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# New Semantic Learning and Generalization in a Patient With Amnesia

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New learning of semantic information is impaired in amnesia. Several reports have demonstrated that "errorless" learning techniques have allowed patients with amnesia to acquire at least some form of new semantic information, although this information appears to be relatively inflexible. Using insights and principles from connectionist modeling of cortical and medial temporal lobe memory systems, the authors describe why errorless learning procedures act as a poor proxy for the medial temporal lobe, suggesting that they artificially eliminate the variability that defines semantic information. The authors trained a patient with severe amnesia on new semantic sentences both with and without variance and then tested him on both repeated and related novel sentences to assess generalization. He successfully learned new semantic information in both conditions but demonstrated better generalization of semantic concepts following training with variance.

*Keywords:* declarative memory, medial temporal lobe, errorless learning

Normally, learning in humans is rapid, and the information learned can be used flexibly to answer the different and often unpredictable demands placed on our memory. For example, one can easily learn new information, such as "The Orioles beat the Yankees." Once having learned this piece of information, one can immediately understand that it is also true that "The Yankees lost to the Orioles" and "The Orioles won." The knowledge gained from learning that "The Orioles beat the Yankees" will not only be available to conscious recollection but can also reveal itself in such automatic processes as the time it takes to verify sentences such as "The Yankees advanced to the playoffs" (e.g., Coltheart et al., 1998) or in the duration of gaze to a picture of the Orioles relative to some unknown team (e.g., Manns, Stark, & Squire, 2000). These capabilities are among those that give normal human memory its power in acquiring and generalizing semantic knowledge.

In contrast, when an individual develops amnesia as a result of damage to medial temporal lobe (MTL) structures, the learning and use of both episodic and semantic knowledge (*declarative memory*) are impaired (see Milner, Squire, & Kandel, 1998, for a review). In severe cases, this impairment can be complete. For example, in the case of patient E.P. (whose damage to the MTL is extensive yet fairly well constrained to the MTL), an array of 42 tests of declarative memory failed to uncover any evidence of intact declarative memory, with E.P. continually making judgments no more accurately than would a coin toss (Hamann & Squire, 1997; Stark & Squire, 2000; Stefanacci, Buffalo, Schmolck, & Squire, 2000). In contrast, tests of implicit or nondeclarative memory in these same studies have repeatedly shown intact performance.

Examples of such striking impairments as these have led numerous researchers to propose a fundamental distinction between declarative or *explicit memory* (memory for facts and events) and *nondeclarative* or *implicit memory* (see Milner et al., 1998; Schacter & Buckner, 1998, for reviews). Declarative memory is often thought to be conscious and facilitated by attention to and elaboration of the material presented, and it is also critically reliant on structures in the MTL (the hippocampal region and the entorhinal, perirhinal, and parahippocampal cortices) for some period of time during and following the initial learning (i.e., a consolidation period). In contrast, nondeclarative or implicit memory reflects learning that is nonconscious, generally unaffected by attention or elaboration, and expressed through changes in performance or biases rather than intentional or conscious recollection. Nondeclarative learning has also proven to be quite specific not only to the task (such as in procedural learning or priming) but also to the materials and to be intact in amnesia following damage to the MTL. Nondeclarative memory is therefore often thought to rely on small changes to connections in cortical or subcortical structures outside the MTL that are involved in task performance.

Even though learning new factual information is impaired in severe amnesia, it is not impossible. For example, Bayley and Squire (2002) tested new semantic learning in E.P. by training him on three-word facts (e.g., "Venom caused seizures") and explicitly asking him to think about the meaning of these sentences. Of note in the data reported by Bayley and Squire was the observation that E.P. was able to recall approximately 20% of the facts learned. Although E.P. was clearly impaired, this was researchers' first

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observation of above-chance performance on a test of long-term recall or recognition in this extensively studied patient with amnesia. In this report and in other observations of factual learning in amnesia (e.g., Baddeley & Wilson, 1994; Glisky, Schacter, & Tulving, 1986a; Holdstock, Mayes, Isaac, Gong, & Roberts, 2002; Wilson, Baddeley, & Evans, 1994), the teaching of new factual information in amnesia has required a learning paradigm that is different from the "errorful" learning paradigms typically used with healthy participants. In *errorful learning,* errors are allowed during the study and test sessions and are then corrected. However, for teaching individuals with amnesia, it has been shown that a far more effective strategy is what has been termed *errorless learning,* which is derived from animal learning paradigms (Savage-Rumbaugh et al., 1993; Terrace, 1963). Errorless learning methods attempt to prevent the participant from making mistakes during learning and testing. Using an errorless learning paradigm, Glisky, Schacter, and Tulving (1986b) were the first to demonstrate learning of new information in memory-impaired individuals. Glisky et al. (1986b) trained memory-impaired individuals on new computer terms over successive trials. If the participant was successful in providing the correct answer with cues, then letters in the cue would gradually be removed, providing less information about the correct answer. If the participant made an error, then a letter was added to the cue to help the participant recall the computer term correctly. With this errorless learning technique, even several individuals with severe amnesia tested by Glisky et al. (1986b) were able to learn the correct answers eventually. Using other errorless learning procedures, memory-impaired individuals have also been able to improve their performance in a cued-recall paradigm (Baddeley & Wilson, 1994; Hunkin, Squires, Parkin, & Tidy, 1998), learn new face–name associations (Clare, Wilson, Breen, & Hodges, 1999), program an electronic memory aid (Wilson et al., 1994), and improve their recall for items of general knowledge (Bayley & Squire, 2002; Holdstock et al., 2002; Wilson et al., 1994).

Although these accomplishments have been impressive, as they appear on the surface to be evidence of declarative memory acquisition in even severe cases of amnesia, the learning is clearly not normal. Not only were a large number of trials required to learn the information, but also the learning that these individuals with amnesia were able to accomplish was hyperspecific. If even small changes were made to the questions used to probe the memory, performance dropped precipitously. For example, although E.P. (Bayley & Squire, 2002) was able to learn many three-word facts (e.g., "Venom *caused* seizures"), when a related verb was substituted for the one actually used in training (e.g., "Venom *induced* ???"), his accuracy dropped from 20.7% to approximately 3%. In contrast, control participants did almost as well with the substitution as they had done with the original form (29% → 24%). The hyperspecificity of this learning has been held to be theoretically important, as it is clear that the patients have not learned the information in the same way as control participants (e.g., perhaps the result of nondeclarative or implicit learning). Several researchers have suggested (N. J. Cohen & Eichenbaum, 1993; Eichenbaum, Otto, & Cohen, 1994; Squire, 1992) that nondeclarative learning is hyperspecific by nature, whereas declarative learning is inherently flexible. Evidence of a loss of flexibility in the application of knowledge has been observed not only in humans with amnesia (Dopkins, Kovner, & Goldmeier, 1990; Glisky et al., 1986b; McKenna & Gerhand, 2002; Milner, 1968; Van der Linden, Meulemans, & Lorrain, 1994) but also in rats and monkeys with damage to the hippocampal region (Eichenbaum, Mathews, & Cohen, 1989; Eichenbaum, Stewart, & Morris, 1990; Saunders & Weiskrantz, 1989).

Although declarative learning is undoubtedly flexible, nondeclarative learning is not necessarily rigid. The basic mechanisms assumed to operate in nondeclarative learning certainly allow for generalization: External stimuli tend to activate more representations than only the target representation; there is also likely to be activation of additional associations from the target item—and from related representations—that could help support generalization (see Gordon, Boatman, Crone, & Lesser, 1997). Flexibility and generalization in nondeclarative memory have been recognized empirically (Barsalou, 1999; Goldstone, 1998, 2000).

When viewed from the standpoint of connectionist models of amnesia (McClelland, McNaughton, & O'Reilly, 1995; O'Reilly & Rudy, 2001), the ideas of flexibility and generalization take on a different character from a dichotomy between flexible declarative and inflexible nondeclarative memory. For example, McClelland et al. (1995) proposed a division between learning in the hippocampus and in the neocortex on the basis of computational principles that govern learning in connectionist models. In this schema, the hippocampal memory system (which may include adjacent structures in the MTL) rapidly learns arbitrary patterns of activity, whereas the neocortical system(s) must learn slowly. The slow learning of the neocortex is a requirement for any system that is able to eventually extract and model the similarity structure in its environment. The rapid learning of the hippocampal system, in contrast, sacrifices the ability to generalize for the ability to rapidly learn arbitrary patterns of activity. When both systems are intact, the hippocampal memory system trains the neocortical learning system through a process of interleaved learning, allowing for the gradual extraction of the similarity structure that is central to generalization.

At face value, such a system would seem to suggest that neocortical learning would be more capable of generalization and flexibility than would hippocampal learning. After all, it is the cortical system that can generalize to similar but novel inputs (following the process of slow, interleaved learning), and it is the hippocampal system that cannot perform such generalization by design (the use of sparse representations that orthogonalize similar input patterns). Why would damage to the hippocampal system (in the model or in patients with amnesia) produce behavior that appears to be hyperspecific? Although hyperspecificity following damage to the hippocampal system might appear counterintuitive in this framework, we argue that it is actually entirely consistent.

First, we echo the proposal by J. Cohen and O'Reilly (1996) and McClelland et al. (1995), who suggested that the flexible use of recently acquired information is not the particular role of the hippocampal system. The hippocampal system (construed broadly for the present purposes to include the hippocampal region and neighboring cortical structures in the MTL) provides the ability to store and retrieve arbitrary patterns of activity—to act as a memory system capable of rapid learning of novel information. The use of that information, and in particular, the flexible application of that information to novel situations, is within the domain of frontal structures (and potentially other structures) that can take recently acquired information provided by the hippocampal system (and also consolidated declarative information provided by the neocortex) to consciously and deliberately apply the information in complex and flexible ways. Thus, damage to the hippocampal system does not impair the flexible application of declarative memory per se but does impair the ability to store and retrieve new factual and episodic memory, which is the prerequisite for its flexible application.

One must still consider, however, why the learning observed in patients with amnesia is hyperspecific. If the learning observed in patients with amnesia uses the slow, interleaved learning in the neocortical system, why does this learning not generalize to novel situations? Why is it that with intact frontal structures, patients with amnesia who have learned information using the errorless technique still cannot generalize this information? Having learned to complete the sentence "Venom caused ???" with the word "seizures" after long periods of training, why can they not complete the phrase "Venom induced ???" in the same way? We propose that the methods used in the errorless learning procedure itself are at the heart of the hyperspecificity in the observed behavior. Drawing on findings from learning in connectionist models (a simple model demonstrating these principles is presented in the Appendix on the Web at http://dx.doi.org/10.1037/0894-4105.19.2.139.supp), we suggest that the errorless learning techniques that have been used to date have artificially eliminated the variability in the stimuli required for the discovery of any shared structure that would allow for generalization. By always presenting the same stimulus in the same context with the same response, virtually the same exact learning will occur on each trial. Although this technique will ensure that an inappropriate response will not be inadvertently strengthened, it will also ensure that irrelevant specifics of the episode are strengthened as well. Ultimately, the learning is not guided to be tolerant of irrelevant information or minor distortions and is not focused on the semantic components of the information.

We propose that the addition of variance into a training set within the errorless learning paradigm might not only allow for the gradual accumulation of the to-be-learned information over many trials but might also allow for the gradual elimination of irrelevant information (information that is not consistent across episodes) and the accrual of the consistent, relevant information. By introducing variability into the training set (e.g., "Venom caused seizures," "Venom resulted in seizures," and "Venom produced seizures"), the core semantic aspect of the information can be trained without specific and irrelevant episodic details that could lead to hyperspecificity. Thus, subsequent retrieval attempts with a novel but semantically related probe (e.g., "Venom induced ???") will have a higher probability of success, as the memory cue now more consistently matches what had been learned (i.e., "induced" more closely matches a semantic representation of a causal link than it matches perceptual or episodic features of seeing the word "caused" in this context). A demonstration of this principle in a simple connectionist model of this task and further discussion is presented in the Appendix on the Web at http://dx.doi.org/10.1037/0894-4105.19.2.139.supp. Once this memory has been retrieved, conscious, deliberate, and flexible application of this information would then be the domain of frontal structures.

This theory suggests that an innovative and in some respects, counterintuitive method to overcome the apparent hyperspecificity of learning in amnesia would be to add variance to the material to be learned (variance geared toward retaining the desired semantic aspects and eliminating the irrelevant specific details). If this approach shows that even some of the hyperspecificity can be overcome, then a revision or reconsideration of some influential theories of the role of the MTL in learning and generalization may be required. These results would be important for developing more effective methods for retraining individuals with memory loss, not only individuals with pure amnesia but also a much larger group with memory problems such as mild cognitive impairment (Chertkow, 2002) and closed head injury (Zec et al., 2001).

We present data from a patient with severe amnesia to investigate whether training with variance leads to a more flexible memory representation. We designed a study using materials similar to those used by Bayley and Squire (2002) in their study of E.P. We taught three-word sentences to T.E. using two versions of an errorless learning procedure: the traditional errorless learning procedure (here called the *no-variance condition*), in which studied items were presented repeatedly in the same form, and a *variance condition,* in which studied items were presented in slightly varied forms (substitution of a semantically related verb). Flexibility of this learning was assessed in both conditions by presenting novel but related sentence cues and testing whether T.E. would be able to generalize to this new version of the sentence. Consistent with previous reports, our findings showed that T.E. was able to learn the three-word sentences in both conditions (with some evidence for better learning in the variance condition). Also consistent with previous reports, our findings showed that T.E.'s learning appeared to be rather inflexible in the traditional no-variance condition, as he demonstrated poor generalization performance to novel versions of these sentences. In contrast, T.E.'s ability to generalize was significantly better in the variance condition than in the no-variance condition when either recall or recognition memory tests were used.

## Method

We used a modification of the paradigm that Bayley and Squire (2002) used with E.P., designing it to include both a near-replication of the Bayley and Squire paradigm (our no-variance condition) and a condition in which variance was inserted into the training session (variance condition). Our aim was to determine whether inserting variability into the training set would affect the ability to generalize performance to novel versions of the trained sentences. Here, we assessed performance in patient T.E. after every four training sessions using both visual cued-recall and visual forced-choice recognition memory paradigms (a total of eight test sessions). In addition, on the last test session, we gave T.E. an auditory version of the cued-recall task and collected confidence ratings on all three tasks.

### Participants

All participants signed a consent form approved by the Western Institutional Review Board (Seattle, Washington), and all testing was in compliance with the approved protocol. All participants received $10 per session for their participation.

*Patient with amnesia.* T.E. (not his real initials) is a 68-year-old, right-handed man with 14 years of education, who spent much of his career in accounting. His amnesia was caused by an anoxic episode following cardiac arrest approximately 2 years prior to our study (in September 2000). Cerebral anoxia has been identified as one of the most significant causes of an isolated amnesic syndrome, causing significant damage to the hippocampus and, sometimes, to the extrahippocampal areas in the MTL (for a review, see Caine & Watson, 2000). The vulnerability to the hippocampus and other gray matter regions can be attributed to a combination of abnormal blood flow, basal metabolic rate, and presence of receptors for excitatory amino acids (Arbelaez, Castillo, & Mukherji, 1999). T.E. had been playing golf with friends when he began to feel some discomfort. They drove him to the hospital, and he became less responsive during the 40-min drive and unresponsive for the last 5–10 min. Upon arrival at the hospital, he was resuscitated and subsequently transferred to an inpatient rehabilitation unit. At present, he is ambulatory and can dress, shower, eat, and conduct other activities of normal daily living.

However, T.E. is profoundly amnesic in everyday life. He does not remember the day or time, does not recall the names of his four grandchildren (all born prior to the anoxic episode), and is completely dependent on his wife to maintain the household. He is unable to maintain a job because of his severe memory loss. Furthermore, not only does he not remember the name or function of the researcher (Shauna Stark) who has tested him in his home over 75 times in the past year, but he is also unaware that the two have ever met.

The severity of his amnesia has been confirmed by formal testing done at the onset of research testing. On the Wechsler Memory Scale—Third Edition (WMS–III, Wechsler, 1997b), he scored 88, 58, 56, and 49 on the Working Memory, Auditory Delayed Memory, Visual Delayed Memory, and General Memory subtests, respectively. Each of these subtests yields mean scores of 100 in the healthy population, with a standard deviation of 15. On the Warrington Word Recognition test (Warrington, 1984), he scored 54% correct (or 27/50) on recognition, again demonstrating profound anterograde amnesia.

T.E. was given the Rey–Osterrieth figure drawing task (Osterrieth, 1944), a task that is quite sensitive to MTL damage (Squire, Clark, & Bayley, 2004). In this task, the participant is presented with a complex line drawing (see Figure 1a) and asked to copy the drawing. The drawing is then removed, and the participant is immediately asked to produce the drawing from memory. After a 10-min delay, the participant is asked to again produce the drawing from memory. The performance of an age-matched control participant is shown in Figure 1b, and T.E.'s performance is shown in Figure 1c. In the immediate test (see Figure 1c, middle), T.E. knew that he had seen the image but forgot it as soon as he started to draw, saying, "OK . . . [puts the pen to the paper] . . . oh damn!" (expletive altered). In the delayed test (see Figure 1c, right), T.E. had no memory of having previously copied the drawing. When asked to draw what he had copied earlier, his response was, "Was it an animal?" When told it was not an animal but to draw the first thing that came to mind, he initially resisted drawing anything. Finally, he produced a figure with only minimal information.

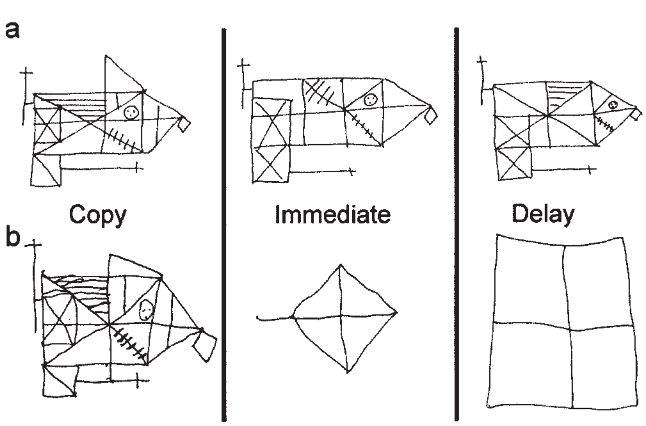


*Figure 1.* Rey–Osterrieth figure drawing task. Participants were asked to copy the original drawing while it was visible (Copy), immediately after it was removed (Immediate), and after a 10-min delay (Delay). a: Performance of an age-matched control participant. b: T.E.'s performance.

Table 1
*Performance on Seven of the Tests From the Semantic Test Battery Reported by Schmolck et al. (2002), Presented Alongside Data From Patient T.E.*

| Semantic Test Battery | Control ($n$ = 8) | HF ($n$ = 2) | MTL+ ($n$ = 3) | T.E. |
|---|---|---|---|---|
| Four Pointing and Naming tasks (% correct) | 98.9 | 100.0 | 78.1 | 90.1[a] |
| Semantic Features (% correct) | 91.9 | 96.9 | 80.9 | 84.4 |
| Category Fluency (no. of items provided) | 128.9 | 112.0 | 75.7 | 54.0[b] |
| Category Sorting (% correct) | 97.0 | 98.5 | 97.0 | 100.0 |

*Note.* HF = damage to the hippocampal region; MTL+ = extensive damage to the medial temporal lobe.
[a] Patient T.E. scored 93.8% on the Pointing tasks and 86.5% on the Naming tasks. [b] Patient H.M. named 42% items total on Category Fluency.

On a recognition memory test of public events (Manns, Hopkins, & Squire, 2003) over the past five decades (1950s through the 1990s), T.E. demonstrated retrograde amnesia, such that his percentage of correct responses for information from the 1950s was 67%; it dropped to 44% for information from the 1990s, with a gradient for the decades in between. In contrast, his general intellectual abilities were still intact, as his Wechsler Adult Intelligence Scale—Third Edition (WAIS–III; Wechsler, 1997a) IQ score of 102 was within the normal range. His digit span was six forward and five backward. In addition, he exhibited appropriate social behavior, had an intact sense of humor, and seemed otherwise cognitively intact.

We tested the condition of his semantic knowledge using the Semantic Test Battery, originally developed by Hodges, Salmon, and Butters (1992). Schmolck, Kensinger, Corkin, and Squire (2002) administered this test, as well as some other tests of semantic knowledge, to patients with hippocampal damage only and to patients with MTL lesions with variable damage to the anterolateral temporal cortex (MTL+), including patients H.M. and E.P. In Table 1, we compare T.E.'s performance on seven of the tests in the Semantic Test Battery (Pointing tasks [pointing to picture name, pointing to picture description], Naming tasks [naming picture, naming description], Semantic Features, Category Fluency, and Category Sorting) with the scores reported by Schmolck et al. (2002). T.E. performed above the mean but within the range of the MTL+ patients' scores that were reported by Schmolck et al. but still below the scores of the hippocampal and control groups. These data indicate that T.E.'s semantic performance is relatively intact and consistent with the semantic performance of other well-characterized MTL+ patients in the literature (such as H.M. and E.P.). Schmolck et al. argued that the severity of the impairment in semantic knowledge in the MTL+ group is related to the extent of damage to the lateral temporal cortex, not damage to the entorhinal, perirhinal, and parahippocampal cortices. For T.E., it appears that the cortical damage that he suffered from his anoxic episode has not disproportionately affected his semantic system.

We also tested T.E.'s frontal lobe functioning with several common tests of executive functioning. On the Wisconsin Card Sorting Test (WCST; Heaton, 1981), T.E. was able to sort the cards into the appropriate categories the full six times (the maximum for the test), making 14 errors (57% perseverative). On the Stroop Color–Word Test (Stroop, 1935), T.E. scored 25 items named correctly in 45 s for the Word Color subtest (for the word *red* printed in blue ink, the correct response is *blue*). Comalli, Wapner, and Werner (1962) reported that subjects aged 65–80 years old averaged 27.2 items named correctly in 45 s. Thus, for his age, T.E. does not appear to be impaired on this task. Finally, we administered the Trail Making Test (Forms A and B; Reitan & Wolfson, 1993), in which we measured the time it took T.E. to connect numbered circles (Form A) or number–letter circles (Form B) in the appropriate order. T.E. took 67 s to complete Form A (25th percentile for his age group) and 76 s to complete Form B (83rd percentile for his age group). On the basis of these measures of frontal lobe functioning, it appears that T.E. has relatively intact executive functioning. Thus, although T.E. does have cortical atrophy consistent with a severe anoxic episode, his neuropsychological testing has indicated a selective impairment in memory, with all other cognitive functions remaining relatively intact.

T.E. has severe damage to the hippocampal region that is clearly visible in structural MRI scans (see Figure 2, white arrows). Both T.E. and 5 age-matched control participants ($M$ age = 65.4 years) underwent structural MRI scans. A one-sample $t$ test of the volume of T.E.'s right hippocampal region (1,851 $mm^3$), compared with that of control participants ($M$ = 3,003 $mm^3$), indicated a significant reduction of 38%, $t(4) = 4.4$, $p < .02$. Similarly, a comparison of the volume in the left hippocampal region (2,011 $mm^3$) with that of control participants ($M$ = 2,898 $mm^3$) indicated a significant reduction of 31%, $t(4) = 4.5$, $p < .02$. In addition to damage to the hippocampal region, T.E. has numerous white matter lesions and cortical atrophy, which are consistent with a severe anoxic episode. Unfortunately, it does not appear to be possible to quantify T.E.'s damage to other MTL structures (entorhinal cortex, perirhinal cortex, and parahippocampal cortex) using current techniques (Insausti et al., 1998; Pruessner et al., 2002). The delineation of the MTL structures requires a definition of the collateral sulcus. Much of T.E.'s collateral sulcus cannot be defined with the degree of accuracy needed for volumetric analysis because the cortex is flat for a large portion of where the collateral sulcus would normally be (apparent in the left hemisphere in Figure 2). Although this anomaly does limit our ability to quantify the damage to his MTL structures outside of the hippocampal region, the severity of his amnesia is consistent with MTL damage that extends beyond the hippocampal region and into the adjacent structures along the parahippocampal gyrus.

Rempel-Clower, Zola, Squire, and Amaral (1996) reported a study of postmortem neuropathological analyses in three patients with amnesia who had hippocampal and other MTL damage. They found that for two patients who had been evaluated by MRI prior to death, the postmortem findings confirmed the decreased hippocampal volume identified with MRI. However, they noted that the "resolution of MRI is not sufficient to provide detailed information about the status of particular tissue, especially when there is cell loss without substantial volume change" (p. 5247). Although the MRI confirmation of damage is useful, it is important to note that the severity of the amnesia may be more telling about the degree of damage and which structures are involved. In the case of T.E., the severity of his amnesia and the relative sparing of his other cognitive faculties indicate that he has severe MTL damage that extends beyond just the hippocampus.

*Control participants.* Three male control participants had a mean age of 67 years (range = 63–72) and a mean education of 14.3 years (range = 12–16). Control participants were recruited from ads posted in the Johns Hopkins Medical Institutions and the local newspapers.

## Materials

Materials consisted of an extension of the same set of three-word sentences (see Table 1) used by Bayley and Squire (2002). In both the variance and no-variance conditions, there were 16 core noun–verb–noun sentences (no nouns or verbs were repeated), which were randomly assigned. For variance training, two semantically similar versions of each core sentence were created by replacing the verb with a synonym (see below). During training, all three variations of the sentence were presented at each study session ($n$ = 48). For training in the no-variance condition, the 16 core sentences were presented three times with no variation ($n$ = 48). Thus, there were a total of 96 sentences per training session. To assess generalization, we created three untrained variations of each of the 32 core sentences, again by replacing the verb with a synonym, for a total of 96 related but untrained sentences (none of these verbs were in any of the training sentences). Therefore, 96 studied sentences and 96 unstudied variations of those sentences could be used during either recognition or recall (visual or auditory) tests.

To evaluate our set of verb synonyms, we asked independent raters ($N$ = 27) to assess each set of verbs for how well they represented the core concept. The raters were students at Johns Hopkins University and received course credit for their participation. Participants were shown 60 sets of verbs (23 sets of six verbs and 37 sets of four verbs) and were instructed to circle the verb that best represented the core concept. The verbs were listed and evaluated independently of the sentence framework. On the basis of these ratings, the word with the highest rating in each group was selected as the training word in the core sentence. For the no-variance condition, this verb was the only one presented during the training. For the variance condition, this verb was presented along with two other verbs chosen randomly from the set. In this way, we chose the most representative verb to establish the core concept for each sentence.

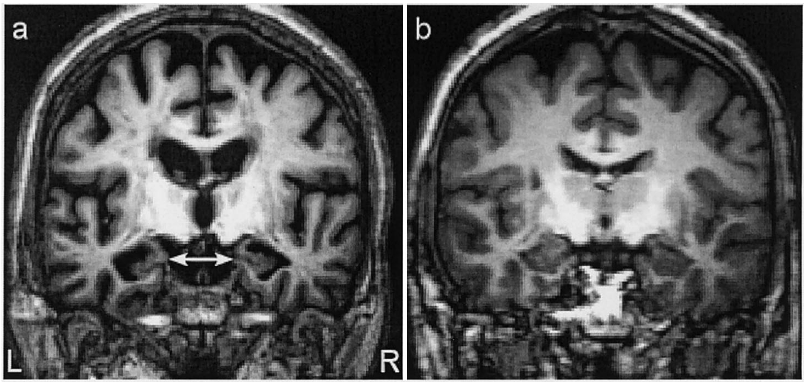


*Figure 2.* a: T1-weighted coronal images of patient T.E. b: An age-matched control participant oriented with the left side of the brain on the left side of the image. The location of the hippocampus is indicated by the white arrows. L = left; R = right.

### Procedure

Prior to any training in the experiment, T.E. and the control group participated in a pretest designed to assess baseline levels of performance. This test was used to select the core sentences described above from a larger set of potential core sentences. During the pretest, two word cues (noun–verb) were presented, and participants were instructed to provide the first word that came to mind to complete each cue. A total of 60 sentences were presented (27 with six verb synonyms suitable for the variance condition, and 33 with four verb synonyms suitable for the no-variance condition). Sentences were filtered out if T.E. responded with the correct target word or consistently responded with any particular target word across the set of related sentences. In these filtered sentences, none of the control participants answered with the correct target word. Sixteen sentences from each group were then randomly selected and used during training for both T.E. and the control participants.

T.E. participated in 31 separate study sessions, each with a total of 96 three-word sentences (three variations of 16 variance, studied sentences and three presentations of the same 16 no-variance, studied sentences; see Table 2). T.E. was tested on cued recall and recognition on a separate day following every 4 study sessions for a total of 8 test sessions. In his final test session, an auditory version of the cued-recall test was administered in a separate session following the visual cued-recall and recognition tests because time constraints prevented him from being tested on all three tests on the same day. On these tests, T.E. provided confidence ratings for his answers immediately after his recall or recognition response using a 5-point scale (see below). Control participants were involved in 2 separate study sessions (compared with T.E.'s 31 study sessions) and were tested 1 week following their 2nd study session. The control participants were tested on visual cued recall, auditory cued recall, and then visual recognition, in that order, providing confidence ratings for their answers on all three tests. In addition, control participants were tested on visual cued recall and visual recognition after an additional 7-week delay in an effort to lower performance.

During each study session, the sentence appeared on the screen for 2 s and remained on the screen, along with the question, *How much sense does this sentence make?*, for an additional 3 s. Participants rated the sentence on the basis of its meaning using the *c* (very little sense) through *m* (a lot of sense) keys (five keys total) on the keyboard. The person administering the test clicked the mouse to proceed to the next trial. During each recall session, the first two words were presented along with three question marks to promote recall of the third word. Participants were given as much time as necessary to provide the word and were allowed to skip the trial if they could not produce any answer. The person administering the test wrote down the answer for each trial and advanced to the next trial. Following the recall portion of the test, a two-word, forced-choice recognition test was administered. Responses were collected with the *1* and *2* keys on the keyboard. When providing their confidence ratings, participants used a 5-point scale (1 = *very sure,* 2 = *pretty sure,* 3 = *maybe,* 4 = *pretty unsure,* and 5 = *very unsure*). Confidence ratings were provided auditorily for the recall tests, and participants were instructed to use the *c* through *m* keys on the keyboard for the recognition test. Participants did not receive feedback regarding their performance on any of the tests.

## Results

### Visual Recognition Test

Figure 3 shows T.E.'s performance on the visual recognition memory test (a) and on the visual recall test (b) across all eight test sessions. Consistent with previous reports following errorless learning, our results showed that T.E.'s recognition memory performance for the studied stimuli in the traditional no-variance condition (61%) was above chance, $t(7) = 3.6$, $p < .01$. Also consistent with previous reports following errorless learning were our results showing that T.E.'s behavior in the no-variance condition was hyperspecific. His recognition memory performance for the not-studied stimuli was only 53% correct, a result that was both reliably below his performance on the studied stimuli, $t(7) = 2.8$, $p < .05$, and not reliably above chance, $t(7) = 1.1$, $p = .31$.

In contrast, T.E.'s recognition memory performance following training in the variance condition was similar for the studied (64%) and the not-studied (61%) items, $t(7) = 1.4$, $p = .21$, both of which were above chance levels of performance ($t$s > 6.2, $p$s < .01). Most critical, when comparing T.E.'s ability to generalize to the not-studied items, we found that his performance following variance training was significantly better than his performance following the traditional no-variance training, $t(7) = 2.5$, $p < .05$. A similar comparison between the two studied conditions revealed similar levels of performance in the two training conditions (64% vs. 61%), $t(7) = 1.0$, $p = .33$.

Table 2
*Sample Visual Recall and Recognition Memory Trials for the Four Conditions*

| Condition | Recall and recognition cue | Recall answer | Recognition choices |
|---|---|---|---|
| Variance, studied | *TRAIN frightened ???*<br>*TRAIN scared ????*<br>*TRAIN startled ???* | "Kangaroo" | *KANGAROO, DOVE* |
| Variance, not studied | *TRAIN shocked ???*<br>*TRAIN surprised ???*<br>*TRAIN terrified ???* | "Kangaroo" | *KANGAROO, DOVE* |
| No variance, studied | *SHEPHERD ate ???*<br>*SHEPHERD ate ???*<br>*SHEPHERD ate ???* | "Apple" | *APPLE, OLIVE* |
| No variance, not studied | *SHEPHERD swallowed ???*<br>*SHEPHERD consumed ???*<br>*SHEPHERD gobbled ???* | "Apple" | *APPLE, OLIVE* |

*Note.* In the recall test, participants were shown the cue and asked to verbally provide the studied target word that completed the sentence. In the recognition test, participants were shown the cue along with the two recognition choices (a studied target and a novel foil) and asked to indicate the correct target word. During the study sessions, the sentences were presented in a similar format (i.e., *TRAIN frightened KANGAROO*).

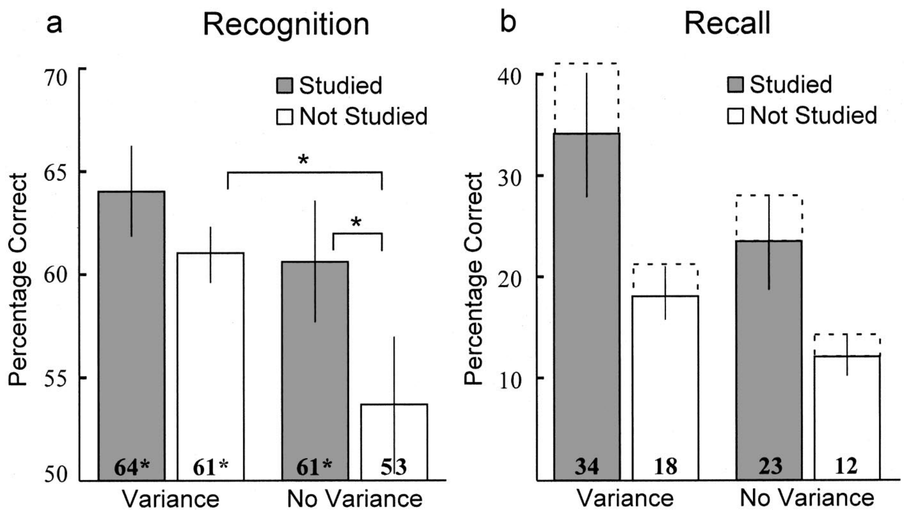


*Figure 3.* a: T.E.'s recognition memory, plotted in terms of percentage of correct items (chance performance is 50%). b: T.E.'s visual cued-recall performance, plotted in terms of percentage of correct items recalled and averaged across the eight test sessions for the variance and no-variance training conditions. Studied items are shown in gray, and nonstudied test items used to assess generalization are shown in white. In the recall task, dotted extensions to the bars indicate recall performance when semantically related items were generated. Bars indicate the standard error of the mean across the eight test sessions, and the asterisks represent significant differences ($p < .05$) between conditions of interest. Even with substantially less training, control participants' recognition memory performance was over 97% in each condition, and they recalled over 84% of the items in each condition.

A repeated measures analysis of variance (ANOVA), treating test session as a random effect, was used to further explore the data and examine the main effects of training task (variance vs. no variance) and of test type (studied vs. not studied) along with potential interactions. Alpha was set at .05. The ANOVA revealed a significant main effect of training task, $F(1, 7) = 15.3$, $p < .01$, such that T.E.'s overall percentage of correct responses in the variance condition (62%) was higher than in the no-variance condition (57%). Additionally, the ANOVA revealed a trend but a nonsignificant main effect of test type, $F(1, 7) = 5.2$, $p = .057$, with T.E.'s overall performance in the studied condition (63%) being somewhat higher than in the not-studied condition (57%). The interaction between training task and test type, however, did not reach significance, $F(1, 7) = 0.9$, $p = .37$, which was potentially the result of variability in T.E.'s performance in the no-variance condition. Although such an interaction would be clear evidence of a difference in generalization across training tasks, the lack of such an interaction does not preclude such a difference.

### *Visual Cued-Recall Test*

Data from T.E.'s eight visual cued-recall test sessions are also shown in Figure 3b. His performance on the visual cued-recall task was similar to his performance on the visual recognition memory task in many ways. For sentences trained in the no-variance condition, T.E. recalled more items in the studied condition (23%) than in the not-studied condition (12%), $t(7) = 2.8$, $p < .05$, demonstrating less than perfect generalization. However, because these items had been prescreened to remove any items that T.E. spontaneously generated prior to testing, a cued-recall rate of 12% may well represent above-chance performance (significantly more data on similarly prescreened but completely unstudied sentences would be required to accurately determine chance behavior).

For sentences trained in the variance condition, T.E. also recalled more items in the studied condition (34%) than in the not-studied condition (18%), $t(7) = 4.4$, $p < .01$. Thus, even in the variance condition, generalization was not perfect. Most critical, however, is that when comparing T.E.'s ability to generalize to the not-studied items, we found that his performance following variance training was significantly better than his performance following the traditional no-variance training, $t(7) = 3.8$, $p < .01$.

A repeated measures ANOVA on the recall percentages was again used to further explore the data and examine main effects of training task (variance vs. no variance) and of test type (studied vs. not studied) along with potential interactions. The ANOVA revealed a significant effect of training task, such that T.E.'s percentage of recall in the variance condition was higher than in the no-variance condition, $F(1, 7) = 22.2$, $p < .01$. There was also a significant main effect of test type, with performance in the studied condition being higher than in the not-studied condition, $F(1, 7) = 15.8$, $p < .01$. The interaction between study condition and test type was not reliable, $F(1, 7) = 3.4$, $p = .109$, however. The main effect of training task is potentially of some interest, especially when coupled with the post hoc observation that his percentage of recalled items in the variance, studied condition was higher than in the no-variance, studied condition (34% vs. 23%), $t(7) = 4.02$, $p < .01$. This advantage was observed despite the fact that each studied sentence was studied three times more in the no-variance condition than in the variance condition. Whether this is the result of an increased number of retrieval cues associated with the variance training or whether another factor may be responsible is unclear from the data at hand, but it does warrant additional study.

Finally, we note that there were several trials in which T.E. failed to generate the target word but did generate a semantically related word. For example, after studying the sentence *Dog attacked grizzly*, he responded with the semantically related word *bear* when presented with *Dog attacked ???* on a number of occasions. When the semantically related responses were included in the percentage of items recalled, the pattern of performance was quite similar, as can be seen in the dashed extensions on the recall graph in Figure 3, giving further support to the conclusion that T.E. had learned some of these items as semantic concepts, not just as simple word associations.

### Auditory Cued-Recall Test

T.E. completed one version of the auditory cued-recall test several days after he completed his final visual cued-recall test. The goal of this test was to determine whether T.E., like patients E.P. and K.C. (Bayley & Squire, 2002; Tulving, 1991), was able to transfer any of his knowledge across domains. In the variance condition, he recalled 25% of the studied items and a similar 23% of the not-studied items. In the no-variance condition, he recalled 10% of the study items and a somewhat greater 17% of the not-studied items. Although this reversal of the expected pattern in the no-variance condition (here showing numerically better performance for the not-studied items than for the studied items) is somewhat confusing, we caution against an overinterpretation of this result. Given the low level of overall performance in the not-studied condition (10 and 16 trials recalled out of 96) and the fact that there was only a single test session in this task, this difference could easily be explained by noise. We suggest, however, that consistent with previous reports (Bayley & Squire, 2002; Tulving, 1991), these results do demonstrate some transfer of knowledge from the visual to the auditory domain.

### Control Data

Because the control participants were given the same stimulus assignments as T.E., their data helped us to determine whether T.E.'s enhanced performance in the variance condition was the result of our manipulation or whether it was the result of an accidental imbalance in the overall ease of learning sentences in the two conditions. The data of the control participants are presented in Table 3. In the visual recognition memory test, control participants performed exceptionally well in the variance (97%) and no-variance (99%) conditions and in the studied (98%) and not-studied (98%) conditions (no significant differences). In the visual cued-recall test, control participants demonstrated similar levels of overall performance in the variance (88%) and no-variance conditions (81%), $t(2) = 4.3$, $p > .05$. They recalled similar numbers of items in the studied (85%) and not-studied (84%) test conditions across both types of training. For the auditory cued-recall test, control participants again performed similarly in recalling the target word in the variance (87%) and no-variance conditions (81%), $t(2) = 4.3$, $p > .05$. Control participants demonstrated equivalent performance for the studied (84%) and not-studied (84%) items across the two training conditions. In summary, the recognition performance of control participants was better than their recall performance, but there was no difference in their recall performance between the visual and auditory presentations.

We were concerned that the exceptionally high level of overall performance in the control data (especially in the recognition memory test) could have masked any difference between the variance and no-variance conditions for the control participants (a difference that could indicate an imbalance in the overall ease of learning sentences in the two conditions). To evaluate this possibility and to remove potential ceiling effects, we gave the control participants the visual cued-recall and recognition tests again after a delay of approximately 7 weeks. Overall performance in the recognition memory test was still very high after a 7-week delay in all conditions: variance (96%), no variance (96%), studied (96%), and not studied (96%). Overall performance in the recall test dropped approximately 20%, however, relative to the immediate testing. Again, however, there were no significant differences between the conditions: variance (63%), no variance (62%), studied (63%), and not studied (61%). Because each condition was associated with similar levels of performance and similarly affected by delay, we conclude that our randomization of sentences was effective in equating the overall level of difficulty across conditions.

### Confidence Ratings

During T.E.'s last test session, he provided confidence ratings (on a 1–5 scale, with 1 corresponding to the highest level of confidence) for his responses in all three tests. In the visual recognition memory test, his ratings averaged 1.95 for his correct responses and 2.13 for his incorrect responses. The distribution of these responses was similar, as assessed by a Kolmogorov–Smirnov test ($Z = .68$, $p = .74$). In the visual recall test, his ratings averaged 1.98 and 2.31, with his distributions again being similar, showing only marginal signs of differentiation ($Z = 1.2$, $p = .11$).

Table 3
*Percentage of Correctly Recalled Items on the Recognition Memory Test Following Two Study Sessions for 3 Age- and Gender-Matched Control Participants*

| | Variance, studied | | Variance, not studied | | No variance, studied | | No variance, not studied | |
|---|---|---|---|---|---|---|---|---|
| Test type | % correct | *SD* | % correct | *SD* | % correct | *SD* | % correct | *SD* |
| Visual cued recall | 88 | 4.2 | 88 | 6.2 | 82 | 7.8 | 81 | 10.2 |
| Auditory cued recall | 87 | 7.2 | 87 | 6.6 | 81 | 10.2 | 81 | 10.8 |
| Visual recognition | 97 | 2.5 | 97 | 2.8 | 99 | 0.7 | 99 | 0.7 |

In the auditory recall test, they averaged similar values of 2.11 and 2.32 for correct and incorrect responses, respectively ($Z = 1.0$, $p = .26$). Thus, his confidence ratings were similar for both correct and incorrect responses.

In contrast, control participants demonstrated a relationship between accuracy and confidence ratings, such that their confidence ratings were lower (meaning more confident) for correct answers. In the visual recognition memory task, their ratings averaged 1.16 and 1.00 for their correct and incorrect responses, respectively. In the visual recall test, their ratings averaged 1.29 and 2.12 for correct and incorrect responses, respectively, and in the auditory recall test, they averaged 1.31 and 1.88 for correct and incorrect responses, respectively. Given the high level of overall accuracy, there were far fewer incorrect trials in the control data than in T.E.'s data. One control participant had two incorrect responses in each of the tests, 1 had only a single incorrect trial in the recognition test, and 1 had no incorrect trials from the recognition test. A statistical analysis of the distribution of confidence ratings for these test runs was impossible. For each of the remaining runs, the distribution of confidence ratings was significantly different for correct and incorrect responses, however (visual recall: $Z = 2.6$, $p < .001$, and $Z = 2.2$, $p < .001$; auditory recall: $Z = 2.3$, $p < .001$, and $Z = 2.3$, $p < .001$). We note that none of the control participants had more than two incorrect responses in the recognition memory test. Thus, the apparent reversal of the expected pattern of confidence scores versus response accuracy cannot be relied on.

### *Performance Across Test Sessions*

The data so far have shown that across all eight test sessions, T.E. was able to learn the novel sentences and, in the case of training with variant forms of the sentences, was able to apply this knowledge in a flexible manner. It is unclear, however, when this knowledge was acquired and whether it was acquired gradually across the training session. In Table 4, we present data from each of T.E.'s eight test sessions across the four conditions for both the visual recognition memory task and the recall task. Unfortunately, no clear learning curve emerges from the data. Whether this is the result of noise in our single-participant measure or whether this reflects some initial amount of learning that saturated after the first few sessions cannot be determined from the data at hand. Future research may be able to address this issue.

## Discussion

We have demonstrated that a patient with severe amnesia was able to learn new semantic information in the form of three-word sentences and was able to generalize that information to related cues. Previous researchers have used errorless learning techniques to facilitate learning in memory-impaired patients using similar materials (Bayley & Squire, 2002; Hamann & Squire, 1995; Hayman, MacDonald, & Tulving, 1993; Tulving, 1991; Wilson, 1992). Consistent with previous reports, our findings demonstrated that, although patient T.E. was able to learn three-word sentences using the errorless learning technique, whatever he learned during this training showed signs of hyperspecificity. Simply rephrasing the cue by replacing the verb with a synonym resulted in a significant reduction in performance. However, we introduced a technique that not only allowed T.E. to demonstrate recall and recognition memory for a set of three-word sentences but also allowed him to apply this knowledge in a flexible way by generalizing well to rephrased versions of the sentences. To our knowledge, this is the first observation of this kind of semantic learning in a patient with severe MTL amnesia that can support this type of generalization. By introducing variance into the training set so that the specific, irrelevant details were not entirely consistent across training trials, we found that T.E. was apparently able to learn the information at a more conceptual level. These results have important implications for theories of semantic acquisition and potential rehabilitation strategies.

There are several other possible interpretations of the data that we must consider before we can confidently conclude that the introduction of variance into the training allowed T.E. to acquire some amount of semantic information that can be flexibly applied. First, we must consider the possibility that T.E. (and the control participants) might simply be forming simple word associations between the subject and the object in the sentence, irrespective of the verb. In a debriefing with control participants, some admitted that often they ignored the verb during the test sessions and relied on the subject word in recalling the object of the sentence. T.E.'s data do not support this conclusion, however. First, if T.E. were

Table 4
*T.E.'s Recognition Memory (RM) and Recall Performance (RP; Percentage of Correct Responses) for Each of the Eight Test Sessions*

| | No variance, studied | | No variance, not studied | | Variance, studied | | Variance, not studied | | Overall average | |
|---|---|---|---|---|---|---|---|---|---|---|
| Session | RM | RP | RM | RP | RM | RP | RM | RP | RM | RP |
| 1 | 67 | 2 | 58 | 4 | 58 | 6 | 60 | 0 | 61 | 3 |
| 2 | 52 | 10 | 50 | 8 | 56 | 19 | 60 | 15 | 55 | 13 |
| 3 | 73 | 15 | 60 | 15 | 67 | 33 | 69 | 21 | 67 | 21 |
| 4 | 62 | 23 | 67 | 6 | 69 | 44 | 60 | 23 | 65 | 23 |
| 5 | 69 | 38 | 54 | 17 | 65 | 48 | 58 | 31 | 61 | 31 |
| 6 | 58 | 35 | 56 | 19 | 73 | 60 | 65 | 34 | 63 | 34 |
| 7 | 52 | 25 | 48 | 19 | 69 | 33 | 56 | 25 | 56 | 25 |
| 8 | 52 | 33 | 35 | 12 | 56 | 31 | 58 | 23 | 50 | 25 |
| Average | 61 | 23 | 53 | 12 | 64 | 34 | 61 | 18 | | |

simply forming an association between the two nouns, his performance in the studied and not-studied conditions should not differ. Although his performance in these two conditions was similar in the recognition memory test, it differed during recall (see Figure 3). To test this possibility more directly, we administered an additional recall test at the end of his final test session, in which he was presented with one of the subject words paired with a verb from another sentence frame. T.E. did not provide the target word for that subject noun on any of these mixed-verb sentence frames, suggesting that he was attending to the verb and not merely learning a subject–object association. When combined with his performance in the not-studied conditions, in which he could show generalization following the replacement of the verb with a synonym, the data suggest that T.E. was at least learning a complex association between the subject noun, some aspect of the meaning of the verb, and the object noun.

An additional potential concern is that because the studied conditions were significantly different from one another, then the degree to which the not-studied conditions were impaired may not be able to be compared in a meaningful way. In other words, the difference in the studied conditions may be indicative of a baseline problem (e.g., the variance task was somehow easier than the no-variance task), and any performance gain in the not-studied condition for variance relative to no variance is a result of a scaling artifact. To address this possibility, we looked at the final cued-recall test session (No. 8) in which T.E.'s percentage recalled performance in the variance, studied (31%) and no-variance, studied (33%) conditions was closely matched. T.E.'s percentage recalled for the variance, not-studied (23%) condition was much higher than his percentage recalled for the no-variance, not-studied (12%) condition. Thus, when performance on the studied items was relatively equal, performance on the generalization items was disproportionately impaired for the no-variance condition. Further, we again point out that not only were the training items screened ahead of time to establish zero levels of performance in T.E. in all conditions, but also that control participants performed identically in the two studied conditions. Therefore, it is unlikely that the stimuli used in the variance condition differed in any significant way from the stimuli used in the no-variance condition.

An argument could be made that the capacity to acquire declarative knowledge by residual tissue in the MTL is responsible for this flexible learning. However, if structures in the MTL were able to acquire this new semantic information in a normal, albeit slower fashion, then T.E. should have been able to generalize in much the same way as control participants. However, whereas control participants demonstrated no difference in their ability to generalize to the novel test set across the two conditions, T.E. demonstrated a marked difference. This finding suggests that T.E.'s learning was qualitatively different from that of control participants. Note that we have characterized the hippocampal system as including the hippocampus proper, as well as the entorhinal, perirhinal, and parahippocampal cortices. Although we do not make any claims here regarding the differences between these structures, it is worth mentioning that there is a popular theory suggesting that semantic learning may depend on a nonhippocampal perirhinal–entorhinal system (Baddeley, Vargha-Khadem, & Mishkin, 2001; Vargha-Khadem et al., 1997). Unfortunately, these data cannot speak to this theory directly because we were unable to quantify the degree of damage to these structures in T.E. However, T.E. does appear to be qualitatively different from Jon, the patient with developmental amnesia, who is seemingly able to acquire semantic information far more easily than can T.E. (Vargha-Khadem et al., 1997).

It is also important to note that information acquired by MTL structures is thought to be available to conscious awareness. Bayley and Squire (2002) reported that E.P.'s knowledge was not available to conscious awareness, as was indicated by equivalent reaction times for correct and incorrect responses. Similarly, T.E.'s learning was not available to conscious awareness, even when he provided the correct answer. There was no difference in his confidence ratings for correct and incorrect answers for the three-word sentences, and as with E.P., there was no difference between his correct and incorrect reaction times during the recognition test for any of the conditions ($p > .05$). In addition, throughout all of the testing sessions, T.E. professed not to remember seeing the sentences before and would often claim not to know the correct answer immediately before providing it. It seems highly unlikely that T.E. was able to use residual MTL functions to acquire this information and generalize it to related cues.

If, as is suggested by the data, T.E. has been able not only to learn new factual information but also to apply this information with some flexibility and in an untrained modality (auditory), we can consider how this learning should be classified. Overall, T.E.'s learning is clearly slow and impaired following his MTL damage, and the learning does not appear to be accessible to conscious awareness (at least not with the amount of training used). As such, it would be classified as nondeclarative, even though it is for factual, semantic information.

Bayley and Squire (2002) raised the question of what kind of nondeclarative memory might support gradual learning of factual information. They concluded that E.P. gradually learned the three-word sentences through something akin to perceptual learning in the neocortex. However, they acknowledged that perceptual learning is typically highly specific to the stimuli that were studied, yet E.P. demonstrated transfer of that learning to an auditory test of the material. E.P. appeared to learn the items more abstractly than one would expect in typical perceptual learning. The results of the current study replicate and extend these results in another patient with amnesia. With variance training, nondeclarative learning can be responsible for acquiring and generalizing semantic or factual information.

Whereas Bayley and Squire (2002) argued that the neocortical learning in this task is perceptual in nature, we relax this description to include learning that is conceptual as well. The results of both studies are consistent with the kind of neocortical learning that is proposed in the McClelland et al. (1995) model discussed in the introduction to this article. In this model, the neocortex can acquire semantic knowledge gradually over many training episodes. When the system is intact with functional MTL structures (e.g., the hippocampus), this hippocampal system helps not only to drive behavior for some period of time, but also to drive the training of the neocortex. In effect, by virtue of having an intact MTL, the neocortex is being presented with errorless learning in a varied environment. We suggest that our technique of including variance in an errorless learning paradigm serves to act as an external, environmental proxy for what the MTL structures are normally doing to help integrate information into the neocortex.

Patients with semantic dementia provide an interesting example of this system when the temporal neocortex is damaged but MTL structures are intact. Graham, Patterson, Pratt, and Hodges (1999) presented a patient with semantic dementia who was able to acquire new vocabulary with repeated training, presumably relying on the MTL structures. However, 6–8 weeks following the cessation of the training, his fluency scores dropped by 60%. The authors argued that the information could not be consolidated into the neocortex adequately because of the damage there and that the time-limited nature of the MTL memory structures could not retain all of the information for that period of time. These results provide a nice contrast to our results with T.E. by demonstrating that the neocortex serves as a permanent store for semantic information once it has been consolidated from the MTL.

Although T.E. was able to acquire semantic information in this study by what we suggest is learning in the neocortex, the quality of the memory is still an open issue that these data are not able to address. We have pointed out that T.E. did not demonstrate a difference in his reaction time or confidence ratings for his correct and incorrect answers, indicating that he did not have conscious awareness of his knowledge for this information. We have argued that this effect reflects T.E.'s inability to use his MTL structures to declaratively (consciously) learn and retrieve this information. However, it is possible that his inability to discriminate between his correct and incorrect responses is a reflection of weaker memory strength relative to that of control participants. Although he demonstrated significant learning in this study, he was still only in the 60% range, compared with the 90% range of the control participants. If he had been given such extensive training that his performance was equated with that of the control participants, would he have been able to consciously retrieve that information from the neocortex? In addition, would he have been able to apply it with the same near-perfect flexibility that the control participants could apply the information? In future research, it would be of interest to determine whether information that is consolidated into the neocortex after being acquired by the MTL structures would be qualitatively different from information that is acquired by the neocortex directly.

The training technique described here has important implications for and suggests possibilities for rehabilitation. Because generalization of acquired knowledge would be a key goal in any rehabilitation program, it would seem beneficial to explore the simple introduction of variability (variability that encourages the abstraction of the central to-be-learned information) into rehabilitative training regimes. In fact, we have made one elementary attempt at this by using the technique to teach T.E. the names of his grandchildren (a task that he was unable to perform following his anoxic episode). In the variance condition, we presented four different pictures of two of the grandchildren, and in the no-variance condition, we presented one picture of the other two grandchildren. In both conditions, each grandchild was presented the same number of times, for a total of 2,000 training trials per child. T.E.'s recall was then tested with a four-choice recognition test with the studied pictures and with novel pictures that had not been studied. Although the lack of experimental control limits our ability to draw firm conclusions from these data (e.g., children were three boys and one girl, with two of the boys' names differing by only one phoneme), we found that his generalization was impaired in the no-variance condition relative to the variance condition, which is consistent with the results presented in this article.

In summary, the data presented here from patient T.E. represent an instance not only of successful acquisition of factual information in a patient with severe amnesia, but also of that patient's ability to flexibly use and generalize this information to performance on a novel test set—the hallmark of semantic information. These data support the hypothesis that, when a version of the errorless learning technique is extended to include variance in the training set, the neocortex can acquire semantic information that can be used flexibly. We propose that this learning is nondeclarative in nature but suggest that it may potentially use the same mechanisms that are responsible for the gradual consolidation of semantic information that normally results from the interaction of MTL structures with the neocortical sites that are the eventual repository of semantic information. Further research will certainly be needed, not only to address the validity of this hypothesis, but also to determine whether the technique demonstrated here (or potential extensions and elaborations) may be useful in rehabilitation applications.

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