53 Memory, Hippocampus, and Brain Systems

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ABSTRACT The topic of memory is considered from a combined psychology and neuroscience perspective. Topics discussed include the nature of retrograde amnesia, the link between recall and recognition memory, the relationship between remembering and knowing, episodic and semantic memory, and the contribution of the frontal lobes to memory. In addition, fact-and-event (declarative) memory is contrasted with a collection of nondeclarative memory abilities including priming, skill and habit learning, and the acquisition of category-level knowledge. Finally, the brain systems that underlie different forms of learning and memory are considered.

Multiple forms of memory

A major theme in current studies of both humans and experimental animals is that memory is not a single entity but is composed of separate systems (Weiskrantz, 1990; Squire, 1992; Schacter and Tulving, 1994). The dissociation between declarative (explicit) and nondeclarative (implicit) memory is based on studies of experimental animals as well as amnesic patients and normal subjects showing that fact-and-event memory is distinct from other kinds of memory (skills, habits, and priming). Figure 53.1 illustrates a way of classifying kinds of memory.

Declarative memory refers to memory for facts and events. It is well suited to storing arbitrary associations after a single trial. Nondeclarative memories are generally acquired gradually across multiple trials (There are exceptions such as priming and taste aversion conditioning, which can occur after a single trial). Declarative knowledge is also flexible and can be readily applied to novel contexts. Nondeclarative memory tends to be inflexible, bound to the learning situation, and

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not readily accessed by response systems that did not participate in the original learning. The most compelling evidence for this property of declarative and nondeclarative memory systems has come from studies of experimental animals (Eichenbaum, Mathews, and Cohen, 1989; Saunders and Weiskrantz, 1989), although there are also some indications that declarative memory in humans is more flexible than nondeclarative memory (Glisky, Schacter, and Tulving, 1986; but see Shimamura and Squire, 1988).

THE DISTINCTION BETWEEN SHORT-TERM AND LONG-TERM MEMORY In human amnesia, short-term (immediate) memory is fully intact (Baddeley and Warrington, 1970; Cave and Squire, 1992b). The distinction between short-term and long-term memory is also present in experimental animals (Kesner and Novak, 1982; Wright et al., 1985; Overman, Ormsby, and Mishkin, 1991; Alvarez-Royo, Zola-Morgan, and Squire, 1992; Alvarez, Zola-Morgan, and Squire, in press; figure 53.2). These findings together demonstrate that the behavioral impairment in experimental animals following damage to the hippocampus and related structures is a memory problem, not an impairment in perception, rule learning, or some other cognitive function. Indeed, all available evidence supports the conclusion that rats, monkeys, and other animals with damage to the hippocampus and related structures provide a good animal model of human amnesia (Zola-Morgan and Squire, 1990; Squire, 1992).

RETROGRADE AMNESIA The brain system that supports declarative memory has only a temporary role in the formation of long-term memory. Retrograde amnesia, the loss of memories that were acquired prior to the onset of amnesia, is usually temporally graded, such that recent memories are lost more easily than remote memories (Ribot, 1881). Retrograde amnesia
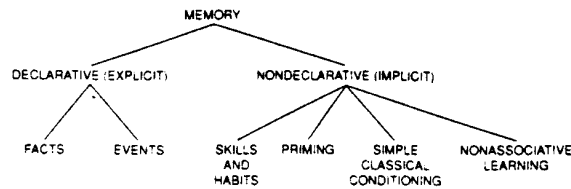
FIGURE 53.1 A taxonomy of long-term memory. (Squire and Zola-Morgan, 1991.)

can sometimes be ungraded and extensive, as in conditions such as encephalitis and head trauma, when damage typically occurs beyond the brain system that supports declarative memory (e.g., Damasio et al., 1985). Nevertheless, in patients with restricted damage within the hippocampal formation, such as patient R. B., retrograde amnesia is brief, perhaps covering a year or two at the most prior to surgery (Zola-Morgan, Squire, and Amaral, 1986). Other patients, who presumably have more extensive damage within the medial temporal lobe, have temporally limited retrograde amnesia that extends back one to two decades (Squire, Haist, and Shimamura, 1989).

Results from experimental animals (Zola-Morgan and Squire, 1990; Kim and Fanselow, 1992; Cho, Beracochea, and Jaffard, 1993) provide evidence for a gradual process of organization and consolidation whereby memory eventually becomes independent of

the medial temporal lobe (figure 53.3). The medial temporal lobe is the target of highly processed information originating from a variety of cortical regions, and it returns projections to these same cortical regions. The hippocampal formation may store conjunctions that tie distributed memory storage sites together until more permanent corticocortical connections are formed. Thus, this system may serve to bind together disparate aspects of a memory and distill them into a coherent memory trace that can subsequently be accessed by many routes. Alternatively, current data leave open the possibility that the medial temporal lobe is the exclusive site of long-term memory storage until a cortical representation is fully developed. Computational models of hippocampal-cortical interactions and single-unit studies of the dynamic properties of cortical long-term memory representations will be needed to decide between these alternatives (e.g., see Alvarez and Squire, in press; McClelland, in press).

RECALL AND RECOGNITION MEMORY Amnesic patients perform poorly on conventional memory tasks that assess recall or recognition. Yet, it has also been proposed that improved perceptual fluency (e.g., the phenomenon of priming) might lead to a sense of familiarity and thereby support recognition memory judgments to some extent, independently of declarative
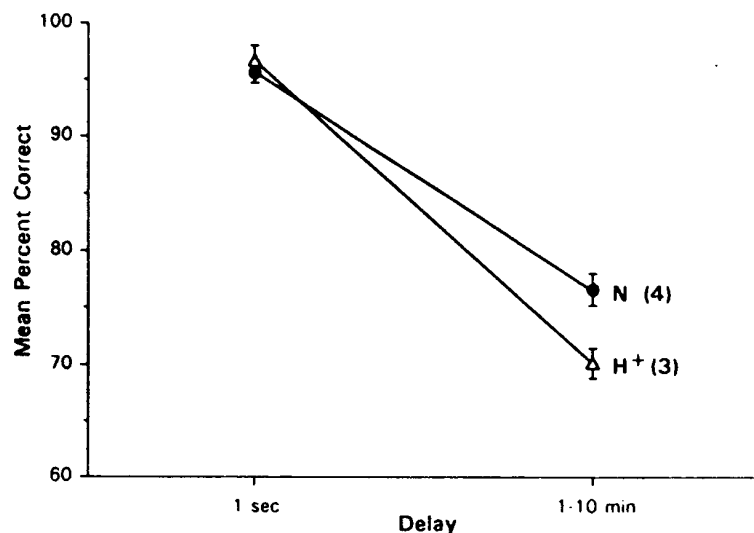

FIGURE 53.2 Percent of correct responses on the delayed nonmatching-to-sample task for 4 normal monkeys (N) and 3 monkeys with damage to the hippocampal formation (H⁺).

Performance of the 2 groups was identical at the 1-s delay, but differed at longer delays. The delays were presented in a mixed order. (Alvarez, Zola-Morgan, and Squire, in press).
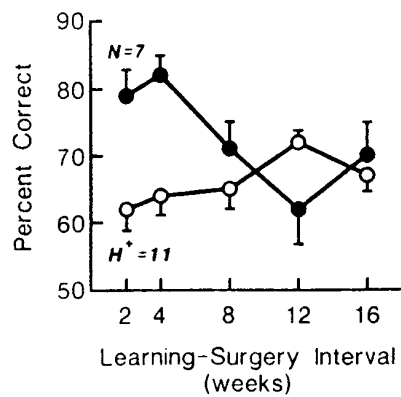
826   MEMORY

FIGURE 53.3 The effect of hippocampal formation lesions on retrograde amnesia. Monkeys with lesions were impaired in remembering information learned 2 to 4 weeks before surgery, but remembered objects learned long ago as normal monkeys. N = 7 normal monkeys; H^+ = 11 monkeys with damage to the hippocampal formation. Brackets show standard error of the mean (Zola-Morgan and Squire, 1990).

memory (Mandler, 1980; Jacoby and Dallas, 1981). In two studies, amnesic patients performed well on a test of recognition as compared to a test of recall (Hirst et al., 1986; Hirst et al., 1988). However, many of these patients may have had frontal lobe pathology, which impairs the effortful search of memory required for recall (Jetter et al., 1986). In a recent study evaluating recall and recognition performance of amnesic patients over a wide range of retention intervals, recognition was impaired proportionately to recall (Haist, Shimamura, and Squire, 1992). The view that recognition performance derives little, if any, benefit from nondeclarative memory is also supported by findings that amnesic patients can sometimes perform at chance levels on measures of recognition memory at the same time that priming is fully intact (Squire, Shimamura, and Graf, 1985; Cave and Squire, 1992). Although nondeclarative memory may not affect recognition memory judgments in typical recognition tests, it remains possible that item fluency, that is, the process that supports priming, could influence recognition judgments under some circumstances (Johnston, Dark, and Jacoby, 1985; Johnston, Hawley, and Eliott, 1991).

The distinction between remembering and knowing

When an item evokes a conscious recollection including specific information about the item and the learning situation, a subject is said to "remember" (R). When a subject is confident an item is familiar and was seen before, but is unable to remember anything about the item in the learning situation, the subject is said to experience "knowing" (K) (Tulving, 1985). In some respects, the distinction between remembering and knowing is similar to the distinction between declarative and nondeclarative memory, and R and K responses can be dissociated in a number of ways that are reminiscent of that distinction. For example, the frequency of R responses is reduced when items are acquired during divided attention, but K responses are not affected (Gardiner and Parkin, 1990). The divided attention manipulation typically affects declarative memory (e.g., recognition memory) more than it affects nondeclarative memory (e.g., priming).

It is also possible that both remembering and knowing are dependent on the limbic and diencephalic brain structures that support declarative memory, but that remembering depends additionally on other brain systems important for source memory such as the frontal lobes (Schacter, Harbluk, and McLachlan, 1984; Janowsky, Shimamura, and Squire, 1989b). In one study, elderly subjects with age-appropriate memory abilities generated fewer R responses and more K responses than young adults (Parkin and Walter, 1992). The frequency of R responses in the elderly subjects correlated negatively with signs of frontal lobe dysfunction.

In another study, event-related potentials (ERPs) from old items that elicited R responses were similar to ERPs from old items that elicited K responses until 500 ms after each item was presented (Smith, 1993). Yet, items that were endorsed as old (i.e., all the items that received either R or K responses) could be distinguished from items that were endorsed as new beginning about 350 ms after item presentation. Moreover, electrical activity in the hippocampal formation during recognition memory performance appears to be most closely related to task performance during the period 400–500 ms after item presentation (Heit, Smith, and Halgren, 1990; see also Smith, 1993). Smith (1993) suggested that both R and K responses result from a common process of recollection, dependent on declarative memory and the hippocampus and related structures. The distinction between R and K responses arises from a postrecollective process, when subjects attend to the products of their retrieval efforts.

The distinction between episodic and semantic memory

Episodic memory refers to autobiographical memory for events, while semantic memory refers to factual memory (Tulving, 1983). Although both episodic and semantic memory are impaired in amnesia, (Shimamura and Squire, 1987; Gabrieli, Cohen, and Corkin, 1988), the possibility remains that amnesic patients have disproportionately impaired episodic memory. However, it is difficult to compare episodic and semantic memory, because episodic memory is specific to events that cannot be repeated. Accordingly, in amnesic patients, the ability to acquire some semantic memory through repetition will always exceed the ability to acquire episodic memory. Second, depending on how one defines semantic memory, there are domains of semantic memory that are severely affected in amnesia (e.g., the ability to learn new facts), and there are domains of semantic memory that are relatively preserved (e.g., the capacity for the gradual learning of artificial grammars and other abilities; see the section later in this chapter on nondeclarative memory).

In one study, the severely amnesic patient K. C. was able to learn simple sentences despite having virtually no episodic memory (Tulving, Hayman, and Mac-Donald). This apparent dissociation between episodic and semantic memory may depend on the fact that patient K. C. became amnesic following head trauma, a condition commonly associated with damage to both the frontal lobe and the temporal lobe. Interestingly, a more recent study found that the severely amnesic patient H. M., who had surgical damage to the medial temporal lobe, did not exhibit successful semantic learning, although the testing procedure used for H. M. was similar to the one used for K. C. (Tulving, personal communication, 1993). Thus, frontal lobe damage can impair episodic memory more than semantic memory. Indeed, episodic memory may be similar to (or in some instances identical to) source memory, which has previously been linked to frontal lobe function.

THE FRONTAL LOBES, THE DIENCEPHALON, AND THE MEDIAL TEMPORAL LOBE Patients with lesions involving the frontal lobes have a variety of deficits that affect performance, such as impaired source memory (Schacter, Harbluk, and McLachlan, 1984; Shimamura and Squire, 1987), impaired metamemory, that is, impaired ability to make judgments and predictions about one's own memory ability (Janowsky, Shimamura, and Squire, 1989a), impaired memory for temporal order (Milner, Petrides, and Smith, 1985; Shimamura, Janowsky, and Squire, 1990), and impaired recall abilities (Jetter et al., 1986). Diencephalic amnesic patients with Korsakoff's syndrome typically exhibit frontal lobe damage in addition to medial diencephalic damage. The presentation of amnesia in Korsakoff's syndrome is therefore somewhat different than in amnesia resulting from other etiologies (Janowsky, Shimamura, and Squire, 1989a; Shimamura, Janowsky, and Squire, 1991).

Other than the cognitive deficits attributable to frontal lobe damage, there is striking similarity between diencephalic amnesia and medial temporal lobe amnesia. Both groups have similar forgetting rates within long-term memory (McKee and Squire, 1992) and similar spatial memory abilities (Cave and Squire, 1991). The similarity between diencephalic and medial temporal lobe amnesia presumably reflects the close anatomical connections between the diencephalic midline and the medial temporal lobe, and suggests that these two regions can be considered to belong to a single functional system. The two regions undoubtedly make somewhat different contributions to memory, but from the perspective of behavioral criteria, the similarities are more prominent than the differences.

Nondeclarative memory

PRIMING Priming refers to the increased ability to identify or detect a stimulus as a result of its recent presentation. The first encounter with an item results in a representation of the item, which can then be subsequently accessed more readily than information about stimuli that have not been presented previously. Amnesic patients exhibit intact priming effects (figure 53.4; for a recent review, see Schacter, Chiu, and Ochsner, 1993). It is important to note that intact priming in amnesic patients has been demonstrated for novel materials that have no preexisting representations (see Schacter, Chiu, and Ochsner, 1993; Squire, Knowlton, and Musen, 1993). These results indicate that priming is not derived simply by activating stored memory representations, but rather is based on the sensory-perceptual traces created by stimulus presentation.

Presentation of items can also influence preferences and judgments about the items. For example, both amnesic patients and normal subjects are more likely
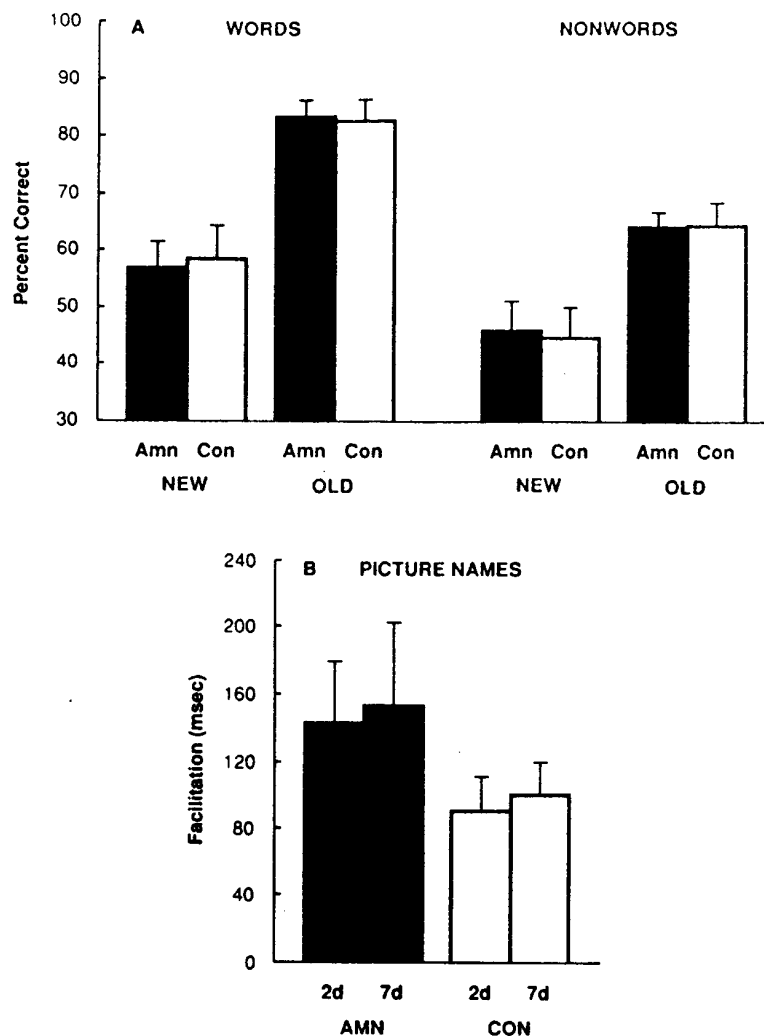
FIGURE 53.4 Intact priming in amnesic patients on two different tests. (A) Percent of words and nonwords correctly identified in a perceptual identification task. Old items had been presented once previously, and the advantage for identifying old items compared to new items indicates priming. (B) Facilitation of picture naming at 2 days (2d) and 7 days (7d) after a single presentation of the pictures. The facilitation score was obtained by subtracting the time required to name 50 old pictures from the time required to name 50 new pictures. Brackets show standard errors of the mean. AMN, amnesic patients; CON, control subjects (Haist et al., 1991; Cave and Squire, 1992a).

to judge a proper name as famous if the name has been presented recently (Neeley and Payne, 1983; Jacoby, Woloshyn, and Kelley, 1989; Squire and McKee, 1992). Normal subjects can suppress this effect in some circumstances because they can draw on declarative memory to recall that the items were just presented (Jacoby et al., 1989). Thus, in one study, only nonfamous names were presented first, then subjects were informed that all the names were nonfamous, then sub-

jects were asked to judge the fame of new famous names together with both old and new nonfamous names. Amnesic patients continued to exhibit a fame judgment bias, but normal subjects did not (Squire and McKee, 1993).

The anatomical locus of priming is probably the neocortex. Studies using positron emission tomography (PET) are consistent with a right posterior neocortical site for word-stem completion priming (Squire et al.,

1992). The finding of a right posterior locus suggests that word-stem completion priming relies importantly on visual, orthographic features of the presented material. Priming across modalities, priming across typefaces, auditory priming, and priming of semantic information presumably depend on other cortical regions.

Although priming can be long-lasting and can result in new representations, priming is nevertheless limited in comparison to declarative memory. While declarative memory is well suited for forming new associations between arbitrary stimuli in a single trial, in nondeclarative memory novel associations are formed more gradually. Thus, implicit learning of novel associations does occur over multiple trials, but one-trial implicit learning of novel associations does not occur readily for either normal subjects or amnesic patients (Musen and Squire, 1993). However, associations that are easily integrated into a single perceptual unit, such as a word and the color in which it is printed, can be learned nondeclaratively in a single trial (Musen and Squire, 1992).

SKILLS AND HABITS The learning of skills and habits is largely nondeclarative in some circumstances, as evidenced by the fact that amnesic patients learn at an entirely normal rate (see Squire, Knowlton, and Musen, 1993, for a review). Amnesic patients can learn normally even when the information to be acquired is not exclusively perceptual or motor. In one study, subjects performed a serial reaction-time task in which they responded successively to a sequence of four illuminated spatial locations (Nissen and Bullemer, 1987). The task was to press one of four keys as rapidly as possible as soon as the location above that key was illuminated. Amnesic patients and normal subjects successfully learned a repeating sequence as indicated by decreasing reaction time for key presses as the sequence repeated itself. When the sequence was changed, reaction times increased again. Subjects were able to learn the sequence even when they were judged to have no declarative knowledge of it. Subjects were judged to have no declarative knowledge when they were unable to generate the sequence in subsequent tests, and were unaware that a sequence had been presented (Nissen and Bullemer, 1987; Willingham, Nissen, and Bullemer, 1989).

A recent study has challenged the idea that sequence learning is implicit, on the basis of findings that subjects were able to recognize and reproduce correct sequences when methods were used that were more sensitive than those used previously (Perruchet and Amorim, 1992). It was suggested that subjects do have declarative knowledge of the material, and that a distinction between memory systems is not required by the data. The findings from amnesic patients are particularly useful in this context, because the patients provide a tool for assessing whether declarative memory is only epiphenomenal or whether it is important for task performance. A finding that amnesic patients learn and remember entirely normally provides strong evidence that long-term declarative memory is not needed for performance. It is possible that some declarative knowledge develops during initial learning, and that even in amnesic patients such knowledge is supported by their intact immediate memory capacity, but it is a different matter whether in normal subjects declarative knowledge for what is learned in a task can or does persist within long-term memory once learning is completed. If performance is intact in amnesia at some time after learning, one has grounds for concluding that performance is supported by nondeclarative memory.

Production systems

In some cases, skills can involve more abstract information, and what is learned is neither perceptual nor motor. For example, subjects can gradually learn to control the level of an output variable by manipulating an input variable that relates to the output variable by a simple formula, although they need not acquire much reportable knowledge about the rule (Berry and Broadbent, 1984). Amnesic patients perform as well as normal subjects during the early learning of this task (Squire and Frambach, 1990). With extended training, normal subjects are able to outperform amnesic patients, and normal subjects are also better than amnesic patients at answering questions about task strategy.

PROBABILISTIC CLASSIFICATION LEARNING In probabilistic category learning, subjects try to predict one of two outcomes based on a set of cues that are probabilistically associated with each outcome. In one such task, a list of one to four symptoms is presented, and
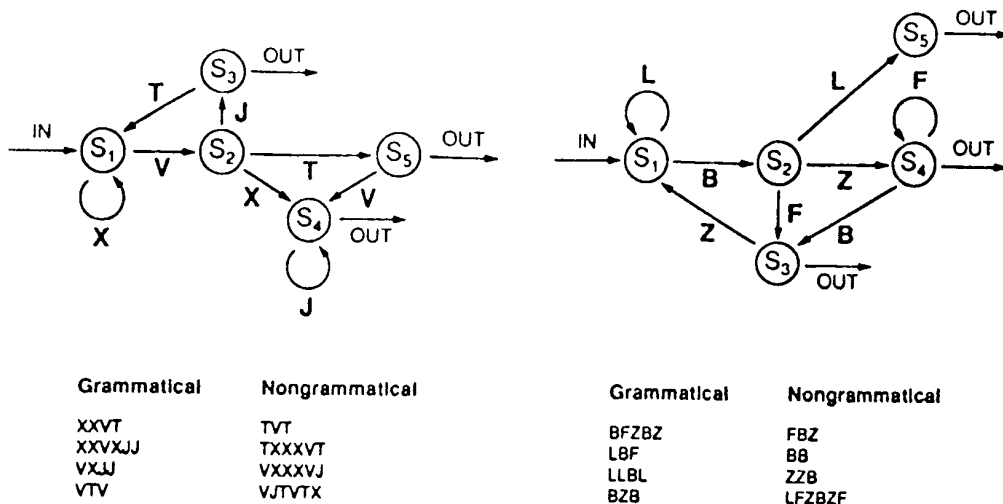
FIGURE 53.5 Two finite-state rule systems used to generate the letter strings of artificial grammars. Examples of grammatical and nongrammatical letter strings are listed below each rule system. (Abrams and Reber, 1989; Knowlton et al., 1992).

Grammatical	Nongrammatical
XXVT	TVT
XXVXJJ	TXXXVT
VXJJ	VXXXVJ
VTV	VJTVTX

Grammatical	Nongrammatical
BFZBZ	FBZ
LBF	BB
LLBL	ZZB
BZB	LFZBZF

each predicts one of two disease outcomes with a particular probability (Gluck and Bower, 1988). This task shares formal aspects with classical conditioning. That is, the separate cues (symptoms) compete for associative strength with the outcome (disease) in much the same way that conditioned stimuli compete for associative strength with the unconditioned stimulus (Gluck and Bower, 1988; Chapman and Robbins, 1990; Shanks, 1991). In three different tasks of probabilistic classification learning, amnesic patients improved their classification performance at the same rate as normal subjects (Knowlton, Squire, and Gluck, submitted). Probabilistic associations may be learned implicitly because information about a single trial is not as useful for performance as information about the probabilistic relationship between cues and outcomes, which necessarily accrues over many trials. In the study, learning occurred at a normal rate for the amnesic patients during approximately the first 50 trials of training. However, with extended training normal subjects surpassed the performance of amnesic patients, presumably because they were able to decipher the task to some extent and to remember some of the relationships explicitly.

ARTIFICIAL GRAMMAR LEARNING In artificial grammar learning, subjects see a series of letter strings

generated by a finite-state rule system (figure 53.5). Subjects are told about the underlying rule system only after viewing the letter strings. They are then asked to judge whether new letter strings adhere or do not adhere to the rules. Although normal subjects are not able to report much explicit knowledge about their judgments, they are able to classify new letter strings at a level above chance (see Reber, 1989, for a review). However, it has also been argued that subjects may be using partially valid declarative knowledge of the grammar to make their judgments, and that declarative knowledge about the grammar can be elicited from subjects using sensitive test measures (Perruchet and Pacteau, 1990; Dulany, Carlson, and Dewey, 1984). Recent studies have helped to resolve this debate by showing that amnesic patients are able to make classification judgments as well as normal subjects in an artificial grammar learning task, despite their severe impairment in the ability to recognize the particular letter strings that were used to teach the grammar (Knowlton, Ramus, and Squire, 1992; Knowlton and Squire, 1994; figure 53.6).

PROTOTYPE ABSTRACTION AND CATEGORY LEARNING When subjects see a series of examples belonging to a single category, they can later classify new examples correctly. One possibility is that subjects abstract a
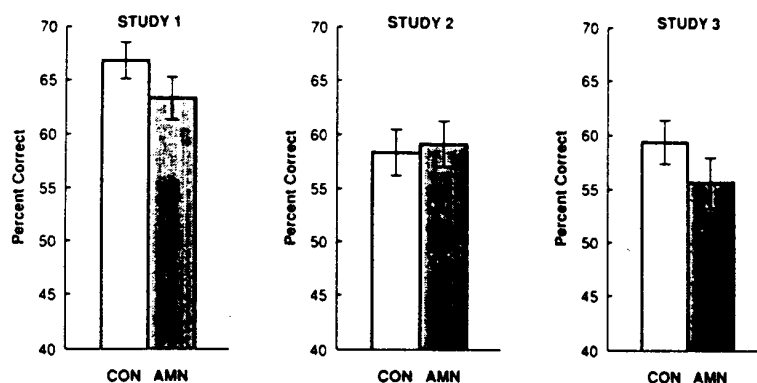
FIGURE 53.6 The results of three separate studies showing normal performance of amnesic patients (AMN) compared to control subjects (CON) on classification tasks based on arti- ficial grammars. Brackets show standard error of the mean. (Knowlton et al., 1992; Knowlton and Squire, 1994).

prototype, or central tendency, from these examples and use the abstracted prototype to classify new items (Posner and Keele, 1968; Rosch, 1973). Alternatively, category judgments may be based on a comparison of test items to examples stored in declarative memory (Medin and Schaffer, 1978; Hintzman, 1986). Studies of amnesic patients should illuminate this issue. Amnesic patients and normal subjects were shown distortions of a prototypic dot pattern during training (Knowlton and Squire, 1993). The two groups performed equivalently on a later classification test, thereby demonstrating that they had abstracted the prototype from the examples. The prototype and low distortions of the prototype were judged to be members of the training category more often than higher distortions (figure 53.7). These results suggest that category-level information is acquired independently of declarative memory for training exemplars. Category-level information might be constructed nondeclaratively (implicitly) either by forming an abstracted prototype or by making comparisons with instances that are stored in implicit memory. In either case, it appears that category-level judgments can be independent of the ability to remember declaratively the particular instances that are encountered during training.
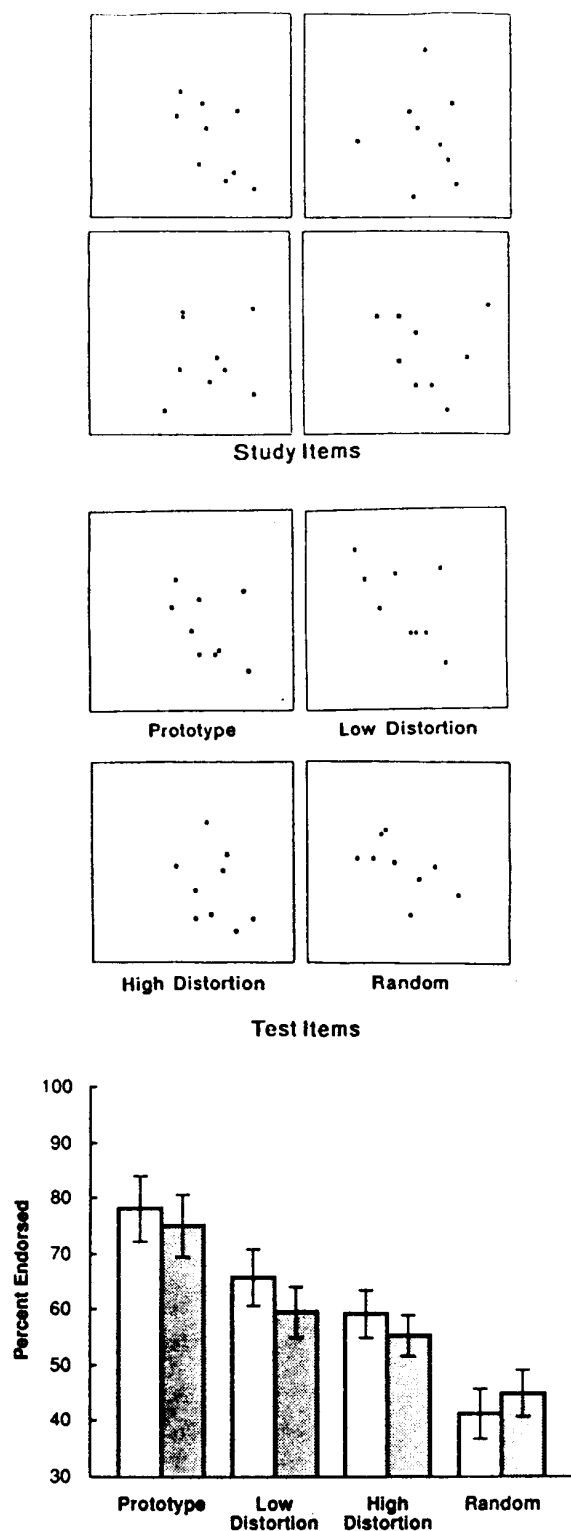
From memory systems to brain systems

Declarative memory is the product of a unique system that is dependent on medial temporal lobe/diencephalic structures, which operate in concert with neocortex (figure 53.8). Studies of nonhuman primates have

elucidated the brain structures and connections that support declarative memory (Mishkin, 1982; Squire and Zola-Morgan, 1991). The important structures in the medial temporal lobe are the hippocampus, the entorhinal cortex, the parahippocampal cortex, and the perirhinal cortex. The amygdala is not part of the medial temporal lobe system for declarative memory (Zola-Morgan, Squire, and Amaral, 1989).

Damage to the hippocampal region, caused either by ischemia or radio frequency lesions, resulted in a significant memory impairment. Yet this level of impairment was increased when the area of the damage was systematically enlarged to include, first, the para-hippocampal cortex and posterior entorhinal cortex (the H^+ lesion). The impairment associated with an H^+ lesion was increased still further when the H^+ lesion was extended forward to include anterior entorhinal cortex and perirhinal cortex (Zola-Morgan et al., 1993; Zola-Morgan, Squire, and Ramus, in press; figure 53.9).

These findings are consistent with the findings from human amnesia. Patient R. B., who exhibited a significant memory impairment following damage to field CA1 of the hippocampus (Zola-Morgan, Squire, and Amaral, 1986) was not nearly so impaired as patient H. M., who sustained much more extensive medial temporal lobe damage (Scoville and Milner, 1957). Thus, the parahippocampal and perirhinal cortices are not simply conduits for sending information to the hippocampus. Damage to the hippocampal region itself causes a relatively mild level of impairment. The fact that memory impairment increases when the adja-

cent cortical regions are damaged indicates that these cortical areas themselves also contribute to memory function.

The information processed by medial temporal lobe structures is also directed to areas in the diencephalon important for declarative memory (Graff-Radford et al., 1990; Zola-Morgan and Squire, 1993). The development of an animal model of alcoholic Korsakoff's syndrome in the rat (Mair et al., 1988) provides a particulary favorable opportunity for investigating the anatomy of diencephalic amnesia.

ANATOMICAL SUBSTRATES OF NONDECLARATIVE MEMORY Brain systems other than the medial temporal lobe and the diencephalic midline are involved in acquiring nondeclarative information. For example, classical conditioning of discrete responses of the skeletal musculature depends on the cerebellum (for a review, see Thompson, 1990), while the conditioning of emotional responses depends on the amygdala (LeDoux, 1987; Davis, 1992). Caudate lesions in rats and monkeys impair the learning of win-stay habits and stimulus response tasks that are insensitive to lesions of the hippocampal formation (Packard, Hirsh, and White, 1989; Wang, Aigner, and Mishkin, 1990).

The neostriatum may also be important for the learning of skills and habits in human subjects. Patients with Huntington's disease were impaired at learning sensorimotor, skill-based tasks (Martone, Butters, and Payne, 1984; Heindel, Butters, and Salmon, 1988; Knopman and Nissen, 1991). Although declarative memory is not normal in these patients, the same patients who performed more poorly than amnesic patients on sensorimotor skill learning tasks performed better than amnesic patients on tests of declarative memory. Patients with Huntington's disease may be impaired on the sensorimotor tasks because they are deficient at forming motor programs. An important

FIGURE 53.7 (Top) Examples of 4 study items and 4 test items used to assess classification learning. The study items are all arithmetic distortions of a prototype dot pattern that subjects do not see. The test items include the prototype pattern, novel distortions of the prototype, and random dot patterns that provide a measure of baseline classification performance. (Bottom) Performance on the dot pattern classification task according to type of test item. Open bars, control subjects; shaded bars, amnesic patients. Brackets show standard error of the mean. (Knowlton and Squire, 1993).
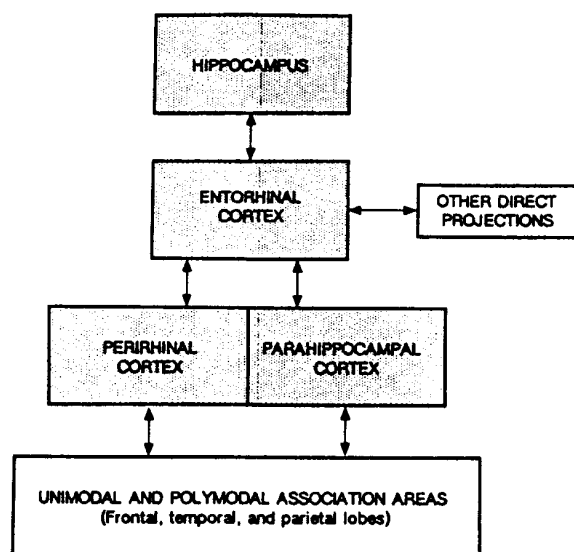
FIGURE 53.8 A schematic view of the structures and connections important for declarative memory. Shaded areas indicate structures within the medial temporal lobe.

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FIGURE 53.9 Mean z scores based on 4 measures of memory for 10 normal monkeys (N), 8 monkeys with damage to the hippocampal region (H), 8 monkeys with damage that also included the adjacent entorhinal and parahippocampal cortices (H^+), and 4 monkeys in which the H^+ lesion was extended forward to include the anterior entorhinal cortex and the perirhinal cortex (H^{++}). As more components of the medial temporal lobe memory system were included in the lesion, the severity of memory impairment increased. Brackets show standard errors of the mean (Zola-Morgan, Squire, and Ramus, in press).

question is whether patients with Huntington's disease would be impaired on the learning of habit-like tasks that do not have a motor component, such as artificial grammar learning or probabilistic classification learning. Alternatively, the neostriatum might not participate in this kind of learning. The processing of exemplars in neocortex might gradually lead to a corti-
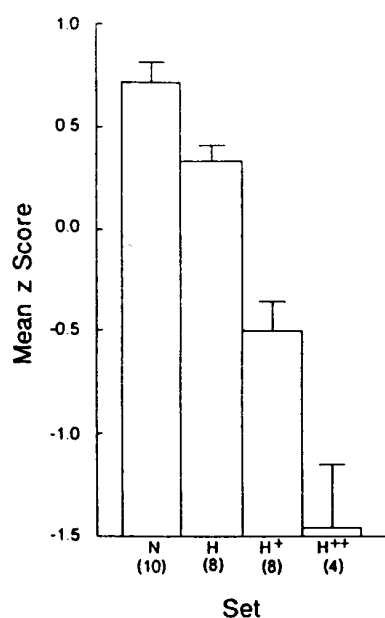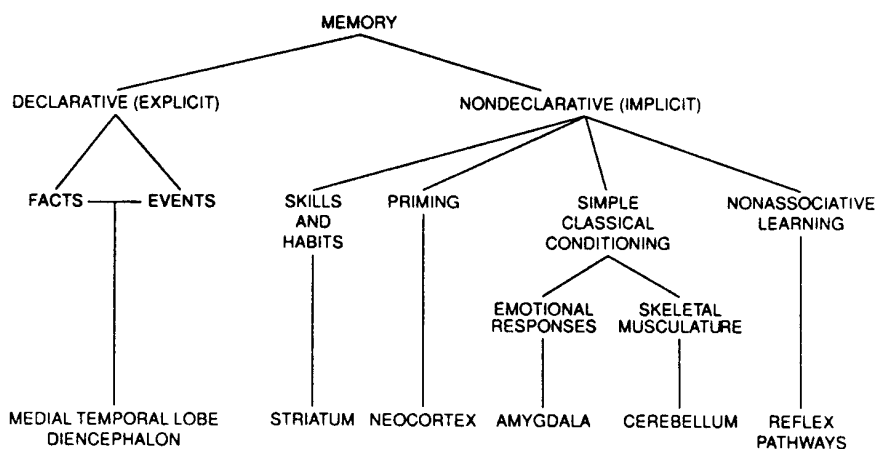

FIGURE 53.10 A taxonomy of long-term memory and associated brain structures.

cal representation of the commonalities between the training items, and the resulting cortical representation could provide a basis for category-level judgments.

It is now possible to link particular brain regions and systems to various kinds of memory (figure 53.10). The next challenge for cognitive neuroscience is to make these links specific. Ultimately, this means identifying where the synaptic changes occur that support different kinds of memory.

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