

Images of Medial Temporal Lobe Functions in Human Learning and Memory

John D. E. Gabrieli,*† James B. Brewer,† and Russell A. Poldrack*

**Department of Psychology and †Neurosciences Program, Stanford University,
Stanford, California 94305*

Investigations of the neural basis of mammalian memory have focused more often on the medial temporal lobe (MTL) than on any other brain region. In humans, the amnesic syndrome revealed the essential importance of the multiple structures located in the MTL system for declarative memory (the remembrance of events and facts). Other neural systems mediate procedural forms of memory, including delay eyeblink conditioning, which depends on the cerebellum, and cognitive skill learning, which depends on the striatum. We review three functional imaging studies that reveal different patterns of MTL activation associated with declarative and procedural memory tasks. One study shows separate MTL activations during the encoding or retrieval of declarative memories. A second study shows MTL activation that occurs in parallel with cerebellum-dependent delay eyeblink conditioning, but does not appear to influence that form of procedural memory. A third study reveals suppression of the MTL during striatum-dependent cognitive skill learning. These studies provide images of MTL activations that are correlated with, independent from, or antagonistic to memory performance. © 1998 Academic Press

Investigations of the neural basis of mammalian memory have probably focused more often on the medial temporal lobe (MTL) than on any other brain region. The importance of this region in memory was revealed by the case study of H.M., who underwent bilateral MTL resections for otherwise intractable epilepsy in 1953 (Scoville & Milner, 1957). The resections resulted in a syndrome of global amnesia, a severe and pervasive deficit in remembering events and facts encountered after the surgery (anterograde amnesia). The specificity of MTL contributions to long-term memory was shown by the sparing of short-term memory and of nonmnemonic perceptual, motor, and cognitive abilities. The essential and circumscribed contribution of the MTL region to mammalian memory has inspired a major program of interrelated cognitive neuroscience research in the rat, monkey, and human (reviewed in Cohen & Eichenbaum, 1993; Squire, 1992).

Two ironies have emerged from the fact that the critical role of the MTL region in memory was discovered in a human. First, most subsequent advances in understanding the mnemonic role of the MTL have come from rat and monkey studies, rather than from human studies. Second, most advances in

Address requests for reprints and correspondence to John Gabrieli, Department of Psychology, Jordan Hall, Stanford University, Stanford, CA 94305. Fax: 650-725-5699. E-mail: gabrieli@psych.stanford.edu.

understanding the mnemonic role of the human MTL have occurred through discoveries of what memory capacities are not subserved by the MTL.

Direct analysis of MTL contributions to human memory have, until recently, been limited largely to behavioral analysis of the consequence of happenstance lesions that traverse anatomical boundaries. Animal studies, therefore, had two major advantages over human studies. First, electrophysiological recording studies could complement lesion studies. Second, selective lesions could be made in the multiple structures located in the MTL, including the amygdala, parahippocampal and perirhinal cortices, entorhinal cortex, subiculum, CA fields, and dentate gyrus. Therefore, elucidation of specific mnemonic functions of the human MTL have yielded only three consensus insights: (1) left and right medial temporal regions mediate verbal and nonverbal memory processes, respectively (Milner, 1971); (2) the amygdala participates narrowly in emotional modulation of memory but is not otherwise essential for many aspects of memory (Bechara, Tranel, Damasio, Adolphs, Rockland, & Damasio, 1995; Cahill, Babinsky, Markowitsch, & McGaugh, 1995; Cahill, Haier, Fallon, Alkire, Tang, Keator, Wu, & McGaugh, 1996; LaBar, LeDoux, Spencer, & Phelps, 1995); and (3) more extensive damage to the medial-temporal region results in more severe amnesia (Corkin, Amaral, Gonzalez, Johnson & Hyman, 1997; Rempel-Clower, Zola, Squire, & Amaral, 1996). A question as simple, however, as whether the MTL participates in the recording of experience into memory (encoding) and/or the recovery of experience from memory (retrieval) has remained unanswered in lesion studies.

With such limited methods available to examine what the MTL does in human memory, researchers have focused on what the MTL does not do by studying memory processes that are preserved in amnesic patients with MTL lesions. Amnesic patients with bilateral MTL lesions have shown intact classical eyeblink conditioning (e.g., Gabrieli, McGlinchey-Berroth, Carrillo, Cermak, Gluck, & Disterhoft, 1995), motor skill learning (e.g., Milner, 1962), visual skill learning (e.g., Cohen & Squire, 1980), cognitive skill learning (e.g., Cohen, Eichenbaum, Deacedo, & Corkin, 1985; Knowlton, Squire, & Gluck, 1994), perceptual repetition priming (e.g., Cermak, Talbot, Chandler, & Wolbarst, 1985; Gabrieli, Milberg, Keane, & Corkin, 1990; Graf, Squire, & Mandler, 1984), and conceptual repetition priming (e.g., Graf, Shimamura, & Squire, 1985; Keane, Gabrieli, Monti, Fleischman, Cantor, & Noland, 1997; Vaidya, Gabrieli, Keane, & Monti, 1995). These various forms of spared learning and memory are known to depend on separable cortical, striatal, and cerebellar systems (reviewed in Gabrieli, 1998).

Studies of forms of learning and memory that do not depend on the MTL have had two broad benefits. First, they have revealed the identities of many other memory systems of the human brain. Indeed, the wide variety of forms of preserved learning in amnesia and their subsequent linkage with many different brain regions have suggested that all brain regions are involved in distinctive forms of learning and memory. Second, the dissociations between impaired and intact forms of learning in amnesia have provided the empirical basis for theoretical distinctions between two major classes of memory. One class is that of declarative memory, as assessed via direct, explicit measures of recall and recognition for facts and events (Cohen & Squire, 1980; Graf & Schacter, 1985), which depends on integrity of the MTL. The other class is procedural memory, as assessed via indirect, implicit measures of experience-

induced changes in performance, which does not depend on integrity of the MTL. These theories have provided conceptual frameworks that integrate studies of normal and brain-injured humans and animals.

Progress in functional neuroimaging with positron emission tomography (PET) and functional magnetic resonance imaging (fMRI), however, has broken the shackles of cognitive neuroscience memory research with humans. Now, it is possible to complement lesion studies with systematic experimental recording studies of the MTL. Further, the resolution of imaging studies allows for the delineation of specific structure–function relations within the MTL. Such studies can examine the activity of the MTL not only in declarative memory, but also during procedural memory.

MTL ACTIVITY DURING THE ENCODING AND RETRIEVAL OF DECLARATIVE MEMORY

Human and nonhuman lesion studies have established the essential importance of the MTL for declarative memory, so it was somewhat of a surprise when a number of functional neuroimaging studies did not detect MTL activity during the encoding or retrieval of declarative memories (e.g., Buckner, Peterson, Ojemann, Miezin, Squire, & Raichle, 1995; Kapur, Craik, Tulving, Wilson, Houle, & Brown, 1994; Shallice, Fletcher, Frith, Grasby, Frackowiak, & Dolan, 1994). Other studies, however, have shown MTL activity during the encoding (Grady, Mcintosh, Horwitz, Maisog, Ungerleider, Mentis, Pietrini, Schapiro, & Haxby, 1995; Tulving, Kapur, Markowitsch, Craik, Habib, & Houle, 1994; Stern, Corkin, Gonzalez, Guimares, Baker, Jennings, Carr, Sugiura, Vedantham, & Rosen, 1996) or retrieval (Nyberg, Mcintosh, Houle, Nilsson, & Tulving, 1996; Rugg, Fletcher, Frith, Frackowiak, & Dolan, 1997; Schacter, Alpert, Savage, Rauch, & Albert, 1996; Squire, Ojemann, Miezin, Peterson, Videen, & Raichle, 1992) of memories.

In an fMRI study, we examined whether different components of the human MTL make distinct contributions to the encoding and retrieval of declarative memories (Gabrieli, Brewer, Desmond, & Glover, 1997). To evoke MTL activity during encoding, healthy young subjects were scanned while viewing color pictures of complex indoor and outdoor scenes. They were instructed to classify each picture as that of an indoor or outdoor scene, and to remember each picture for a later test of memory. One condition maximized encoding demands by requiring subjects to encode novel pictures seen once only. The other condition minimized encoding demands by requiring subjects to encode familiar pictures shown repeatedly. In five of six subjects, there was greater activation in a posterior MTL location when subjects encoded novel relative to familiar pictures. The activation was bilateral and focused in the parahippocampal gyrus. This finding replicated a similar prior study (Stern et al., 1996).

To evoke MTL activity during retrieval, subjects studied line drawings of common objects and animals prior to scanning. During scanning, subjects saw words and were asked to judge whether they were the names of the previously studied line drawings. One condition maximized the retrieval of memories by presenting mostly words that were the names of studied line drawings. The other condition minimized the retrieval of memories by presenting mostly words that were not the names of studied line drawings. Five of six subjects showed greater activation in an anterior MTL location when the words were

mostly the names of studied pictures. This bilateral activation was focused in the subiculum. The association between MTL activation and successful retrieval of declarative memories is consistent with other imaging studies (e.g., Rugg et al., 1997; Schacter, Reiman, Uecker, Polster, Yun, & Cooper, 1995; Schacter et al., 1996). The anterior MTL location of activation is consistent with a correlation between anterior activation and recognition memory accuracy found in a PET study (Nyberg et al., 1996).

The present results showed a dissociation between two MTL activations: a posterior activation during an encoding task that was greatest for novel stimuli and an anterior activation during a retrieval task that was greatest for remembered stimuli. These results demonstrate that in humans different structures in the MTL make different contributions to declarative memory. The precise nature of the psychological processes signified by these activations remains to be elucidated, however. For example, the posterior, parahippocampal activation that occurred for novelty encoding may provide an index of stimulus familiarity to a subject. This region is variably damaged in cases of severe amnesia. It is now known that some posterior, parahippocampal tissue was not resected in the amnesic patient H.M. (Corkin et al., 1997). This tissue is completely damaged in another severely amnesic patient, E.P. (Squire & Knowlton, 1995). Although H.M. and E.P. are similarly and severely amnesic in many respects, they differ in at least one important way. When presented with extended study of complex color scenes, similar to those used in the fMRI study, H.M.'s recognition accuracy was equal to that of normal control subjects who had studied the pictures more briefly (Freed, Corkin, & Cohen, 1987). Extended study, however, did not elevate E.P.'s recognition above chance (Reed, Hamann, Stefanacci, & Squire, 1997). Thus, spared posterior, parahippocampal tissue could provide an index of stimulus familiarity for H.M., but could not for E.P. These findings support the possibility that this region participates in recognition familiarity.

MTL ACTIVITY DURING THE ENCODING AND RETRIEVAL OF PROCEDURAL MEMORY

Functional neuroimaging studies can provide new insights into the interactions of declarative and procedural memory systems during skill learning. Skill learning is typically measured by improvement in performance across multiple trials, so encoding and retrieval are not separable in time as they are in declarative memory paradigms.

Classical eyeblink conditioning is sometimes classified separately from skill learning tasks, although it is measured as an improvement in performance across trials. In the typical delay paradigm, a 250- to 500-ms tone (conditioned stimulus or CS) is repeatedly followed by an air puff (unconditioned stimulus or US) delivered to the eye that elicits reflexively a blink, the unconditioned response (UR). The tone and air puff coterminate. With repeated CS-US pairings, subjects learn to associate the tone with the air puff and initiate an eyeblink (conditioned response or CR) to the CS before the onset of the US. In the rabbit, electrophysiological activity in the cerebellum (McCormick & Thompson, 1987) and in the hippocampus (Disterhoft, Coulter, & Alkon, 1986) parallels the development of behavioral CRs. Lesions of the cerebellar dentate-interpositus nuclei prevent acquisition or abolish retention of the conditioned

association (Clark, McCormick, Lavond, & Thompson, 1984; Glickstein, Hardiman, & Yeo, 1983). Hippocampal lesions, however, do not impair delay conditioning in the rabbit (Schmaltz & Theios, 1972). Presumably, CR-correlated electrophysiological activity in the hippocampus reflects a parallel learning circuit that does not mediate delay conditioning. Hippocampal lesions, however, do impair closely related forms of eyeblink conditioning, including trace conditioning, which differs from delay only by inserting a short period, a second or less, between the offset of the CS and the onset of the US (Solomon, Vander Schaaf, Thompson, & Weisz, 1986).

The combination of lesion and functional neuroimaging studies provides a strikingly similar picture of cerebellar and MTL contributions to human eyeblink conditioning. First, cerebellar lesions in humans abolish delay eyeblink conditioning (Daum, Schugens, Ackermann, Lutzenberger, Dichgans, & Birbaumer, 1993). Second, delay eyeblink conditioning is intact in amnesic patients with bilateral MTL lesions (Gabrieli et al., 1995). Third, PET studies have reported both cerebellar and medial-temporal activations associated with delay conditioning that parallel the development of behavioral CRs (Blaxton, Zeffiro, Gabrieli, Bookheimer, Carrillo, Theodore, & Disterhoft, 1996; Logan & Grafton 1995). Fourth, amnesic patients with MTL lesions who are unimpaired on delay conditioning show impaired trace conditioning with CS-US trace intervals as short as 500 ms (McGlinchey-Berroth, Carillo, Gabrieli, Brawn & Disterhoft, 1997). Thus, the learning of delay eyeblink conditioning in humans appears to depend on a cerebellar memory system, but parallel learning occurs simultaneously in the MTL. The MTL learning is irrelevant for delay conditioning, but critical for other sorts of conditioning such as trace eyeblink conditioning.

The cerebellar and MTL systems appear to operate independently (delay conditioning) or cooperatively (trace conditioning) during eyeblink conditioning. However, in another form of skill learning, probabilistic classification, procedural and declarative systems may operate competitively. In this task, subjects make classification judgments about stimuli that have probabilistic, or fuzzy, category membership. Subjects are presented with a set of symbols and asked to decide whether the stimuli predict one of two possible weather outcomes ("rain" or "sunshine"). Stimuli are probabilistically, rather than absolutely, related to each category (e.g., one set of symbols is associated with rain 80% of the time and sunshine 20%), so that explicit memory for specific trials can be misleading as a basis for categorization. Instead, the task requires abstraction of information about cue-outcome associations over a number of trials, despite contradictory trials, for successful learning. Amnesic patients with MTL lesions learn to perform this task as well as normal subjects early in training, but are impaired later in training (Knowlton, Squire, & Gluck, 1994). Damage to the basal ganglia, as in Huntington's disease and Parkinson's disease, impairs learning of probabilistic classification (Knowlton, Mangels, & Squire, 1996a; Knowlton, Squire, Paulsen, Swerdlow, Swenson, & Butters, 1996b). These findings demonstrate that cognitive skill learning in this task depends on a striatal procedural system in early learning, but then comes to depend on a declarative system in late learning.

We examined activity in memory systems via fMRI during the learning of the cognitive skill underlying probabilistic classification (Poldrack, Prabhakaran, Seger, Desmond, Glover, & Gabrieli, submitted). Eight subjects participated

in four successive fMRI scans during which they alternated between performing the weather prediction task and a baseline task with similar perceptual and motor, but minimal cognitive and no learning, demands. Classification performance (consistency of responses with the dominant probabilities) improved from 61 to 72% across the four scans as subjects gained their cognitive skill. The critical imaging findings were (1) activation of the right caudate and several prefrontal areas during classification relative to baseline performance, and (2) deactivation of bilateral MTL regions during classification relative to baseline performance. During learning, the deactivation of the left MTL region increased from scan 1 to scan 2, and then decreased (approached baseline) from scans 2 to 4.

These results are the first to show striatal activation during cognitive skill learning in humans, an activation consistent with the deleterious consequences of striatal lesions on cognitive skill learning (Saint-Cyr, Taylor, & Lang, 1988; Knowlton et al., 1996a, 1996b). They also suggest that an antagonistic relation between frontostriatal working memory and MTL declarative memory systems early in such learning. Because declarative retrieval of specific previous trials can impede performance early in training (due to the probabilistic cue–outcome relationship), subjects may have suppressed declarative memory retrieval early in training. This suppression resulted in below-baseline MTL activation, and the suppression became greater from scan 1 to scan 2. In later learning, subjects may have begun to revert to a declarative memory strategy after the larger number of trials came to accurately reflect the cue–response probabilities, and this was reflected in a relaxation of left MTL suppression from scans 2 through 4. This change in MTL activation from naive to skilled levels of performance is consistent with the finding that amnesic patients with MTL damage learn the weather prediction task as well as normal subjects early in training (through the first 50 trials) but are impaired later in training (Knowlton et al., 1994).

CONCLUSIONS

Functional neuroimaging revealed three contrasting relations between MTL activation and memory performance across three memory tasks. For declarative memory retrieval, MTL activation was associated with superior accuracy. For delay eyeblink conditioning, MTL activation appears to reflect a parallel learning circuit that does not modulate cerebellum-mediated procedural learning. For probabilistic classification, MTL activation appears to reflect a competition between striatal-mediated procedural learning that is essential for early cognitive skill learning and MTL-mediated declarative learning that is essential for late learning. In combination, these studies reveal with increasing precision the anatomical specificity and dynamic nature of MTL contributions to human memory.

REFERENCES

- Bechara, A., Tranel, D., Damasio, H., Adolphs, R., Rockland, C., & Damasio, A. R. (1995). Double dissociation of conditioning and declarative knowledge relative to the amygdala and hippocampus in humans. *Science*, **269**, 1115–1118.
- Blaxton, T. A., Zeffiro, T. A., Gabrieli, J. D. E., Bookheimer, S. Y., Carrillo, M. C., Theodore, W. H., & Disterhoft, J. F. (1996). Functional mapping of human learning: A positron emission

- tomography activation study of eyeblink conditioning. *Journal of Neuroscience*, **16**, 4032–4040.
- Buckner, R. L., Peterson, S. E., Ojemann, J. G., Miezin, F. M., Squire, L. R., & Raichle, M. E. (1995). Functional anatomical studies of explicit and implicit retrieval tasks. *Journal of Neuroscience*, **15**, 12–29.
- Cahill, L., Babinsky, R., Markowitsch, H. J., & McGaugh, J. L. (1995). The amygdala and emotional memory. *Nature*, **377**, 295–296.
- Cahill, L., Haier, R. J., Fallon, J., Alkire, M. T., Tang, C., Keator, D., Wu, J., & McGaugh, J. L. (1996). Amygdala activity at encoding correlated with long-term, free recall of emotional information. *Proceedings of the National Academy of Sciences of the United States of America*, **93**, 8016–8021.
- Cermak, L. S., Talbot, N., Chandler, K., & Wolbarst, L. R. (1985). The perceptual priming phenomenon in amnesia. *Neuropsychologia*, **23**, 615–622.
- Clark, G. A., McCormick, D. A., Lavond, D. G., & Thompson, R. F. (1988). Effects of lesions of cerebellar nuclei on conditioned behavioral and hippocampal neuronal responses. *Brain Research*, **29**, 125–136.
- Cohen, N. J., & Eichenbaum, H. (1993). *Memory, amnesia and the hippocampal system*. Cambridge, MA: MIT Press.
- Cohen, N. J., Eichenbaum, H., Deacado, B. S., & Corkin, S. (1985). Different memory systems underlying acquisition of procedural and declarative knowledge. *Annals of New York Academy of Science*, **444**, 54–71.
- Cohen, N. J., & Squire, L. R. (1980). Preserved learning and retention of pattern-analyzing skill in amnesia: Dissociation of knowing how and knowing that. *Science*, **210**, 207–210.
- Corkin, S., Amaral, D. G., Gonzalez, R. G., Johnson, K. A., & Hyman, B. T. (1997). H.M.'s medial temporal-lobe lesion: Findings from MRI. *Journal of Neuroscience*, **17**, 3964–3979.
- Daum, I., Schugens, M. M., Ackermann, H., Lutzenberger, W., Dichgans, J., & Birbaumer, N. (1993). Classical conditioning after cerebellar lesions in humans. *Behavioral Neuroscience*, **107**, 748–756.
- Disterhoft, J. F., Coulter, D. A., & Alkon, D. L. (1986). Conditioning-specific membrane changes of rabbit hippocampal neurons measured in vitro. *Proceedings of the National Academy of Sciences of the United States of America*, **83**, 2733–2737.
- Freed, D. M., Corkin, S., & Cohen, N. J. (1987). Forgetting in H.M: A second look. *Neuropsychologia*, **25**, 461–471.
- Gabrieli, J. D. E. (1998). Cognitive neuroscience of human memory. *Annual Reviews of Psychology*, **47**, 87–115.
- Gabrieli, J. D. E., Brewer, J. B., Desmond, J. E., & Glover, G. H. (1997). Separate neural bases of two fundamental memory processes in the human medial temporal lobe. *Science*, **276**, 264–266.
- Gabrieli, J. D. E., McGlinchey-Berroth, R., Carrillo, M. C., Cermak, L. S., Gluck, M. A., & Disterhoft, J. F. (1995). Intact delay-eyeblink classical conditioning in amnesia. *Behavioral Neuroscience*, **109**, 819–827.
- Gabrieli, J. D. E., Milberg, W., Keane, M. W., & Corkin, S. (1990). Intact priming of patterns despite impaired memory. *Neuropsychologia*, **28**, 417–427.
- Glickstein, M., Hardiman, M. J., & Yeo, C. H. (1983). The effects of cerebellar lesions on the conditioned nictitating response of the rabbit. *Journal of Physiology (London)*, **341**, 30–31.
- Grady, C. L., Mcintosh, A. R., Horwitz, B., Maisog, J. M., Ungerleider, L. G., Mentis, M. J., Pietrini, P., Schapiro, M. B., & Haxby, J. V. (1995). Age-related reductions in human recognition memory due to impaired encoding. *Science*, **269**, 218–221.
- Graf, P., Shimamura, A. P., & Squire, L. R. (1985). Priming across modalities and priming across category levels: Extending the domain of preserved function in amnesia. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, **11**, 386–396.
- Graf, P., & Schacter, D. L. (1985). Implicit and explicit memory for new associations in normal and amnesic subjects. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, **11**, 501–518.

- Graf, P., Squire, L. R., & Mandler, G. (1984). The information that amnesic patients do not forget. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, **10**, 164–178.
- Kapur, S., Craik, F. I. M., Tulving, E., Wilson, A. A., Houle, S., & Brown, G. M. (1994). Neuroanatomical correlates of encoding in episodic memory: Levels of processing effect. *Proceedings of the National Academy of Sciences of the United States of America*, **91**, 2008–2011.
- Keane, M. M., Gabrieli, J. D. E., Monti, L. A., Fleischman, D. A., Cantor, J. M., & Noland, J. S. (1997). Intact and impaired conceptual memory processing in amnesia. *Neuropsychology*, **11**, 59–69.
- Knowlton, B. J., Mangels, L. S., & Squire, L. R. (1996a). A neostriatal habit learning system in humans. *Science*, **273**, 1399–1402.
- Knowlton, B. J., Squire, L. R., & Gluck, M. (1994). Probabilistic classification learning in amnesia. *Learning and Memory*, **1**, 106–120.
- Knowlton, B. J., Squire, L. R., Paulsen, J. S., Swerdlow, N. R., Swenson, M., & Butters, N. (1996b). Dissociations within nondeclarative memory in Huntington's disease. *Neuropsychology*, **10**, 538–548.
- LaBar, K. S., LeDoux, J. E., Spencer, D. D., & Phelps, E. A. (1995). Impaired fear conditioning following unilateral temporal lobectomy in humans. *Journal of Neuroscience*, **15**, 6846–6855.
- Logan, C. G., & Grafton, S. T. (1995). Functional anatomy of human eyeblink conditioning determined with regional cerebral glucose metabolism and positron-emission-tomography. *Proceedings of the National Academy of Sciences of the United States of America*, **92**, 7500–7504.
- McCormick, D. A., & Thompson, R. F. (1987). Neuronal responses of the rabbit cerebellum during the activation and performance of a classically conditioned NM-eyelid response. *Journal of Neuroscience*, **4**, 2811–2822.
- Milner, B. (1962). Physiologie de l'hippocampe. In P. Passouant (Ed.), *Les troubles de la memoire accompagnant des lésions hippocampiques bilaterales* (pp.257–272). Paris: Centre National de la Recherche Scientifique.
- Milner, B. (1971). Interhemispheric differences in localization of psychological processes in man. *British Journal of Medicine*, **27**, 272–277.
- Nyberg, L., McIntosh, A. R., Houle, S., Nilsson, L. G., & Tulving, E. (1996). Activation of medial temporal structures during episodic memory retrieval. *Nature*, **380**, 715–717.
- Poldrack, R. A., Prabhakaran, V., Seger, C. A., Desmond, J. E., Glover, G. H., & Gabrieli, J. D. E. (submitted). Suppression of the declarative memory system during habit learning.
- Reed, J. M., Hamann, S. B., Stefanacci, L., & Squire, L. R. (1997). When amnesic patients perform well on recognition memory tests. *Behavioral Neuroscience*, **111**, 1163–1170.
- Rempel-Clower, N. L., Zola, S. M., Squire, L. R., & Amaral, D. G. (1996). Three cases of enduring memory impairment after bilateral damage limited to the hippocampal formation. *Journal of Neuroscience*, **16**, 5233–5255.
- Rugg, M. D., Fletcher, P. C., Frith, C. D., Frackowiak, R. S. J., & Dolan, R. J. (1997). Brain regions supporting intentional and incidental memory: A PET study. *Learning and Memory*, **8**, 1283–1287.
- Saint-Cyr, J. A., & Taylor, A. E. (1988). Procedural learning and neostriatal dysfunction in man. *Brain*, **111**, 941–959.
- Schacter, D. L., Alpert, N. M., Savage, C. R., Rauch, S. L., & Albert, M. S. (1996). Conscious recollection and the human hippocampal formation: Evidence from positron emission- topography. *Proceedings of the National Academy of Sciences of the United States of America*, **93**, 321–325.
- Schacter, D. L., Reiman, E., Uecker, A., Polster, M. R., Yun, L. S., & Cooper, L. A. (1995). Brain regions associated with retrieval of structurally coherent visual information. *Nature*, **376**, 587–590.
- Schmaltz, L. W., & Theios, J. (1972). Acquisition and extinction of a classically conditioned response in hippocampectomized rabbits (*Oryctolagus cuniculus*). *Journal of Comparative and Physiological Psychology*, **79**, 328–333.
- Scoville, W. B., & Milner, B. (1957). Loss of recent memory after bilateral hippocampal lesions. *Journal of Neurology, Neurosurgery, and Psychiatry*, **20**, 11–21.
- Shallice, T., Fletcher, P., Frith, C. D., Grasby, P., Frackowiak, R. S. J., & Dolan, R. J. (1994). Brain

- regions associated with acquisition and retrieval of verbal episodic memory. *Nature*, **368**, 633–635.
- Solomon, P. R., Vander Schaaf, E. R., Thompson, R. F., & Weisz, D. J. (1986). Hippocampus and trace conditioning of the rabbits classically conditioned nictitating membrane response. *Behavioral Neuroscience*, **100**, 729–744.
- Squire, L. R. (1992). Memory and the hippocampus: A synthesis from findings with rats, monkeys, and humans. *Psychological Review*, **99**, 195–231.
- Squire, L. R., & Knowlton, B. J. (1995). Learning about categories in the absence of memory. *Proceedings of the National Academy of Sciences of the United States of America*, **92**, 12470–12474.
- Squire, L. R., Ojemann, J. G., Miezin, F. M., Peterson, S. E., Videen, T. O., & Raichle, M. E. (1992). Activation of the hippocampus in normal humans: A functional anatomical study of memory. *Proceedings of the National Academy of Sciences of the United States of America*, **89**, 1837–1841.
- Stern, C. E., Corkin, S., Gonzalez, R. G., Guimares, A. R., Baker, J. R., Jennings, P. J., Carr, C. A., Sugiura, R. M., Vedantham, V., & Rosen, B. R. (1996). The hippocampal formation participates in novel picture encoding: Evidence from functional magnetic resonance image. *Proceedings of the National Academy of Sciences of the United States of America*, **93**, 8660–8665.
- Tulving, E., Kapur, S., Markowitsch, H. J., Craik, F. I. M., Habib, R., & Houle, S. (1994). Neuroanatomical correlates of retrieval in episodic memory: Auditory sentence recognition. *Proceedings of the National Academy of Sciences of the United States of America*, **91**, 2012–2015.
- Vaidya, C. J., Gabrieli, J. D. E., Keane, M. M., & Monti, L. A. (1995). Perceptual and conceptual memory processes in amnesia. *Neuropsychology*, **9**, 580–591.