Neurobiology of Learning and Memory **77,** 125–184 (2002)
doi:10.1006/nlme.2001.4008, available online at http://www.idealibrary.com on IDEAL®

THEORETICAL REVIEW

Multiple Parallel Memory Systems in the Brain of the Rat

Norman M. White* and Robert J. McDonald†

**Department of Psychology, McGill University, Montreal, Canada; and*
†Department of Psychology, University of Toronto, Toronto, Canada

Published online October 25, 2001

A theory of multiple parallel memory systems in the brain of the rat is described. Each system consists of a series of interconnected neural structures. The "central structures" of the three systems described are the hippocampus, the matrix compartment of the dorsal striatum (caudate-putamen), and the amygdala. Information, coded as neural signals, flows independently through each system. All systems have access to the same information from situations in which learning occurs, but each system is specialized to represent a different kind of relationship among the elements (stimulus events, responses, reinforcers) of the information that flows through it. The speed and accuracy with which a system forms a coherent representation of a learning situation depend on the correspondence between the specialization of the system and the relationship among the elements of the situation. The coherence of these stored representations determines the degree of control exerted by each system on behavior in the situation. Although they process information independently the systems interact in at least two ways: by simultaneous parallel influence on behavioral output and by directly influencing each other. These interactions can be cooperative (leading to similar behaviors) or competitive (leading to different behaviors). Experimental findings consistent with these ideas, mostly from experiments with rats, are reviewed.

I. INTRODUCTION

This paper discusses the idea that several neural systems in the brain function simultaneously and with some degree of independence to process and store information about events that occur during the life of an individual. Although the systems have access to much of the same information, each deals with it in a different way. These differences in the information *processing style* of the systems constitute the essence of the theory.

Address correspondence and reprint requests to Norman White, Department of Psychology, McGill University, 1205 Dr. Penfield Avenue, Montreal, Quebec H3A 1B1, Canada. Fax: (514) 398-4896. E-mail: nwhite@psych.mcgill.ca.

1074-7427/02 $35.00

The ideas that there are different kinds of memory (Hilgard & Marquis, 1940; Hilgard & Bower, 1966; Amsel, 1980; Horn, 1985; Sherry & Schacter, 1987; Weiskrantz, 1990; Polster, Nadel, & Schacter, 1991; Moscovitch, 1992; Nadel, 1992; Shettleworth, 1993; Moscovitch, 1994; McClelland, McNaughton, & O'Reilly, 1995; Willingham, 1997; Tolman, 1949; Dickinson, 1985; Dickinson & Balleine, 1994; Dickinson, 1994) and that these are mediated in different parts of the brain (Scoville & Milner, 1957; Milner, Corkin, & Teuber, 1968; O'Keefe & Nadel, 1978; Hirsh, 1974; Cohen, 1984; Mishkin, Malamut, & Bachevalier, 1984; Kesner & DiMattia, 1987; Kesner, 1998; Butters, Martone, White, Granholm, & Wolfe, 1986; Phillips & Carr, 1987; Squire, Knowlton, & Musen, 1993) are not new. Some of the present theory constitutes a summary and reorganization of ideas presented by these and other authors. Although the paper deals mainly with data from the rat, many of the considerations raised are applicable to the organization of information processing and memory functions in all mammalian brains.

The present version of a multiple parallel memory systems (MPMS) theory deals with three hypothesized neural systems. Each has a *central structure*: these are the hippocampus, the matrix compartment of the dorsal striatum, and the amygdala. Each system includes its central structure and the efferent and afferent connections of this structure. Each system receives information, processes it in its own style, stores some of it under certain circumstances, and influences behavior. Each system is capable of performing these functions independently of the other systems. The processing style of each system is assumed to be the result of its neural architecture. Therefore, the processing styles of the systems are fixed.

The systems are referred to by the anatomical names of their central structures: the *hippocampus system*, the *dorsal striatum system*, and the *amygdala system*. These names are intended to include the entire anatomical systems of which each central structure forms a part (discussed in section VI. Anatomy of Systems).

Differences in the effects of lesions to the central structures on the acquisition and expression of learned behaviors suggest the proposed differences in the information processing styles of the systems. Data on the responsiveness of neurons in these structures and on posttraining manipulations of them are consistent with these ideas. Information on the afferent and efferent connections of the central structures provides an initial idea of the anatomical extent of the systems.

Although supported by much empirical evidence, the proposed systems remain theoretical entities. In each case, there is evidence that none of the systems function as simply or as uniformly as is suggested by the conceptualizations described here. For example, although the hippocampus is designated as a central structure, it is dependent for its memory-related functions on other medial temporal lobe structures (Zanatta et al., 1996; Cho, Kesner, & Brodale, 1995; Myers, Gluck, & Granger, 1995). Furthermore, while they are treated as unitary structures in the present theory, there is evidence that both the amygdala (Hatfield, Graham, & Gallagher, 1992; Grijalva, Levin, Morgan, Roland, & Martin, 1990; Hiroi & White, 1991; Gallagher & Chiba, 1996; Gallagher & Holland, 1994; Ono, Nishijo, & Uwano, 1995; Aggleton, 1993) and dorsal striatum (Divac & Oberg, 1979; Divac, 1968; White, 1997; Graybiel, 1995; Wise, Murray, & Gerfen, 1996; Alexander & Crutcher, 1990; Alexander, Crutcher, & DeLong, 1990; Devan, McDonald, & White, 1998) are functionally heterogeneous with respect to both memory and other functions. The present treatment is in no way intended to ignore or deny these issues, but

rather to provide a framework within which the specific functions of each system can be studied.

Theories of memory are often confined to ideas about how information is stored in the brain or about how knowledge is organized as a cognitive process; the present approach also considers the functions of motivational and emotional factors in learning and memory. These factors are organized under the concept of *reinforcement*. Reinforcement is a process by which certain events promote changes in behavior (White & Milner, 1992). Examples of events with this property, sometimes called *reinforcers* or *unconditioned stimuli*, include encountering food, water, a sexual partner, or some fear- or pain-producing situation. Thus, there are two basic types of reinforcers: positive (rewarding) and negative (aversive). In the present theory reinforcers promote behavior change because they produce a specific class of responses with little or no previous experience. These responses include specific patterns of neural activity (which may correspond to particular behaviors), neurotransmitter release, and autonomic and hormonal changes. These responses interact with each of the memory systems in a different way to promote changes in behavior. Understanding these interactions is critical to a complete understanding of how experience alters behavior.

The Systems Concept

A basic assumption of the present theory is that normal behavior involves a continuous flow of information through each of the hypothesized independent brain systems. The systems process (i.e., filter, combine, associate, and otherwise alter) this information. The resulting output from these systems ultimately controls behavior, directly or indirectly. Under certain circumstances some part or parts of a neural system may be changed by the information being processed, and this change will alter the processing of similar information on future occasions, resulting in a corresponding change in the output of the system. When altered behavior resulting from this changed output is observed it is usually attributed to a process called "learning," and this in turn leads to the inference of the existence of a "memory." This inferred entity refers to the changes in the information-processing substrate that produced the new behavior. Thus, the study of memory involves the localization and characterization of these changes.

Parallel processing. The idea that more than one neural system continually processes information and influences behavior leads to the concept of *parallel processing*. As illustrated in Fig. 1, this concept means that at least three more-or-less independent neural systems mediate-information processing and storage functions simultaneously and in parallel in the normal brain. These are the neural systems that include the hippocampus, the amygdala, and the dorsal striatum.

A more parsimonious model of the learning and memory functions of the brain would be based on a single set of learning concepts involving a single processing style. The suggestion that several different brain systems simultaneously process information pertaining to the same behavioral situation raises the question of how such apparently redundant systems evolved. Ideas about the evolution of brain function as a series of functional adaptations to problems of survival are notoriously facile and can be used to support any theoretical position. The evolutionary concept of "exaptation" as described by Sherry and Schacter (1987) is useful in this context. Exaptation denotes that not every function of an adaptation is related to the problem of survival that originally selected for it. To use

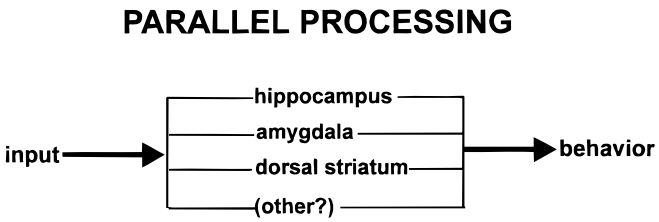

FIG. 1. The concept of parallel processing. The hippocampus, dorsal striatum, and amygdala are central structures in three neural systems, each of which can function independently. Each system receives similar information about situations in which learning can occur and each processes that information according to a different set of principles that emphasize different relationships among the elements of the situation (processing style). The systems all influence the behavior of the individual in either a cooperative or competitive manner. Processing within each system can lead to the storage of information (memory) that influences the processing of similar information in the future.

their example: "Human memory is clearly not an adaptation for remembering telephone numbers, though it performs this function fairly well, nor is it an adaptation for learning to drive a car, though it handles this rather different problem effectively, too" (Sherry & Schacter, 1987, p. 449). This means that it may be impossible to know exactly what environmental circumstances led to the evolution of multiple memory systems. For this reason no explanation in evolutionary terms of the MPMS concept is attempted here. Rather, the theory results from an attempt to account for the results of studies of the relation between brain function and behavior.

Memory and information processing. The idea that information "flows" through neural systems and is processed or altered as it does so makes learning and memory subsidiary to the general, ongoing, information processing, behavior-producing functions of the brain (Vanderwolf & Cain, 1994). In fact, it suggests that a study of learning and memory processes can lead to an improved understanding of the organization of these more general processes. This differs somewhat from the more usual view of memory simply as the representation and storage of new information (Polster et al., 1991). The work of Kesner (Kesner & DiMattia, 1987; Kesner, 1998; Kesner & Gilbert, 2000), who has used an extensive series of memory tasks to gather information about the cognitive processes mediated in a large number of different brain areas, illustrates the advantages of integrating the investigation of cognitive and memory functions.

These considerations mean that learning and memory processes can be understood as functions of these information processing systems. The major purpose of the present theory is to suggest the ways in which each of the hypothesized neural systems processes information: their processing styles. The fixed processing style of each system determines the nature of the information that can be represented in that system and this in turn determines the kind of information that can be stored in the system.

Other substrates of learning and memory. Although the present theory deals with three memory systems it is unlikely that they account for all aspects of learning and memory. Most obviously, a large amount of literature on the cerebellum (Thompson, 1990; Thompson & Krupa, 1994) and the cerebral cortex (Young, Otto, Fox, & Eichenbaum, 1997; Merzenich & Sameshima, 1993; Desimone, 1992; McNaughton, Leonard, & Chen, 1989; Kaas, 1987; Alkon et al., 1991; Kirkwood, Dudek, Gold, Aizenman, & Bear, 1993;

DiMattia & Kesner, 1988; Kesner, Farnsworth, & DiMattia, 1989; Kesner, Berman, & Tardif, 1992; Cho et al., 1995) suggests the existence of learning- and memory-related functions in these areas, and the three systems dealt with here undoubtedly interact with these substrates. It is also sometimes suggested that plasticity is a general property of the nervous system, and that experience-related changes in information processing functions can occur everywhere in the brain. Regardless of the extent to which this may be true, the evidence to be considered here suggests a degree of specifiable specialization of information processing styles within each of the three systems, making them a good starting point for studying the information processing and memory functions of multiple parallel neural systems and their implications for behavior.

Neuroplasticity. Although much effort is currently expended on understanding the synaptic basis of memory storage, particularly in the hippocampus, it is arguable that the issues dealt with in this paper logically precede such investigations. The general problem of understanding how information is represented by synaptic change requires precise specification of the information represented by any particular synaptic mechanism under study. Since information stored in the brain cannot be observed directly, this must be inferred from behavior. However, if the behavior of an organism is influenced by several different neural systems operating on different principles, knowledge of exactly what information is stored by the specific synapses under study becomes critical. Accurate inferences from behavior about the specific information processed and stored by the synapses in any one neural system at any given time require knowledge of what information is being processed by all systems at that time.

The neuroplasticity that represents the information stored in each system is assumed to be localized exclusively within that system. Evidence for independence of the systems can therefore be taken as evidence for the independence of the neuroplastic representation of the memories stored in the systems. By postulating that memory systems rather than individual structures are the locus of the neuroplasticity that stores information, the present hypothesis does not require the assumption that a lesion affects performance of a learned task because it damages the substrate that stores the information required to perform the task. Instead, the MPMS concept leads to the conclusion that lesions with specific effects have simply damaged some part of a system that represents and stores the information that normally produces the affected behaviors. Although the theory requires no assumption about the specific location of the stored information, the presence of neuroplasticity of the type thought to mediate memory storage in each of the central structures (Collingridge, 1992; Malenka & Nicoll, 1993; McNaughton, 1993; Calabresi, Pisani, Mercuri, & Bernardi, 1996; Calabresi, Maj, Pisani, Mercuri, & Bernardi, 1992; Calabresi, Pisani, Mercuri, & Bernardi, 1992; Johnston, Williams, Jaffe, & Gray, 1992; Ono et al., 1995) must be regarded as suggestive.

Relationship between Memory Systems and Learned Information

The present theory is based on an experiment (McDonald & White, 1993) that suggested a dissociation of the processing styles of the neural systems. Three similar memory tasks were used. The *elements* (stimuli, responses, reinforcers) of these tasks were identical, but the *relationships among the elements* differed. In each task, the relationship among the elements was contrived to correspond to a preexisting hypothesis about the innate

processing style of one of the neural systems. The main evidence leading to the present MPMS theory is the finding that acquisition of each task was impaired by disabling a different neural system, a triple dissociation.

Coherence. The concept of parallel processing (Fig. 1) implies that information about all ongoing contexts and activities, regardless of their nature, reaches and activates all three information processing systems. Which system(s) represents (and therefore potentially stores) information pertaining to a given situation depends on the degree of correspondence between the relationship among the elements of the situation and the fixed information processing style of each system. A situation that corresponds closely to the processing style of a system produces *coherent neural activity* in the system. Coherence denotes that the neural activity in the system is organized or synchronized into a uniform pattern or patterns that represent the situation (evidence for the existence of such patterns is discussed in Section V. Evidence From Other Experiments). A coherent representation of a situation in a system means that information processed and stored in the system produces coherent output which has a powerful influence on behavior in that situation. Another system with a processing style that corresponds less closely to the situation forms a less coherent representation resulting in less coherent output in that situation, with less influence on behavior in the situation.

Thus, the coherence of the representation of a situation in a system is, in the first instance, determined by the match between the relationship among the elements of the situation and the processing style of the system. Subsequently, the coherence of a representation is also a function of amount of exposure to the situation. If the pattern of neural activity produced by a single exposure to a situation is of sufficient coherence (due to the degree of matching) to produce the permanent neural changes that store information in the system, a representation of the situation, which could range from strong and accurate to weak and imperfect, is stored. This representation might not in itself produce detectable changes in behavior on subsequent exposure to the situation. However, the processing of the neural activity in the system produced by such exposure would be altered, resulting in activity of increased coherence and additional permanent changes, improving the coherence of the representation. With repeated exposures, coherence would increase to the point where a change in behavior would be detectable. Thus, coherence is a function of matching and amount of exposure.

Patterns of representation among systems. The relationship among the elements of a memory task could be identical to the processing style of one, and only one, neural system. This would be a *pure task.* Such a perfect match between the relationship among the elements of a task and the fixed processing style of a memory system might be expected to produce a high degree of coherent neural activity within that system with relatively little exposure to the learning situation, resulting in output with a powerful influence on behavior. Little or no coherent activity would exist in the other systems. Disabling the neural system that corresponds to a pure task would completely and permanently eliminate the ability to learn or recall the task. Disabling any other system would have no effect on learning the task. Although completely pure tasks are probably nonexistent, relatively pure tasks (however artificial) are very useful because an examination of the relationships among their elements can provide information about the processing style of the system that is critical for learning them. In the triple dissociation experiment described below, a

series of relatively pure tasks was used to make inferences about the processing styles of each of the proposed memory systems.

Most memory tasks are not pure. Some learning situations may not be accurately representable by any one system because the relationships among their elements do not correspond closely to the processing style of any of the systems. Components of such tasks may be represented by different systems, and performance of these tasks may require cooperative output from each of the systems. Disabling any system processing a critical component of such a task would impair performance.

Other situations may be representable by more than one system. Each system could represent a different set of relationships among the same situational elements, but both representations could lead to similar behaviors. If such representations were of equivalent coherence disabling either system would have no observable effect; both systems would have to be disabled to impair performance. However, multiple representations of a situation would not necessarily be equivalent; the relationships among the elements of a task might correspond more closely to the processing style of one of the systems. With repeated exposure to the situation, coherent activity in that system would occur first. Representations in other systems might take longer to form and could be less specific, resulting in less accurate performance. In this case disabling the primary system before the start of training might simply retard acquisition of the task. The effect of disabling the primary system at some point after the start of training would be a degree of impairment that depended on the amount of coherence that had developed in the secondary system at the time of the damage, and performance might continue to improve with further training as the coherence of the representation in the secondary system continued to improve. In contrast, disabling the secondary system in an otherwise normal animal would have little effect on learning or performance.

In the above discussion it is assumed that multiple representations of a situation are *cooperative* in the sense that they promote similar behaviors. It is also possible for representations of a situation by different systems to result in *competitive* outputs that promote different behaviors (Hirsh & Krajden, 1982). This could occur when the processing styles of two systems accord different degrees of importance to the elements of a situation, leading to the development of coherent representations of different aspects of the same situation. As suggested by Fig. 1, the outputs of the systems would compete in such cases. The system in which coherence developed first would presumably influence behavior early in training, but further training could lead to the development of more coherence in another system, resulting in a more competitive output and a possible change in the resulting behavior. In this case, disabling one system would eliminate its competitive output and allow the output of another system to exert greater control over behavior. Depending on the variables measured in a particular experiment, this could result in supernormal acquisition and performance.

These kinds of interactions are based on the idea that outputs of independently functioning systems converge to influence behavior by cooperating or competing (Fig. 1). The systems can also interact with each other through direct and indirect anatomical connections. Interactions of these kinds are illustrated in subsequent sections.

The dissociation technique. In dissociation experiments, the effects of lesions to several different brain areas on each of a number of memory tasks are tested. If a lesion

impairs performance on only one of the tasks in the series the inference is that the damaged brain structure processes information related to some unique feature(s) of that task. If the other lesions have no effect on performance of that task the inference is that those structures are not required to process the same information. Within the present theoretical framework, the degree of correspondence between the relationships among the elements of a task and the processing style of a neural system determines the specificity of the impairment produced by each of the lesions. When the impairment is specific to one task, an analysis of the relationship among the elements of that task can lead to inferences about the information processing style of the neural system that contains the lesioned structure.

Two issues pertaining to these inferences require consideration. First, impairment of the performance of a task by a lesion could be due to factors other than elimination of the system required to represent the relationships among the elements of the task. Normal learning and memory also require normal perceptual, motivational, and motor functions. In a dissociation experiment, an attempt is made to hold these factors constant across all tasks used. If the only differences among the tasks are those in the relationships among their elements, impairments produced by lesions must be due to functional specificity in the processing and representation of these relationships.

Second, in a dissociation experiment the complete impairment of a task by damage to one brain system and the lack of effect of damage to the other systems is taken to suggest that the other systems play no role in the task. Two exceptions to this conclusion are possible. As already discussed, this finding does not eliminate the possibility that normal performance requires representation of different components of the task by different systems. In this case, lesions of more than one system should impair performance of the task. It is also possible that a system other than the one lesioned may participate in controlling behavior when a normal animal performs the task, even if the contribution of that system is not sufficient to produce normal behavior in the lesioned animal.

The triple dissociation. The triple dissociation was carried out by disabling each of the three systems under consideration, one at a time. This was done by lesioning the central structure of one of the systems (dorsal striatum), part of the central structure of another (lateral nucleus of the amygdala—LNA), or a part of a system other than the central structure, the fimbria-fornix, which is a major but not the only input-output pathway of the hippocampus (Peterson, 1994; Blaker, Armstrong, & Gage, 1988; Chronister & DeFrance, 1979; Votaw & Lauer, 1963; Jones, 1993; Amaral & Witter, 1995). The effects of these lesions on acquisition of three memory tasks were examined. The tasks were chosen on the basis of previous evidence that each of them is impaired by lesions similar to those used in the dissociation experiment. The effect of hippocampus (Jarrard, 1986, 1991, 1993) and fimbria-fornix (Olton & Samuelson, 1976; Olton & Papas, 1979) lesions on win-shift behavior in the radial maze was well documented. The impairment of certain relatively simple behaviors by lesions of the dorsal striatum had been reported several times (Viaud & White, 1989; Divac, 1968; Prado-Alcala et al., 1975; Packard & McGaugh, 1992); and Packard, Hirsh, and White (1989) had reported a double dissociation of the effects of fimbria-fornix and dorsal striatum lesions on the win-shift and win-stay tasks. The elimination of the conditioned cue preference (CCP; also known as conditioned place preference) by lesions of the lateral part of the amygdala (Cador, Robbins, & Everitt,

1989; Everitt, Morris, O'Brien, & Robbins, 1991), but not by fimbria-fornix lesions (Hiroi et al., 1991), had also been demonstrated.

Based on this evidence, it was hypothesized that these three tasks are relatively pure, and it was predicted that each would be impaired by one, and only one, of the lesions. In this event it became possible to infer, to a first approximation, the processing style of each of the three systems from an analysis of the relationships among the elements of each task.

II. THE THEORY

The descriptions of the information processing styles of the three hypothesized systems are presented as a set of inferences from the findings of the triple dissociation experiment. The focus on a single experiment in this section is a convenient way of organizing the concepts to be presented. These concepts are not derived solely from this experiment but in each case from a large preexisting theoretical and experimental literature. A summary of this evidence is presented in section V. Evidence from Other Experiments.

The model learning situation. Together with the description of the experiment a series of models describing the processing style of each system is presented. The elements of a generalized learning situation (Fig. 2) form the basis of these system models. These include both neutral cues (S) and a reinforcer (S*). The three types of responses normally elicited by reinforcers are shown. First, observable approach or escape responses (R*) correspond to patterns of neural activity specific to each type of reinforcer. Second, patterns of unobservable central and autonomic responses (r…r) include neural activity, neurotransmitter release, and hormonal changes. Depending on the reinforcer, the effect of such an array of responses is thought to constitute a rewarding or aversive affective state (Izard, 1972; Candland et al., 1977; Malmo, 1975; Young, 1959; Cabanac, Minaire, & Adair, 1968; Wise, 1982; Shizgal, 1997; Kagan, 1994). These states constitute an internal affective stimulus (Sa). The third type of response (which may be a subset of the second type) is the modulation (M) (i.e., strengthening or enhancement) of recently acquired memories (Landauer, 1969; Gold & McGaugh, 1975; Huston, Mueller, & Mondadori, 1977; Vaccarino, Schiff, & Glickman, 1989; Gold, 1992; White & Milner, 1992; McGaugh & Herz, 1972).

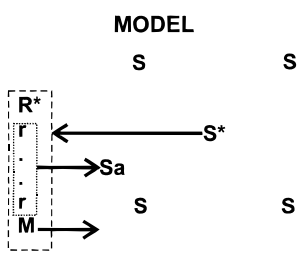

FIG. 2. The elements of learning situations. This model of the elements of a general learning situation is used in Figs. 3–5 to illustrate hypotheses about the processing style of the three proposed systems. The elements include an array of neutral cues (S) and a reinforcer (S*). Reinforcers can elicit three different types of responses: neural activity that results in observable approach or escape responses (R*), an array of relatively unobservable central and autonomic responses (r..r) that may be the basis of positive (rewarding) or negative (aversive) affective states (Sa), and memory modulation (M), the strengthening or enhancement of recently acquired memories.

In the following descriptions this model is used to represent the elements of the memory tasks (which are the same for all tasks) and the relationships among their elements (which are different for each task).

The experiment. All tasks were run on a standard 8-arm radial maze (a central platform with arms radiating out from it) that remained in the same position in the same room for all tasks. The rats were food deprived and were required to learn about the location of food on the maze in all tasks. The tasks differed only in how information about the location of food was presented (the operationalization of the differing relationships among the elements).

Lesions of the fimbria-fornix impaired the rats' ability to learn the location of food in the win-shift task, but had no effect on their ability to do so in the win-stay or CCP tasks. Lesions of the dorsal striatum impaired learning the location of food in the win-stay situation, but had no effect on win-shift or CCP learning. Lesions of the LNA impaired learning the location of food in the CCP situation, but had no effect on the rats' ability to learn it in the win-shift or win-stay tasks. These findings led to the conclusion that learning the location of food in each situation required some unique information processing capacity of one, and only one, of the lesioned structures. The rather complete nature of the dissociation led to the following analysis of the information processing requirements of each of the tasks and to the attribution of these information processing and memory functions to the neural systems that contain each of the lesioned structures.

Hippocampus System

Win-Shift Task

On the win-shift task a single food pellet was placed at the end of each of the arms. A rat was placed on the central platform and allowed to run freely on the maze until it had obtained all 8 pellets. When a rat obtained a pellet from an arm no further pellets were placed there, and subsequent entries into that arm were scored as errors. To obtain the 8 pellets most efficiently a rat had to enter each arm once only, avoiding locations in which food was previously obtained. This required a rat to remember which arms it had visited on that trial, a function known as "working memory" (Honig, 1978; Olton & Papas, 1979; Beatty & Shavalia, 1980; Solomon, 1980). This "list" of visited arms applied only to a single trial, and had to be created as the trial proceeded. Accordingly, the neural system that includes the fimbria-fornix and hippocampus must be able to store new information quickly, based on a single brief experience.

To remember which arms it had visited, a rat must have been able to discriminate the arms from each other. It is usually suggested (Suzuki, Augerinos, & Black, 1980; O'Keefe & Conway, 1978; Eichenbaum, Stewart, & Morris, 1990b) that this ability is based on the formation of a "cognitive" or "spatial map" of the maze and its environment that identifies each arm on the basis of its relationship to other cues in the environment. This type of information remains constant over trials and is sometimes called "reference memory" (Olton & Papas, 1979). By itself, this relational information has no implications for behavior; however, it can apparently be represented and stored by some part of the hippocampus system and subsequently used to direct win-shift behavior by serving as the basis for remembering which arms have been visited during a trial. This requires the

incorporation of specific information about each arm visited and depleted of food as the trial proceeds. That is, it requires the integration of working with reference memory.

What Is Learned

The acquisition of the relational information that forms a spatial map and its use to direct ongoing behavior by incorporating information about current experiences is the unique information processing capacity of the hippocampus system suggested by the effect of damage to this system on performance of the win-shift task. In the model illustrated in Fig. 3, the hippocampus system acquires representations of the relationships among the cues and events (S, S*) in a situation. As explained further in a subsequent section, internal affective stimuli (Sa) resulting from contact with reinforcers can be part of the same relational array as the external stimuli. One property of this type of relational information is that each individual stimulus (S, Sa) is associated with several others. This type of learning involves only the acquisition of information; no responses or behavior are implied by the information that is acquired, and none are learned. However, any number of different responses can be elaborated on future occasions when the stored information interacts with ongoing information processing in the system.

This is the type of learning originally contemplated by Tolman (Tolman, Hall, & Bretnall, 1932; Tolman, Ritchie, & Kalish, 1946; Tolman, 1948), which he labeled "S-S" to symbolize the idea that it involves learning about relationships among stimuli (cues). Because it includes no information about any behavior or responses, this learning model was famously criticized by Guthrie (1959) for leaving the rat at the choice point of the maze "lost in thought." It is sometimes referred to as "cognitive" learning.

Role of Reinforcers

Reinforcers interact with this system in three ways. The first is as a stimulus or event in the environment. All stimuli have several different properties, or "dimensions" (Hirsh,

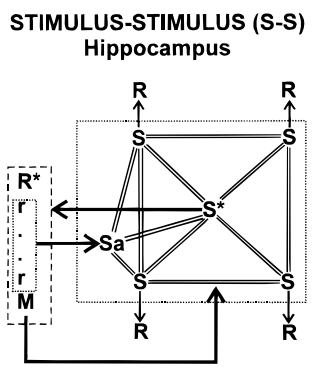

FIG. 3. Stimulus-stimulus (S-S) learning (Attributed to the hippocampus system). The diagram illustrates how the information in the model learning situation (Fig. 2) is processed by the hippocampus system. The large dotted rectangle encloses the parts of the process that go on within the system; the double lines indicate associative bonds. All individual stimuli (S) have more than one association with other stimuli, including the stimulus properties of the reinforcer (S*). The internal affective state (Sa: the hypothesized result of the central and autonomic responses (r…r) elicited by the reinforcer) is also part of this relational array. A number of different responses (R) can be generated based on information appropriate to the situation stored in the hippocampus system, but no information about these responses is stored in the system. The modulatory response (M) acts on the associations that represent the relationships among the elements of the learning situation.

1980), such as colour, size, smell, tactual properties, taste, and location and/or time of occurrence with respect to the other stimuli in the environment. The system represented by this model acquires information about these properties of the stimuli, including the reinforcer. These are the items of information, the relationships among which constitute a nonliteral "map" of the spatial environment (Hirsh, 1980). In performing the win-shift task, this would include information about the remaining food locations after each arm had been visited and the food there consumed.

Second, there is evidence that internal affective states (Sa) such as those thought to be produced by the reinforcer are available to the hippocampus system (Hirsh, Leber, & Gillman, 1978; Davidson, Flynn, & Jarrard, 1992; Davidson & Jarrard, 1993) (see also White, 1996, for a discussion of evidence for hippocampal involvement in mediating the affective properties of addictive drugs) and that this information can be used, together with other stored and current information, to generate behaviors that maximize rewarding and minimize aversive states (Young, 1959). Third, as discussed further in a subsequent section, the memory-modulation response produced by reinforcers acts to facilitate the storage of recently acquired information in the hippocampus.

Dorsal Striatum System

Win-Stay Task

For this learning task lights were placed at the entrances to each of the arms of the radial maze. When a rat was placed on the center platform 4 arms were lit and only those 4 arms contained food pellets. A new random selection of 4 lit/food arms was made every day. When a rat obtained the pellet from a lit arm a second pellet was placed there. When a rat obtained the second pellet from an arm the light at the entrance to that arm was extinguished and no more food was placed there. Thus, the rats obtained 8 food pellets by visiting each of 4 lit arms twice. Entries into unlit arms were scored as errors.

On this task the rats learned to approach lit arms and/or avoid unlit arms. Since the arms containing food were always lit, the rats did not have to remember which arms they had already visited, nor did they have to learn to distinguish the arms from each other. These features distinguish win-stay from win-shift learning.

What Is Learned

In this type of learning (Fig. 4) animals may adventitiously make any response (R) in the presence of an environmental stimulus (S). If a reinforcer (S*) is encountered at around the same time as these events an association between the stimulus and response is strengthened, or enhanced, increasing the probability that the stimulus will elicit the response in the future. In the S-R model, any response that is performed can, in theory, become associated with any stimulus that happens to be present if the two are temporally contiguous with a reinforcer.

This function of reinforcers was originally described by Thorndike (1911; Thorndike, 1933a, 1933b), who referred to it as the "stamping-in" of stimulus-response (S-R) bonds. The basic mechanism was adopted by Hull (1943) for his theory of learning, and later elaborated by others (Estes, 1959; Schacter, Chiu, & Ochsner, 1993; Dickinson & Balleine, 1994). Because this type of learning is thought to proceed in an automatic, unconscious

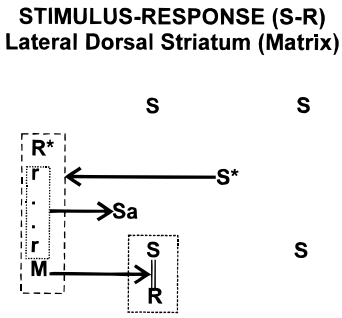

FIG. 4. Stimulus-response (S-R) learning (Attributed to the dorsal striatum system). The diagram illustrates how the information in the model learning situation (Fig. 2) is processed by the dorsal striatum system. The dotted rectangle encloses the parts of the process that go on within the system; the double lines indicate associative bonds. Associative bonds between neural representations of any stimulus (S) and any response (R) are strengthened by the memory-modulating response (M) elicited by the reinforcer. The strength of the association increases with repeated conjunctions of S, R, and M, leading to an increased probability that S will elicit R on future occasions. Each S-R association involves a single stimulus (or array of stimuli treated as a unit) and a single response and includes no information about the reinforcer itself or about the affective response it elicits.

manner, it has also been called "habit" learning (Mishkin & Petri, 1984; Mishkin et al., 1984).

Role of Reinforcers

Only the memory-modulating response elicited by reinforcers acts to facilitate the storage of recently experienced S-R associations in this system. The stimulus properties of, and affective states produced by reinforcers are not involved in this form of learning.

Amygdala System

Conditioned Cue Preference

On the CCP task the rats were confined on successive days in one of the maze arms with a large supply of food and in another arm with no food. This 2-day procedure constituted a training trial, and the rats experienced four such trials over 8 days. The maze was surrounded by curtains to attenuate extra-maze cues. One of the two arms assigned to each rat had a small light in it, the other arm was dark (counterbalanced with respect to the location of the food). On the day following the last training trial the rats were given a choice between the two arms, neither of which contained food. Normal animals entered and spent more time in the arm that formerly contained food than the other arm, regardless of whether it was the lit or the dark arm. Thus, in this form of learning the animals approached and remained close to a cue (light or dark) that had been present while they ate during the training trials. Note that the rats consumed the food during the training trials but did not make the response (entering the arm that formerly contained food) that resulted in the conditioned cue preference during the test trial.

What Is Learned

As illustrated in Fig. 5, the learned behavior observed in this task is based on the association of a neutral stimulus in the arm that contained food (S) with the food reinforcer

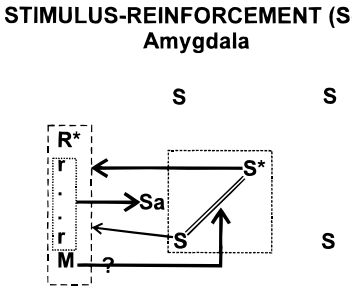

FIG. 5. Stimulus-reinforcer (S-Rf) learning (attributed to the amygdala system). The diagram illustrates how the information in the model learning situation (Fig. 2) is processed by the amygdala system. The dotted rectangle encloses the parts of the process that go on within the system; the double lines indicate associative bonds. The formation of an association between the stimulus properties of the reinforcer (S*) and a neutral stimulus (S) results in the ability of S to elicit the array of responses (R*, r…r, M, and Sa) normally produced by the reinforcer. The learned responses elicited by S (now a conditioned stimulus) are conditioned responses. S-Rf learning is limited to responses that are normally elicited by reinforcers.

(S*). This association allows the now-conditioned stimulus (S) to elicit an array of conditioned responses similar to those initially elicited by the reinforcer itself. Two of the responses in this array could lead to the observed behavior. One is a conditioned approach response (R*); a tendency to approach and maintain contact with the conditioned stimulus.

The conditioned affective response (Sa) could also lead to the observed behavior. By itself this conditioned response, elicited by the conditioned cues in the arm that formerly contained food, has no particular implications for behavior. When it is experienced for the first time (while the rat explores the apparatus on the test day) the relationship of the conditioned affective response to the stimulus that produces it must be acquired through experience. As already mentioned, learning about the relationship between internal affective states and external stimuli is thought to be hippocampus-based (Fig. 3), making this form of CCP learning a task requiring the cooperative function of two independent systems. This two-stage learning process is similar to the "two-factor theory" proposed some time ago by Mowrer (1947) to explain avoidance learning (McAllister & McAllister, 1995).

Lesions to either system should impair performance of this form of CCP learning. Since fimbria-fornix lesions had no effect in this case, this instance of CCP learning was probably based on a simple conditioned approach response rather than on hippocampus-based learning about an amygdala-based conditioned affective response.

The type of learning in which responses normally elicited by reinforcers come to be elicited by conditioned stimuli (Fig. 5) was originally described by Pavlov (1927), and is commonly referred to as Pavlovian or Classical conditioning. Within that scheme, the reinforcer is the unconditioned stimulus (US) and the neutral cues are the conditioned stimuli (CS). The observable or unobservable responses elicited by the US constitute the unconditioned response (UR) and the responses elicited by the CS are the conditioned response (CR). As shown in Fig. 5, and as suggested by Pavlov and numerous empirical and theoretical investigations (Williams, 1965; Mackintosh, 1974; Klopf, 1988; Rescorla, 1988), Pavlovian conditioning is a form of S-S learning that is restricted to associations between neutral stimuli and reinforcers. For this reason it is labeled here as S-Rf learning.

In the present scheme (Fig. 5), S-Rf learning involves conditioned approach and escape responses, their corresponding constellations of conditioned internal responses that are thought to constitute affective states, and the conditioned memory modulation response (Holahan & White, 1998). The restriction of amygdala-based S-Rf learning to responses elicited by reinforcers differentiates it from both S-S and S-R learning. Amygdala-based learning is also differentiated from S-R learning because the new responses that appear after conditioning do not have to be performed to be learned. It is differentiated from S-S learning because the stimuli involved are single cues or stimulus arrays that are treated as single cues.

Role of Reinforcers

Considerable evidence suggests that the amygdala is a critical structure for the acquisition and performance of conditioned approach-reward responses (Henke, 1972; Henke & Maxwell, 1973; Everitt et al., 1991; Kemble & Schwartzbaum, 1969; Peinado-Manzano, 1988), conditioned escape/freezing-aversive responses (LeDoux, 1993; Sutherland & McDonald, 1990; Davis, 1992; Gallagher & Chiba, 1996; Fanselow & LeDoux, 1999; Fendt & Fanselow, 1999), and the memory modulation response (McGaugh, Cahill, & Roozendaal, 1996; McGaugh et al., 1993; McGaugh, Introini-Collison, Cahill, Kim, & Liang, 1992). There is also good evidence that the amygdala-mediated modulation response affects recently acquired memories in the hippocampus and dorsal striatum systems (Packard, Cahill, & McGaugh, 1994; Packard & Teather, 1998a); however, the question of whether this amygdala-mediated response can influence amygdala-based learning remains open.

By one way of reckoning five different types of conditioned responses are attributed to the amygdala in the preceding paragraph: approach response, rewarding affective state, avoidance response, aversive affective state, and memory modulation. These conditioned responses influence behavior directly (approach and avoidance), and indirectly (by the use of affective information in hippocampus-based learning and by modulation of learning in other systems). The question of whether these functions are mediated by the same or different parts of the amygdala is unsettled.

III. FACTORS DETERMINING SYSTEMS INVOLVEMENT IN SPATIAL LEARNING

The present MPMS theory postulates that the involvement of a neural system in processing and storing information in a learning situation is determined by the degree of correspondence between the relationships among the elements of the situation and the fixed processing style of the system. The experiments reviewed in this section manipulated the elements of spatial learning situations to study how specific relationships among them determine the participation of each system. As in the triple dissociation, the experiments involved learning the location of food on a radial maze.

Stimulus Factors

On the win-shift task only distal, environmental cues (stimuli) in the testing room were available to the rats, while in the win-stay and CCP tasks the critical cues were lights in

the maze arms (light vs dark). Distal environmental cues are thought to be used by the hippocampus system to form spatial maps. The question addressed here is whether and how the dorsal striatum and amygdala systems utilize these distal cues.

Hippocampus and Dorsal Striatum Systems

A comparison of how these two systems use distal environmental cues was made in experiments (Packard, 1989; Packard & White, 1990) that compared the effects of lesions to the hippocampus system (fimbria-fornix) and dorsal striatum on the 4/8 radial maze task (Olton & Papas, 1979). In this task the rats are given one trial per day. The maze is open to the environmental cues and the same 4 arms contain food on each trial. The other 4 arms are always empty. Normal rats learn to enter each of the food arms once only on each trial and to avoid entering the arms that never contain food. Rats with fimbria-fornix lesions learned to enter the food arms and avoid the no-food arms as well as controls, showing that they could discriminate between food and no-food locations with a nonfunctional hippocampus system using only distal cues. These rats made errors by reentering food arms, a working-memory deficit consistent with that of animals with fimbria-fornix or hippocampus lesions on the standard win-shift task, and with the model of S-S information processing in Fig. 3.

The rats with dorsal striatum lesions usually entered each of the 8 arms only once per trial, showing that they could discriminate among the arm locations and had normal working memory. However, they tended to enter all 8 arms equally often, suggesting that the ability to discriminate between the food and no-food locations depended on information normally processed by the dorsal striatum system. This is consistent with the S-R model of information processing for this system (Fig. 4) because the approach response to each food arm was consistently associated with the distal cues visible from those arms and always followed by reinforcement (food consumption). Since there was never any food in the other arms no responses to cues visible from those locations were reinforced. This combination of reinforced and unreinforced S-R associations resulted in the discrimination behavior, implying that dorsal striatum-based learning occurs with distal as well as with proximal cues. Consistency of reinforced S-R associations rather than the type or location of the stimuli involved appears to be the critical factor for this system.

The findings also imply that the hippocampus system, which was intact in the rats with dorsal striatum lesions, was unable to process this type of consistent win-stay information within the number of daily trials given in the experiment. A similar conclusion applies to the win-stay task in the triple dissociation experiment. According to the present theory, this is because the relationship among the elements of a win-stay situation is incompatible with the processing style of the hippocampus system.

The findings of the 4/8 experiment are also consistent with the idea that different kinds of learning occur simultaneously in different systems. In this task information processing involving the same environmental cues goes on simultaneously in both the hippocampus and dorsal striatum systems, leading to different types of behavior in each case. Other experiments leading to a similar conclusion are described in subsequent sections.

Amygdala System

The CCP task used in the triple dissociation experiment required rats to find food by discriminating among maze arms on the basis of a cue within each arm (light vs dark)

with attenuated environmental cues (curtains around the maze). The importance of cue type for amygdala-based learning was examined in a CCP experiment on a radial maze with no curtains (White & McDonald, 1993). Each rat was assigned a food arm and a no-food arm separated by at least two other arms, and was given four training trials. To prevent the use of local cues the maze was turned before each trial so that a different arm occupied each location. Normal rats acquired a preference for the location of the food arm, demonstrating that CCP learning occurs with distal environmental cues. Rats with lesions of the fimbria-fornix and/or dorsal striatum acquired CCPs, but rats with lesions of the lateral amygdala failed to acquire CCPs. These findings show that CCP learning occurs with distal environmental cues and that the critical information processing substrate is the amygdala system, as is the case for the CCP with proximal cues.

Individual Cues vs Relations among Cues

As already discussed, the hippocampus system is thought to process information about the relationships among distal environmental cues visible from the maze. The conclusion that the amygdala and dorsal striatum systems also process information involving the same cues raises the question of how these systems utilize this information. (Although it is assumed that visual cues are the major ones in these situations other modalities could also be involved.)

This question was addressed in a series of experiments (McDonald & White, 1995b) that manipulated the angular distance between the radial maze arms defining the spatial locations that rats were required to discriminate. In the experiments already described the locations to be discriminated were defined by arms separated by at least two other arms (angular distance of 135–180 degrees). In this situation, there is little overlap among the sets of cues visible from the two arms. Learned associations between either of these sets and a reinforcer (amygdala system) or a response (dorsal striatum system) should be possible, and should not be affected by learning or extinction involving the cues visible from the other arm. In contrast, with adjacent arm locations (angular distance of 45 degrees) there is a large degree of overlap among the cues visible from the two arms. Therefore, conditioned responses to these cues, acquired while eating on the arm that contained food, would be extinguished on the no-food arm in the presence of the same cues. Because differential reinforcement of individual cues is impossible, it would be difficult for a system that does not process information about the relationships among cues (as the hippocampus system does) to represent the differences between locations defined by adjacent arms of a radial maze.

These ideas were tested in two experiments. In a CCP experiment (McDonald & White, 1995b) with adjacent food and no-food arms, normal rats failed to exhibit a preference for the food arm after 8 training trials (compared to 3–4 trials with separated arms). Since CCP learning is thought to be processed by the amygdala system (CCP learning with separated arms is impaired only by amygdala lesions), this finding suggests that the amygdala system either does not process the information required to discriminate between adjacent arm locations or processes it very inefficiently.

In a second experiment (McDonald & White, 1995b) rats were trained with daily sessions consisting of 10 discrete trials each. The rats were required to chose among radial maze arms by running into them from the center platform. Normal rats easily learned to

discriminate among three adjacent arm locations when one of the arms always contained food. Rats with lesions of the lateral amygdala or of the dorsal striatum performed this task normally, but rats with fimbria-fornix lesions were unable to learn it, suggesting that this discrimination task requires the relational information processing properties of the hippocampus system, and that the dorsal striatum and amygdala systems do not process this information well, if at all. This conclusion is consistent with that suggested by the finding that only hippocampus-system lesions impair the win-shift task (McDonald & White, 1993), performance of which also requires discriminations among locations defined by adjacent arms of a radial maze.

According to the present theory, the amygdala system has difficulty with the adjacent arm discrimination because of its inability to process the information that the set of cues visible from both arms is associated with reward in one arm but not in the other. The dorsal striatum system has difficulty processing information in this system because the S-R association that is reinforced when the rats enter the food arm is extinguished when they enter the no-food arm. However, a small proportion of the cues visible from each arm, on the edge of the visible field distal from the other arm, cannot be seen from the other arm, and is therefore subject to differential reinforcement. Differential reinforcement of this small proportion of unique cues visible from each arm (Estes, 1959) would be the basis of adjacent arm discriminations by the amygdala and dorsal striatum systems, were they to appear after a large number of training trials. This would be an instance of slow learning due to a low level of compatibility between the relationship among the elements of a task and the processing styles of two of the systems.

In a final experiment (McDonald & White, 1995b) normal rats easily learned to discriminate between locations defined by two widely separated radial maze arms when they ran into them from the center platform in a series of daily sessions, each consisting of 10 discrete choice trials. Lesions of the fimbria-fornix, the lateral nucleus of the amygdala, or the dorsal striatum had no effect on this behavior, but combined lesions of dorsal striatum and fimbria-fornix severely impaired acquisition of this discrimination. Combined lesions of fimbria-fornix and amygdala, or of amygdala and dorsal striatum did not impair the discrimination. These findings suggest that information available in the discrete choice paradigm with separated arms is processed by two systems simultaneously, each of which can independently produce the correct behavior. The dorsal striatum system produced the correct behavior because the consistent relationship between the approach response and the cues visible from the food arm, followed by reinforcement, resulted in the formation of an S-R association. Because the arms were widely separated, there was no interference from unreinforced entries into the no-food arm. At the same time the hippocampus system acquired a spatial map of the environment and was able to incorporate information about the location of food into this map during the daily sessions, allowing selection of the correct arm.

In summary, information processed by the hippocampus system involving the cues visible from adjacent or separated arms led to behaviors that discriminated between the locations defined by the arms. Information processed by the dorsal striatum and amygdala systems involving cues visible from separated arms led to different behaviors that discriminated between the locations, but information processed by the latter systems involving cues visible from adjacent arms did not lead to such behaviors. This may be because these systems can only process information about individual cues. Such individual cues

could be either salient features of the environment, or they could consist of "snapshots" that include the entire scene visible from particular locations (Amsel, 1993). Somewhat paradoxically, it appears that if the hippocampus processes information about consistently reinforced responses to individual cues its ability to store such information is slow and inefficient, at best.

Movement and Temporal Factors

In the experiments just described normal animals were able to discriminate between adjacent locations when they ran into the arms from the central platform of the maze, but failed to learn the same discrimination (after 8 training trials) in the CCP situation, in which they were prevented from moving around on the maze during the training trials because they were confined in the food or no-food arms. This suggests that movement may be a factor determining system involvement in processing stimulus information. Another difference between the two procedures was the time between exposures to the two arm locations. In the CCP paradigm 24 h elapsed between exposures to the food and no-food arms; in the discrete trial paradigm the rats visited both arms several times within a 10-min trial. This difference is similar to that between the win-stay components of the triple dissociation and 4/8 tasks (24 h between trials) and the discrete trial separated arms task (multiple trials in the same session).

The importance of these movement and temporal factors was examined by comparing rats' ability to discriminate between maze arm locations using two different training procedures (White & Ouellet, 1997). One was the standard CCP procedure, in which rats were exposed to the food and no-food arms for 30 min at a time, 24 h apart. In the other procedure, the rats were moved between the two arms by the experimenter five times (at 5-min intervals) during each 30-min training session. The total time spent on the food and no-food arms was equal in the two procedures. As previously described, normal rats trained with the 24-h procedure failed to discriminate between adjacent arm locations; however, rats trained with the 5-min procedure learned this discrimination (i.e., they spent significantly more time in the food arm than in the no-food arm when given a preference test between the two empty arms). Acquisition of this discrimination was impaired by fimbria-fornix lesions, but unaffected by lateral amygdala lesions.

These findings are consistent with the conclusion that the relational information processing function of the hippocampus system is required to discriminate the cues visible from locations defined by adjacent arms in the 8-arm radial maze within a few trials. They also show the importance of a temporal factor in this form of learning. Exposure to the cues visible from the two arm locations within 30 min of each other resulted in the required learning, and exposure to the cues from the same two locations with a 24-h delay did not. Presumably, the actual maximum delay between exposures to the cues from the two locations that permits this form of learning is somewhere between these two times. Experiments with the win-shift task, which requires the same type of discrimination and provides exposure to the environmental cues from eight locations plus the center platform, suggest that this time may be approximately 4 h (Beatty & Shavalia, 1980; Maki, Beatty, Hoffman, Bierley, & Clouse, 1984; Packard, Regenold, Quirion, & White, 1990).

These findings also have implications for the role of movement in hippocampus-based spatial information processing (Vanderwolf, Bland, & Whishaw, 1973; Sutherland, 1985).

They show that voluntary, self-generated movement is not required for the system to acquire and process information that can subsequently produce spatial discriminations in ambiguous situations. Rather, the function of self-generated movement is to create the condition in which the system acquires information about the cues visible from at least two locations in the environment within some limited time. Acquisition of this information leads to the computation of the spatial map. The findings of this experiment do not preclude the possibility that some form of sensory feedback during movement to and from the maze and/or between the arms, as suggested by the concept of "path integration" (Etienne, Maurer, & Séguinot, 1996; Whishaw, 1998), could also have formed part of the information processed by the hippocampus system leading to the adjacent location discrimination.

Some conclusions about the importance of movement for the information processed by the other systems can also be made. The fact that the dorsal striatum had to be lesioned to impair the separated location discrimination when the rats ran into the maze arms suggests that this system processed information that led to an approach response to the cues visible from the arm that contained food. The importance of movement for the information processing style of this system is emphasized by the failure of dorsal striatum lesions to impair the same discrimination in the passive CCP paradigm. In this case, the importance of movement may lie in the fact that it is part of the learned association. This means that a response must be performed for it to become part of a dorsal striatum-based S-R association.

The failure of lesions involving the amygdala, either alone or in combination with another central structure, to impair the rats' ability to discriminate widely separated locations in the active learning paradigm is in contrast to the complete elimination by these lesions of the ability to learn the same discrimination in the passive CCP paradigm (White & McDonald, 1993). This suggests that when the animals moved around on the maze amygdala-based processing of information involving the distal cues either did not occur or was minor. Possibly some minimum continuous period of passive exposure to the cues and the reinforcer is required for this system to process information that leads to this form of discrimination behavior.

Summary

The experiments reviewed illustrate factors that determine the involvement of each of the systems in processing and learning spatial information. The data suggest that the hippocampus system processes information about the relations among the cues in an environment (Fig. 3) if the rat experiences those cues from at least two locations in the environment within some limited period of time. Normally, this condition is probably produced by self-generated movement. This relational information (a "spatial map") can be used to discriminate largely overlapping sets of ambiguous cues (such as those defined by adjacent radial arm locations) within a few trials. In more general terms, the findings suggest that the hippocampus system processes information about environmental cues that, when temporally integrated, constitute a definition of a space (i.e., the spatial environment). This process of integrating the relationships among events over time may also apply to other types of information processed and learned by the hippocampus system.

There are apparently limits on hippocampus-based information processing and storage.

Lesions of the dorsal striatum alone impaired acquisition of the win-stay task, and amygdala lesions alone impaired acquisition of the CCP. The inability of rats with intact hippocampus systems that acquired the win-shift task to learn the win-stay and CCP tasks or the reference memory component of the 4/8 task may mean that the processing style of the hippocampus system is limited to information (spatial or nonspatial) requiring the temporal integration of individual sensory elements. The data presented also suggest that although the temporal information processing (working memory) function of the hippocampus system may process subsequently acquired information about specific features of the environment (e.g., the location of food), this information is not permanently incorporated into the stored spatial map.

The dorsal striatum system processes information involving individual cues (which can be of the complex, "snapshot" type). Movement is not required to process such cues, but the response that becomes associated with the stimulus in this form of learning must be performed for the S-R association to be formed. In addition to the empirical evidence presented for this conclusion, it follows logically from the assumption that any stimulus can become associated with any response. Thus, when discriminations between separated locations resulted from stored information processed in the dorsal striatum system, they were due to reinforced approach responses to cues visible from the location that formerly contained food (Fig. 4).

The amygdala system also processes information involving individual environmental cues, perception of which does not require movement. Moreover, since amygdala-based learning occurred when the rats were passively exposed to the learning situation, responses generated from the information processed by this system must have another source. According to the present theory of S-Rf learning (Fig. 5), this source is the responses (observable and unobservable) normally elicited by reinforcers. When environmental cues become associated with reinforcers, these conditioned cues elicit these responses even though they were never made during the training trials. According to this model, the amygdala-based CCP involving discrimination between separated locations is due to the conditioned approach response elicited by cues visible from the location that formerly contained food. Another form of the CCP discrimination is discussed in the next section.

IV. INTERACTIONS AMONG THE SYSTEMS

The concept of parallel processing implies that several different kinds of information processing are usually going on in a single brain, each in a different system. At least two kinds of interactions among these processes are possible. First, the output of the systems must interact (or merge) at one or more points (see VI. Anatomy of Systems) so that the behavioral tendencies produced by the systems can interact, cooperatively or competitively. Second, there are direct anatomical connections between the systems. Some form of activity in one system could act directly on another system to promote or impede information processing and synaptic changes that may be ongoing in the latter system. Such direct influences could also result in cooperative or competitive interactions.

Learning the active discrimination between widely separated arms of the radial maze (McDonald & White, 1995b) is an instance of cooperative interaction, in which similar behaviors were learned by the dorsal striatum and hippocampus systems. Accordingly,

pretraining lesions of either system had little effect on acquisition; only simultaneous lesions to both systems impaired learning the discrimination.

Competitive interactions occur in situations where systems produce different behavioral tendencies. In such cases, the behavior produced by one of the systems will lead to "correct" performance of the task defined by the experimenter, and the behavior produced by the other system will necessarily be "incorrect," resulting in interference with the correct behavior. It follows that disabling the system producing the incorrect behavior will result in more correct responding earlier in training. Operationally, this means that on certain tasks the performance of subjects with certain lesions will be better than that of normal subjects.

Competitive interactions of this type are taken as strong evidence for the independent functioning of the information processing systems proposed by the present MPMS theory. Several instances of this phenomenon, involving all three systems are described here and in section V. Evidence from other Experiments.

Caudate vs Hippocampus in Win-Stay

In two experiments (Packard, et al., 1989; McDonald & White, 1993) dorsal striatum lesions impaired, but hippocampus system (fimbria-fornix) lesions, facilitated acquisition of the win-stay task. In this task, approaching the lit arms is thought to be learned as a reinforced S-R association that depends on the unique information processing capacity of the dorsal striatum system. Facilitation of this behavior in rats with hippocampus system lesions suggests that in normal animals information processed by that system leads to behavior that interferes with the win-stay behavior produced by the dorsal striatum system, or that interferes directly with information processing in the dorsal striatum system. The incapacity of the hippocampus system to represent simple S-R associations has already been discussed. An analysis of the learning situation suggests the possibility that the hippocampus system acquires a spatial map of the maze environment during the first few daily trials, and that this coherent representation of the irrelevant distal cues in the situation would be the dominant influence on the animals' behavior during the early trials, possibly producing a tendency to avoid arms already reinforced on the same trial (win-shift). Acquisition of the incrementally reinforced light-approach association by the dorsal striatum system would require considerably more trials to attain a degree of coherence that could compete successfully with the output of the hippocampus system for control of the animal's behavior. Disabling the hippocampus system with a fimbria-fornix lesion would eliminate its competition with the output of the dorsal striatum system, allowing the influence of that system to be observed after fewer trials.

Additional evidence for this explanation of the interfering action of hippocampus-based information processing with win-stay learning comes from the finding (Packard, 1987) that win-stay performance on a radial maze located in a room containing numerous environmental cues was significantly improved by surrounding the maze with curtains that attenuated those cues. This is consistent with the hypothesis that environmental cues provide the information that contributes to interference with win-stay performance. This interference can be reduced by attenuating the cues or by disabling the hippocampus system that normally processes them.

Hippocampus vs Caudate in Water Maze

In this experiment (McDonald & White, 1994) rats were trained to swim from four points on the edge of a large circular pool to a visible platform in a constant location in the pool. After 12 days of training, with hidden (submerged) platform trials on every third day, normal rats were able to swim directly to the platform from all starting locations, regardless of whether it was visible or hidden. They were then tested with a visible platform in a new location. Among 8 normal rats tested, 4 swam directly to the visible platform, but the other 4 swam first to the location the platform had occupied during the previous training trials.

An explanation of this observation is suggested by the effects of lesions on this behavior. Among 8 rats with fimbria-fornix lesions, all swam directly to the visible platform, suggesting that disabling the hippocampus system eliminated the tendency of some rats to swim to the previously learned spatial location of the platform. Among 9 rats with dorsal striatum lesions, 7 swam to the old platform location first and then to the visible platform, suggesting that these lesions impaired a previously learned tendency to approach the visible platform cue. This pattern of effects is consistent with the idea that the brains of the normal rats simultaneously processed both a spatial map of the environment and a tendency to approach the visible platform. The dissociation of the lesion effects suggests that these two kinds of information were processed in different neural systems. Disabling each of them allowed unimpeded expression of the behavioral tendency produced by the other system.

Amygdala vs Hippocampus in CCP

Normal rats required four training trials to acquire the CCP on the radial maze when locations marked by clearly discriminable cues (widely separated arms) were used, and lesions of the lateral amygdala, but not of fimbria-fornix or dorsal striatum, eliminated this form of learning (McDonald & White, 1993; White & McDonald, 1993). In these experiments all rats were "habituated" to the experimental situation by being placed on the maze with no food for a 10-min "preexposure" session on the day before CCP training began. Subsequent investigation of this procedure (McDonald & White, 1995a) revealed that elimination of the preexposure session resulted in the acquisition of a large CCP after only one or two training trials. Moreover, preexposing the rats on a similar maze in a different room resulted in similarly accelerated CCP acquisition, suggesting that the rats acquired information specific to the maze environment during preexposure, and that this information retarded subsequent CCP learning in the same environment (using the same cues).

In a parallel experiment (White & McDonald, 1993) rats with fimbria-fornix lesions that were preexposed to the maze environment also exhibited accelerated CCP learning in the same environment. Rats with combined lateral amygdala and fimbria-fornix lesions did not acquire a CCP, showing that the facilitated CCP produced by fimbria-fornix lesions depends on an intact amygdala. These findings suggest that the environment-specific information acquired during preexposure depends on an intact hippocampus system, and that this form of learning interferes with subsequent amygdala-based CCP learning. However, when this hypothesis was tested further it was found that neurotoxic lesions of the hippocampus had no effect on the retardation of CCP learning produced by preexposure

to the maze environment (White & Wallet, 2000). A similar finding, the failure of large electrolytic lesions of the hippocampus to impair latent learning (Kimble & BreMiller, 1981; Kimble, Jordan, & BreMiller, 1982), had been previously reported.

This surprising finding has several implications for understanding the function of the hippocampus system. Notwithstanding its label in the present theory, the system does not appear to require an intact hippocampus for all of its functions. Since there were no reinforcers on the maze during the preexposure sessions the learning that occurred involved only the acquisition of "pure" information about the maze environment, presumably in the form of S-S associations, with no specific implications for behavior. Possibly the function of the hippocampus is only required when an internal affective state resulting from the presence of a reinforcer is part of the "map" acquired during exposure to the situation. Alternatively, hippocampal function may be required when the information acquired results in some specific behavior (due to the presence of a reinforcer) or when this behavior is expressed, as has been suggested by some recent findings on spatial navigation and other behaviors (Whishaw, 1998; Oddie, Kirk, Whishaw, & Bland, 1997). Since the fimbria-fornix has direct connections with parts of the hippocampus system such as subiculum, entorhinal cortex, and other parahippocampal structures (see VI. Anatomy of Systems), the finding suggests that "pure" spatial learning may involve a subcircuit of the system, with hippocampal involvement only under certain circumstances.

One indication of these circumstances may be provided by the finding that large, neurotoxic lesions of dorsal and ventral hippocampus impaired separated arm CCP learning in rats that were preexposed to the maze environment (Ferbinteanu & McDonald, 2000) but had no effect on a similar CCP learning task in rats that were not preexposed (White & Wallet, 2000). This suggests the possibility that, in the presence of a spatial map of the environment, acquisition and storage of which do not require a functional hippocampus, CCP learning utilizes the available spatial information. This utilization process does require hippocampal function, and a normal amygdala. In rats not given the opportunity to acquire a spatial map, amygdala-based CCP learning may occur without requiring involvement of the hippocampus. This parallels findings for certain types of aversive learning (Phillips & LeDoux, 1992, 1994; Sutherland & McDonald, 1990), in which "contextual" conditioning is impaired by both hippocampus and amygdala lesions, but conditioning with a simple stimulus as the CS is impaired only by amygdala lesions.

In summary, during exploration of the maze prior to CCP training the hippocampus system appears to acquire (spatial) information about the maze environment that later interferes with acquisition or expression of the amygdala-based CCP. Acquisition of the spatial information requires an intact fimbria-fornix, but not an intact hippocampus. Since this form of hippocampus system learning does not involve any specific behavior, this interference could not be due to competitive output from this system. Rather, it seems likely that the interference is due to a direct action of the hippocampus system on the amygdala system. This action, which may involve the transfer of spatial information, may be the basis of the CCP observed in rats that have been preexposed to the maze in the absence of reinforcers. This is consistent with the finding that the CCP in preexposed rats is impaired by both hippocampus (but not fimbria-fornix) and amygdala lesions. However, only an intact amygdala is required for the CCP in rats not preexposed to the environment.

V. EVIDENCE FROM OTHER EXPERIMENTS

Three kinds of additional evidence, most of which preexisted and provided the context for the present MPMS theory, convergently suggest information-processing and memory functions for each proposed system similar to those suggested by the MPMS theory. These include studies of the effects of lesions to the central structures, studies on the behavioral correlates of single unit activity within the central structures, and reports of behavior-specific effects of posttraining manipulations, including electrical stimulation and localized intracranial injection of drugs into the central structures.

Effects of Lesions

Even when limited to studies involving the central structures, the literature on the effects of lesions on behavior is large and highly variable. According to MPMS theory, the limited number of pure learning tasks (with properties that are processed by a single system) is a major cause of this variability. Most lesion studies use tasks mediated by more than one system. The effect of a lesion to any central structure on such tasks will depend partly on which other system(s) is involved in mediating it, and partly on the stage of learning at which the lesions were made. Due to limitations of space, scope, and information, the following brief review does not attempt extensive analyses of these factors in studies that may appear to contradict certain aspects of the present hypothesis.

Hippocampus

Impairment of win-shift behavior on the 8-arm radial maze is a well-established behavioral effect of damage to both the hippocampus (Jarrard, 1993) and fimbria-fornix (Olton & Samuelson, 1976; Olton & Papas, 1979). Evidence that rats use cues in the maze environment to perform this task (Suzuki et al., 1980) is consistent with the idea that the behavior affected by these lesions depends on learning that involves relationships among these cues, as illustrated in Fig. 3.

Another reliable effect of damage to the hippocampus (Morris, Garrud, Rawlins, & O'Keefe, 1982; Sutherland, Kolb, & Whishaw, 1982; Sutherland, Whishaw, & Kolb, 1983; DiMattia & Kesner, 1988) and fornix (Nilsson, Shapiro, Gage, Olton, & Bjorklund, 1987; Sutherland & Rodriguez, 1989; McDonald & White, 1994) in the rat is the disruption of both acquisition and retention of place learning on the hidden platform version of the water maze task. In this task rats learn the location of an escape platform hidden under the surface of a swimming pool. Two features of this situation correspond to the hippocampus system S-S model. First, no proximal cue shows the location of the platform, forcing the rat to use information about the relationship of its location to distal cues in the room. Second, the use of different starting points around the edge of the pool prevents the use of any specific response strategy for locating the platform. Therefore, hippocampus system lesions impair the processing of information about the spatial relationships among the available environmental cues.

Damage to the hippocampus system in rats also impairs acquisition of other types of discriminations involving spatial information (Barnes, 1988; Rasmussen, Barnes, & McNaughton, 1989; van der Staay, Raaijmakers, Lammers, & Tonnaer, 1989). In one such

study (Aggleton, Hunt, & Rawlins, 1986) rats with hippocampal lesions were impaired on a forced choice alternation task between two arms in a T-maze from which environmental cues were visible, but were normal on a similar task in which the arms of the maze were differentiated with patterns on the maze walls, even when there was a delay between successive choices. In other studies, rats were impaired on tasks involving spatial working (Kesner, Crutcher, & Beers, 1988) and recognition (Kesner, Bolland, & Dakis, 1993) memory. Hippocampus lesions also impaired the ability of rats to discriminate a new radial maze arm from a series that had previously been presented (using the spatial cues visible from each arm) (Hunt, Kesner, & Evans, 1994), but similar lesions had no effect when rats were required to discriminate 3-dimensional objects (Jackson-Smith, Kesner, & Chiba, 1993). However, hippocampal lesions impaired the ability of rats to discriminate similar objects when they were presented less than 1 m apart on an open field (Gilbert, Kesner, & DeCoteau, 1998), a finding similar to that already described for the distance between arms on a radial maze (McDonald & White, 1995b).

Certain spatial (Eichenbaum, Stewart, & Morris, 1990a; White & McDonald, 1993) and other (Gallagher & Holland, 1992; Whishaw & Tomie, 1991; Cho & Kesner, 1995) tasks that can be modeled as S-S learning are not affected by hippocampus system lesions. Although these tasks have certain features that correspond to the S-S model, in each case they also have features in common with one or more other models. According to MPMS theory, this means that such tasks correspond to the processing style of one or more of the other systems, and that these systems develop coherent output in the situation before the hippocampus system. In general, it is often not possible to predict which of the models corresponds more closely to a specific task, and therefore which system will first develop coherent output in the situation. In such cases an investigation of the effects of lesions to individual and combinations of the central structures may be required to determine how the task is mediated by the brain.

Negative patterning (Rudy & Sutherland, 1989) is a nonspatial task that can be modeled as S-S learning because rats must learn to make a response to a cue when it occurs alone, and a different response when it occurs together with a second cue. Rats with neurotoxic damage to the hippocampus are impaired on this discrimination (Rudy & Sutherland, 1989; Sutherland & Rudy, 1989; Sutherland, McDonald, Hill, & Rudy, 1989; Rudy & Sutherland, 1995; Sutherland & McDonald, 1990; McDonald et al., 1997), although at least one exception to this general finding has been reported (Davidson, McKernan, & Jarrard, 1993). Other instances of learning situations that are formally negative patterning tasks (Gallagher & Holland, 1992) but can also be modeled as amygdala- or dorsal striatum-based tasks are not affected by lesions to the hippocampus system.

In addition to the hippocampus itself, structures such as subiculum and entorhinal and perirhinal cortex, that are parts of the hippocampus system, have been implicated in various forms of memory that require an intact hippocampus system (Wiig & Bilkey, 1994, 1995; Hunt et al., 1994; Baxter & Gallagher, 1996; Nagahara, Otto, & Gallagher, 1995; Eichenbaum, Schoenbaum, Young, & Bunsey, 1996). The specific functions of the various parts of the system remain the subject of investigation.

Lesions of the hippocampus have also been reported to impair (Sutherland & McDonald, 1990; Kim & Fanselow, 1992; Phillips & LeDoux, 1992; Selden, Everitt, Jarrard, & Robbins, 1991; Blanchard, Blanchard, & Fial, 1970) or to have no effect on (Phillips & LeDoux, 1994; Frankland, Cestari, Filipkowski, McDonald, & Silva, 1998) the acquisition

of conditioned aversive responses (conditioned "fear") when the CS is a "context": that is, an array of stimuli similar to those that can be seen from an arm of a radial maze. McDonald and colleagues (McDonald, Koerner, & Sutherland, 1995; Frankland et al., 1998) have shown that aversive conditioning is unaffected by hippocampal lesions in situations where a single set of stimuli serves as the CS, but that this form of conditioning is impaired when the CS is a context that must be discriminated from one or more other contexts that share common elements, making the discrimination ambiguous. This finding is similar to that for learning to discriminate between arms of a radial maze. In that situation, the hippocampus system is required only for learning to discriminate between the cues visible from adjacent arms which also contain common elements, making them ambiguous.

Thus, the pattern of deficits following hippocampal damage in rats suggests that there is a subset of spatial and contextual learning tasks that can be represented only in the hippocampus system. One of the characteristics of these tasks is that they require discriminations between sets of cues that are ambiguous because they contain common elements.

Dorsal Striatum

Simple discrimination tasks, in which a response made in the presence of a stimulus is repeatedly followed by a reinforcer (e.g., the win-stay task), are instances of S-R learning attributed to the dorsal striatum system (Fig. 4). In one of the earliest studies of this type, dorsal striatum lesions impaired acquisition of a visual discrimination task in monkeys (Divac, Rosvold, & Szwarcbart, 1967), and there is evidence consistent with this idea from a variety of species (Divac, 1968; Chozick, 1983; Kimura, 1995). The impairment by damage to the dorsal striatum of maze learning in which food is always found in a fixed direction from a rat's starting position (Thompson, Guilford, & Hicks, 1980; Brasted, Humby, Dunnett, & Robbins, 1997) is a frequently studied example. Cook and Kesner (1988) compared the effects of dorsal striatum lesions on four tasks. The rats were impaired on two response-dependent egocentric tasks on a radial maze (entering the adjacent arm from a random start arm and choosing between the right and left arms of randomly selected pairs) but normal on two tasks that depended on spatial cues.

Recently, impairment of S-R tasks has been demonstrated with lesions restricted to the lateral part of dorsal striatum; lesions to the medial part of the structure impaired S-S learning and were anatomically associated with the hippocampus system in this function (Devan, 1997; Devan et al., 1998). These findings are consistent with the hypothesis that the dorsal striatum S-R learning system includes the matrix compartment (White, 1989) which predominates in the lateral dorsal striatum of the rat. The findings also begin to account for effects of dorsal striatum lesions that include the medial part of the structure on a variety of non-S-R tasks (e.g., Devan, Blank, & Petri, 1992; Devan et al., 1998; Whishaw, Mittleman, Bunch, & Dunnett, 1987; Colombo, Davis, & Volpe, 1989; Furtado & Mazurek, 1996).

Rats with dorsal striatum lesions are also impaired on various tasks involving escape and avoidance responses. Green, Beatty, and Schwartzbaum (1967) showed that dorsal striatum lesions impair acquisition of a two-chamber active avoidance response, and there are numerous other reports of similar effects (Allen & Mitcham, 1972; Green et al., 1967; Kirkby & Polgar, 1974; Mitcham & Thomas, 1972; Winocur, 1974; Viaud and White,

1989; Neill & Grossman, 1970). These tasks can be represented as S-R associations between environmental cues (usually explicit) and simple running responses. When shock is received during training it acts to modulate these associations.

These findings are consistent with the hypothesis that an intact dorsal striatum is necessary for the acquisition and maintenance of simple S-R tasks conforming to the model illustrated in Fig. 4.

Hippocampus-Dorsal Striatum Dissociations

Three additional experiments dissociating the hippocampus and dorsal striatum systems are consistent with the present hypothesis. Kesner et al., (1993) found that performance of a spatial delayed-matching-to-sample task, in which rats entered a randomly chosen arm of a radial maze and then had to select that arm over a novel arm, was impaired by hippocampal but not by dorsal striatum lesions. This task required the use of spatial cues. In contrast, performance of a task requiring rats to maintain the direction of a turn on successive trials regardless of the starting point was impaired by dorsal striatum, but not by hippocampus lesions. This task required the rats to ignore the spatial cues in the situation and to rely solely on egocentric cues. This double dissociation is consistent with other evidence concerning the kinds of information processed by the two systems, and with the idea that they function independently of each other.

In the second experiment, Packard and McGaugh (1992) trained rats in a water maze to distinguish between two local cues that were moved to a new location on each trial: one cue always led to escape from water (on a hidden platform), the other did not. Acquisition of this task, based on a consistent response to a local cue, was impaired by dorsal striatum lesions, but unaffected by fimbria-fornix lesions. On a different task the locations of the cues (and the hidden platform) remained constant but the cues themselves were exchanged randomly, forcing the rats to use spatial cues to locate the platform. Acquisition of this task was impaired by fimbria-fornix lesions but unaffected by lesions of dorsal striatum. This double dissociation of the functions of the hippocampus and dorsal striatum systems is similar to those already described for the radial and water mazes.

In the final experiment (Packard & McGaugh, 1996), rats were trained to find food in a T-maze by making a consistently reinforced right turn at the choice point, and were then tested by having them approach the same choice point from the opposite direction (Blodgett & McCutchan, 1947, 1948). When tested after 8 days of training most of the control rats turned toward the location of the food, a response that was opposite (left turn instead of right turn) to the one that had been reinforced during training. Bilateral inactivation of the hippocampus with lidocaine eliminated this tendency; inactivation of the dorsal striatum had no effect. When tested after 16 days of training, most control rats made the right turn response that was reinforced during training (i.e., they turned away from the food). Inactivation of the hippocampus had no effect on this behavior. Inactivation of the dorsal striatum eliminated the tendency to repeat the reinforced response and reinstated the behavior that led to the food location.

These findings suggest that early in training the rats' behavior was controlled by information about the location of food processed in the hippocampus system. Later in training their behavior was controlled by a consistently reinforced S-R association processed in the dorsal striatum system. The fact that behavior leading to the location of the

food replaced the reinforced response when the hippocampus was inactivated is consistent with the idea that the two forms of information processing occurred in independent neural systems. The findings also illustrate how differences in learning rate that are properties of the systems (the hippocampus-based behavior was acquired more quickly than the dorsal striatum-based behavior) lead to different effects of lesions made at different stages of learning.

Improvements in Learning Produced by Hippocampus-System Lesions: Evidence for Independent Function

Place learning. In an experiment with much in common with the radial maze studies already described, O'Keefe, Nadel, Keightley, and Kill (1975) trained rats to find food hidden in wells in the surface of a large circular runway. When the only information available about the location of the food was its relation to distal room cues animals with fimbria-fornix lesions were impaired compared to normal controls. When the location of food was indicated by a spotlight that illuminated the correct well the lesioned animals were better than normal animals at finding the food. According to MPMS theory the superior performance of the lesioned animals was due to their inability to form hippocampus system-based spatial representations of the maze environment. In normal animals the presence of this information interfered with the expression of a dorsal striatum-based S-R association between the cue indicating the correct well and an approach response.

Avoidance. One of the earliest reports of improved performance following lesions (Isaacson & Douglas, 1961) involved two-way active avoidance learning by rats with hippocampal ablations produced by aspiration. The rats learned to avoid foot shock by running back and forth in a test chamber whenever a buzzer sounded. While learning to respond to the buzzer the animals received shock on both sides of the chamber. According to MPMS theory, the hippocampus system of normal animals processed representations of the places where shock was received, resulting in a tendency to avoid those places when the buzzer sounded. Simultaneously but more slowly, the dorsal striatum system processed an S-R association between the buzzer and the running response, reinforced by the contiguous foot shock, leading to shock avoidance. Disabling the hippocampus system eliminated its competitive output resulting in quicker appearance of the avoidance response.

Olfactory discrimination learning. Eichenbaum, Fagan, Matthews, and Cohen (1988) found that rats with fimbria-fornix lesions acquired an olfactory discrimination faster than normal rats. The task required the animals to keep their noses in a hole for at least 2 s when the correct odor was presented, but for less than 2 s when the incorrect odor was presented. This task could have been represented as a single S-R association consisting of a prolonged nose poke to the correct odor or as two independent S-R associations consisting of a long nose poke to the correct odor and a short one to the incorrect odor. The authors assume that some form of redundant information processed in the hippocampus system interfered with the S-R associations that produced the correct responses, but were unable to specify the precise nature of this information.

Amygdala

The model of S-Rf information processing in the amygdala system (Fig. 5) predicts that lesions of the amygdala should impair conditioning based on responses normally elicited by reinforcers. Some effects of these lesions on approach/reward and escape/aversion responses are described here.

Approach/reward responses. Weiskrantz (1956) provided the first evidence in monkeys that lesions of the amygdala impair learning that involves "biologically significant events," called reinforcers in the present scheme. The term "stimulus-reinforcement learning" was first applied to amygdala function by Jones and Mishkin (1972). Their findings suggested that the formation of object-reward associations in monkeys depends on the integrity of the amygdala (see also Spiegler & Mishkin, 1981).

In rats, neurotoxic lesions of the lateral amygdala made after training on a CCP task with a sucrose solution as the reinforcer eliminated the conditioned preference for the sucrose-paired location (Everitt et al., 1991). This finding shows that the lateral amygdala is critical for expression of this paradigmatic S-Rf task after it has been acquired.

In another study (Kesner, Walser, & Winzenried, 1989) rats with lesions of the central nucleus of the amygdala failed to discriminate between arms of a radial maze that contained one or seven pieces of food, suggesting that they lacked the ability to discriminate "magnitude of reward." Peinado-Manzano (1988) trained rats on a go-no go bar-pressing task with bright and dim lights as the discriminative stimuli. Approaching and pressing the bar were reinforced for only one of the stimuli. Neurotoxic lesions of the amygdala severely retarded acquisition of the task and produced a severe impairment of performance when made after training. With additional training both the pre- and posttraining lesion groups eventually learned the discrimination. The impairment of acquisition and performance of this task by amygdala lesions suggests that it was initially learned as a conditioned approach response to the positive discriminative stimulus. The fact that the lesioned rats acquired the task with additional training suggests that it may also have been learned at a slower rate as a dorsal striatum-based S-R association.

Kesner and Williams (1995) trained rats to use the presentation of two kinds of cereal containing different amounts of sugar as a discriminative stimulus signaling the availability of a reward. Rats with amygdala lesions failed to learn this discrimination, but rats with hippocampus lesions learned it normally. Taken together with the other evidence presented, this finding suggests that a neural system that includes the amygdala but not the hippocampus is required for processing responses elicited by reinforcers. The finding suggests that different magnitudes of reward elicit responses with different amplitudes.

Conditioned reinforcement. Conditioned reinforcement is the tendency for a conditioned stimulus to produce a new learned behavior when it is made contingent on that behavior. In one series of experiments (Cador et al., 1989; Burns, Robbins, & Everitt, 1993) rats were trained to push a panel to obtain water or a sucrose solution. Panel pushing was accompanied by a compound CS that elicited the behavior without the reinforcer after training. Neurotoxic lesions of the amygdala retarded but did not prevent learning this response. Subsequently the rats were offered two bars; pressing one of them produced the compound CS (only), pressing the other had no consequences. Control rats pressed

the CS bar about twice as often as the non-CS bar, demonstrating conditioned reinforcement; the amygdala-lesioned rats pressed the CS bar about 1.2 times as often as the non-CS bar (Burns et al., 1993), demonstrating an impairment of conditioned reinforcement. The difference in the effects of amygdala lesions on the response reinforced by sucrose, which could be learned by more than one system, and on the response reinforced by the CS, which required an intact amygdala, is consistent with the notion of parallel processing in the present MPMS theory.

In another experiment (Everitt, Cador, & Robbins, 1989) male rats learned to press a bar for access to an estrous female in the presence of a CS (a light). After this behavior was learned the males were trained to press a bar for the CS only. After this behavior was learned (due to the conditioned reinforcing properties of the CS) amygdala lesions were made. The lesioned rats' rate of bar pressing was about 57% that of the sham-lesioned rats, suggesting that the lesions impaired the conditioned reinforcing properties of the CS.

According to MPMS theory, these instances of amygdala-based conditioned reinforcement could be produced by two different forms of S-Rf learning (Fig. 5). First, the CS could elicit conditioned rewarding responses when presented contingently upon some new response, leading to new hippocampus-based learning about the conditions that produce the conditioned rewarding state and, in turn, more frequent performance of the response.

Second, the CS could elicit a conditioned memory modulation response (Holahan et al., 1998). This response would facilitate acquisition of contemporaneously occurring S-S and/or S-R associations, increasing the tendency for the behaviors they represent to be repeated.

Escape/aversion. Bagshaw and Benzies (1968) showed that amygdala damage in monkeys impairs acquisition of an aversive conditioned response. Presentations of light were paired with offset of an electric shock to the paw. The galvanic skin response (GSR) of normal monkeys increased during presentation of both the light and the shock; the GSR of monkeys with amygdala lesions increased during the shock only. This suggests that the amygdala lesion blocked a conditioned GSR to the light, a learned S-Rf response similar to that modeled in Fig. 5.

Several groups of investigators have extended this finding to the rat and contributed information about the anatomy and function of the neural system that mediates both the unconditioned and conditioned aversive responses. Kapp and colleagues (Kapp, Frysinger, Gallagher, & Haselton, 1979) showed that rabbits with damage to the amygdala fail to acquire a classically conditioned bradycardia (UR) produced by presentations of an electric shock (US), or to retain the response if it was learned before the lesions were made. Davis (1986) and colleagues used a fear-potentiated startle paradigm in which pairings of light and shock causes the light to acquire conditioned stimulus properties. In normal rats the amplitude of the startle response elicited by a loud noise was increased in the presence of this CS, but in rats with amygdala lesions this potentiation of the startle response was absent (Davis, Gendelman, Tischler, & Gendelman, 1982). LeDoux (1993) and colleagues used a paradigm in which shock-produced increases in behavioral freezing (immobility) and arterial blood pressure were elicited by a tone (CS) after tone-shock pairings. Rats with damage to the amygdala showed increased responding to the shock, but not to the tone (LeDoux, Cicchetti, Xagoraris, & Romanski, 1990). Fanselow and co-workers (Kim,

Rison, & Fanselow, 1993; Fanselow & Kim, 1994; Maren, Aharonov, & Fanselow, 1996) have demonstrated the involvement of NMDA-based neuroplasticity in the amygdala, apparently mediating the conditioned freezing response.

There is also considerable evidence that amygdala lesions impair the acquisition and expression of the conditioned taste aversion (Nachman & Ashe, 1974; Yamamoto & Fujimoto, 1991; Kesner et al., 1992) a paradigm in which a novel taste is paired with illness, leading to a reduction in consumption of foods or fluids with that taste. This is generally agreed to be a classically conditioned response (Garcia, Hankins, & Rusiniak, 1976).

These findings show that lesions of the amygdala impair conditioned aversive behaviors, including freezing, escape, and taste aversion. The same lesions impair the conditioned autonomic responses that may contribute to the aversive central state sometimes called "fear."

Neural Activity

This evidence is based on correlations between the appearance of learned behaviors during training and changes in the activity patterns of single neurons or groups of neurons in the central structures. Since the idea of parallel processing (Fig. 1) suggests that all systems process information about similar elements of a learning situation, some neurons in each system (or central structure) should respond to the individual elements of most situations regardless of the match between the situation and the processing style of the system. However, the postulate that a match between a learning situation and the processing style of a system results in an increase in the coherence of neural activity in that system predicts an increase in the probability of observing altered neural activity that corresponds to some relationship among the elements of the situation. The degree of matching between the situation and the processing style of a system will determine how quickly and with what probability such changes in neural activity are observed in that system.

Hippocampus

The development of "place fields" by neurons in the hippocampus (O'Keefe & Dostrovsky, 1971; O'Keefe, 1979) soon after rats are placed into a new environment is perhaps the clearest known instance of the development of a form of coherent neural activity in a system as information about the relationships among the elements of the situation is processed by the system. The activity of these cells is probably based on stimuli from different modalities (O'Keefe & Conway, 1978), including representation of the motivational context of the situation (Breese, Hampson, & Deadwyler, 1989; Eichenbaum, Kuperstein, Fagan, & Nagode, 1987; Ehlers, Somes, Lopez, & Robledo, 1998; Shapiro & Eichenbaum, 1999), and is not generally related to movement (Muller, Kubie, & Ranck, 1987), although it may be related to certain learned behaviors (Wiener, Paul, & Eichenbaum, 1989). The early discoveries of this type were the main impetus for the development of the "cognitive mapping" theory of hippocampal function (O'Keefe & Nadel, 1978).

O'Keefe and Speakman (1987) showed that neurons in the hippocampus appear to process information about topographical relationships among environmental stimuli. They found that place units can persist even if some of the controlling cues are removed in the

presence of the animal (see also Quirk, Muller, & Kubie, 1990). The finding that a rat's position in space about 1 s in the future is better correlated with place unit firing than its current position (Muller & Kubie, 1989) also suggests that complex coding of spatial information is represented in the hippocampus in certain circumstances. The fact that the development of place fields is impaired in rats treated with NMDA receptor blockers (Kentros et al., 1998) and in mice lacking NMDA receptors in the hippocampal CA1 field (McHugh, Blum, Tsien, Tonegawa, & Wilson, 1996; Rotenberg, Mayford, Hawkins, Kandel, & Muller, 1996) also provides a link between the information-processing functions of these neurons and neuroplastic processes in this system. However, consistent with the previous discussion suggesting that an intact fimbria-fornix is required for the acquisition of spatial information, it has been reported that rats with lesions of these structures do not acquire consistent place fields related to distal environmental cues (Shapiro et al., 1989).

Nonspatial correlates of neuronal activity in the hippocampus have been demonstrated using a delayed nonmatch to sample task (Wible et al., 1986): firing rates correlated with some nonspatial features of the apparatus and task such as brightness of goal boxes and type of trial. The activity of hippocampal neurons has also been related to the configuration of olfactory cues in an odor discrimination task (Eichenbaum et al., 1987) and with other nonspatial features of learning situations (Wood, Dudchenko, & Eichenbaum, 1999; Wiener et al., 1989). There is also evidence for hippocampal neural activity specific to eating and drinking or the internal states related to these behaviors (Breese et al., 1989; Hampson, Heyser, & Deadwyler, 1993).

Dorsal Striatum

The MPMS theory attributes S-R learning to the matrix compartment of the dorsal striatum (Fig. 4), and therefore predicts that the activity of single units in this compartment should reflect the acquisition of S-R associations. Although the matrix predominates in the lateral striatum and the striosomes are mainly located in the anterior-medial part, both compartments are present throughout the entire structure. Therefore, unless specific procedures are used to differentiate the compartments histologically it is not possible to know which compartment any given neuronal recording is from. These procedures have been used in a few studies (Heidenreich, Trytek, Schroeder, Sengelaub, & Rebec, 1994; Onn & Grace, 1994), and it has been shown that neurons with activity that is coincident with head and body movements tend to be located in the matrix, sometimes on the border of a striosome (Trytek, White, Schroeder, Heidenreich, & Rebec, 1996; Onn, Berger, Grace, & Onn, 1994). However, no studies in which units have been recorded during learning have made this determination directly, making the information they provide difficult to interpret with respect to the theory. Nevertheless, there are some data that could be compatible with processing representations of stimuli, responses, and their association.

When recorded during performance of a lever release avoidance task (White & Rebec, 1993), the activity of neurons in the medial dorsal striatum tended to correspond to the sensory elements of the task, while neurons in the lateral parts of the structure responded more in conjunction with the response. A certain number of neurons in both locations responded to both aspects of the task. A similar pattern of responding of striatal neurons was reported in rats that had been trained to perform a conditioned head-turning movement

(Gardiner & Kitai, 1992); in this case the activity of a large proportion of the neurons studied correlated with both the stimulus and the response elements of the task.

Wiener (1993) recorded from units in the anteromedial striatum while rats performed a learned sequence of movements to find water in an arena. About 25% responded (by significantly increasing or decreasing their firing rates) to specific quadrants of the arena, but only when the rat was performing a specific series of movements. Other neurons exhibited head-direction responses. When the arena was darkened and turned these neurons maintained their orientation to cues in the arena rather than to cues from the surrounding room. The responses of an additional 30% of the neurons correlated with the rat's movement. These findings show that at least some striatal neurons respond preferentially to repeatedly reinforced local cues. In contrast, when hippocampal pyramidal cell activity was recorded during performance of the same task (Sanghera, Rolls, & Roper-Hall, 1979), these neurons maintained their orientation to the room cues rather than to the arena cues.

Amygdala

The S-Rf learning model attributed to the amygdala system (Fig. 5) predicts that prior to training, unit activity related to the presence of neutral sensory cues and reinforcers should be observed. During and after conditioning, unit responses to conditioned cues should change. There is ample evidence that neurons in the amygdala respond to cues in most sensory modalities including olfactory (O'Keefe & Bouma, 1969; Cain & Bindra, 1972), visual (Brown & Buchwald, 1973; Ben-Ari, Le Gal le Salle, & Champagnat, 1974; Sanghera et al., 1979), auditory (Jacobs & McGinty, 1972; Ben-Ari et al., 1974; Bordi & LeDoux, 1992; Pascoe & Kapp, 1985), and somatosensory (Ben-Ari et al., 1974). Intrinsic neurons of the amygdala are also responsive to the presence of rewarding or aversive reinforcers (O'Keefe & Bouma, 1969; Fuster & Uyeda, 1971; Jacobs & McGinty, 1972; Brothers, Ring, & Kling, 1990).

Many evoked responses to neutral cues in the amygdala habituate quickly (Ben-Ari & Le Gal la Salle, 1974; Bordi & Le Doux, 1992) unless they are temporally contiguous with the occurrence of a reinforcer. In classical conditioning situations amygdala neurons responded more to stimuli previously paired with shock (Applegate, Frysinger, Kapp, & Gallagher, 1982; Pascoe & Kapp, 1985) or food (Sanghera et al., 1979) than to stimuli not associated with those reinforcers. The development of selective neural activity in the presence of conditioned stimuli has also been reported for aversive conditioning (Applegate et al., 1982; Pascoe & Kapp, 1985). These observations are consistent with the processing of associations between neutral cues and reinforcers, leading to the elicitation of conditioned responses by these cues.

Posttraining Manipulations

The major experimental paradigm for demonstrating the memory modulation response elicited by reinforcers involves presenting the reinforcers during the period immediately after the training trials on a memory task. This procedure is based on the theory of memory consolidation (McGaugh & Hertz, 1972; Gold & McGaugh, 1975; McGaugh et al., 1996; White & Milner, 1992), the idea that, during the period immediately after they are first formed, neural representations of information undergo a structural change that makes

them more permanent. Thus, newly acquired memories are subject to disruption by a variety of events unrelated to the stored information that represents them. With the passage of time these memories become more resistant to the effects of the same events. To differentiate effects of a treatment on memory functions from generally disruptive effects on perception, motor behavior, or motivation the treatment must be administered at two different times between the end of the training session and the start of the test session. Behavior learned during the training session must be disrupted in subjects given the earlier treatment (before consolidation was complete), but unaffected in subjects given the later treatment (after consolidation was complete).

Electroconvulsive shock was one of the first disruptive modulatory events studied according to these criteria (Zubin & Barrera, 1941; Duncan, 1949). It was then reasoned that similar disruptions by electrical stimulation confined to specific brain areas might provide information about the involvement of those areas in memory functions (Kesner & Wilburn, 1974). Many different brain areas have been tested using various stimulation paradigms (Kesner & Wilburn, 1974), and there is clear evidence that effects meeting the above criteria are obtained with stimulation of the hippocampus (Berman & Kesner, 1976; Kapp, Gallagher, Holmquist, & Theall, 1978), the amygdala (Berman & Kesner, 1976; Gold, Hankins, & Rose, 1977; Kesner & Andrus, 1982), and the dorsal striatum (Wyers, Peeke, Williston, & Herz, 1968; Gold & King, 1972; Wyers & Deadwyler, 1972). Demonstration of such time-dependent effects on learned behaviors by manipulation of the central structures is the major form of evidence that the systems have mnemonic as well as information-processing functions.

Drug Injections

Similar logic concerning posttraining treatments was applied to the modulatory improvements in memory produced by systemic, posttraining injections of drugs such as amphetamine (Doty & Doty, 1966; Krivanek & McGaugh, 1969). Two experiments have used intracerebral injections of amphetamine to dissociate the mnemonic functions of the hippocampus and dorsal striatum. In one (Packard & White, 1991), immediate posttraining injections of amphetamine into the hippocampus but not into the dorsal striatum improved performance on a delayed version of the win-shift task. In another group of rats immediate posttraining injections of amphetamine into dorsal striatum but not into hippocampus improved performance on the win-stay task. When the two effective injections were delayed for 2 h after the training trial they had no effect. This double dissociation of system-specific, time-dependent, posttraining memory modulation effects is consistent with the effects of lesions to the same systems on the same tasks.

In a similar demonstration using a water maze (Packard et al., 1994), immediate posttraining injections of amphetamine into hippocampus but not into dorsal striatum improved performance on a task that required rats to remember the location of a hidden platform. In contrast, immediate posttraining injections of amphetamine into dorsal striatum but not into hippocampus improved performance on a task that required rats to swim directly to a visible platform that was in a new location on each trial. These findings also constitute a double dissociation of the modulatory effects on specific behaviors of time-dependent, posttraining injections of amphetamine into hippocampus and dorsal striatum. The results of both experiments are consistent with the MPMS theory.

Performance of the CCP task is improved by systemic posttraining injections of amphetamine (White & Carr, 1985), and posttraining intraamygdala injections of the dopamine D3 agonist, 7-OH-DPAT improved stimulus-reward learning (Hitchcott, Bonardi, & Phillips, 1997) but had no effect on an instrumental learning task (Hitchcott & Phillips, 1998).

The modulatory action of the amygdala itself has also been demonstrated using this technique (Packard et al., 1994; Packard & Teater, 1998a). Posttraining intra-amygdala injections of amphetamine improved performance on both hippocampus and caudate-mediated water maze tasks just described. Moreover, inactivation of the amygdala with lidocaine during testing had no effect on the improved performance produced by previously administered posttraining intraamygdala amphetamine. These findings show that activation of an amygdala-based mechanism with amphetamine during the posttraining period modulates memories thought to be mediated independently by the hippocampus and dorsal striatum systems.

In summary, although it has not been exploited to the same extent as the lesion technique, the posttraining intracranial injection technique provides an additional line of evidence for the independence of the hippocampus, dorsal striatum, and amygdala systems. Moreover, the time-dependent effects of these posttraining modulatory treatments are consistent with the hypothesis that the functions of these systems include the independent storage of new information.

VI. ANATOMY OF SYSTEMS

The preceding discussion of MPMS theory focuses mainly on three brain structures, each of which is thought to be the central structure in an information processing and storage system. The concept of parallel processing (Fig. 1) includes the ideas that similar information reaches and "flows through" each of the systems, that the outputs of the systems converge at some point(s) to influence behavior, and that the systems can influence each other directly. This section attempts to provide a preliminary description of the anatomy of each system in these functional terms.

Hippocampus System

The hippocampus, or *hippocampal formation*, is a set of cortical fields grouped together because of the dominant associational projections that interconnect them (Amaral, 1987). The structure consists of the entorhinal cortex, dentate gyrus, CA-1–3 subfields, and the subicular complex (Cajal, 1968; Swanson, Wyss, & Cowan, 1978; Swanson, 1983).

As shown in Fig. 6, the entorhinal cortex receives extensive input from all cortical sensory association areas (Turner & Zimmer, 1984; Veening, 1978a; Wyss, 1981; Kosel, Van Hoesen, & West, 1981; Kosel, Van Hoesen, & Rosene, 1983), suggesting that information about all sensory events in the individual's environment is received in this part of the brain. This information flows from entorhinal cortex to the dentate gyrus via the perforant path (Andersen, Holmqvist, & Voorhoeve, 1966; Hjorth-Simonsen & Jeune, 1972; Hjorth-Simonsen, 1972; Steward & Scoville, 1976). From the dentate gyrus the information flows to the CA-3 region (Blackstad, Brink, Hem, & Jeune, 1970; Gaarskjaer, 1978a,b), then to the CA-1 subfield (Swanson et al., 1978), to the subiculum (Swanson et al., 1978), and then back to the entorhinal cortex (Beckstead, 1978). This is the classic

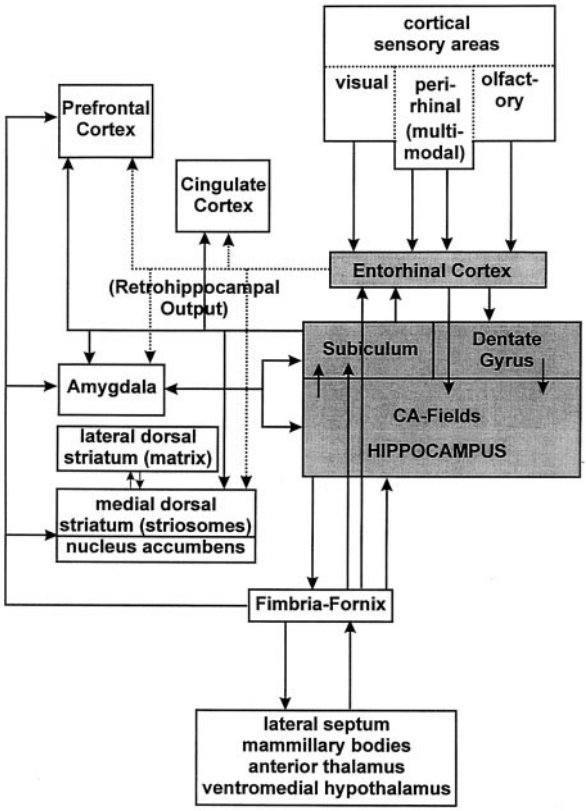

FIG. 6. The hippocampus system. Major anatomical connections of the hippocampal formation, the central structure of the hippocampus-system. Information flows into the system from all sensory cortical areas. The major outputs from the system include prefrontal and cingulate cortex, amygdala and medial dorsal striatum, and subcortical areas including the septum, mammillary bodies, and anterior thalamus. These interconnections could provide the substrate of a neural system that processes and stores information about the relationships among environmental stimuli and events (S-S learning, Fig. 3), the output of which influences ongoing behavior. Note projections from subiculum directly to amygdala and indirectly via medial dorsal striatum to lateral dorsal striatum, providing a basis for direct influences of this system on the other two systems.

trisynaptic circuit of the hippocampus. The existence of plasticity at each of the synapses in this circuit (Malenka & Nicoll, 1993; McNaughton, 1993) has led to the suggestion that they may be a substrate of memory storage in the hippocampal system.

The hippocampal formation connects to other brain structures via two main routes. The fimbria-fornix is a bidirectional connection between the hippocampus and the subcortical regions including the lateral septum (Siegel, Edinger, & Ogami, 1974), nucleus accumbens (Kelley & Domesick, 1982), mammillary bodies (Meibach & Siegel, 1975), anterior thalamus, and ventral medial hypothalamus (Irle & Markowitsch, 1982). There is also evidence that fibers from the septal region, traveling via the fimbria-fornix, communicate with entorhinal cortex without involving the hippocampus (Gaykema, Luiten, Nyakas, & Traber, 1990; Swanson, 1977). The other major hippocampal output projection, sometimes called the "retrohippocampal output," connects the subiculum to the entorhinal cortex and to the cingulate and prefrontal cortices (Swanson & Kohler, 1986).

Taken together, the sensory input, the trisynaptic circuit, and the major output systems

constitute a route by which information can enter, flow through, and exit from the hippocampus (Andersen, Bliss, & Skrede, 1971). The hippocampus also has two major associational fiber systems that move information along its longitudinal axis (Amaral & Witter, 1989), creating a flow of information orthogonal to the one represented by the trisynaptic circuit. This suggests that the information-processing function of the hippocampus is highly distributed within the structure.

The hippocampal formation also receives secondary, modulatory input from both cholinergic (Fonnum, 1970; Lewis, Shute, & Silver, 1967; Wainer, Levey, Rye, Mesulam, & Mufson, 1985) and monoaminergic (Lindvall & Bjorklund, 1974; Swanson, 1982) cell groups in the basal forebrain. The ventral portion of the hippocampus also receives input directly from the amygdala (Pitkanen, Pikkarainen, Nurminen, & Ylinen, 2000) providing a possible route for the informational component of both unconditioned and conditioned affective responses to reach this structure, as suggested in the previous discussion.

The flow of information through the hippocampus system and its output to high level structures such as prefrontal cortex and cingulate gyrus are consistent with the idea that the hippocampal system processes mainly information about the individual's environment, and that this information can modulate ongoing behavior (Rezai et al., 1993; Stuss, Shallice, Alexander, & Picton, 1995). The flow of information to subcortical structures provides this same information to lower level systems where it can also influence motivational and reinforcement mechanisms, and afferent connections along these same routes supply information about these functions to the hippocampus system.

Dorsal Striatum System

The neostriatum is divided into dorsal (caudate-putamen in the rat) and ventral (nucleus accumbens, olfactory tubercle) parts, based on anatomical and neurochemical differences (Heimer, Alheid, & Zaborsky, 1985). As illustrated in Fig. 7 the rat dorsal striatum is heavily innervated by both sensory and motor areas of the neocortex. The corticostriatal projections to the lateral dorsal striatum, which contains most of the matrix tissue, are topographically organized (McGeorge & Faull, 1987; McGeorge, Faull, & Faull, 1989; Webster, 1961; 1965) and correspond to the functions of specific subregions of the lateral part of the dorsal striatum (Carelli & West, 1991). These topographically organized projections overlap with input from midline thalamic nuclei (Grofova, 1979; Kalil, 1978; Gerfen, Baimbridge, & Thibault, 1987; Royce, 1978) and topographically organized projections from the pars reticulata of the substantia nigra (Gerfen, Herkenham, & Thibault, 1987) that may provide for the convergence of sensory information with information about movement sequences (Graybiel, 1995; Flaherty & Graybiel, 1994; Graybiel, Aosaki, Flaherty, & Kimura, 1994; Brown, 1992).

The major outputs of the matrix compartment of the lateral dorsal striatum are to globus pallidus and substantia nigra (Gerfen, 1985), areas implicated in higher order motor functions. The latter structure also projects to the anterior thalamus, which in turn innervates the prefrontal cortex. Thus information about the sensory environment and (possibly) two forms of efference copy from the motor system—from motor cortex and substantia nigra—are available to form S-R associations. Dopaminergic input from substantia nigra may provide the reinforcement required to modulate or strengthen these associations (White, 1989; White & Milner, 1992).

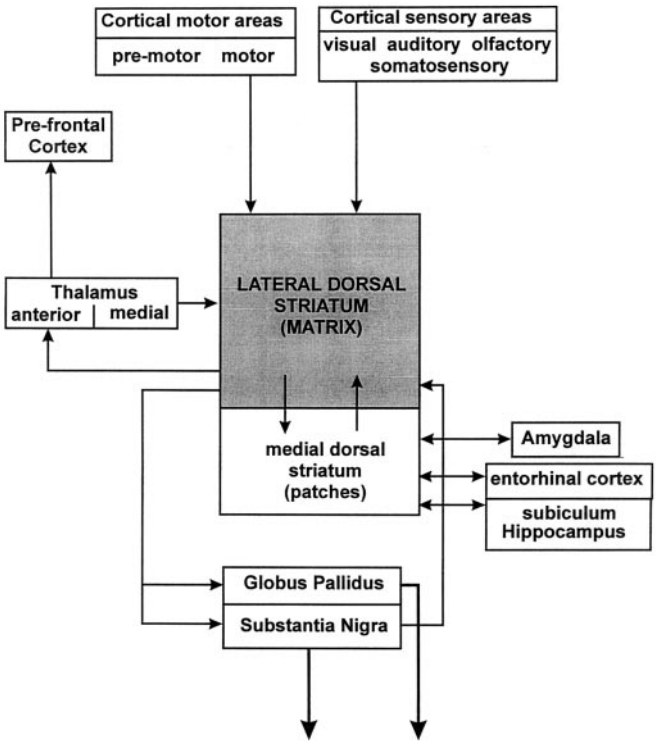

FIG. 7. The dorsal striatum system. Major anatomical connections of the lateral dorsal striatum (matrix compartment), the central structure of the dorsal striatum system. Information about both sensory events and motor movements (efference copy) reaches the lateral dorsal striatum from the cortex, thalamus, and substantia nigra. In addition to outputs to the thalamus and prefrontal cortex, the major flow of information from this system is to high level motor structures, including globus pallidus and substantia nigra, which in turn influence midbrain motor organization mechanisms. The system could provide the substrate required to process S-R learning (Fig. 4). Note projections via medial dorsal striatum to both amygdala and subiculum, providing for the possibility of direct influences by this system on the other two systems.

Amygdala System

The amygdala has been divided into subgroups of nuclei (De Olmos, Alheid, & Beltramino, 1985), three of which—the lateral, basolateral and central nuclei—have been implicated in learning and memory functions. As shown in Fig. 8, the lateral and basolateral nuclei receive extensive projections from cortical areas in the temporal lobes: rhinal, entorhinal, prepyriform and periamygdala cortex (Ottersen, 1982; Deacon, Eichenbaum, Rosenberg, & Eckmann, 1983). In turn, these cortical areas receive input from most sensory cortical areas (Turner & Zimmer, 1984; Veening, 1978a; Wyss, 1981). Thus, the lateral and basolateral nuclei receive highly processed polymodal sensory information from the cortex. The same nuclei also receive primary sensory information from the thalamus (Veening, 1978b; Kretteck & Price, 1977; Herkenham, 1978; Ottersen & Ben-Ari, 1979; Turner & Herkenham, 1991). There is also a major cholinergic input to basolateral amygdala from basal forebrain (Woolf & Butcher, 1982; Nagai et al., 1982; Carlsen, Zaborszky, & Heimer, 1985).

The lateral and basolateral nuclei also receive afferents from brain areas known to

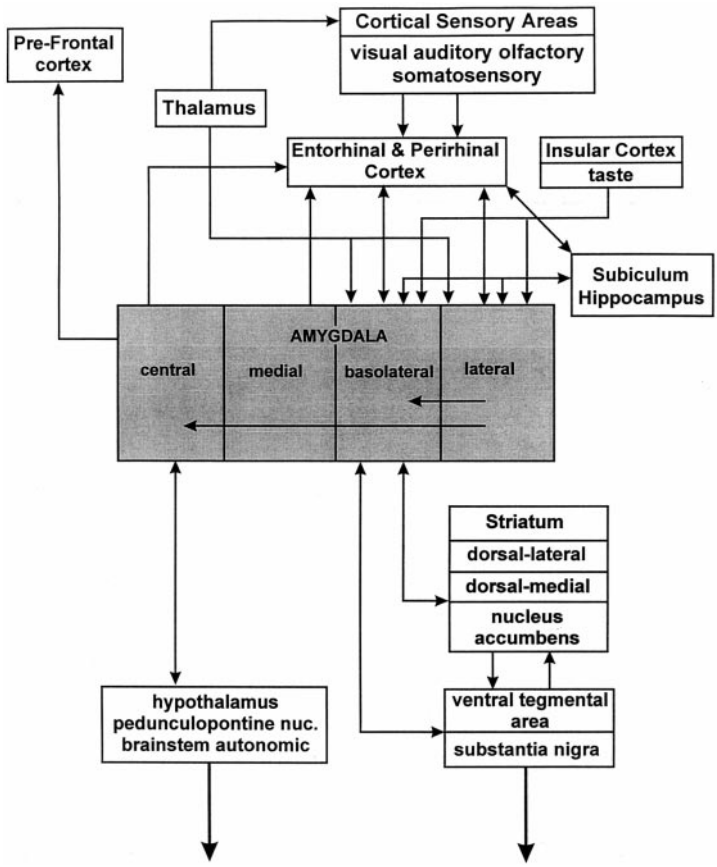

FIG. 8. The amygdala system. Major anatomical connections of the amygdala subnuclei implicated in learning and memory processes, the central structure in the amygdala system. Information about sensory events reaches the amygdala from the cortex (via the entorhinal and perirhinal cortex) and from the thalamus, providing potential conditioned stimuli. Afferents from subcortical structures (and insular cortex) provide information about responses elicited by reinforcers, the unconditioned stimuli. Assuming that these two types of information become associated in the amygdala (S-Rf learning, Fig. 5), the output to subcortical brainstem structures produces the conditioned responses. Note indirect projections from amygdala to dorsolateral striatum via dorsomedial striatum, and to subiculum via entorhinal and perirhinal cortex, providing a basis for direct influences of this system on the other two systems.

process visceral and affective information, such as substantia nigra (Beckstead, Domesick, & Nauta, 1979), diagonal band and ventral tegmental area (Simon, Le Moal, & Calas, 1979; Phillipson, 1979), nucleus accumbens (Fallon & Moore, 1978), hypothalamus, basal diencephalon (Ottersen, 1980), pedunculopontine nucleus (Saper & Loewy, 1982), and other brainstem (Norgren, 1976) and autonomic (Ottersen, 1981) areas. The insular cortex receives converging projections from midbrain autonomic nuclei and from limbic cortex, and a major efferent projection of insular cortex is to the basolateral amygdala (Saper, 1982). Thus, the amygdala receives both modality-specific sensory information about the environment that is thought to constitute CSs (Turner & Zimmer, 1984) and affective, gustatory, and visceral input from brain structures that mediate both rewarding and aversive responses to reinforcers (UCRs). The convergence of these two types of information in the lateral amygdala would allow the formation of CSs.

Nuclei of the amygdala have afferent projections to striatum (Veening, Cornelissen, & Lieven, 1980; Kelley, Domesick, & Nauta, 1982), cerebral cortex and thalamus (Kretteck & Price, 1977), hypothalamus (Post & Mai, 1980), VTA (Simon et al., 1979; Phillipson, 1979), nucleus of the solitary tract (van der Kooy, Koda, McGinty, Gerfen, & Bloom, 1984), and portions of the brainstem including the parabrachial nuclei, caudal medulla, nucleus of the solitary tract (van der Kooy et al., 1984), and periaqueductal gray (Veening, 1978b; Jackson & Crossman, 1981; Koh & Ricardo, 1978; Post & Mai, 1980). The central nucleus also has reciprocal connections with various portions of the hypothalamus (Ottersen, 1980; 1982; Veening, 1978b; Berk & Finkelstein, 1981). Since most of these connections are reciprocal, they provide an anatomical basis for the amygdala to produce CRs that resemble the UCRs produced by UCSs. The lateral and basolateral nuclei also project directly to the ventral hippocampus and subiculum, and to entorhinal cortex which, in turn, also projects to the hippocampus (Pikkarainen, Ronkko, Savander, Insausti, & Pitkanen, 1999; Pitkanen et al., 2000). As previously mentioned, these projections provide a basis for the transmission of affective information to the hippocampus, and for the modulation of hippocampal memory processes by output from amygdala (Packard et al., 1994; Packard & Teather, 1998a, 1998b).

This brief review shows that two major types of information converge in the central and basolateral amygdala. The first, from cortical and thalamic areas, is sensory information from all modalities that represent an animal's external environment, forming the basis of what will become the conditioned stimuli. The second is from areas of the brain that respond to rewarding (food, water, sexual partners, social contact) or aversive (electric shock, cold water, loud auditory stimuli, predators) events (reinforcers), each of which elicits the three types of UCRs described in Section 2 (Fig. 5). Information from areas mediating these responses (brainstem, hypothalamus, nucleus accumbens, substantia nigra, VTA) reaches the amygdala, constituting the UCSs. The internal circuitry of the amygdala is thought to provide the basis for the association of the two forms of stimulus information. The output pathways from the amygdala to subcortical structures mediate the CRs.

Interactions among the Systems

Two forms of interaction among the systems have been discussed: direct facilitatory or retarding effects by information stored in one system on the function of another system, and cooperative or competitive interactions among the outputs of the systems. Figures 6–8 illustrate possible anatomical bases for direct effects of the systems on each other. The figures also suggest points of convergence of the outputs of the systems. Consistent with the response-producing aspects of their processing styles, both the dorsal striatum and amygdala systems project to higher order motor structures (globus pallidus and substantia nigra) providing a basis for cooperative or competitive interactions among the outputs of these systems on structures that organize motor behavior.

Perhaps most obviously, all three systems have direct projections to the prefrontal cortex providing what could be the major site of interaction among the outputs of the systems. The prefrontal cortex does not directly influence individual responses, but is known to affect ongoing behavior. The wide variety of approaches to understanding its function (Jonides et al., 1993; Williams & Goldman-Rakic, 1995; McCarthy et al., 1996; Miller, Erickson, & Desimone, 1996; Frith & Dolan, 1996; Robbins, 1996; Damasio, 1995; Kolb,

Buhrmann, McDonald, & Sutherland, 1994; Williams & Goldman-Rakic, 1995; McCarthy et al., 1996) could be taken as consistent with the convergence in this area of several different kinds of information, each leading to different kinds of response tendencies. Recently, a scheme in which the prefrontal cortex utilizes information received from subcortical areas to activate selectively the information processing and memory functions of other cortical areas has been proposed (Wise et al., 1996). Taken together with its receipt of the outputs of all three systems, the presence of neuroplasticity in the prefrontal cortex (Mulder, Arts, & Lopes da Silva, 1997; Williams & Goldman-Rakic, 1995) also suggests the possibility that this structure participates in the memory storage functions of all three systems.

VII. CONCLUSION

This paper has presented a theory suggesting that the ongoing information processing and memory functions of the brain are organized into a series of independent conceptual modules that function in parallel, and that each of these modules is instantiated in a specifiable anatomical system. The evidence presented for the theory consists mainly of the behavioral effects of manipulating the proposed neural substrates of the systems. Although the experimental data considered are mainly from rats, there are strong parallels for many of the findings and conclusions in the human literature (Milner et al., 1968; Tulving, 1972; Cohen & Squire, 1980; Milner, 1985; Butters et al., 1986; Brandt, Folstein, & Folstein, 1988; Helkala, Laulumaa, Soininen, & Riekkinen, 1988; Morris et al., 1988; Sahakian et al., 1988; Daum, Channon, & Canaran, 1989; Heindel, Salmon, Shults, Walicke, & Butters, 1989; Damasio & Tranel, 1990; Solomon, Levine, Bein, & Pendlebury, 1991; Squire & Zola-Morgan, 1991; Knowlton, Ramus, & Squire, 1992; Butters, Salmon, & Heindel, 1994; Moscovitch, 1994; Bechara et al., 1995; Knowlton, Mangels, & Squire, 1996; Winocur, Moscovitch, & Stuss, 1996).

The main postulates of the theory are:

1. There are at least three definable neural systems in the brain for processing and storing information that influences behavior. Each of the systems is capable of functioning independently of the others.

2. Each system consists of a central structure together with other structures afferent and efferent to it. The three central structures are the hippocampus, the matrix compartment of the dorsal striatum, and the amygdala.

3. Information, in the form of neural representations of stimuli and events in the external (and sometimes internal) environment, "flows through" each system where it is processed: integrated with ongoing activity and information stored in the system to produce output that promotes certain specific responses or behavioral tendencies.

4. The structure of each system is compatible with a specific form of neural activity produced when the various elements of a situation exist in a specific relationship to each other. These sets of relationships constitute the processing styles of the systems. The processing styles of the three systems considered correspond to stimulus-stimulus (S-S), stimulus-response (S-R), and stimulus-reinforcer (S-Rf) learning.

5. Activation of a system by a situation compatible with its processing style results in coherent activity in that system leading to strong, coordinated output. Coherent activity in a system has the potential to alter the system, leaving some record of itself that will

influence the way similar information is processed in the future, altering the output of the system. This is the function called "memory." Degree of coherence and the "modulatory response" elicited by reinforcers are two factors determining the storage of information in a system.

6. Although they function independently, the systems interact in two ways. First, one system can directly influence another to facilitate or retard its function. Second, the outputs of the systems converge producing either cooperative facilitation of the same response or behavioral tendency, or competitive facilitation of different responses or behavioral tendencies in the same situation.

Notwithstanding its length, this paper has presented only an outline of the main points of a theory of multiple parallel memory systems. Many important issues have been ignored and much data, both compatible and incompatible with the theory, have been omitted. In particular, each of the proposed neural systems is considerably more complex than discussed here, and it is likely that each of them can be fractionated into several functionally distinct subsystems.

Finally, an important implication of the MPMS theory is that progress in understanding the precise relationship between learned behavior and the function of any given neural substrate depends on recognition of the possibility that several forms of learning and memory may be going on simultaneously in parts of the brain other than the one under study. For any given behavior, therefore, it is essential to know the precise nature and degree of involvement of each neural system before the contribution of any one of them to memory for the behavior can be usefully studied using electrophysiological, neurochemical, or molecular techniques.

REFERENCES

Aggleton, J. P. (1993). The contribution of the amygdala to normal and abnormal emotional states. *Trends in Neurosciences,* **16,** 328–333.

Aggleton, J. P., Hunt, P. R., & Rawlins, J. N. P. (1986). The effects of hippocampal lesions upon spatial and non-spatial tests of working memory. *Behavioural Brain Research,* **19,** 133–146.

Alexander, G. E., & Crutcher, M. D. (1990). Functional architecture of basal ganglia circuits: Neural substrates of parallel processing. *Trends in Neurosciences,* **13,** 265–270.

Alexander, G. E., Crutcher, M. D., & DeLong, M. R. (1990). Basal ganglia-thalamocortical circuits: Parallel substrates for motor, oculomotor, "prefrontal" and "limbic" functions. *Progress in Brain Research,* **85,** 119–146.

Alkon, D. L., Amaral, D. G., Bear, M. F., Black, J., Carew, T. J., Cohen, N. J., Disterhoft, J. F., Eichenbaum, H., Golski, S., Gorman, L. K., Lynch, G., McNaughton, B. L., Mishkin, M., Moyer, J. R., Jr., Olds, J. L., Olton, D. S., Otto, T., Squire, L. R., Staubli, U., Thompson, L. T., & Wible, C. (1991). Learning and memory. *Brain Research Reviews,* **16,** 193–220.

Allen, J. D., & Mitcham, J. C. (1972). Effects of caudate lesions on the acquisition and retention of Sidman avoidance in the rat. *Psychonomic Science,* **27,** 157–160.

Amaral, D. G. (1987). Memory: Anatomical organization of candidate brain regions. *In* V. D. Mountcastle, F. Plum, & S. R. Geiger (Eds.), *Handbook of physiology, section 1: The nervous system, part 1* (2nd ed., pp. 211–294). Bethesda, MD: American Physiological Society.

Amaral, D. G., & Witter, M. P. (1989). The three-dimensional organization of the hippocampal formation: A review of anatomical data. *Neuroscience,* **31,** 571–591.

Amaral, D. G., & Witter, M. P. (1995). Hippocampal formation. *In* G. Paxinos (Ed.), *The rat nervous system* (2nd ed., pp. 443–493). San Diego: Academic Press.

Amsel, A. (1980). *Behaviorism, neobehaviorism and cognitivism in learning theory: Historical and contemporary perspectives.* Hillsdale, NJ: Earlbaum.

Amsel, A. (1993). Hippocampal function in the rat: Cognitive mapping or vicarious trial and error. *Hippocampus,* **3,** 251–256.

Andersen, P., Bliss, T. V. P., & Skrede, K. K. (1971). Lamellar organization of hippocampal excitatory pathways. *Experimental Brain Research,* **13,** 222–238.

Andersen, P., Holmqvist, B., & Voorhoeve, P. E. (1966). Entorhinal activation of dentate granule cells. *Acta Physiologica Scandinavica,* **66,** 448–460.

Applegate, C. D., Frysinger, R. C., Kapp, B. S., & Gallagher, M. (1982). Multiple unit activity recorded from amygdala central nucleus during Pavlovian heart rate conditioning in rabbit. *Brain Research,* **238,** 457–462.

Bagshaw, M., & Benzies, S. (1968). Multiple measures of the orienting raction and their dissociation after amygdalectomy in monkeys. *Experimental Neurology,* **20,** 175–187.

Barnes, C. A. (1988). Spatial learning and memory processes: The search for their neurobiological mechanisms in the rat. *Trends in Neurosciences,* **11,** 163–169.

Baxter, M. G., & Gallagher, M. (1996). Intact spatial learning in both young and aged rats following selective removal of hippocampal cholinergic input. *Behavioral Neuroscience,* **110,** 460–467.

Beatty, W. W., & Shavalia, D. A. (1980). Spatial memory in rats: Time course of working memory and effect of anesthetics. *Behavioral & Neural Biology,* **28,** 454–462.

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.

Beckstead, R. M. (1978). Afferent connections of the entorhinal area in the rat as demonstrated by retrograde cell-labeling with horseradish peroxidase. *Brain Research,* **152,** 249–264.

Beckstead, R. M., Domesick, V. B., & Nauta, W. J. H. (1979). Efferent connections of the substantia nigra and ventral tegmental area in the rat. *Brain Research,* **175,** 191–217.

Ben-Ari, Y., & Le Gal la Salle, G. (1974). Lateral amygdala unit activity: II. Habituating and non-habituating neurons. *Electroencephalography & Clinical Neurophysiology,* **37,** 463–472.

Ben-Ari, Y., Le Gal le Salle, G., & Champagnat, J. C. (1974). Lateral amygdala unit acitvity: I. Relationship between spontaneous and evoked activity. *Electroencephalography & Clinical Neurophysiology,* **37,** 449–461.

Berk, M. L., & Finkelstein, J. A. (1981). Afferent projections to the preoptic area and hypothalamic regions in the rat brain. *Neuroscience,* **6,** 1601–1624.

Berman, R. F., & Kesner, R. P. (1976). Posttrial hippocampal, amygdaloid, and lateral hypothalamic electrical stimulation: Effects on short- and long-term memory of an appetitive experience. *Journal of Comparative & Physiological Psychology,* **90,** 260–267.

Blackstad, T. W., Brink, K., Hem, J., & Jeune, B. (1970). Distribution of hippocampal mossy fibers in the rat. An experimental study with silver impregnation methods. *Journal of Comparative Neurology,* **138,** 433–449.

Blaker, S. N., Armstrong, D. M., & Gage, F. H. (1988). Cholinergic neurons within the rat hippocampus: Response to fimbria-fornix transection. *Journal of Comparative Neurology,* **272,** 127–138.

Blanchard, R. J., Blanchard, D. C., & Fial, R. A. (1970). Hippocampal lesions in rats and their effect on activity, avoidance, and aggression. *Journal of Comparative & Physiological Psychology,* **71,** 92–101.

Blodgett, H. C., & McCutchan, K. (1947). Place versus response learning in the simple T-maze. *Journal of Experimental Psychology,* **37,** 412–422.

Blodgett, H. C., & McCutchan, K. (1948). Relative strength of place and response learning in the T-maze. *Journal of Comparative & Physiological Psychology,* **41,** 17–24.

Bordi, F., & LeDoux, J. E. (1992). Sensory tuning beyond the sensory system: An initial analysis of auditory response properties of neurons in the lateral amygdaloid nucleus and overlying areas of the striatum. *Journal of Neuroscience,* **12,** 2493–2503.

Brandt, J., Folstein, S. E., & Folstein, M. F. (1988). Differential cognitive impairment in Alzheimer's disease and Huntington's disease. *Annals of Neurology,* **23,** 555–561.

Brasted, P. J., Humby, T., Dunnett, S. B., & Robbins, T. W. (1997). Unilateral lesions of the dorsal striatum in rats disrupt responding in egocentric space. *Journal of Neuroscience,* **17,** 8919–8926.

Breese, C. R., Hampson, R. E., & Deadwyler, S. A. (1989). Hippocampal place cells: Stereotypy and plasticity. *Journal of Neuroscience,* **9,** 1097–1111.

Brothers, L., Ring, B., & Kling, A. (1990). Response of neurons in the macaque amygdala to complex social stimuli. *Behavioural Brain Research,* **41,** 199–213.

Brown, K. A., & Buchwald, J. S. (1973). Acoustic responses and plasticity of limbic units in cats. *Experimental Neurology,* **40,** 608–631.

Brown, L. L. (1992). Somatotopic organization in rat striatum: Evidence for a combinational map. *Proceedings of the National Academy of Sciences, U.S.A.,* **89,** 7403–7407.

Burns, L. H., Robbins, T. W., & Everitt, B. J. (1993). Differential effects of excitotoxic lesions of the basolateral amygdala, ventral subiculum and medial prefrontal cortex on responding with conditioned reinforcement and locomotor activity potentiated by intra-accumbens infusions of D-amphetamine. *Behavioural Brain Research,* **55,** 167–183.

Butters, N., Martone, M., White, B., Granholm, E., & Wolfe, J. (1986). Clinical validators: Comparisons of demented and amnesic patients. *In* L. Poon (Ed.), *Handbook of clinical assessment of memory* (pp. 337–352). Washington, DC: American Psychological Association.

Butters, N., Salmon, D., & Heindel, W. C. (1994). Specificity of the memory deficits associated with basal ganglia dysfunction. *Revue Neurologique,* **150,** 580–587.

Cabanac, M., Minaire, Y., & Adair, E. R. (1968). Influence of internal factors on the pleasantness of a gustative sweet sensation. *Communications in Behavioral Biology,* **1,** 77–82.

Cador, M., Robbins, T. W., & Everitt, B. J. (1989). Involvement of the amygdala in stimulus-reward associations: Interaction with the ventral striatum. *Neuroscience,* **30,** 77–86.

Cain, D. P., & Bindra, D. (1972). Responses of amygdala single units to odors in the rat. *Experimental Neurology,* **35,** 98–110.

Cajal, S. R. Y. (1968). *The structure of Ammon's horn.* Springfield, IL: Thomas. Calabresi, P., Maj, R., Pisani, A., Mercuri, N. B., & Bernardi, G. (1992). Long-term synaptic depression in the striatum: Physiological and pharmacological characterization. *Journal of Neuroscience,* **12,** 4224–4233.

Calabresi, P., Pisani, A., Mercuri, N. B., & Bernardi, G. (1992). Long-term potentiation in the striatum is unmasked by removing the voltage-dependent magnesium block of NMDA receptor channels. *European Journal of Neuroscience,* **4,** 929–935.

Calabresi, P., Pisani, A., Mercuri, N. B., & Bernardi, G. (1996). The corticostriatal projection: From synaptic plasticity to dysfunctions of the basal ganglia. *Trends in Neurosciences,* **19,** 19–24.

Candland, D. K., Fell, J. P., Keen, E., Leshner, A. I., Tarpy, R. M., & Plutchik, R. (1977). *Emotion.* Monterey, CA: Brooks-Cole.

Carelli, R. M., & West, M. O. (1991). Representation of the body by single neurons in the dorsolateral striatum of the awake, unrestrained rat. *Journal of Comparative Neurology,* **309,** 231–249.

Carlsen, J., Zaborszky, L., & Heimer, L. (1985). Cholinergic projections from the basal forebrain to the basolateral amygdaloid complex: A combined retrograde fluorescent and immunohistochemical study. *Journal of Comparative Neurology,* **234,** 155–167.

Cho, Y. H., & Kesner, R. P. (1995). Relational object association learning in rats with hippocampal lesions. *Behavioural Brain Research,* **67,** 91–98.

Cho, Y. H., Kesner, R. P., & Brodale, S. (1995). Retrograde and anterograde amnesia for spatial discrimination in rats: Role of hippocampus, entorhinal cortex, and parietal cortex. *Psychobiology,* **23,** 185–194.

Chozick, B. S. (1983). The behavioral effects of lesions of the corpus striatum: A review. *International Journal of Neuroscience,* **19,** 143–160.

Chronister, R. B., & DeFrance, J. F. (1979). Organization of projection neurons of the hippocampus. *Experimental Neurology,* **66,** 509–523.

Cohen, N. J. (1984). Preserved learning capacity in amnesia: Evidence for multiple memory systems. *In* N. Butters & L. R. Squire (Eds.), *Neuropsychology of memory* (pp. 83–103). New York: Guilford.

Cohen, N. J., & Squire, L. R. (1980). Preserved learning and retention of pattern-analyzing skill in amnesia: Dissociation of knowing how and knowing what. *Science,* **210,** 207–209.

Collingridge, G. L. (1992). The mechanism of induction of NMDA receptor-dependent long-term potentiation in the hippocampus. *Experimental Physiology,* **77,** 771–797.

Colombo, P. J., Davis, H. P., & Volpe, B. T. (1989). Allocentric spatial and tactile memory impairments in rats with dorsal caudate lesions are affected by preoperative behavioral training. *Behavioral Neuroscience,* **103,** 1242–1250.

Cook, D., & Kesner, R. P. (1988). Caudate nucleus and memory for egocentric localization. *Behavioral & Neural Biology,* **49,** 332–343.

Damasio, A. R. (1995). On some functions of the human prefrontal cortex. *Annals of the New York Academy of Sciences,* **769,** 241–251.

Damasio, A. R., & Tranel, D. (1990). Knowing that 'Colorado' goes with 'Denver' does not imply knowledge that 'Denver' is in 'Colorado'. *Behavioural Brain Research,* **40,** 193–200.

Daum, I., Channon, S., & Canaran, A. G. M. (1989). Classical conditioning in patients with severe memory problems. *Journal of Neurophysiology,* **52,** 47–51.

Davidson, T. L., Flynn, F. W., & Jarrard, L. E. (1992). Potency of food deprivation intensity cues as discriminative stimuli. *Journal of Experimental Psychology: Animal Behavior Processes,* **18,** 174–181.

Davidson, T. L., & Jarrard, L. E. (1993). A role for hippocampus in the utilization of hunger signals. *Behavioral & Neural Biology,* **59,** 167–171.

Davidson, T. L., McKernan, M. G., & Jarrard, L. E. (1993). Hippocampal lesions do not impair negative patterning: A challenge to configural association theory. *Behavioral Neuroscience,* **107,** 227–234.

Davis, M. (1986). Pharmacological and anatomical analysis of fear conditioning using the fear-potentiated startle paradigm. *Behavioral Neuroscience,* **100,** 814–824.

Davis, M. (1992). The role of the amygdala in fear and anxiety. *Annual Review of Neuroscience,* **15,** 353–375.

Davis, M., Gendelman, D. S., Tischler, M. D., & Gendelman, P. M. (1982). A primary acoustic startle circuit: Lesion and stimulation studies. *Journal of Neuroscience,* **2,** 791–805.

De Olmos, J., Alheid, G. F., & Beltramino, C. A. (1985). Amygdala. *In* G.Paxinos (Ed.), *The rat nervous system, Volume 1* (pp. 223–334). Sydney: Academic Press.

Deacon, T. W., Eichenbaum, H., Rosenberg, P., & Eckmann, K. W. (1983). Afferent connections of the perirhinal cortex in the rat. *Journal of Comparative Neurology,* **220,** 168–190.

Desimone, R. (1992). The physiology of memory: Recordings of things past. *Science,* **258,** 245–246.

Devan, B. D. (1997). *Functional organization of the dorsal striatum: Comparison to the hippocampal system.* Montreal: McGill University.

Devan, B. D., Blank, G. S., & Petri, H. L. (1992). Place navigation in the Morris water task: Effects of reduced platform interval lighting and pseudorandom platform positioning. *Psychobiology,* **20,** 120–126.

Devan, B. D., McDonald, R. J., & White, N. M. (1998). Effects of medial and lateral caudate-putamen lesions on place- and cue-guided behaviors in the water maze: Relation to thigmotaxis. *Behavioural Brain Research.*

Dickinson, A. (1985). Actions and habits: The development of behavioural autonomy. *In* L. Weiskrantz (Ed.), *Animal intelligence* (pp. 67–78). Oxford: Clarendon.

Dickinson, A. (1994). Instrumental conditioning. *In Animal learning and cognition* (pp. 45–79). New York: Academic Press.

Dickinson, A., & Balleine, B. (1994). Motivational control of goal-directed action. *Animal Learning and Behavior,* **22,** 1–18.

DiMattia, B. D., & Kesner, R. P. (1988). Spatial cognitive maps: Differential role of parietal cortex and hippocampal formation. *Behavioral Neuroscience,* **102,** 471–480.

Divac, I. (1968). Functions of the caudate nucleus. *Acta Biologiae Experimentalis (Warsaw),* **28,** 107–120.

Divac, I., & Oberg, R. G. (1979). Current conceptions of neostriatal function: History and evaluation. *In* I. Divac & R. G. Oberg (Eds.), *The neostriatum.* Oxford: Pergamon.

Divac, I., Rosvold, H. E., & Szwarcbart, M. K. (1967). Behavioral effects of selective ablation of the caudate nucleus. *Journal of Comparative & Physiological Psychology,* **63,** 183–190.

Doty, B., & Doty, L. (1966). Facilitating effects of amphetamine on avoidance conditioning in relation to age and problem difficulty. *Psychopharmacology,* **9,** 234–241.

Duncan, C. P. (1949). The retroactive effect of electroshock on learning. *Journal of Comparative & Physiological Psychology,* **42,** 32–44.

Ehlers, C. L., Somes, C., Lopez, A. L., & Robledo, P. (1998). Long latency event-related potentials in rats: Response of amygdala, nucleus accumbens, dorsal hippocampus and frontal cortex to changes in reward characteristics of conditioned stimuli. *Brain Research,* **780,** 138–142.

Eichenbaum, H., Fagan, A., Matthews, P., & Cohen, N. J. (1988). Hippocampal system dysfunction and odor discrimination learning in rats: Impairment or facilitation depending on representational demands. *Behavioral Neuroscience,* **102,** 331–339.

Eichenbaum, H., Kuperstein, M., Fagan, A., & Nagode, J. (1987). Cue-sampling and goal-approach correlates of hippocampal unit activity in rats performing an odor-discrimination task. *Journal of Neuroscience,* **7,** 716–732.

Eichenbaum, H., Schoenbaum, G., Young, B., & Bunsey, M. (1996). Functional organization of the hippocampal memory system. *Proceedings of the National Academy of Sciences, U.S.A.,* **93,** 13500–13507.

Eichenbaum, H., Stewart, C., & Morris, R. G. M. (1990a). Hippocampal representation in place learning. *Journal of Neuroscience,* **10,** 3531–3542.

Eichenbaum, H., Stewart, C., & Morris, R. G. M. (1990b). Hippocampal representation in spatial learning. *Journal of Neuroscience,* **10,** 331–339.

Estes, W. K. (1959). The statistical approach to learning theory. *In* S. Koch (Ed.), *Psychology: A study of a science.* New York: McGraw-Hill.

Etienne, A. S., Maurer, R., & Séguinot, V. (1996). Path integration in mammals and its interaction with visual landmarks. *Journal of Experimental Biology,* **199,** 201–209.

Everitt, B. J., Cador, M., & Robbins, T. W. (1989). Interactions between the amygdala and ventral striatum in stimulus-reward associations: Studies using a second-order schedule of sexual reinforcement. *Neuroscience,* **30,** 63–75.

Everitt, B. J., Morris, K. A., O'Brien, A., & Robbins, T. W. (1991). The basolateral amygdala-ventral striatal system and conditioned place preference: Further evidence of limbic-striatal interactions underlying reward-related processes. *Neuroscience,* **42,** 1–18.

Fallon, J. H., & Moore, R. Y. (1978). Catecholamine innervation of the basal forebrain: IV Topography of the dopamine projection to the basal forebrain and neostriatum. *Journal of Comparative Neurology,* **180,** 545–579.

Fanselow, M. S., & Kim, J. J. (1994). Acquisition of contextual Pavlovian fear conditioning is blocked by application of an NMDA receptor antagonist D, L-2-amino-5- phosphonovaleric acid to the basolateral amygdala. *Behavioral Neuroscience,* **108,** 210–212.

Fanselow, M. S., & LeDoux, J. E. (1999). Why we think plasticity underlying Pavlovian fear conditioning occurs in the basolateral amygdala. *Neuron,* **23,** 229–232.

Fendt, M., & Fanselow, M. S. (1999). The neuroanatomical and neurochemical basis of conditioned fear. *Neuroscience & Biobehavioral Reviews,* **23,** 743–760.

Ferbinteanu, J., & McDonald, R. J. (2000). Dorsal/ventral hippocampus and conditioned place preference. *Hippocampus, in press.*

Flaherty, A. W., & Graybiel, A. M. (1994). Input-output organization of the sensorimotor striatum in the squirrel monkey. *Journal of Neuroscience,* **14,** 599–610.

Fonnum, F. (1970). Topographical and subcellular localization of choline acetyltransferase in rat hippocampal region. *Journal of Neurochemistry,* **17,** 1029–1037.

Frankland, P. W., Cestari, V., Filipkowski, R. K., McDonald, R. J., & Silva, A. J. (1998). The dorsal hippocampus is essential for context discrimination but not for contextual conditioning. *Behavioral Neuroscience,* **112,** 863–874.

Frith, C., & Dolan, R. (1996). The role of the prefrontal cortex in higher cognitive functions. *Cognitive Brain Research,* **5,** 175–181.

Furtado, J. C. S., & Mazurek, M. F. (1996). Behavioral characterization of quinolinate-induced lesions of the medial striatum: Relevance for Huntington's disease. *Experimental Neurology,* **138,** 158–168.

Fuster, J. M., & Uyeda, A. A. (1971). Reactivity of limbic neurons of the monkey to appetitive and aversive signals. *Electroencephalography & Clinical Neurophysiology,* **30,** 281–293.

Gaarskjaer, F. B. (1978a). Organization of the mossy fiber system of the rat studied in extended hippocampi. I. Terminal area related to number of granule and pyramidal cells. *Journal of Comparative Neurology,* **178,** 49–72.

Gaarskjaer, F. B. (1978b). Organization of the mossy fiber system of the rat studied in extended hippocampi. II. Experimental analysis of fiber distribution with silver impregnation methods. *Journal of Comparative Neurology,* **178,** 73–88.

Gallagher, M., & Chiba, A. A. (1996). The amygdala and emotion. *Current Opinion in Neurobiology,* **6,** 221–227.

Gallagher, M., & Holland, P. C. (1992). Preserved configural learning and spatial learning impairment in rats with hippocampal damage. *Hippocampus,* **2,** 81–88.

Gallagher, M., & Holland, P. C. (1994). The amygdala complex: Multiple roles in associative learning and attention. *Proceedings of the National Academy of Sciences, U.S.A.,* **91,** 11771–11776.

Garcia, J., Hankins, W. G., & Rusiniak, K. W. (1976). Flavor aversion studies. *Science,* **192,** 265–266.

Gardiner, T. W., & Kitai, S. T. (1992). Single-unit activity in the globus pallidus and neostriatum of the rat during performance of a trained head movement. *Experimental Brain Research,* **88,** 517–530.

Gaykema, R. P., Luiten, P. G., Nyakas, C., & Traber, J. (1990). Cortical projection patterns of the medial septum-diagonal band complex. *Journal of Comparative Neurology,* **293,** 103–124.

Gerfen, C. R. (1985). The neostriatal mosaic: I. Compartmental organization of projections from the striatum to the substantia nigra in the rat. *Journal of Comparative Neurology,* **236,** 454–476.

Gerfen, C. R., Baimbridge, K. G., & Thibault, J. (1987). The neostriatal mosaic: III. Biochemical and developmental dissociation of patch-matrix mesostriatal systems. *Journal of Neuroscience,* **7,** 3935–3944.

Gerfen, C. R., Herkenham, M., & Thibault, J. (1987). The neostriatal mosaic: II. Patch- and matrix-directed mesostriatal dopaminergic and non-dopaminergic systems. *Journal of Neuroscience,* **7,** 3915–3934.

Gilbert, P. E., Kesner, R. P., & DeCoteau, W. E. (1998). Memory for spatial location: Role of the hippocampus in mediating spatial pattern separation. *Journal of Neuroscience,* **18,** 804–810.

Gold, P. E. (1992). Modulation of memory processing: Enhancement of memory in rodents and humans. *In* L. R. Squire & N. Butters (Eds.), *Neuropsychology of memory* (2nd ed., pp. 402–414). New York: Guilford.

Gold, P. E., Hankins, L. L., & Rose, R. P. (1977). Time-dependent post-trial changes in the localization of amnestic electrical stimulation sites within the amygdala in rats. *Behavioral Biology,* **20,** 32–40.

Gold, P. E., & King, R. A. (1972). Caudate stimulation and retrograde amnesia: Amnesia threshold and gradient. *Behavioral Biology,* **7,** 709–715.

Gold, P. E., & McGaugh, J. L. (1975). A single trace, two process view of memory storage processes. *In* D. Deutsch & J. A. Deutsch (Eds.), *Short term memory.* New York: Academic Press.

Graybiel, A. M. (1995). Building action repertoires: Memory and learning functions of the basal ganglia. *Current Opinion in Neurobiology,* **5,** 733–741.

Graybiel, A. M., Aosaki, T., Flaherty, A. W., & Kimura, M. (1994). The basal ganglia and adaptive motor control. *Science,* **265,** 1826–1831.

Green, R. H., Beatty, W. W., & Schwartzbaum, J. S. (1967). Comparative effects of septo-hippocampal and caudate lesions on avoidance behavior in rats. *Journal of Comparative & Physiological Psychology,* **64,** 444–452.

Grijalva, C. V., Levin, E. D., Morgan, M., Roland, B., & Martin, F. C. (1990). Contrasting effects of centromedial and basolateral amygdaloid lesions on stress-related responses in the rat. *Physiology & Behavior,* **48,** 495–500.

Grofova, I. (1979). Extrinsic connections of the striatum. *In* I. Divac & R. G. E. Oberg (Eds.), *The neostriatum* (pp. 37–51). Oxford: Pergamon.

Guthrie, E. R. (1959). Association by contiguity. *In* S. Koch (Ed.), *Psychology: A study of a science.* New York: McGraw-Hill.

Hampson, R. E., Heyser, C. J., & Deadwyler, S. A. (1993). Hippocampal cell firing correlates of delayed-match-to-sample performance in the rat. *Behavioral Neuroscience,* **107,** 715–739.

Hatfield, T., Graham, P. W., & Gallagher, M. (1992). Taste-potentiated odor aversion learning: Role of the amygdaloid basolateral complex and central nucleus. *Behavioral Neuroscience,* **106,** 286–293.

Heidenreich, B. A., Trytek, E. S., Schroeder, D. M., Sengelaub, D. R., & Rebec, G. V. (1994). A methodology for determining the patch-matrix compartmental location of extracellular single-unit recordings in the striatum of freely moving rats. *Journal of Neuroscience Methods,* **52,** 169–174.

Heimer, L., Alheid, G. F., & Zaborsky, L. (1985). Basal ganglia. *In* G. Paxinos (Ed.), *The rat nervous system: Vol. 1. Forebrain and midbrain* (pp. 37–86). Sydney: Academic Press.

Heindel, W. C., Salmon, D. P., Shults, C. W., Walicke, P. A., & Butters, N. (1989). Neuropsychological evidence for multiple implicit memory systems: A comparison of Alzheimer's, Huntington's, and Parkinson's disease patients. *Journal of Neuroscience,* **9,** 582–587.

Helkala, E.-L., Laulumaa, V., Soininen, H., & Riekkinen, P. J. (1988). Recall and recognition memory in patients with Alzheimer's and Parkinson's diseases. *Annals of Neurology,* **24,** 214–217.

Henke, P. G. (1972). Effect of lesions in the amygdala on behavioral contrast. *Physiology & Behavior,* **8,** 173–176.

Henke, P. G., & Maxwell, D. (1973). Lesions in the amygdala and the frustration effect. *Physiology & Behavior,* **10,** 647–650.

Herkenham, M. (1978). The connections of the nucleus reuniens thalami: Evidence for a direct thalamo-hippocampal pathway in the rat. *Journal of Comparative Neurology,* **177,** 589–610.

Hilgard, E. R., & Bower, G. H. (1966). *Theories of learning.* (3rd ed.) New York: Appleton-Century-Crofts.

Hilgard, E. R., & Marquis, D. G. (1940). *Conditioning and learning.* New York: Appleton-Century.

Hiroi, N., & White, N. M. (1991). The lateral nucleus of the amygdala mediates expression of the amphetamine conditioned place preference. *Journal of Neuroscience,* **11,** 2107–2116.

Hirsh, R. (1974). The hippocampus and contextual retrieval of information from memory: A theory. *Behavioral Biology,* **12,** 421–444.

Hirsh, R. (1980). The hippocampus, conditional operations and cognition. *Physiological Psychology,* **8,** 175–182.

Hirsh, R., & Krajden, J. (1982). The hippocampus and the expression of knowledge. *In* R. L. Isaacson & N. E. Spear (Eds.), *The expression of knowledge* (pp. 213–241). New York: Plenum.

Hirsh, R., Leber, B., & Gillman, R. (1978). Fornix fibers and motivational states as controllers of behavior: A study stimulated by the contextual retrieval theory. *Behavioral Biology,* **22,** 463–475.

Hitchcott, P. K., Bonardi, C. M., & Phillips, G. D. (1997). Enhanced stimulus-reward learning by intra-amygdala administration of a D_3 dopamine receptor agonist. *Psychopharmacology,* **133,** 240–248.

Hitchcott, P. K., & Phillips, G. D. (1998). Double dissociation of the behavioural effects of R(+) 7-OH-DPAT infusions in the central and basolateral amygdala nuclei upon Pavlovian and instrumental conditioned appetitive behaviours. *Psychopharmacology,* **140,** 458–469.

Hjorth-Simonsen, A. (1972). Projection of the lateral part of the entorhinal area to the hippocampus and fascia dentata. *Journal of Comparative Neurology,* **146,** 219–232.

Hjorth-Simonsen, A., & Jeune, B. (1972). Origin and termination of the hippocampal perforant path in the rat studied by silver impregnation. *Journal of Comparative Neurology,* **144,** 215–232.

Holahan, M. R., & White, N. M. Memory modulation produced by post-training exposure to an aversive conditioned stimulus. *Society for Neuroscience Abstracts* **24,** 1683, 1998. (Abstract)

Honig, W. K. (1978). Working memory in pigeons. *In* S. H. Hulse, W. K. Honig, & H. Fowler (Eds.), *Cognitive aspects of animal behavior.* Hillsdale, NJ: Erlbaum.

Horn, G. (1985). *Memory, imprinting and the brain: An inquiry into mechanisms.* Oxford: Clarendon.

Hull, C. L. (1943). *Principles of behavior.* New York: Appleton-Century-Crofts.

Hunt, M. E., Kesner, R. P., & Evans, R. B. (1994). Memory for spatial location: Functional dissociation of entorhinal cortex and hippocampus. *Psychobiology,* **22,** 186–194.

Huston, J. P., Mueller, C. C., & Mondadori, C. (1977). Memory facilitation by posttrial hypothalamic stimulation and other reinforcers: A central theory of reinforcement. *Biobehavioral Reviews,* **1,** 143–150.

Irle, E., & Markowitsch, H. J. (1982). Connections of the hippocampal formation, mamillary bodies, anterior thalamus and cingulate cortex. A retrograde study using horseradish peroxidase in the cat. *Experimental Brain Research,* **47,** 79–94.

Isaacson, R. L., & Douglas, R. J. (1961). The effect of radical hippocampal ablation on acquisition of avoidance response. *Journal of Comparative & Physiological Psychology,* **54,** 625–628.

Izard, C. E. (1972). *Patterns of emotions.* New York: Academic Press.

Jackson-Smith, P., Kesner, R. P., & Chiba, A. A. (1993). Continuous recognition of spatial and nonspatial stimuli in hippocampal-lesioned rats. *Behavioral & Neural Biology,* **59,** 107–119.

Jackson, A., & Crossman, A. R. (1981). Basal ganglia and other afferent projections to the peribrachial region in the rat: A study using retrograde and anterograde transport of horseradish peroxidase. *Neuroscience,* **6,** 1537–1549.

Jacobs, B. L., & McGinty, D. J. (1972). Participation of the amygdala in complex stimulus recognition and behavioral inhibition: Evidence from unit studies. *Brain Research,* **36,** 431–436.

Jarrard, L. E. (1986). Selective hippocampal lesions and behavior: Implications for current research and theorizing. *In* R. L. Isaacson & K. H. Pribram (Eds.), *The hippocampus* (pp. 93–126). New York: Plenum.

Jarrard, L. E. (1991). On the neural bases of the spatial mapping system: Hippocampus vs. hippocampal formation. *Hippocampus,* **1,** 236–239.

Jarrard, L. E. (1993). On the role of the hippocampus in learning and memory in the rat. *Behavioral & Neural Biology,* **60,** 9–26.

Johnston, D., Williams, S., Jaffe, D., & Gray, R. (1992). NMDA-receptor-independent long-term potentiation. *Annual Review of Physiology,* **54,** 489–505.

Jones, B., & Mishkin, M. (1972). Limbic lesions and the problem of stimulus-reinforcement associations. *Experimental Neurology,* **36,** 362–377.

Jones, R. S. G. (1993). Entorhinal-hippocampal connections: A speculative view of their function. *Trends in Neurosciences,* **16,** 58–64.

Jonides, J., Smith, E. E., Koeppe, R. A., Awh, E., Minoshima, S., & Mintun, M. A. (1993). Spatial working memory in humans as revealed by PET. *Nature,* **363,** 623–625.

Kaas, J. H. (1987). The organization of neocortex in mammals: Implications for theories of brain function. *Annual Review of Psychology,* **38,** 129–151.

Kagan, J. (1994). On the nature of emotion. *Monographs of the Society for Research in Child Development,* **59,** 7–24.

Kalil, K. (1978). Patch-like terminations of thalamic fibers in the putamen of the rhesus monkey: An autoradiographic study. *Brain Research,* **140,** 333–339.

Kapp, B. S., Frysinger, R. C., Gallagher, M., & Haselton, J. R. (1979). Amygdala central nucleus lesions: Effect on heart rate conditioning in the rabbit. *Physiology & Behavior,* **23,** 1109–1117.

Kapp, B. S., Gallagher, M., Holmquist, B. K., & Theall, C. L. (1978). Retrograde amnesia and hippocampal stimulation: Dependence upon the nature of associations formed during conditioning. *Behavioral Biology,* **24,** 1–23.

Kelley, A. E., & Domesick, V. B. (1982). The distribution of the projection from the hippocampal formation to the nucleus accumbens in the rat: an anterograde- and retrograde-horseradish peroxidase study. *Neuroscience,* **7,** 2321–2335.

Kelley, A. E., Domesick, V. B., & Nauta, W. J. H. (1982). The amygdalo-striatal projection in the rat—An anatomical study by anterograde and retrograde tracing methods. *Neuroscience,* **7,** 615–630.

Kemble, E. D., & Schwartzbaum, J. S. (1969). Reactivity to taste properties of solutions following amygdaloid lesions. *Physiology & Behavior,* **4,** 981–985.

Kentros, C., Hargreaves, E. L., Hawkins, R. D., Kandel, E. R., Shapiro, M. L., & Muller, R. U. (1998). Abolition of long-term stability of new hippocampal place cell maps by NMDA receptor blockade. *Science,* **280,** 2121–2126.

Kesner, R. P. (1998). Neuurobiological views of memory. *In* J. L. Martinez & R. P. Kesner (Eds.), *Neurobiology of learning and memory* (3rd ed., pp. 361–416). San Diego: Academic Press.

Kesner, R. P., & Andrus, R. G. (1982). Amygdala stimulation disrupts the magnitude of reinforcement contribution to long-term memory. *Physiological Psychology,* **10,** 55–59.

Kesner, R. P., Berman, R. F., & Tardif, R. (1992). Place and taste aversion learning: Role of basal forebrain, parietal cortex, and amygdala. *Brain Research Bulletin,* **29,** 345–353.

Kesner, R. P., Bolland, B. L., & Dakis, M. (1993). Memory for spatial locations, motor responses and objects: Triple dissociation among the hippocampus, caudate nucleus and extrastriate visual cortex. *Experimental Brain Research,* **93,** 462–470.

Kesner, R. P., Crutcher, K., & Beers, D. R. (1988). Serial position curves for item (spatial location) information: Role of the dorsal hippocampal formation and medial septum. *Brain Research,* **454,** 219–226.

Kesner, R. P., & DiMattia, B. D. (1987). Neurobiology of an attribute model of memory. *Progress in Psychobiology and Physiological Psychology,* **12,** 207–278.

Kesner, R. P., Farnsworth, G., & DiMattia, B. D. (1989). Double dissociation of egocentric and allocentric space following medial pre-frontal cortex and parietal cortex lesions in the rat. *Behavioral Neuroscience,* **103,** 956–961.

Kesner, R. P., & Gilbert, P. E. (2000). A process oriented view of amygdala and hippocampus mediation of reward value and spatial location information. *In* P. E. Gold & W. T. Greenough (Eds.), *Four decades of memory: A festschrift honoring James L. McGaugh.* Irvine, CA: American Psychological Association: University of California.

Kesner, R. P., Walser, R. D., & Winzenried, G. (1989). Central but not basolateral amygdala mediates memory for positive affective experiences. *Behavioural Brain Research,* **33,** 189–195.

Kesner, R. P., & Wilburn, M. W. (1974). A review of electrical stimulation of the brain in the context of learning and retention. *Behavioral Biology,* **10,** 259–292.

Kesner, R. P., & Williams, J. M. (1995). Memory for magnitude of reinforcement: Dissociation between the amygdala and hippocampus. *Neurobiology of Learning & Memory,* **64,** 237–244.

Kim, J. J., & Fanselow, M. S. (1992). Modality-specific retrograde amnesia of fear. *Science,* **256,** 675–677.

Kim, J. J., Rison, R. A., & Fanselow, M. S. (1993). Effects of amygdala, hippocampus, and periaqueductal gray lesions on short- and long-term contextual fear. *Behavioral Neuroscience,* **107,** 1093–1098.

Kimble, D. P., & BreMiller, R. (1981). Latent learning in hippocampal lesioned rats. *Physiology & Behavior,* **26,** 1055–1059.

Kimble, D. P., Jordan, W. P., & BreMiller, R. (1982). Further evidence for latent learning in hippocampal-lesioned rats. *Physiology & Behavior,* **29,** 401–407.

Kimura, M. (1995). Role of basal ganglia in behavioral learning. *Neuroscience Research,* **22,** 353–358.

Kirkby, R. J., & Polgar, S. (1974). Active avoidance in the laboratory rat following lesions of the dorsal or ventral caudate nucleus. *Physiological Psychology,* **2,** 301–306.

Kirkwood, A., Dudek, S. M., Gold, J. T., Aizenman, C. D., & Bear, M. F. (1993). Common forms of synaptic plasticity in the hippocampus and neocortex in vitro. *Science,* **260,** 1518-1521.

Klopf, A. H. (1988). A neuronal model of classical conditioning. *Psychobiology,* **16,** 85–125.

Knowlton, B. J., Mangels, J. A., & Squire, L. R. (1996). A neostriatal habit learning system in humans. *Science,* **273,** 1399–1402.

Knowlton, B. J., Ramus, S. J., & Squire, L. R. (1992). Intact artifical grammar learning in amnesia: Dissociation of classification learning and explicit memory for specific instances. *Psychological Science,* **3,** 172–179.

Koh, E. T., & Ricardo, J. A. (1978). Afferents and efferents of the parabrachial region in the rat: Evidence for parallel ascending gustatory versus viscereceptive systems arising from the nucleus of the solitary tract. *Anatomical Record,* **190,** 449.

Kolb, B., Buhrmann, K., McDonald, R. J., & Sutherland, R. J. (1994). Dissociation of the medial prefrontal, posterior parietal, and posterior temporal cortex for spatial navigation and recognition memory in the rat. *Cerebral Cortex,* **4,** 664–680.

Kosel, K. C., Van Hoesen, G. W., & Rosene, D. L. (1983). A direct projection from the perirhinal cortex (area 35) to the subiculum in the rat. *Brain Research,* **269,** 347–351.

Kosel, K. C., Van Hoesen, G. W., & West, J. R. (1981). Olfactory bulb projections to the parahippocampal area of the rat. *Journal of Comparative Neurology,* **198,** 467–482.

Kretteck, J. E., & Price, J. L. (1977). Projections from the amygdaloid complex to the cerebral cortex and thalamus in the rat and cat. *Journal of Comparative Neurology,* **172,** 687–722.

Krivanek, J., & McGaugh, J. L. (1969). Facilitating effects of pre- and post-training amphetamine administration on discrimination learning in mice. *Agents and Actions,* **1,** 36–42.

Landauer, T. K. (1969). Reinforcement as consolidation. *Psychological Review,* **76,** 82–96.

LeDoux, J. E. (1993). Emotional memory systems in the brain. *Behavioural Brain Research,* **58,** 69–79.

LeDoux, J. E., Cicchetti, P., Xagoraris, A., & Romanski, L. M. (1990). The lateral amygdaloid nucleus: Sensory interface of the amygdala in fear conditioning. *Journal of Neuroscience,* **10,** 1062–1069.

Lewis, P. R., Shute, C. C., & Silver, A. (1967). Confirmation from choline acetylase analyses of a massive cholinergic innervation to the rat hippocampus. *Journal of Physiology,* **191,** 215–224.

Lindvall, O., & Bjorklund, A. (1974). The organziation of the ascending catecholamine neuron systems in the rat brain. *Acta Physiologica Scandinavica, Supp.* **412,** 1–48.

Mackintosh, N. J. (1974). *The psychology of animal learning.* London: Academic Press.

Maki, W. S., Beatty, W. W., Hoffman, N., Bierley, R. A., & Clouse, B. A. (1984). Spatial memory over long retention intervals: Nonmemorial factors are not necessary for accurate performance on the radial-arm maze by rats. *Behavioral & Neural Biology,* **41,** 1–6.

Malenka, R. C., & Nicoll, R. A. (1993). NMDA-receptor-dependent synaptic plasticity: Multiple forms and mechanisms. *Trends in Neurosciences,* **12,** 521–527.

Malmo, R. B. (1975). *On emotions, needs, and our archaic brain.* New York: Holt, Rinehart & Winston.

Maren, S., Aharonov, G., & Fanselow, M. S. (1996). Retrograde abolition of conditional fear after excitotoxic lesions in the basolateral amygdala of rats: Absence of a temporal gradient. *Behavioral Neuroscience,* **110,** 718–726.

McAllister, W. R., & McAllister, D. E. (1995). Two-factor fear theory: Implications for understanding anxiety-based clinical phenomena. *In* W. T. O'Donohue & L. Krasner (Eds.), *Theories of behavior therapy: Exploring behavior change* (pp. 145–171). Washington, DC: American Psychological Association.

McCarthy, G., Puce, A., Constable, R. T., Krystal, J. H., Gore, J. C., & Goldman-Rakic, P. S. (1996). Activation of human prefrontal cortex during spatial and nonspatial working memory tasks measured by functional MRI. *Cerebral Cortex,* **6,** 600–611.

McClelland, J. L., McNaughton, B. L., & O'Reilly, R. C. (1995). Why there are complementary learning systems in the hippocampus and neocortex: Insights from the successes and failures of connectionist models of learning and memory. *Psychological Review,* **102,** 419–457.

McDonald, R. J., Koerner, A., & Sutherland, R. J. (1995). Contextual fear conditioning and the hippocampus. *Society for Neuroscience Abstracts,* **21,** 1218.

McDonald, R. J., Murphy, R. A., Guarrachi, F. A., Gortler, J. R., White, N. M., & Baker, A. G. (1997). A systematic comparison of the effects of hippocampal and fornix-fimbria lesions on acqusition of three configural discrimination tasks. *Hippocampus,* **7,** 371–388.

McDonald, R. J., & White, N. M. (1993). A triple dissociation of memory systems: Hippocampus, amygdala and dorsal striatum. *Behavioral Neuroscience,* **107,** 3–22.

McDonald, R. J., & White, N. M. (1994). Parallel information processing in the water maze: Evidence for independent memory systems involving dorsal striatum and hippocampus. *Behavioral & Neural Biology,* **61,** 260–270.

McDonald, R. J., & White, N. M. (1995a). Information acquired by the hippocampus interferes with acquisition of the amygdala-based conditioned cue preference (CCP) in the rat. *Hippocampus,* **5,** 189–197.

McDonald, R. J., & White, N. M. (1995b). Hippocampal and non-hippocampal contributions to place learning. *Behavioral Neuroscience,* **109,** 579–593.

McGaugh, J. L., Cahill, L. F., & Roozendaal, B. (1996). Involvement of the amygdala in memory storage: Interactions with other brain systems. *Proceedings of the National Academy of Sciences, U.S.A.,* **93,** 13508–13514.

McGaugh, J. L., & Herz, M. J. (1972). *Memory consolidation.* San Francisco: Albion.

McGaugh, J. L., Introini-Collison, I. B., Cahill, L. F., Castellano, C., Dalmaz, C., Parent, M. B., & Williams, C. L. (1993). Neuromodulatory systems and memory storage: Role of the amygdala. *Behavioural Brain Research,* **58,** 81–90.

McGaugh, J. L., Introini-Collison, I. B., Cahill, L. F., Kim, M., & Liang, K. C. (1992). Involvement of the amygdala in neuromodulatory influences on memory storage. *In* J. P. Aggleton (Ed.), *The amygdala: Neurobiological aspects of emotion, memory and mental dysfunction* (pp. 431–451). New York: Wiley-Liss.

McGeorge, A. J., & Faull, R. L. (1987). The organization and collateralization of corticostriate neurones in the motor and sensory cortex of the rat brain. *Brain Research,* **423,** 318–324.

McGeorge, A. J., Faull, R. L. M., & Faull, R. L. (1989). The organization of the projection from the cerebral cortex to the striatum in the rat. *Neuroscience,* **29,** 503–537.

McHugh, T. J., Blum, K. I., Tsien, J. Z., Tonegawa, S., & Wilson, M. A. (1996). Impaired hippocampal representation of space in CA1-specific NMDAR1 knockout mice. *Cell,* **87,** 1339–1349.

McNaughton, B. L. (1993). The mechanism of expression of long-term enhancement of hippocampal synapses: Current issues and theoretical implications. *Annual Review of Physiology,* **55,** 375–396.

McNaughton, B. L., Leonard, B., & Chen, L. (1989). Cortical-hippocampal interactions and cognitive mapping: A hypothesis based on reintegration of the parietal and inferotemporal pathways for visual processing. *Psychobiology,* **17,** 230–235.

Meibach, R. C., & Siegel, A. (1975). The origin of fornix fibers which project to the mammillary bodies in the rat: A horseradish peroxidase study. *Brain Research,* **88,** 508–512.

Merzenich, M. M., & Sameshima, K. (1993). Cortical plasticity and memory. *Current Opinion in Neurobiology,* **3,** 187–196.

Miller, E. K., Erickson, C. A., & Desimone, R. (1996). Neural mechanisms of visual working memory in prefrontal cortex of the macaque. *Journal of Neuroscience,* **16,** 5154–5167.

Milner, B. (1985). Memory and the human brain. *In* M. Shafto (Ed.), *How we know: Nobel conference XX* (pp. 31–59). San Francisco: Harper & Row.

Milner, B., Corkin, S., & Teuber, H.-L. (1968). Further analysis of the hippocampal amnesic syndrome: 14-year follow-up study of H.M. *Neuropsychologia,* **6,** 215–234.

Mishkin, M., Malamut, B., & Bachevalier, J. (1984). Memories and habits: Two neural systems. *In* G. Lynch, J. L. McGaugh, & N. M. Weinberger (Eds.), *Neurobiology of human memory and learning* (pp. 65–77). New York: Guilford.

Mishkin, M., & Petri, H. L. (1984). Memories and Habits: Some implications for the analysis of learning and retention. *In* L. R. Squire & N. Butters (Eds.), *Neuropsychology of memory* (pp. 287–296). New York: Guilford.

Mitcham, J. D., & Thomas, Jr. R. K. (1972). Effects of substantia nigra and caudate nucleus lesions on avoidance learning in rats. *Journal of Comparative & Physiological Psychology,* **81,** 101–107.

Morris, R. G., Downes, J. J., Sahakian, B. J., Evenden, J. L., Heald, A., & Robbins, T. W. (1988). Planning and spatial working memory in Parkinson's disease. *Journal of Neurology, Neurosurgery and Psychiatry,* **51,** 757–766.

Morris, R. G. M., Garrud, P., Rawlins, J. N. P., & O'Keefe, J. (1982). Place navigation impaired in rats with hippocampal lesions. *Nature,* **297,** 681–683.

Moscovitch, M. (1992). Memory and working-with-memory: A component process model based on modules and central systems. *Journal of Cognitive Neuroscience,* **4,** 258–267.

Moscovitch, M. (1994). Memory and working with memory: Evaluation of a component process model and comparisons with other models. *In* D. L. Schacter & E. Tulving (Eds.), *Memory systems 1994* (pp. 269–310). Cambridge, MA: MIT Press.

Mowrer, O. H. (1947). On the dual nature of learning—A reinterpretation of "conditioning" and "problem solving." *Harvard Educational Review,* **17,** 102–148.

Mulder, A. B., Arts, M. P., & Lopes da Silva, F. H. (1997). Short- and long-term plasticity of the hippocampus to nucleus accumbens and prefrontal cortex pathways in the rat, in vivo. *European Journal of Neuroscience,* **9,** 1603–1611.

Muller, R. U., & Kubie, J. L. (1989). The firing of hippocampal place cells predicts the future position of freely moving rats. *Journal of Neuroscience,* **9,** 4101–4110.

Muller, R. U., Kubie, J. L., & Ranck, J. B. (1987). Spatial firing patterns of hippocampal complex-spike cells in a fixed environment. *Journal of Neuroscience,* **7,** 1935–1950.

Myers, C. E., Gluck, M. A., & Granger, R. (1995). Dissociation of hippocampal and entorhinal function in associative learning: A computational approach. *Psychobiology,* **23,** 116–138.

Nachman, M., & Ashe, J. H. (1974). Effects of basolateral amygdala lesions on neophobia, learned taste aversions, and sodium appetite in rats. *Journal of Comparative & Physiological Psychology,* **87,** 622–643.

Nadel, L. (1992). Multiple memory systems: When and why. *Journal of Cognitive Neuroscience,* **4,** 179–188.

Nagahara, A. H., Otto, T., & Gallagher, M. (1995). Entorhinal-perirhinal lesions impair performance of rats on two versions of place learning in the Morris water maze. *Behavioral Neuroscience,* **109,** 3–9.

Nagai, T., Kimura, H., Maeda, T., McGeer, P. L., Peng, F., & McGeer, E. G. (1982). Cholinergic projections from the basal forebrain of rat to the amygdala. *Journal of Neuroscience,* **2,** 513–520.

Neill, D. B., & Grossman, S. P. (1970). Behavioral effects of lesions or cholinergic blockade of the dorsal and ventral caudate of rats. *Journal of Comparative & Physiological Psychology,* **71,** 311–317.

Nilsson, O. G., Shapiro, M. L., Gage, F. H., Olton, D. S., & Bjorklund, A. (1987). Spatial learning and memory following fimbria-fornix transection and grafting of fetal septal neurons to the hippocampus. *Experimental Brain Research,* **67,** 195–215.

Norgren, R. (1976). Taste pathways to hypothalamus and amygdala. *Journal of Comparative Neurology,* **166,** 17–30.

O'Keefe, J. (1979). A review of the hippocampal place cells. *Progress in Neurobiology,* **13,** 419–439.

O'Keefe, J., & Bouma, H. (1969). Complex sensory properties of certain amygadala units in the freely moving cat. *Experimental Neurology,* **23,** 384–398.

O'Keefe, J., & Conway, D. H. (1978). Hippocampal place cells in the freely moving rat: Why they fire where they fire. *Experimental Brain Research,* **31,** 573–590.

O'Keefe, J., & Dostrovsky, J. (1971). The hippocampus as a spatial map. Preliminary evidence from unit activity in the freely-moving rat. *Brain Research,* **34,** 171–175.

O'Keefe, J., & Nadel, L. (1978). *The hippocampus as a cognitive map.* Oxford: Oxford University Press.

O'Keefe, J., Nadel, L., Keightley, S., & Kill, D. (1975). Fornix lesions selectively abolish place learning in the rat. *Experimental Neurology,* **48,** 152–166.

O'Keefe, J., & Speakman, A. (1987). Single unit activity in the rat hippocampus during a spatial memory task. *Experimental Brain Research,* **68,** 1–27.

Oddie, S. D., Kirk, I. J., Whishaw, I. Q., & Bland, B. H. (1997). Hippocampal formation is involved in movement selection: Evidence from medial septal cholinergic modulation and concurrent slow-wave (theta rhythm) recording. *Behavioural Brain Research,* **88,** 169–180.

Olton, D. S., & Papas, B. C. (1979). Spatial memory and hippocampal function. *Neuropsychologia,* **17,** 669–682.

Olton, D. S., & Samuelson, R. J. (1976). Remembrances of places past: Spatial memory in the rat. *Journal of Experimental Psychology: Animal Behavior Processes,* **2,** 97–116.

Onn, S.-P., Berger, T. W., Grace, A. A., & Onn, S. P. (1994). Identification and characterization of striatal cell subtypes using in vivo intracellular recording and dye-labeling in rats: III. Morphological correlates and compartmental localization. *Synapse,* **16,** 231–254.

Onn, S. P., & Grace, A. A. (1994). Dye coupling between rat striatal neurons recorded in vivo: Compartmental organization and modulation by dopamine. *Journal of Neurophysiology,* **71,** 1917–1934.

Ono, T., Nishijo, H., & Uwano, T. (1995). Amygdala role in conditioned associative learning. *Progress in Neurobiology,* **46,** 401–422.

Ottersen, O. P. (1980). Afferent connections to amygdaloid complex of the rat and cat: II. Afferents from the hypothalamus and basal telencephalon. *Journal of Comparative Neurology,* **194,** 267–289.

Ottersen, O. P. (1981). Afferent connections to the amygdaloid complex of the rat with some observations in the cat: III. Afferents from the lower brain stem. *Journal of Comparative Neurology,* **202,** 335–356.

Ottersen, O. P. (1982). Connections of the amygdala of the rat: IV. Corticoamygdaloid and intraamygdaloid connections as studied with axonal transport of horseradish peroxidase. *Journal of Comparative Neurology,* **205,** 30–48.

Ottersen, O. P., & Ben-Ari, Y. (1979). Afferent connections to the amygdaloid complex of the rat and cat: I. Projections from the thalamus. *Journal of Comparative Neurology,* **187,** 401–424.

Packard, M. G. (1987). *Differential roles of hippocampus and caudate nulceus in memory: Selective mediation of "cognitive" and "associative" memory.* M.Sc. thesis, McGill University, Montreal.

Packard, M. G. (1989). *Organization of memory in the brain: Role of caudate nucleus and hippocampus.* Ph.D. thesis, McGill University, Montreal.

Packard, M. G., Cahill, L. F., & McGaugh, J. L. (1994). Amygdala modulation of hippocampal-dependent and caudate nucleus-dependent memory processes. *Proceedings of the National Academy of Sciences, U.S.A.,* **91,** 8477–8481.

Packard, M. G., Hirsh, R., & White, N. M. (1989). Differential effects of fornix and caudate nucleus lesions on two radial maze tasks: Evidence for multiple memory systems. *Journal of Neuroscience,* **9,** 1465–1472.

Packard, M. G., & McGaugh, J. L. (1992). Double dissociation of fornix and caudate nucleus lesions on acquisition of two water maze tasks: Further evidence for multiple memory systems. *Behavioral Neuroscience,* **106,** 439–446.

Packard, M. G., & McGaugh, J. L. (1996). Inactivation of hippocampus or caudate nucleus with lidocaine differentially affects expression of place and response learning. *Neurobiology of Learning & Memory,* **65,** 66–72.

Packard, M. G., Regenold, W., Quirion, R., & White, N. M. (1990). Post-training injection of the acetylcholine M_2 receptor antagonist AF-DX 116 improves memory. *Brain Research,* **524,** 72–76.

Packard, M. G., & Teather, L. A. (1998a). Amygdala modulation of multiple memory systems: Hippocampus and caudate-putamen. *Neurobiology of Learning & Memory,* **69,** 163–203.

Packard, M. G., & Teather, L. A. (1998b). Amygdala modulation of multiple memory systems: Hippocampus and caudate-putamen. (Review), 108 refs *Neurobiology of Learning & Memory,* **69,** 163–203.

Packard, M. G., & White, N. M. (1990). Lesions of the caudate nucleus selectively impair 'reference memory' acquisition in the radial maze. *Behavioral & Neural Biology,* **53,** 39–50.

Packard, M. G., & White, N. M. (1991). Dissociation of hippocampal and caudate nucleus memory systems by post-training intracerebral injection of dopamine agonists. *Behavioral Neuroscience,* **105,** 295–306.

Pascoe, J. P., & Kapp, B. S. (1985). Electrophysiological characteristics of amygdaloid central nucleus neurons during Pavlovian fear conditioning in the rabbit. *Behavioural Brain Research,* **16,** 117–133.

Pavlov, I. P. (1927). *Conditioned reflexes.* Oxford: Oxford University Press.

Peinado-Manzano, M. A. (1988). Effects of biateral lesions of the central and lateral amygdala on free operant successive discrimination. *Behavioural Brain Research,* **29,** 61–72.

Peterson, G. M. (1994). Differential projections to the hippocampus by neurons of the medial septum and vertical limb of the diagonal band. *Brain Research,* **646,** 129–134.

Phillips, A. G., & Carr, G. D. (1987). Cognition and the basal ganglia: A possible substrate for procedural knowledge. *Canadian Journal of Neurological Science,* **14,** 381–385.

Phillips, R. G., & LeDoux, J. E. (1992). Differential contribution of amygdala and hippocampus to cued and contextual fear conditioning. *Behavioral Neuroscience,* **106,** 274–285.

Phillips, R. G., & LeDoux, J. E. (1994). Lesions of the dorsal hippocampal formation interfere with background but not foreground contextual fear conditioning. *Learning and Memory,* **1,** 34–44.

Phillipson, O. T. (1979). Afferent projections to the ventral tegmental area of Tsai and interfascicular nucleus: A horseradish peroxidase study in the rat. *Journal of Comparative Neurology,* **187,** 117–143.

Pikkarainen, M., Ronkko, S., Savander, V., Insausti, R., & Pitkanen, A. (1999). Projections from the lateral, basal, and accessory basal nuclei of the amygdala to the hippocampal formation in rat. *Journal of Comparative Neurology,* **403,** 229–260.

Pitkanen, A., Pikkarainen, M., Nurminen, N., & Ylinen, A. (2000). Reciprocal connections between the amygdala and the hippocampal formation, perirhinal cortex, and postrhinal cortex in rat. A review. *Annals of the New York Academy of Sciences,* **911,** 369–391.

Polster, M. R., Nadel, L., & Schacter, D. L. (1991). Cognitive neuroscience analyses of memory: A historical perspective. *Journal of Cognitive Neuroscience,* **3,** 95–116.

Post, S., & Mai, J. K. (1980). Contribution to the amygdaloid projection field in the rat. A quantitative autoradiographic study. *Journal fur Hirnforschung,* **21,** 199–225.

Prado-Alcala, R. A., Grinberg, Z. J., Arditti, Z. L., Garcia, M. M., Prieto, H. G., & Brust-Carmona, H. (1975). Learning deficits produced by chronic and reversible lesions of the corpus striatum in rats. *Physiology & Behavior,* **15,** 283–287.

Quirk, G. J., Muller, R. U., & Kubie, J. L. (1990). The firing of hippocampal place cells in the dark depends on the rat's recent experience. *Journal of Neuroscience,* **10,** 2008–2017.

Rasmussen, M., Barnes, C. A., & McNaughton, B. I. (1989). A systematic test of cognitive mapping, working-memory, and temporal discontiguity theories of hippocampal function. *Psychobiology,* **17,** 335–348.

Rescorla, R. A. (1988). Behavioral studies of Pavlovian conditioning. *Annual Review of Neuroscience,* **11,** 329–352.

Rezai, K., Andreasen, N. C., Alliger, R., Cohen, G., Swayze, V., II, & O'Leary, D. S. (1993). The neuropsychology of the prefrontal cortex. *Archives of Neurology,* **50,** 636–642.

Robbins, T. W. (1996). Dissociating executive functions of the prefrontal cortex. *Philosophical Transactions of the Royal Society of London. B: Biological Sciences,* **351,** 1463–1470.

Rotenberg, A., Mayford, M., Hawkins, R. D., Kandel, E. R., & Muller, R. U. (1996). Mice expressing activated CaMKII lack low frequency LTP and do not form stable place cells in the CA1 region of the hippocampus. *Cell,* **87,** 1351–1361.

Royce, G. J. (1978). Autoradiographic evidence for a discontinuous projection to the caudate nucleus from the centromedian nucleus in the cat. *Brain Research,* **146,** 145–150.

Rudy, J. W., & Sutherland, R. J. (1989). The hippocampal formation is necessary for rats to learn and remember configural discriminations. *Behavioural Brain Research,* **34,** 97–109.

Rudy, J. W., & Sutherland, R. J. (1995). Configural association theory and the hippocampus: An appraisal and reconfiguration. *Hippocampus,* **5,** 375–389.

Sahakian, B. J., Morris, R. G., Evenden, J. L., Heald, A., Levy, R., Philpot, M., & Robbins, T. W. (1988). A comparative study of visuospatial memory and learning in Alzheimer-type dementia and Parkinson's disease. *Brain,* **111,** 695–718.

Sanghera, M. K., Rolls, E. T., & Roper-Hall, A. (1979). Visual responses of neurons in the dorsolateral amygdala of the alert monkey. *Experimental Neurology,* **63,** 610–626.

Saper, C. B. (1982). Convergence of autonomic and limbic connections in the insular cortex of the rat. *Journal of Comparative Neurology,* **210,** 163–173.

Saper, C. B., & Loewy, A. D. (1982). Projections of the pedunculopontine tegmental nucleus in the rat: Evidence for additional extrapyramidal circuitry. *Brain Research,* **252,** 367–372.

Schacter, D. L., Chiu, C.-Y. P., & Ochsner, K. N. (1993). Implicit memory: A selective review. *Annual Review of Neuroscience,* **16,** 159–182.

Scoville, W. B., & Milner, B. (1957). Loss of recent memory after bilateral hippocampal lesions. *Journal of Neurology, Neurosurgery and Psychiatry,* **20,** 11–21.

Selden, N. R. W., Everitt, B. J., Jarrard, L. E., & Robbins, T. W. (1991). Complementary roles for the amygdala and hippocampus in aversive conditioning to explicit and contextual cues. *Neuroscience,* **42,** 335–350.

Shapiro, M. L., & Eichenbaum, H. (1999). Hippocampus as a memory map: Synaptic plasticity and memory encoding by hippocampal neurons. *Hippocampus,* **9,** 365–384.

Shapiro, M. L., Simon, D. K., Olton, D. S., Gage, F. H., III, Nilsson, O. G., & Bjorklund, A. (1989). Intrahippocampal grafts of fetal basal forebrain tissue alter place fields in the hippocampus of rats with fimbria- fornix lesions. *Neuroscience,* **32,** 1–18.

Sherry, D. F., & Schacter, D. L. (1987). The evolution of multiple memory systems. *Psychological Review,* **94,** 439–454.

Shettleworth, S. J. (1993). Varieties of learning and memory in animals. *Journal of Experimental Psychology: Animal Behavior, Processes,* **19,** 5–14.

Shizgal, P. (1997). Neural basis of utility estimation. *Current Opinion in Neurobiology,* **7,** 198–208.

Siegel, A., Edinger, H., & Ogami, S. (1974). The topographical organization of the hippocampal projection to the septal area: A comparative neuroanatomical analysis in the gerbil, rat, rabbit, and cat. *Journal of Comparative Neurology,* **157,** 359–377.

Simon, H., Le Moal, M., & Calas, A. (1979). Efferents and afferents of the ventral tegmental-A10 region studied after local injection of [3H]leucine and horseradish peroxidase. *Brain Research,* **178,** 17–40.

Solomon, P. R. (1980). A time and a place for everything? Temporal processing views of hippocampal function with special reference to attention. *Physiological Psychology,* **8,** 254–261.

Solomon, P. R., Levine, E., Bein, T., & Pendlebury, W. W. (1991). Disruption of classical conditioning in patients with Alzheimer's disease. *Neurobiology of Aging,* **12,** 283–287.

Spiegler, B. J., & Mishkin, M. (1981). Evidence for the sequential participation of inferior temporal cortex and amygdala in the acquisition of stimulus-reward associations. *Behavioural Brain Research,* **3,** 303–317.

Squire, L. R., Knowlton, B. J., & Musen, G. (1993). The structure and organization of memory. *Annual Review of Psychology,* **44,** 453–495.

Squire, L. R., & Zola-Morgan, S. (1991). The medial temporal lobe memory system. *Science,* **253,** 1380–1386.

Steward, O., & Scoville, S. A. (1976). Cells of origin of entorhinal cortical afferents to the hippocampus and fascia dentata of the rat. *Journal of Comparative Neurology,* **169,** 347–370.

Stuss, D. T., Shallice, T., Alexander, M. P., & Picton, T. W. (1995). A multidisciplinary approach to anterior attentional functions. *Annals of the New York Academy of Sciences,* **769,** 191–211.

Sutherland, R. J. (1985). The navigating hippocampus: An individual medley of movement, space and memory. *In* G. Buzsaki & C. H. Vanderwolf (Eds.), *Electrical activity of the archicortex* (pp. 255–279). Budapest: Akademiai Kiado.

Sutherland, R. J., Kolb, B., & Whishaw, I. Q. (1982). Spatial mapping: Definitive disruption by hippocampal or medial frontal cortical damage in the rat. *Neuroscience Letters,* **31,** 271–276.

Sutherland, R. J., & McDonald, R. J. (1990). Hippocampus, amygdala and memory deficits in rats. *Behavioural Brain Research,* **37,** 57–79.

Sutherland, R. J., McDonald, R. J., Hill, C. R., & Rudy, J. W. (1989). Damage to the hippocampal formation in rats selectively impairs the ability to learn cue relationships. *Behavioral & Neural Biology,* **52,** 331–356.

Sutherland, R. J., & Rodriguez, A. J. (1989). The role of the fornix/fimbria and some related subcortical structures in place learning and memory. *Behavioural Brain Research,* **32,** 265–278.

Sutherland, R. J., & Rudy, J. W. (1989). Configural association theory: The role of the hippocampal formation in learning, memory and amnesia. *Psychobiology,* **17,** 129–144.

Sutherland, R. J., Whishaw, I. Q., & Kolb, B. (1983). A behavioural analysis of spatial localization following electrolytic, kainate- or colchicine-induced damage to the hippocampal formation in the rat. *Behavioural Brain Research,* **7,** 133–153.

Suzuki, S., Augerinos, G., & Black, A. H. (1980). Stimulus control of spatial behavior on the eight-arm maze in rats. *Learning and Motivation,* **11,** 1–18.

Swanson, L. W. (1977). The anatomical organization of septo-hippocampal projections. *Ciba Foundation Symposium,* **58,** 25–48.

Swanson, L. W. (1982). The projections of the ventral tegmental area and adjacent regions: A combined fluorescent retrograde tracer and immunofluorescence study in the rat. *Brain Research Bulletin,* **9,** 321–353.

Swanson, L. W. (1983). The hippocampus and the concept of the limbic system. *In The neurobiology of the hippocampus* (pp. 3–19). New York: Academic Press.

Swanson, L. W., & Kohler, C. (1986). Anatomical evidence for direct projections from the entorhinal area to the entire cortical mantle in the rat. *Journal of Neuroscience,* **6,** 3010–3023.

Swanson, L. W., Wyss, J. M., & Cowan, W. M. (1978). An autoradiographic study of the organization of intrahippocampal association pathways in the rat. *Journal of Comparative Neurology,* **181,** 681–715.

Thompson, R. F. (1990). Neural mechanisms of classical conditioning in mammals. *Philosophical Transactions of the Royal Society of London. B: Biological Sciences,* **329,** 161–170.

Thompson, R. F., & Krupa, D. J. (1994). Organization of memory traces in the mammalian brain. *Annual Review of Neuroscience,* **17,** 519–549.

Thompson, W. G., Guilford, M. O., & Hicks, L. H. (1980). Effects of caudate and cortical lesions on place and response learning in rats. *Physiological Psychology,* **8**(4), 473–479.

Thorndike, E. L. (1911). *Animal intelligence.* New York: Macmillan.

Thorndike, E. L. (1933a). A proof of the law of effect. *Science,* **77,** 173–175.

Thorndike, E. L. (1933b). A theory of the action of the after-effects of a connection upon it. *Psychological Review,* **40,** 434–439.

Tolman, E. C. (1948). Cognitive maps in rats and men. *Psychological Review,* **56,** 144–155.

Tolman, E. C. (1949). There is more than one kind of learning. *Psychological Review,* **56,** 144–155.

Tolman, E. C., Hall, C. S., & Bretnall, E. P. (1932). A disproof of the law of effect and a substitution of the laws of emphasis, motivation and disruption. *Journal of Experimental Psychology: General,* **15,** 601–615.

Tolman, E. C., Ritchie, B. F., & Kalish, D. (1946). Studies in spatial learning II place learning versus response learning. *Journal of Experimental Psychology: General,* **36,** 221–229.

Trytek, E. S., White, I. M., Schroeder, D. M., Heidenreich, B. A., & Rebec, G. V. (1996). Localization of motor- and nonmotor-related neurons within the matrix-striosome organization of rat striatum. *Brain Research,* **707,** 221–227.

Tulving, E. (1972). Episodic and semantic memory. *In* E. Tulving & W. Donaldson (Eds.), *Organization of memory.* New York: Academic Press.

Turner, B. H., & Herkenham, M. (1991). Thalamoamygdaloid projections in the rat: A test of the amygdala's role in sensory processing. *Journal of Comparative Neurology,* **313,** 295–325.

Turner, B. H., & Zimmer, J. (1984). The architecture and some of the interconnections of the rat's amygdala and lateral periallocortex. *Journal of Comparative Neurology,* **227,** 540–557.

Vaccarino, F. J., Schiff, B. B., & Glickman, S. E. (1989). Biological view of reinforcement. *In* S. B. Klein & R. R. Mowrer (Eds.), *Contemporary learning theories* (pp. 111–141). Nutley, NJ: Earlbaum.

van der Kooy, D., Koda, L. Y., McGinty, J. F., Gerfen, C. R., & Bloom, F. E. (1984). The organization of projections from the cortex, amygdala, and hypothalamus to the nucleus of the solitary tract in rat. *Journal of Comparative Neurology,* **224,** 1–24.

van der Staay, F. J., Raaijmakers, W. G. M., Lammers, A. J. J. C., & Tonnaer, J. A. D. M. (1989). Selective fimbria lesions impair acquisition of working and reference memory of rats in a complex spatial discrimination task. *Behavioural Brain Research,* **32,** 151–161.

Vanderwolf, C. H., Bland, B. H., & Whishaw, I. Q. (1973). Diencephalic, hippocampal, and neocortical mechanisms in voluntary movement. *In* J. D. Maser (Ed.), *Efferent organization and the integration of behavior* (pp. 229–262). New York: Academic Press.

Vanderwolf, C. H., & Cain, D. P. (1994). The behavioral neurobiology of learning and memory: A conceptual reorientation. *Brain Research Reviews,* **19,** 264–297.

Veening, J. G. (1978a). Cortical afferents of the amygdaloid complex in the rat: An HRP study. *Neuroscience Letters,* **8,** 191–195.

Veening, J. G. (1978b). Subcortical afferents of the amygdaloid complex in the rat: An HRP study. *Neuroscience Letters,* **8,** 197–202.

Veening, J. G., Cornelissen, F. M., & Lieven, P. A. J. M. (1980). The topical organization of the afferents to the caudatoputamen of the rat. A horseradish peroxidase study. *Neuroscience,* **5,** 1253–1268.

Viaud, M. D., & White, N. M. (1989). Dissociation of visual and olfactory conditioning in the neostriatum of rats. *Behavioural Brain Research,* **32,** 31–42.

Votaw, C. L., & Lauer, E. W. (1963). An afferent hippocampal fiber system in the fornix of the monkey. *Journal of Comparative Neurology,* **121,** 195–206.

Wainer, B. H., Levey, A. I., Rye, D. B., Mesulam, M. M., & Mufson, E. J. (1985). Cholinergic and non-cholinergic septohippocampal pathways. *Neuroscience Letters,* **54,** 45–52.

Webster, K. E. (1961). The cortico-striatal projection in the albino rat. *Journal of Anatomy,* **95,** 532–564.

Webster, K. E. (1965). The cortico-striatal projection in the cat. *Journal of Anatomy,* **99,** 329–337.

Weiskrantz, L. (1956). Behavioral changes associated with ablation of the amygdaloid complex in monkeys. *Journal of Comparative & Physiological Psychology,* **49,** 381–391.

Weiskrantz, L. (1990). Problems of learning and memory: One or multiple memory systems. *Philosophical Transactions of the Royal Society of London. B: Biological Sciences,* **329,** 99–108.

Whishaw, I. Q. (1998). Place learning in hippocampal rats and the path integration hypothesis. *Neuroscience & Biobehavioral Reviews,* **22,** 209–220.

Whishaw, I. Q., Mittleman, G., Bunch, S. T., & Dunnett, S. B. (1987). Impairments in the acquisition,retention and selection of spatial navigation strategies after medial caudate-putamen lesions in rats. *Behavioural Brain Research,* **24,** 125–138.

Whishaw, I. Q., & Tomie, J.-A. (1991). Acquisition and retention by hippocampal rats of simple, conditional, and configural tasks using tactile and olfactory cues: Implications for hippocampal function. *Behavioral Neuroscience,* **105,** 787–797.

White, I. M., & Rebec, G. V. (1993). Responses of rat striatal neurons during performance of a lever- release version of the conditioned avoidance response task. *Brain Research,* **616,** 71–82.

White, N. M. (1989). A functional hypothesis concerning the striatal matrix and patches: Mediation of S-R memory and reward. *Life Sciences,* **45,** 1943–1957.

White, N. M. (1996). Addictive drugs as reinforcers: Multiple partial actions on memory systems. *Addiction,* **91,** 921–949.

White, N. M. (1997). Mnemonic functions of the basal ganglia. *Current Opinion in Neurobiology,* **7,** 164–169.

White, N. M., & Carr, G. D. (1985). The conditioned place preference is affected by two independent reinforcement processes. *Pharmacology, Biochemistry & Behavior,* **23,** 37–42.

White, N. M., & McDonald, R. J. (1993). Acquisition of a spatial conditioned place preference is impaired by amygdala lesions and improved by fornix lesions. *Behavioural Brain Research,* **55,** 269–281.

White, N. M., & Milner, P. M. (1992). The psychobiology of reinforcers. *Annual Review of Psychology,* **43,** 443–471.

White, N. M., & Ouellet, M.-C. (1997). Roles of movement and temporal factors in spatial learning. *Hippocampus,* **7,** 501–510.

White, N. M., & Wallet, P. (2000). Dorsal hippocampus function in unreinforced spatial learning. *Hippocampus,* **10,** 226–235.

Wible, C. G., Findling, R. L., Shapiro, M. L., Lang, E. J., Crane, S., & Olton, D. S. (1986). Mnemonic correlates of unit activity in the hippocampus. *Brain Research,* **399,** 97–110.

Wiener, S. I. (1993). Spatial and behavioral correlates of striatal neurons in rats performing a self-initiated navigation task. *Journal of Neuroscience,* **13,** 3802–3817.

Wiener, S. I., Paul, C. A., & Eichenbaum, H. (1989). Spatial and behavioral correlates of hippocampal neuronal activity. *Journal of Neuroscience,* **9,** 2737–2763.

Wiig, K. A., & Bilkey, D. K. (1994). The effects of perirhinal cortical lesions on spatial reference memory in the rat. *Behavioural Brain Research,* **63,** 101–109.

Wiig, K. A., & Bilkey, D. K. (1995). Lesions of rat perirhinal cortex exacerbate the memory deficit observed following damage to the fimbria-fornix. *Behavioral Neuroscience,* **109,** 620–630.

Williams, D. R. (1965). Classical conditioning and incentive motivation. *In* W. F. Prokasy (Ed.), Classical conditioning: A symposium (pp. 340–357). New York: Appleton-Century-Crofts.

Williams, G. V., & Goldman-Rakic, P. S. (1995). Modulation of memory fields by dopamine D1 receptors in prefrontal cortex. *Nature,* **376,** 572–575.

Willingham, D. B. (1997). Systems of memory in the human brain. *Neuron,* **18,** 5–8.

Winocur, G. (1974). Functional dissociation within the caudate nucleus of rats. *Journal of Comparative & Physiological Psychology,* **86,** 432–439.

Winocur, G., Moscovitch, M., & Stuss, D. T. (1996). Explicit and implicit memory in the elderly: Evidence for double dissociation involving medial temporal- and frontal-lobe functions. *Neuropsychologia,* **10,** 57–65.

Wise, R. A. (1982). Neuroleptics and operant behavior: The anhedonia hypothesis. *Behavioral & Brain Sciences,* **5,** 39–87.

Wise, S. P., Murray, E. A., & Gerfen, C. R. (1996). The frontal cortex-basal ganglia system in primates. *Critical Reviews in Neurobiology,* **10,** 317–356.

Wood, E. R., Dudchenko, P. A., & Eichenbaum, H. (1999). The global record of memory in hippocampal neuronal activity. *Nature,* **397,** 613–616.

Woolf, N. J., & Butcher, L. L. (1982). Cholinergic projections to the basolateral amygdala: A combined Evans blue and acetylcholinesterase analysis. *Brain Research Bulletin,* **8,** 751–763.

Wyers, E. J., & Deadwyler, S. A. (1972). Duration and nature of retrograde amnesia produced by stimulation of caudate nucleus. *Physiology & Behavior,* **6,** 97–103.

Wyers, E. J., Peeke, H. V., Williston, J. S., & Herz, M. J. (1968). Retroactive impairment of passive avoidance learning by stimulation of the caudate nucleus. *Experimental Neurology,* **22,** 350–366.

Wyss, J. M. (1981). An autoradiographic study of the efferent connections of the entorhinal cortex in the rat. *Journal of Comparative Neurology,* **199,** 495–512.

Yamamoto, T., & Fujimoto, Y. (1991). Brain mechanisms of taste aversion learning in the rat. *Brain Research Bulletin,* **27,** 403–406.

Young, B. J., Otto, T., Fox, G. D., & Eichenbaum, H. (1997). Memory representation within the parahippocampal region. *Journal of Neuroscience,* **17,** 5183–5195.

Young, P. T. (1959). The role of affective processes in learning and motivation. *Psychological Review,* **66,** 104–125.

Zanatta, M. S., Schaeffer, E., Schmitz, P. K., Medina, J. H., Quevedo, J., Quillfeldt, J. A., & Izquierdo, I. (1996). Sequential involvement of NMDA receptor-dependent processes in hippocampus, amygdala, entorhinal cortex and parietal cortex in memory processing. *Behavioural Pharmacology,* **7,** 341–345.

Zubin, J., & Barrera, S. E. (1941). Effect of electric convulsive therapy on memory. *Proceedings of the Society for Experimental Biology and Medicine,* **48,** 596–597.