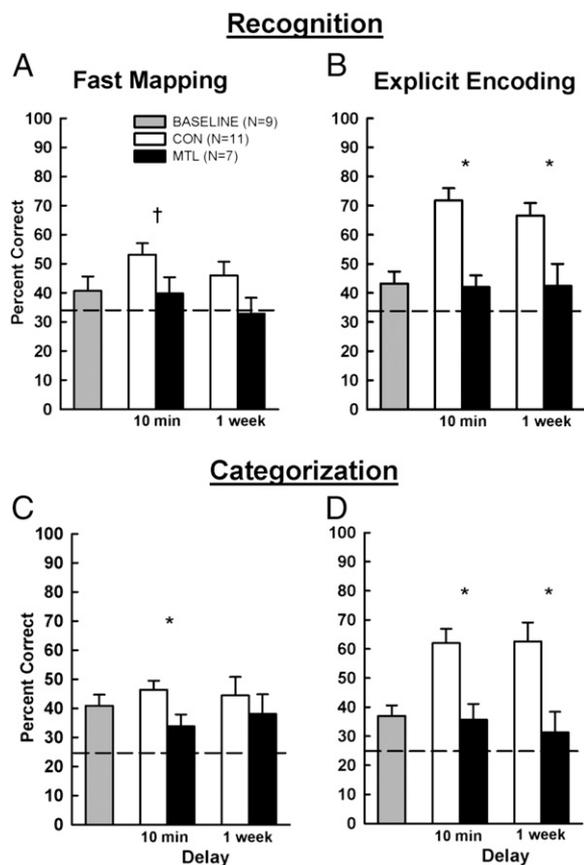
## Significance

**Declarative memory for rapidly learned, novel associations is thought to depend on structures in the medial temporal lobe (MTL). A recent study suggested that rapidly learned associations can nevertheless be supported by structures outside the MTL when a promising, incidental encoding procedure termed “fast mapping” (FM) is used. In two experiments with memory-impaired patients, we found that the FM procedure yielded the same deficits in learning and memory that have been obtained with the use of other more traditional paradigms. We suggest that the effects of the FM procedure are not robust and, if replicable, depend on yet-unknown aspects of how the test is given.**

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The authors declare no conflict of interest.

<sup>1</sup>To whom correspondence should be addressed. E-mail: lsquire@ucsd.edu.



**Fig. 1.** Experiment 1. Accuracy of recognition performance (A and B) and categorization performance (C and D). For controls (CON) and patients (MTL), the tasks were administered 10 min and 1 wk after the study session. The baseline group did not study material before testing. (A) For recognition, controls benefited marginally from the FM procedure at the short delay. Patients performed similarly to the baseline group at both delays. (B) In the EE condition, controls performed better than the patient and baseline groups at both delays. Patients performed similarly to the baseline group. (C) In the FM condition, controls performed numerically better than the baseline group when categorizing the study items (bird, flower, fruit/vegetable, or animal). Patients performed worse than controls at the 10-min delay and similarly to the baseline group at both delays. (D) In the EE condition, controls performed better than the patient and baseline groups at both delays. Patients performed similarly to the baseline group. Dashed line indicates chance performance for the recognition task (33%) and for the categorization task (25%). (\* $P < 0.05$  and <sup>†</sup> $P = 0.06$ .)

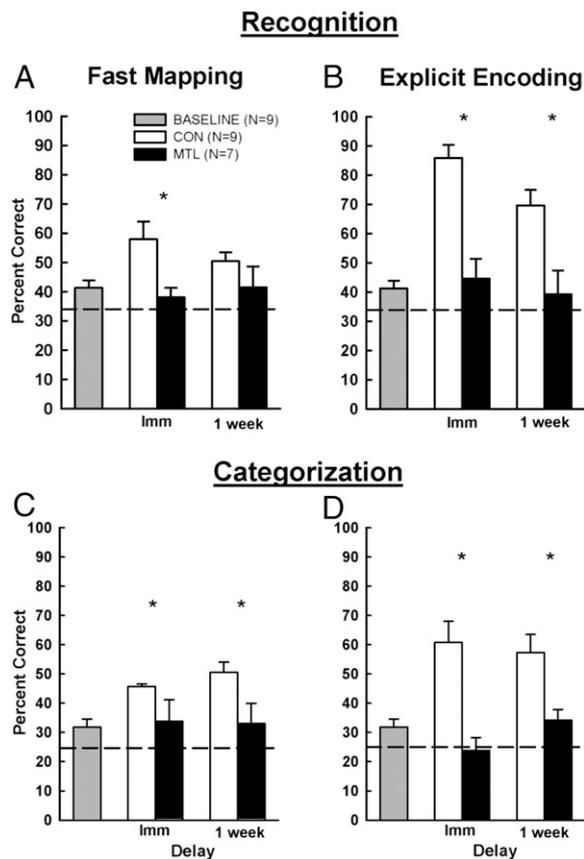
patient and baseline groups at both delays (all  $P < 0.05$ ). Patients performed no better than the baseline group at either delay.

**Confidence ratings.** Controls gave higher confidence ratings for their correct responses than for their incorrect responses in all conditions of experiment 1 (in the FM and EE conditions, for both recognition and categorization, and at both delays;  $P$  values ranged from  $P < 0.001$  to  $P < 0.09$ ). The baseline group also tended to give higher confidence ratings for their correct responses than for their incorrect responses ( $P \leq 0.05$  in all conditions except the categorization task in the EE condition). However, the confidence ratings given by the baseline group were much lower than the ratings given by controls (baseline group, overall means of 2.0 and 1.6 for correct and incorrect responses, respectively, compared with 3.3 and 2.7 in controls). In contrast, across the same conditions, the confidence ratings given by the patients did not differ for correct and incorrect responses (overall means of 3.3 and 3.2 for correct and incorrect responses, respectively;  $P > 0.1$  in all conditions).

**Experiment 2.** The controls in experiment 1 performed slightly poorer than the controls in the earlier study (4). To improve performance, experiment 2 provided more opportunity to study the material (four study repetitions instead of two) and involved a reduced study–test interval (no delay instead of 10 min). In addition, to obtain a more reliable measure of performance, the test consisted of 24 items instead of 16.

The results of experiment 2 were similar to the results of experiment 1.

**Recognition.** Immediately after study, controls in the FM condition (Fig. 2A) performed better than the patient and baseline groups at selecting the correct study item ( $57.9 \pm 6.1\%$  correct vs.  $38.1 \pm 3.2\%$  and  $41.3 \pm 2.6\%$ ; all  $P < 0.05$ ). Patients performed similarly to the baseline group. Thus, controls benefited from the FM procedure, but patients did not. One week later, control performance declined but was still better than baseline performance ( $P < 0.05$ ). Patients performed like the baseline group. In the EE condition (Fig. 2B), controls performed better than in the FM condition ( $P < 0.01$ ) and better than the patient and baseline groups



**Fig. 2.** Experiment 2. Accuracy of recognition performance (A and B) and categorization performance (C and D). For controls (CON) and patients (MTL), the tasks were administered immediately and 1 wk after the study session. The baseline group did not study material before testing. (A) For recognition, controls performed better than the baseline group at both delays and better than patients at the short delay. Patients did not benefit from the FM procedure and performed similarly to the baseline group at both delays. (B) In the EE condition, controls performed better than the patient and baseline groups at both delays. Patients performed similarly to the baseline group. (C and D) Controls categorized the test items better than the patient and baseline groups at both delays. Patients performed similarly to the baseline group. Dashed line indicates chance performance for the recognition task (33%) and for the categorization task (25%). Imm., immediate. (\* $P < 0.05$ .)

at both delays ( $P < 0.01$ ). Patients performed similarly to the baseline group at both delays.

**Categorization.** In the FM condition (Fig. 2C), controls did better than the patient and baseline groups at categorizing the study items at both delays (all  $P < 0.05$ ). Patients performed like the baseline group at both delays. In the EE condition (Fig. 2D), controls did marginally better than in the FM condition (all  $P \leq 0.10$ ) and significantly better than the patient and baseline groups at both delays ( $P < 0.05$ ). Patients performed like the baseline group at both delays.

**Confidence ratings.** Controls gave higher confidence ratings for their correct responses than for their incorrect responses in all conditions of experiment 2 (in the FM and EE conditions, for both recognition and categorization, and at both delays;  $P$  values ranged from  $P < 0.001$  to  $P = 0.1$ ). In contrast, across the same conditions, the confidence ratings given by the patients did not differ for correct and incorrect responses (overall means of 3.2 and 2.9 for correct and incorrect responses;  $P > 0.10$  in all conditions). Similarly, the confidence ratings given by the baseline group did not differ for correct and incorrect responses. Note also that the confidence ratings given by the baseline group were lower than the ratings given by controls (baseline group, overall means of 2.4 and 2.2 for correct and incorrect responses, respectively, compared with 3.3 and 2.8 in controls).

## Discussion

In two experiments, memory-impaired patients with hippocampal lesions or larger lesions of the MTL attempted to learn name-object associations under two different conditions. One condition used a traditional learning procedure in which EE instructions were given, and participants tried to learn the associations. The other condition used an incidental learning procedure (i.e., FM) that had been reported to substantially benefit the learning of memory-impaired patients. In both experiments, the findings were that patients were markedly impaired under FM and EE learning procedures (Figs. 1 and 2). Indeed, in both experiments and for both FM and EE learning procedures, patients performed no better than a group that was given the tests but had not studied the test material.

We also explored whether memory acquired in the FM condition exhibited characteristics of declarative memory. Sharon et al. (4) reported (for a separate control group and for one patient who was available for follow-up testing) that confidence ratings in the FM condition were higher for correct trials than for incorrect trials. This finding suggests that participants had conscious access to what had been learned. We conducted a similar analysis for the control groups in our two experiments and found that the control groups consistently gave higher confidence ratings for correct trials than for incorrect trials in all conditions (in the FM and EE conditions and for both recognition and categorization tests). Accordingly, it appears that successful performance in FM and EE conditions was supported by declarative memory.

Interestingly, this effect of confidence ratings (higher for correct than incorrect trials) was also observed in the baseline control group in experiment 1 (but not in experiment 2), although confidence ratings were low overall. By contrast, as might be expected given the absence of learning, the patients as a group did not exhibit this effect in any of the conditions. Note that one patient in experiment 1 who, despite scoring poorly on the recognition test in the FM condition, nevertheless gave higher confidence ratings for correct than for incorrect trials (4.0 vs. 2.5). In the study of Sharon et al. (4), the one patient who was tested also exhibited this effect.

We suggest that, when real-world stimuli are used, one can occasionally observe an association between recognition performance and confidence judgments even when significant learning has not occurred (as was the case for the baseline group in experiment 1) and even in an individual participant who otherwise performed poorly (as occurred in experiment 1). Why might a correspondence emerge between accuracy and confidence

ratings in control participants who had not studied the material or in a patient who performed poorly on the task? Perhaps, based on a lifetime of experience with the kinds of names normally associated with different kinds of items (animals, plants, and foods), individuals can sometimes intuit the correct answer based on what is presented (e.g., “tenrec” might seem more like an animal name than a fruit name). If participants then rated their decision on such trials with higher confidence than their decisions on other trials, an association between accuracy and confidence could be observed. Note that performance was numerically better than chance for the baseline group in all conditions, consistent with the idea that participants could have intuited correctly on a few trials and given a high confidence rating in those cases.

Another characteristic of declarative memory is that the acquired information can be expressed flexibly. That is, memory can be exhibited even when the procedures used during training and testing are quite different. Following the recognition test, Sharon et al. (4) gave a categorization test to a separate control group and one patient to ask if participants could express their knowledge in a novel way. Participants were asked to decide whether the name they had learned was an animal, bird, fruit/vegetable, or flower. In the FM and EE conditions, good performance on the recognition test predicted good performance on the categorization test for their control group as well as for their single patient. We found a similar relationship between recognition performance and categorization performance for our controls. Thus, like the findings for confidence ratings, the findings for categorization performance indicate that successful performance was supported by declarative memory.

Note that, in the present study, the same relationship between recognition and categorization performance was also observed for the patients (in some conditions) and for the baseline groups in both experiments. Again, we suggest that this particular finding reflects the fact that participants could occasionally intuit the correct answer from their real-world knowledge. If participants could intuit a few answers correctly on the recognition test, one would expect them to respond correctly for the same items on the categorization test.

The fact remains that, in an earlier study, the FM procedure greatly benefited the learning of memory-impaired patients (4), whereas this procedure conferred no benefit to the memory-impaired patients in the present study. One important factor in comparisons between memory-impaired patients from different studies is that the severity of the memory deficit might differ. The severity of amnesia is known to determine whether special training procedures can be fruitful in improving performance. For example, the noted patient HM (7) had very severe memory impairment, yet his performance still benefited from increased exposure time to study material (8). By contrast, patient EP (9) exhibited even more severe memory impairment than HM, and EP was unable to benefit from the same increases in exposure time (10). For the patients in the present study, the mean anterograde memory score was  $-4.5 \pm 0.2$  SDs below control performance (range,  $-3.7$  to  $-5.4$ ; scores are average z-scores for five standard tests of anterograde memory; see ref. 11). In contrast, the average anterograde memory score for the patients from the study of Sharon et al. (4) was  $-2.1 \pm 0.3$  SDs below control performance (range,  $-1.3$  to  $-2.6$ ; scores are average z-scores for four to seven standard tests of anterograde memory; see supporting information in ref. 4). Accordingly, the patients in the earlier study may have been less impaired than the patients in the present study. Perhaps FM learning strategies can benefit memory-impaired patients only when memory is not severely impaired. This possibility seems unlikely when one considers that the healthy elderly individuals who served as controls in the present study performed even worse in the FM condition than in the EE condition.

**Table 1. Characteristics of memory-impaired patients**

Patient	Sex	Age, y	Education, y	WAIS-III IQ	WMS-Revised				
					Attention	Verbal	Visual	General	Delay
DA	M	30	12	95	104	90	91	90	56
KE	M	71	13.5	108	114	64	84	72	55
LJ	F	74	12	101	105	83	60	69	<50
RS	M	55	12	99	99	85	81	82	<50
GW	M	52	12	108	105	67	86	70	<50
JRW	M	48	12	90	87	65	95	70	<50
GP	M	65	16	90	102	79	62	66	50

WMS-Revised does not provide numerical scores for individuals who score below 50. IQ scores for patients RS and JRW are from the WAIS-Revised, and the IQ score for patient DA is from the WAIS-IV. IQ, intelligence quotient; WAIS, Wechsler Adult Intelligence Scale; WMS, Wechsler Memory Scale.

It is also the case that the control group in the earlier study (4) was younger (~10 y) and performed better than the control group in our experiment 1. (The patient groups were nearly the same age.) Experiment 2 provided an opportunity to improve control performance (more study repetitions and a reduced study–test interval). Although performance of our controls did improve in experiment 2 (by 14% in the EE condition and by 5% in the FM condition), the patients still obtained no benefit from the FM learning procedure. Accordingly, it seems unlikely that level of control performance (and, by inference, task difficulty) could account for our findings. We suggest that the effects of the FM procedure are not robust and, if replicable, depend on yet-unknown aspects of how the instructions are delivered and how the test is administered.

## Materials and Methods

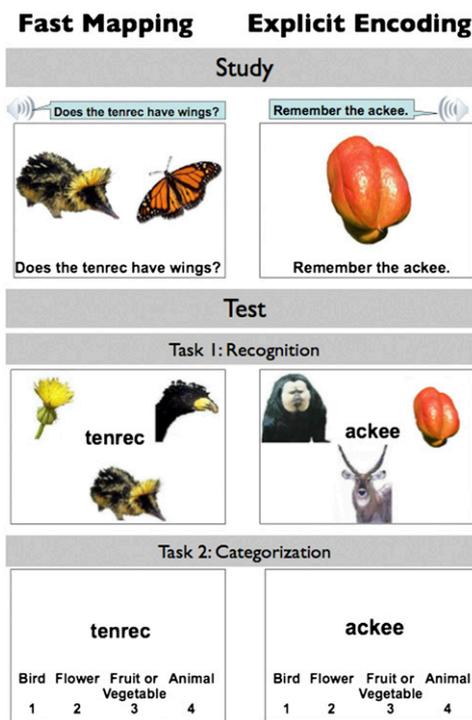
**Experiment 1. Participants.** Seven memory-impaired patients participated (Table 1), six with bilateral lesions thought to be limited to the hippocampus (CA fields, dentate gyrus, and subicular complex) and one with larger MTL lesions. Patient KE became amnesic in 2004 after an episode of ischemia associated with kidney failure and toxic shock syndrome. Patient LJ (the only female patient) became amnesic in 1988 during a 6-mo period with no known precipitating event. Her memory impairment has been stable since that time. Patients RS, GW, and DA became amnesic in 1998, 2001, and 2011, respectively, following a drug overdose and associated respiratory failure. Patient JRW became amnesic in 1990 following an anoxic episode associated with cardiac arrest. Estimates of MTL damage were based on quantitative analysis of MRI images from 19 age-matched healthy males for patients GW, KE, JRW, and RS, eight younger healthy males for DA, and 11 age-matched healthy females for patient LJ (12). Patients GW, KE, LJ, RS, JRW, and DA have average reductions in hippocampal volume of 48%, 49%, 46%, 33%, 44%, and 35%, respectively (all values more than 2.9 SDs from the control mean). On the basis of two patients (LM and WH) with similar bilateral volume loss, for whom detailed postmortem neurohistological information was obtained, the degree of volume loss in the present patient group likely reflects nearly complete loss of hippocampal neurons (13). The volume of the parahippocampal gyrus is reduced by 10%, 11%, –17%, –5%, 12%, and –5% for GW, KE, LJ, RS, JRW, and DA, respectively (all values within 2 SDs of the control mean). These values differ slightly from the volumes reported previously for these patients and are based on newly published, more detailed guidelines for identifying the caudal border of the gyrus (14).

Patient GP has severe memory impairment resulting from viral encephalitis in 1987. He has demonstrated virtually no new learning since the onset of his amnesia and, during repeated testing over many weeks, does not recognize that he has been tested before (15). Patient GP has an average bilateral reduction in hippocampal volume of 96%. The volume of the parahippocampal gyrus is reduced by 94%. Eight coronal MRI images from each patient, together with detailed descriptions of the lesions, can be found in the work of Knutson et al. (16).

A group of 11 healthy volunteers participated as controls (two females; mean age,  $61 \pm 3.5$  y; mean education,  $15.3 \pm 0.5$  y). A second group of nine healthy volunteers participated as a baseline group (four females; mean age,  $62 \pm 5.2$  y; mean education,  $15.1 \pm 0.8$  y). All procedures were approved by the institutional review board at the University of California at San Diego, and participants gave written informed consent before participation.

**Materials and procedure.** The stimuli were generously provided by Asaf Gilboa, Rotman Research Institute at Baycrest and Center for Stroke Recovery, Department of Psychology, University of Toronto, Toronto. For experiment 1, the stimuli and procedures were the same as in an earlier study (4). There were two conditions, FM and EE. In the FM condition, stimuli were presented but without explicit instructions to learn. In the EE condition, explicit instructions were given to remember the stimuli. In each condition, participants were given 48 trials involving pictures of fruits/vegetables, animals, flowers, or birds that were intended to be unfamiliar (e.g., mangosteen, tenrec) or familiar (e.g., butterfly, sparrow). The study session of each condition was preceded by 10 practice trials involving familiar and unfamiliar stimuli that did not appear again.

**FM condition.** The materials consisted of 24 unfamiliar items and 24 familiar items, each of which appeared twice during the study session. On each trial, participants first heard a question and, at the same time, saw it displayed on the screen. After the question was asked, participants saw two pictures displayed on the screen, together with the printed question (Fig. 3). One of the pictures always represented a familiar item and the other represented an unfamiliar item. On 32 of the 48 trials, the question pertained to the



**Fig. 3.** Illustration of the FM and EE conditions of experiment 1 for the study session, the recognition test, and the categorization test. In the study session, the question was spoken and also displayed on the screen immediately before the items appeared.

unfamiliar item (e.g., “Does the tenrec have wings?” when the tenrec was paired with a butterfly, as in Fig. 3). It was presumed that participants would infer that the label (tenrec) referred to the unfamiliar item and that they would therefore respond correctly (in this case “no”). With such a procedure, they could potentially learn the name of the item queried about. Responses (yes or no) were made on a keyboard. On 16 of the 48 trials, the question pertained to the familiar item (e.g., “Is the sparrow red?”). In this case, it was not possible to learn the name of the unfamiliar item because the name was not presented. Accordingly, memory for the unfamiliar items that appeared on these trials was not subsequently tested. Each item that was to be later tested appeared on two different trials during the study session, always on a different side of the screen, and always paired with a different familiar picture. The response to the question was “yes” one of the times that an item appeared and “no” the other time. Because there were only 32 trials on which the unfamiliar item was queried about (16 items appeared twice), subsequent testing for incidental learning involved those 16 unfamiliar items.

Following the study session, memory for the 16 unfamiliar items was tested with a recognition task and then with a categorization task (Fig. 3). These tasks were administered after a 10-min, conversation-filled delay and also after 1 wk (At the 1-wk delay, only five of the seven patients were available for testing). For the recognition task (16 trials), participants saw three pictures together with one name and were asked to select the picture that had been associated with the name. The three pictures in each display had appeared during the study session as one of the 16 unfamiliar items that had been queried about. For each trial, participants indicated a confidence rating for their choice on a scale from 1 to 5 (1, a pure guess; 5, very sure). Responses were made by key press.

For the categorization task (16 trials), participants saw one of the 16 unfamiliar names and were asked to select the appropriate category (bird, flower, fruit/vegetable, or animal). They also indicated a confidence rating for their selection (1–5 scale).

At the end of the first test session, participants saw each of the unfamiliar items again and were asked if they had prior knowledge of any of them. Items designated as previously familiar were excluded from data analysis for that participant (mean 0.5 items per participant for the FM condition). In addition, an item that received incorrect responses both times the item was presented during the study session was excluded from data analysis for that participant (mean 0.3 items per participant). Overall, controls were 94.1% accurate in the study session, and patients were 91.7% accurate. All testing was self-paced. **EE condition.** The EE condition was given after all testing in the FM condition was completed. This condition used a new set of stimuli (16 unfamiliar items and 8 familiar items). The procedure was the same as in the FM condition except for the study phase (Fig. 3). Specifically, each item appeared alone rather than paired with another item. On 32 of the 48 trials, participants were instructed to remember an unfamiliar item (e.g., “remember the ackee” when an ackee appeared on the screen). On 16 of the 48 trials, participants were instructed to remember a familiar item (e.g., “remember the lion” when a lion appeared on the screen). No response was required. Each item was displayed for 2.4 s, as in the study by Sharon et al. (4). Testing then proceeded exactly as in the FM condition (16 trials for recognition followed by 16 trials for categorization). A mean of 0.1 items per participant was designated as previously familiar and excluded from analysis. The same patients and controls participated in the FM and EE conditions.

**Baseline group.** Because of general knowledge or intuition, certain names might seem more appropriate for one category than another (e.g., “tenrec” might seem more like an animal name than a fruit name). Thus, we did not assume that chance performance would necessarily be 33.3% correct for the recognition test and 25.0% correct for the categorization test. Instead,

a second group of participants ( $n = 9$ ) was given the recognition and categorization tasks from both conditions without previously studying the items. For each test trial, participants tried to guess the correct answer. As in the FM and EE conditions, items were subsequently excluded from analysis when they were identified as familiar before testing (mean 0.6 items per participant). The baseline score obtained by this group was used to evaluate the learning achieved in the FM and EE conditions.

**Experiment 2. Participants.** The same seven memory-impaired patients from experiment 1 participated in experiment 2. Nine healthy volunteers participated as controls (four female patients; mean age,  $62 \pm 5.2$  y; mean education,  $15.1 \pm 0.8$  y). These were the same individuals who constituted the baseline group in experiment 1. A second group of nine healthy volunteers participated as a baseline group in experiment 2 (two female patients; mean age,  $58 \pm 4.6$  y; mean education,  $14.6 \pm 0.5$  y). These nine individuals had participated in the FM and EE conditions of experiment 1 as controls. Note that all controls completed experiment 1 or 2 prior to participating in a baseline group. All procedures were approved by the institutional review board at the University of California at San Diego, and participants gave written informed consent.

**Materials and procedure.** Experiment 2 involved the same two conditions (FM and EE) as experiment 1 but with new stimuli. Here the procedure was modified so that there were more items that could be learned (24 instead of 16) and greater opportunity for learning each item (four presentations per item instead of two). In addition, instead of presenting eight items that were not later queried about in the recognition and categorization tasks, as in experiment 1, there were only four such items, each of which appeared four times. Accordingly, for the FM condition, there were a total of 112 trials. On 96 of the 112 trials, familiar and unfamiliar items appeared side by side, and the question asked about the unfamiliar item (e.g., cornuta). On 16 of the 112 trials, the question was asked about the familiar item. Subsequent testing for incidental learning involved the 24 unfamiliar items. The EE condition proceeded in the same way as in experiment 1, but with 112 trials (24 unfamiliar items appeared alone four different times and four familiar items appeared alone four different times).

Two other modifications were introduced in experiment 2. First, the initial test session for the FM and EE conditions followed immediately after the study session rather than after a 10-min delay. (The second test session was given after 1 wk as in experiment 1. Again, only five of the seven patients were available for testing.) Second, the materials were counterbalanced across conditions, such that a given item appeared in the FM condition for half of the participants and in the EE condition for the other half of the participants.

In all other respects, experiment 2 followed the procedure of experiment 1 (study session, recognition test, and categorization test in the FM and EE conditions). Means of 0.4, 0.6, and 0.8 items per participant were designated as previously familiar and excluded from analysis for the FM condition, the EE condition, and the baseline group, respectively. In addition, for the FM condition, an item that received incorrect responses all four times the item was presented during the study session was excluded from data analysis for that participant (mean 0.2 items per participant). Overall, controls were 90.8% accurate in the study session of the FM condition, and patients were 85.3% accurate.

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- Gabrieli JDE (1998) Cognitive neuroscience of human memory. *Annu Rev Psychol* 49:87–115.
- Tulving E, Schacter DL (1990) Priming and human memory systems. *Science* 247:301–306.
- Squire LR (1992) Memory and the hippocampus: A synthesis from findings with rats, monkeys, and humans. *Psychol Rev* 99(2):195–231.
- Sharon T, Moscovitch M, Gilboa A (2011) Rapid neocortical acquisition of long-term arbitrary associations independent of the hippocampus. *Proc Natl Acad Sci USA* 108(3):1146–1151.
- Brown RW (1957) Linguistic determinism and the part of speech. *J Abnorm Psychol* 55(1):1–5.
- Carey S, Bartlett E (1978) Acquiring a single new word. *Proc Stanford Child Language Conf* 15:17–29.
- Scoville WB, Milner B (1957) Loss of recent memory after bilateral hippocampal lesions. *J Neurol Neurosurg Psychiatry* 20(1):11–21.
- Freed DM, Corkin S, Cohen NJ (1987) Forgetting in H.M.: A second look. *Neuropsychologia* 25(3):461–471.
- Insausti R, Anness J, Amaral DG, Squire LR (2013) Human amnesia and the medial temporal lobe illuminated by neuropsychological and neurohistological findings for patient E.P. *Proc Natl Acad Sci USA* 110(21):E1953–E1962.
- Reed JM, Hamann SB, Stefanacci L, Squire LR (1997) When amnesic patients perform well on recognition memory tests. *Behav Neurosci* 111(6):1163–1170.
- Smith CN, Frascino JC, Hopkins RO, Squire LR (2013) The nature of anterograde and retrograde memory impairment after damage to the medial temporal lobe. *Neuropsychologia* 51(13):2709–2714.
- Gold JJ, Squire LR (2005) Quantifying medial temporal lobe damage in memory-impaired patients. *Hippocampus* 15(1):79–85.
- Rempel-Clower NL, Zola SM, Squire LR, Amaral DG (1996) Three cases of enduring memory impairment after bilateral damage limited to the hippocampal formation. *J Neurosci* 16(16):5233–5255.
- Frankó E, Insausti AM, Artacho-Péruela E, Insausti R, Chavoix C (2014) Identification of the human medial temporal lobe regions on magnetic resonance images. *Hum Brain Mapp* 35:248–256.
- Bayle PJ, Frascino JC, Squire LR (2005) Robust habit learning in the absence of awareness and independent of the medial temporal lobe. *Nature* 436(7050):550–553.
- Knutson AR, Hopkins RO, Squire LR (2013) A pencil rescues impaired performance on a visual discrimination task in patients with medial temporal lobe lesions. *Learn Mem* 20(11):607–610.