Behavioral Neuroscience
1993, Vol. 107, No. 1, 3–22

0735-7044/93/$3.00

A Triple Dissociation of Memory Systems: Hippocampus, Amygdala, and Dorsal Striatum

Robert J. McDonald and Norman M. White

This study investigated the respective roles of the hippocampus, the amygdala, and the dorsal striatum in learning and memory. A standard set of experimental conditions for studying the effects of lesions to the three brain areas using an 8-arm radial maze was used: a win–shift version, a conditioned cue preference (CCP) version, and a win–stay version. Damage to the hippocampal system impaired acquisition of the win–shift task but not the CCP or win–stay tasks. Damage to the lateral amygdala impaired acquisition of the CCP task but not the win–shift or win–stay tasks. Damage to the dorsal striatum impaired acquisition of the win–stay task but not the win–shift or CCP tasks. These results are consistent with the hypothesis that the mammalian brain may be capable of acquiring different kinds of information with different, more-or-less independent neural systems. A neural system that includes the hippocampus may acquire information about the relationships among stimuli and events. A neural system that includes the amygdala may mediate the rapid acquisition of behaviors based on biologically significant events with affective properties. A neural system that includes the dorsal striatum may mediate the formation of reinforced stimulus–response associations.

The idea that there is more than one kind of learning is not a new one (Tolman, 1949), nor is the idea that learning and memory in the mammalian nervous system are subserved by several more-or-less independent substrates. The first suggestion of the existence of multiple memory systems came from Scoville and Milner's (1957) discovery that patients with large temporal lobe lesions have a memory deficit that is selective for certain types of new information. However, early attempts to produce an animal model of this temporal lobe amnesic syndrome failed (Douglas, 1967; Isaacson, Douglas, & Moore, 1961; Kimble, 1963).

The publication of Hirsh's (1974) contextual retrieval theory and O'Keefe and Nadel's (1978) cognitive mapping theory provided new insights into these issues. These theories explained the contradictory findings in humans and animals with hippocampal damage, they provided the basis for the development of the idea of multiple memory systems, and they addressed one of the fundamental problems of learning theory by suggesting how the type of learning they attributed to the hippocampus enabled a particular cue or event to have more than one meaning based on the presence of another cue.

A large number of more-or-less related dual memory theories have followed these influential studies, based on research with rats (Cormier, 1981; Eichenbaum, Cohen, Otto, & Wible, in press; Kesner & DiMiattia, 1987; Olton, Becker, & Handelmann, 1979; Rawlins, 1985; Sutherland & Rudy, 1989; Wickelgren, 1979; Winocur, 1980), monkeys (Gabriel, Foster, Orona, Saltwick, & Stanton, 1980; Gaffan, 1974; Kinsbourne & Wood, 1975; Mishkin, Malamut, & Bachevalier, 1984; Ridley, Aitken, & Baker, 1989), and humans (Bruner, 1969; Cohen, 1984; Cohen & Squire, 1980; Graf, Mandler, & Haden, 1982; Hirst, 1982; Huppert & Piercy, 1976; Ryle, 1949; Schacter & Tulving, 1982; Squire, 1987; Stern, 1981; Tulving, 1972; Warrington & Weiskrantz, 1982). Most of these investigators focus on the type of learning that is associated with the hippocampus. They usually recognize the existence of the other types of memory and other neural systems but do not pay much attention to them.

Studies using posttraining electrical stimulation and posttraining drug administration provide another line of evidence that supports the multiple memory systems idea. Posttraining stimulation of the hippocampus (Lidsky & Slotnick, 1970), amygdala (Bresnahan & Routtenberg, 1972; Kesner & Wilburn, 1974), and dorsal striatum (Peeke & Herz, 1971; Wyers, Peeke, Williston, & Herz, 1968) produce memory deficits. Posttraining memory improvement effects have been demonstrated using indirect and direct dopamine agonists injected directly into the hippocampus or dorsal striatum (Packard & White, 1991). The results of these studies suggest that the hippocampus, amygdala, and dorsal striatum may be involved in some type of learning and memory.

Lesion data from animal experiments are consistent with the idea that the three brain areas are involved in memory and suggest that each may mediate acquisition of a different type of information.

A normal hippocampus appears to be necessary for tasks that require the use of information about relationships among stimuli (Eichenbaum et al., in press; Hirsh, 1974, 1980;

Robert J. McDonald and Norman M. White, Department of Psychology, McGill University, Montréal, Québec, Canada.

This research was supported by grants from the Medical Research Council of Canada and from Fonds pour la Formation des Chercheurs et l'Aide à la Recherche (Province de Québec) and formed the basis of a thesis submitted in partial fulfillment of the requirements for M.S. by Robert J. McDonald.

We thank Noboru Hiroi, M. Packard, R. Hirsh, M. Shapiro, P. Milner, J. McGaugh, and D. S. Olton for their helpful discussions concerning the present findings. We also thank Janet Raymond and Carmelo Milo for their technical assistance.

Correspondence concerning this article should be addressed to Robert McDonald, McGill University, Department of Psychology, 1205 Dr. Penfield Avenue, Montréal, Québec, Canada H3A 1B1.

O'Keefe & Nadel, 1978; Sutherland & Rudy, 1989). Rats with damage to the hippocampal system are impaired on the Morris water maze (Morris, Garrud, Rawlins, & O'Keefe, 1982; Sutherland, Kolb, & Whishaw, 1982; Sutherland, Whishaw, & Kolb, 1983), the eight-arm radial maze task (Harley, 1979; Olton, Walker, & Gage, 1978), tasks that require discriminations among places containing food (Aggleton, Hunt, & Rawlins, 1986; Bouffard & Jarrard, 1988; O'Keefe et al., 1975; Okaichi, 1987; Rasmussen, Barnes, & McNaughton, 1989; Sutherland, 1985; van der Staay, Raaijmakers, Lammers, & Tonnaer, 1989), contextual conditioning (Black, Nadel & O'Keefe, 1977; Blanchard, Blanchard, & Fial, 1970; Selden, Everitt, Jarrard, & Robbins, 1991; Sutherland & McDonald, 1990), and various nonspatial mnemonic tasks (Alvarado & Rudy, 1989; Best & Orr, 1973; Eichenbaum, Matthews, & Cohen, 1989; Good & Honey, 1991; Hirsh, Leber, & Gillman, 1978; Hsaio & Isaacson, 1971; Kaye & Pearce, 1987; Rickert, Lorden, Dawson, Smyly, & Callahan, 1979; Rudy & Sutherland,1989; Solomon & Moore, 1975; Sutherland & McDonald, 1990; Sutherland, McDonald, Hill, & Rudy, 1989). Lesions to the hippocampal system in other species have similar effects on learning and memory (Mahut, 1971, 1972; Parkinson, Murray, & Mishkin, 1988; Saunders & Weiskrantz, 1989; Sherry & Vaccarino, 1989).

Following the early research of Brown and Schaeffer (1888) and Kluver and Bucy (1939), Weiskrantz (1956) provided preliminary evidence that the amygdala was involved in learning and memory by demonstrating a variety of learning deficits in monkeys with amygdaloid damage. These initial reports stimulated research directed at the role of the amygdala in emotional behavior. A large body of evidence has accumulated suggesting a role for the amygdala in behavioral tasks that require associations of neutral stimuli with incentive stimuli.

Rats with lesions of the amygdala are impaired on the fear-potentiated startle reflex in which shock is associated with a neutral stimulus (Davis, 1986; Davis, Gendelman, Tischler, & Gendelman, 1982), avoidance tasks (Cahill & McGaugh, 1990; Dunn & Everitt, 1988; Horvath, 1963; Jellestad, Markowska, Bakke, & Walther, 1986; Kemble & Tapp, 1968; Pellegrino, 1968; Slotnick, 1973), acquisition of conditioned emotional responses (CER; Dafters, 1976; Selden et. al., 1991; Spevack, Campbell, & Drake, 1975), neophobic responses (Fitzgerald & Burton, 1981; Rolls & Rolls, 1973; Sutherland & McDonald, 1990), acquisition of conditioned taste aversion (Nachman & Ashe, 1974), autonomic conditioning (Bagshaw and Benzies, 1968; Kapp, Frysinger, Gallagher, & Haselton, 1979; Ledoux, Cicchetti, Xagoraris, & Romanski, 1990; Sanares & Campbell, 1989), and conditioned reaction to threat (Blanchard & Blanchard, 1972).

Animals with amygdaloid lesions are also impaired on conditioned appetitive tasks such as those involving differences in magnitude of reinforcement (Goomas & Steele, 1980; Henke, Allen, & Davison, 1972; Henke & Maxwell, 1973; Kemble & Beckman, 1970; McGleary, 1966; Peinado-Manzano, 1989; Pellegrino, 1968) and conditioned reward tasks in which previously neutral stimuli are associated with stimuli that elicit approach (Baylis & Gaffan, 1991; Cador, Robbins, & Everitt, 1989; Everitt, Cador, & Robbins, 1989; Everitt, Morris, O'Brien, & Robbins, 1991; Gaffan & Harrison, 1987; Gaffan, Gaffan, & Harrison, 1989; Gallagher, Graham, & Holland, 1990; Hiroi & White, 1991; Jones & Mishkin, 1972; Kentridge, Shaw, & Aggleton, 1991; Speigler & Mishkin, 1981).

Recent investigations have been directed at dissociating the functions of the various nuclei of the amygdala. The central and lateral nuclei have been implicated in associations of neutral stimuli with aversive events (Davis, 1986; Kapp et al., 1979; LeDoux et al., 1990). The basolateral and lateral nuclei have been implicated in similar associations with appetitive events (Cador et al., 1989; Everitt et al., 1991; Hiroi & White, 1991; Peinado-Manzano, 1989).

Lesions of the dorsal striatum impair learning of tasks in which a particular motor response is reinforced in the presence of a single cue. Rats with damage to the dorsal striatum are impaired on brightness discriminations (Schwartzbaum & Donovick, 1968), runway learning (Kirkby, Polgar, & Coyle, 1981), avoidance learning (Allen & Davison, 1973; Allen, Mitcham, & Byrd, 1972; Green, Beatty, & Schwartzbaum, 1967; Kirkby & Polgar, 1974; Neill & Grossman, 1971; Prado-Alcala et al., 1975; Winocur, 1974), egocentric maze learning (Cook & Kesner, 1988; Potegal, 1969), reversal learning (Hannon & Bader, 1974), alternation (Chorover & Gross, 1963; Gross, Chorover, & Cohen, 1965), and cued radial maze learning (Packard, Hirsh, & White, 1989).

The present series of experiments was intended to characterize the different contributions made by the hippocampus, amygdala, and dorsal striatum to normal learning and memory. The underlying hypothesis was that each of these structures is part of a more-or-less independent learning and memory system. In any learning situation, each of these systems may act simultaneously and in parallel to acquire different types of information.

The system that includes the hippocampus is thought to acquire information about the relationships among stimuli. This type of information could decrease ambiguity in learning situations that require a particular stimulus to have different meanings based on the presence or absence of other stimuli. This type of processing would aid in identifying and remembering multiple spatial locations. In the present study, this type of memory was tested using a win–shift version of the eight-arm radial maze task (Olton et al., 1979). The neural system that includes the amygdala may mediate the formation of behaviors based on the association of neutral stimuli with biologically significant events that have affective properties. The amygdala could be considered a simple Pavlovian memory system in which neutral stimuli are associated with unconditioned stimuli (food, shock) and the unconditioned responses associated with them (dopamine release, increases in heart rate). In the present study, this type of memory was tested using a conditioned cue preference (CCP) task developed for the radial maze. The neural system that includes the dorsal striatum may mediate the formation of reinforced stimulus–response associations. This memory system could be considered a simple associative learning system in which neutral stimuli come to elicit specific motor responses because the association between these stimuli and responses was repeatedly reinforced. In the present study, this type of memory was tested using a win–stay version of the radial maze task (Packard et al., 1989).

Separate groups of rats with electrolytic lesions of the fornix–fimbria, the lateral nucleus of the amygdala, or the dorsal striatum were trained on each of the three radial maze tasks. If a particular lesion produced a behavioral deficit on any of the tasks, then that experiment was repeated using rats with neurotoxic damage to the implicated structure. This was done to determine whether the behavioral deficit was due to damage to intrinsic neurons or to fibers of passage.

General Method

Subjects

Three hundred twelve male Long-Evans rats were used. The animals were individually housed in single cages and were maintained on a 12:12-hr light–dark cycle. The rats weighed approximately 300-325 g at the beginning of the experiment. The animals were maintained on a food-deprivation schedule that reduced them to 85% of their free-feeding body weights.

Apparatus

An eight-arm radial maze that was made of wood and painted flat gray was used. The maze was 60 cm from the floor. The center platform was 40 cm in diameter. Each arm was 60 cm long and 9 cm wide. A recessed food well was located at the end of each arm. In each of the experiments some modifications were made to the maze.

Surgery

The rats were anesthetized with sodium pentobarbital (65 mg/kg ip). All lesions were stereotaxically placed with coordinates based on the atlas of Paxinos and Watson (1982). All coordinates were measured in relation to bregma and the skull surface. The fornix was damaged with radio-frequency current. Two lesions were made on each side of the brain. The coordinates were posterior (P) = 1.5 mm, lateral (L) = 0.8 and 2.2 mm, and ventral = 4.5 mm. Current (6 mA for 40 s) was passed through a nichrome electrode that was insulated except for an exposed portion (0.8 mm) at the tip. Testing began 1 week after surgery was completed.

The lateral amygdala was damaged with direct current. The coordinates for the lateral amygdala lesions were P = 3.5 mm, L = 5.5 mm, and V = 8.5 mm. Anodal current (1.5 mA for 20 s) was passed through a nichrome electrode that was insulated except for an exposed portion (0.5 mm) at the tip. Testing began 1 week after surgery.

The dorsal striatum was damaged with direct current at both the anterior and posterior sites. The coordinates for the anterior site were anterior (A) = 1.5 mm, L = 2.8 mm, and V = 6.2 mm. Anodal current (5 mA for 20 s) was passed through a nichrome electrode that was insulated except for an exposed portion (0.8 mm) at the tip. The coordinates for the posterior site were A = 0.2 mm, L = 4.3 mm, and P = 6.7 mm. Anodal current (4 mA for 15 s) was passed through an electrode similar to the one used for the anterior lesion. These lesions were made in two stages. Both the anterior and posterior sites were damaged on one side, and the animals were allowed to recover for 2 weeks. Two lesions were then made on the other side, followed by another 2-week recovery period. During the recovery periods, the animals were fed wet rat chow mash twice a day, and rat chow pellets were placed inside their cages.

All sham animals were treated identically to their appropriate lesion groups except that no current was passed through their electrodes.

Neurotoxic lesions of the hippocampus were produced by injections of a mixture of 2 μg colchicine and 0.1 μg kainic acid per 0.5 μl of normal saline. The solution was injected into the hippocampus at 3 injection sites per hemisphere. The coordinates were P = 3.3 mm, L = 1.5 mm, and V = 3.7 mm; P = 4.8 mm, L = 3.2 mm, and V = 4.2 mm; and P = 5.8 mm, L = 5.0 mm, and V = 7.5 mm (Sutherland & McDonald, 1990). Each microinjection (0.4 μl) was infused through a 30-gauge cannula for 8 min using a Harvard minipump. After each injection, the cannula was left in place for another 5 min. Sham lesions consisted of injections of 0.9% saline solution using identical procedures. Testing began 1 week after surgery.

Neurotoxic lesions of the lateral amygdala and dorsal striatum were produced by injections of *N*-methyl-D-aspartate (NMDA; 0.25 M in phosphate buffer, pH 7.0). The solution was injected into the lateral amygdala at one site on each side. The coordinates were P = 3.5 mm, L = 5.5 mm, and V = 8.0 mm. The microinjections (0.3 μl) were infused through 30-gauge cannulas for 6 min. After each injection the cannula was left in place for another 5 min. Sham lesions consisted of injections of phosphate buffer using identical procedures. Testing began 1 week after surgery.

Bilateral NMDA injections into the dorsal striatum were completed in one stage. The coordinates for the anterior site were A = 1.5 mm, L = 3.2 mm, and V = 4.4 mm. The coordinates for the posterior site were A = 0.2 mm, L = 4.0 mm, and V = 4.8 mm. The microinjections (0.3 μl) were infused through 30-gauge cannulas for 6 min. After each injection the cannula was left in place for another 5 min. Sham lesions consisted of injections of phosphate buffer using identical procedures. Testing began 1 week after surgery.

Animals that received microinjections of neurotoxins were monitored for any behavioral signs of seizure activity. If seizure activity was observed, then the animal was given injections of valium (10 mg/kg ip). Monitoring of the animals' seizure activity continued for 3 hr after surgery.

Histology

At the completion of behavioral testing, the rats were deeply anesthetized with an injection of 30% chloral hydrate and perfused with 0.9% saline, which was followed by a 10% formol–saline solution. The brains were removed and stored in 10% formol–saline solution. They were frozen and sliced at 30 μm, and every fifth section through the lesion site was mounted on glass slides. The slides were then stained with cresyl violet and examined.

The histological data presented in Figures 1 and 2 illustrate the maximum and minimum extent of damage to the neural structures of animals that were retained for the data analysis. Figures 3, 4, and 5 show representative examples of neurotoxic damage and sham lesions to the neural structures of animals that were retained for the data analysis. Anatomical criteria were established for deciding which animals to include in the final data analysis. Animals with radio-frequency fornix lesions were included if the fornix–fimbria damage was complete, including both the medial portion and lateral tips. These animals were retained only if there was no damage to the adjacent septal area. Animals with electrolytic lateral amygdala damage were included if the large posterior portions of the nucleus were destroyed and the adjacent nuclei were left intact. Animals with electrolytic lesions of the dorsal striatum were included if both the anterior and posterior portions of the structure sustained extensive damage. If the lesions caused damage to the adjacent septal nuclei, then the animal was eliminated.

Animals with neurotoxic lesions of the hippocampus were included in the data analysis if there was substantial cell loss in all subfields of the hippocampal formation (CA1, CA3, dentate gyrus). Many of these animals sustained some damage to either the subiculum or entorhinal cortex. Animals with neurotoxic lesions of the dorsal striatum were included if there was substantial cell loss and gliosis at both the anterior and posterior portions of the structure. Animals with neurotoxic lesions of the lateral amygdala were included if the lateral

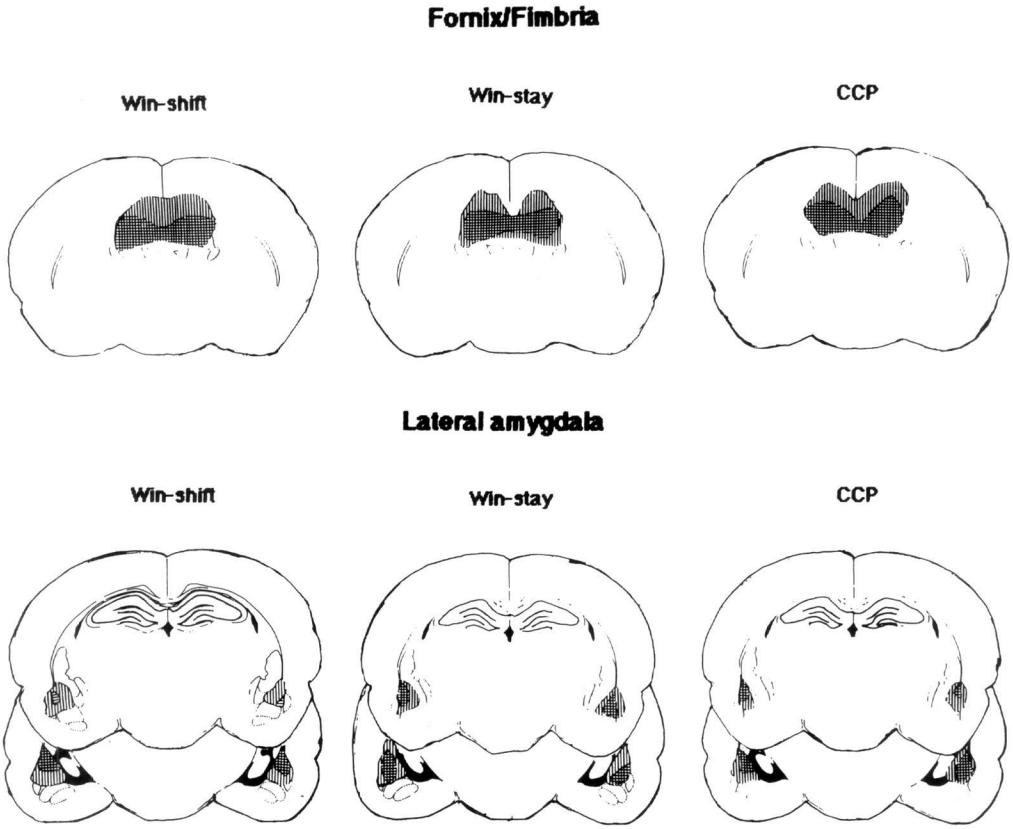

Figure 1. Radio-frequency lesions of the fornix-fimbria (top panel) and electrolytic lesions of the lateral nucleus of the lateral amygdala (bottom panel). (The vertical lines indicate the maximum extent of all lesions, and the cross-hatched areas indicate the minimum extent of lesions for all rats in each experimental condition. CCP = conditioned cue preference.)

nucleus sustained substantial cell loss and gliosis. Many of these animals also sustained damage to the basolateral and central nuclei, portions of the dorsal striatum, and the endopyriform nucleus. Some rats sustained slight damage to portions of the hippocampus adjacent to the lateral nucleus of the amygdala.

Experiment 1: Win–Shift Task

Materials and Method

Subjects For each lesion type, 26 rats were randomly assigned to one of three groups: lesion (n = 10), sham (n = 8), or control (n = 8).

Apparatus. The radial maze that was described in the General Method section was used with minor modifications. A Plexiglas wall (40 cm high) that extended around the circumference of the center platform was used. At the entrance to each arm was an opening that was blocked by a guillotine door. The doors could be raised or lowered by the experimenter. The maze was centrally located in a room with a number of extramaze cues. The dimensions of the room were 140 cm × 120 cm. The wall facing the door had a 30 cm × 22 cm storage box attached to the left corner of the wall. On the center of this wall was a 32 cm × 21 cm poster. The wall to the right of the entrance had an 82 cm × 45 cm closet that started at the far left wall. On the right side of this wall, a black cardboard circle (20 cm in diameter) was located on the center of the wall. The wall to the left of the entrance had a 32 cm × 21 cm poster that was centrally located. The remaining wall, in which the door was located, had a large set of bookshelves.

Procedure. All rats were placed on a food-deprivation schedule and handled daily on 4 successive days for 5 min each. Rats were then placed in the apparatus, and the doors were manipulated randomly for 5 min on each of 2 successive days. There was no food in the maze during these habituation sessions. During this period, the rats were given Froot Loops cereal in their home cage. After these habituation procedures, testing began. A single piece of Froot Loop cereal was placed in the food well of each arm. Each rat was individually placed on the center platform with all of the guillotine doors closed. After 10 s, the doors were opened, and the rat was allowed to choose an arm. At the moment the rat entered an arm, all the doors were closed except for the one at the entrance to the arm the rat occupied. When the rat returned to the center platform, the door was closed, and a 10-s waiting period began. After the waiting period, all of the doors were opened, and the rat was allowed to choose another arm. This procedure continued until all eight cereal pieces had been retrieved or 10 min had elapsed. Each rat was given one such trial per day. Each animal's performance was assessed as the number of revisits to arms from which they had already obtained food within the first eight choices and expressed as number of errors. Daily trials continued until the mean number of errors for the control animals was less than one on each of 2 consecutive days.

Results

The results for the fornix lesions are shown in the top panel of Figure 6. The rats in the sham (n = 7; ns given here and in

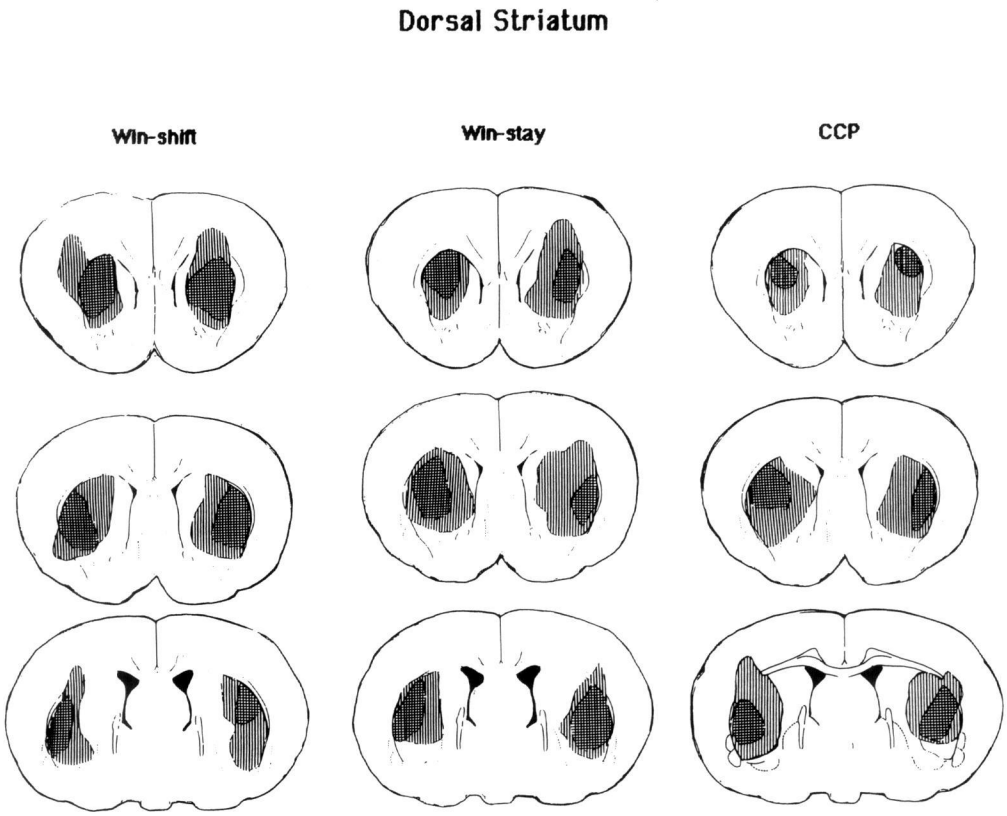

Figure 2. Electrolytic lesions of the dorsal striatum. (The vertical lines indicate the maximum extent, and cross-hatched areas indicate the minimum extent of all lesions in the rats in each experimental condition. CCP = conditioned cue preference.)

the other Results sections are the numbers of animals that completed the experiment and were used in the statistical analysis). and control groups quickly learned to avoid reentering arms in which food had been obtained within that trial. The rats in the fornix group ($n = 7$) made considerably more errors than did the rats in the control groups. An analysis of variance (ANOVA) with repeated measures computed on the errors measure indicated that there was a significant main effect of group, $F(2, 19) = 22.2, p < .0001$, a significant effect of trial, $F(9, 171) = 29.1, p < .0001$, but no significant interaction between group and trial, $F(18, 171) = 1.0, p > .4$. Post hoc tests using Scheffe's method revealed, for the last trial of acquisition, significant differences between the lesion and sham groups ($F = 8.5, p < .05$) and between the lesion and control groups ($F = 8.2, p < .05$). There was no significant difference between the sham and control groups ($F = 0.02$, $p < .05$).

The results for the amygdaloid lesions are shown in the middle panel of Figure 6. Rats with damage to the lateral amygdala ($n = 7$) consistently made fewer errors than did the rats with sham lesions or than did the controls. However, an ANOVA with repeated measures on the error measure revealed no significant main effect of group, $F(2, 20) = 2.62, p < .1$, a significant effect of trial, $F(6, 120) = 33.8, p < .0001$, and no significant interaction between group and trial, $F(12, 120) = .91, p > .5$.

The results for the dorsal striatal lesions are shown in the bottom panel of Figure 6. The results clearly show that dorsal striatal lesions ($n = 7$) had no effect on acquisition of the win–shift task. There was no significant main effect of group, $F(2, 20) = .06, p > .9$, a significant effect of trials, $F(9, 180) = 17.1, p < .0001$, and no significant interaction between group and trial, $F(18, 180) = .83, p > .6$.

Discussion

The results of this first experiment are consistent with those of previous investigations (Becker, Walker, & Olton, 1980; Flaherty, Rowan, Emerich, & Walsh, 1989; Jarrard, 1983; Jarrard, Okaichi, Goldschmidt, & Stewart, 1984; Nadel & McDonald, 1980; Olton & Papas, 1979; Olton et al., 1978; Packard et al., 1989; Rasmussen et al., 1989; Sutherland, 1985; Walker & Olton, 1979; Winocur, 1980) demonstrating that rats with damage to the hippocampal system are impaired on spatial versions of the eight-arm radial maze task. The results are also consistent with the idea that the hippocampal system is necessary for tasks that require the use of information about relationships among cues for accurate performance.

Electrolytic lesions of the lateral nucleus of the amygdala did not impair choice accuracy in the win–shift version of the eight-arm radial maze. In fact, the rats in this lesion group consistently made fewer errors than did those in the sham and

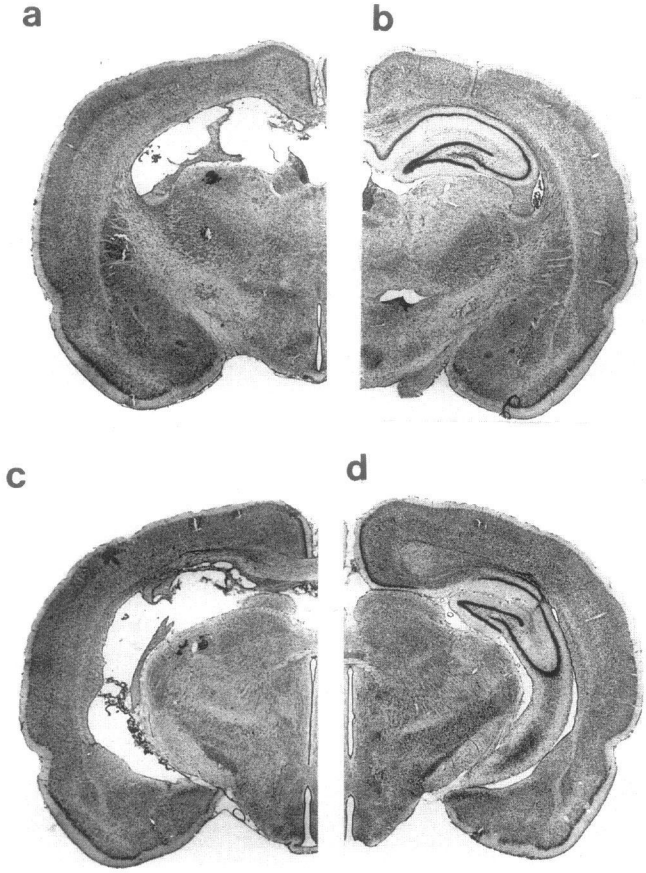

Figure 3. Representative damage after microinjections of neurotoxins into the hippocampal formation at two coronal planes (a and c) or after microinjections of saline into the hippocampal formation (b and d).

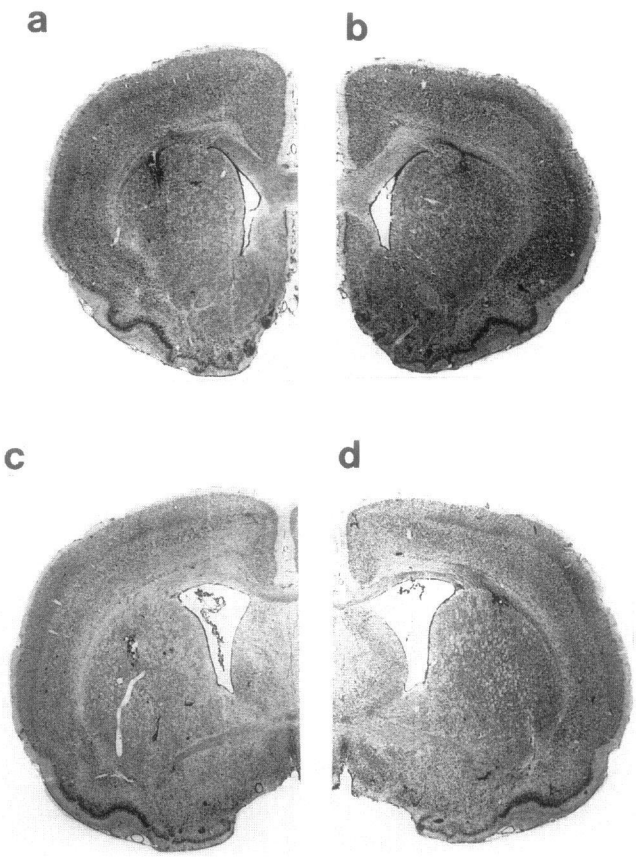

Figure 5. Representative damage after microinjections of neurotoxins into the dorsal striatum at two coronal planes (a and c) or after microinjections of buffer solution (b and d).

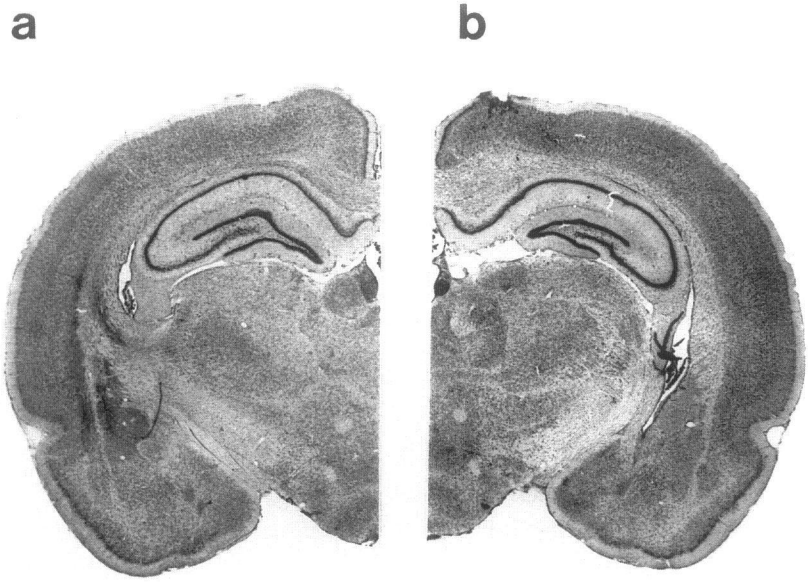

Figure 4. Representative damage after microinjections of neurotoxins into the lateral amygdala (a) or after injections of buffer solution (b).

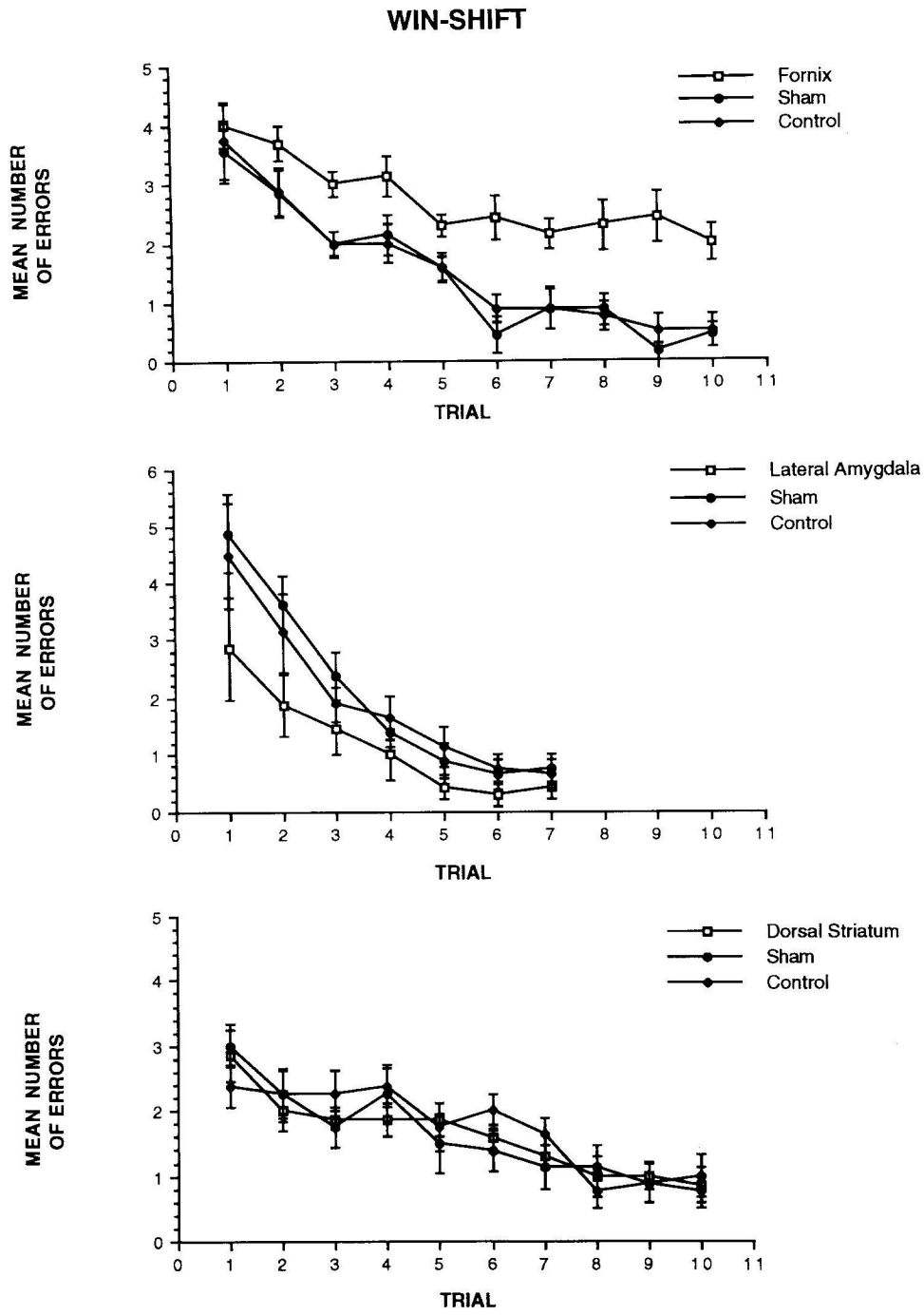

Figure 6. Mean number of errors ($\pm SE$) made by groups of rats with radio-frequency fornix lesions (top panel), electrolytic lateral amygdala lesions (middle panel), or electrolytic dorsal striatal lesions (bottom panel) and their respective sham and control groups on acquisition of the win–shift task.

control groups, although this trend was not statistically significant. The results suggest that an intact lateral amygdala is not necessary for a task that requires the use of information about relationships among cues. These results are consistent with those of other studies of the effects of amygdaloid lesions on this type of task. Becker et al. (1980) found that amygdala-damaged rats were not impaired on the win–shift version of the eight-arm radial maze task. Aggleton et al. (1986) reported that rats with damage to the amygdala were not impaired on a spatial delayed-nonmatching-to-sample (DNMS) task. Parkinson et al. (1988) observed that monkeys with damage to the amygdala were not impaired on an object–place association

task. Sutherland and McDonald (1990) found that rats with damage to the amygdala were unaffected on acquisition of the spatial version of the Morris water maze task. Zola-Morgan, Squire, Alverez-Royo, and Clower (1991) found that damage to the amygdala had no effect on tasks that are sensitive to hippocampal damage in monkeys.

Rats with damage to the dorsal striatum were also able to acquire the present task. These results are consistent with Becker et al.'s (1980) and Packard et al.'s (1989) demonstrations that damage to the dorsal striatum has no apparent effect on acquisition of the win–shift task. Taken together, these results provide support for the idea that an intact dorsal striatum is not necessary for performance of tasks that require knowledge of relationships among cues.

Experiment 2: Conditioned Cue Preference Task

Materials and Method

Subjects For each lesion type, 26 rats were randomly assigned to one of three groups: lesion (n = 10), sham (n = 8), or control (n = 8).

Apparatus. The radial maze that was described in the General Method section was used with minor modifications. The guillotine door system was removed, and the maze was surrounded by a "tent" made of curtains. The animals' behavior was monitored with a video camera that was suspended over the maze (outside the tent). The camera was connected to a video screen that was located outside of the tent. Six of the eight arms of the radial maze were blocked with rectangular wooden blocks (34 cm × 8.5 cm) that fit into the entrances of the arms. Similar wooden blocks were used to confine the rats to specific arms. Light bulbs (7 W) were attached to these blocks on the side facing the arm. Similar bulbs were attached over the entrances to each of the arms.

Procedure. All rats were placed on a food-deprivation schedule and handled daily on 4 successive days for 5 min each. Two randomly chosen arms (adjacent arms excluded) were assigned to each rat, and the other arms were blocked whenever the animal was in the maze. For each rat, one of the two selected arms was designated as the "light" arm. Whenever the animal was in the maze, the light at the entrance to the arm or on the wooden blocks in the arm, as appropriate, was turned on. The other arm was designated as the "dark" arm. In Session 1, both arms and the center platform were open, and the rats were allowed to move freely in the three areas for 10 min.

The CCP training required eight sessions with one session per day. These included four pairings with food (Froot Loops cereal) and four pairings without food. Rats in each treatment group were randomly assigned to the cells of a 2 × 2 factorial design. One factor was pairing arm (light or dark), and the other was food pairing order. Half of the rats in each group had access to 70 pieces of Froot Loops cereal while confined in the light arm, and the other half had access to the food while confined in the dark arm. Within each of these subgroups, half of the rats had access to food on even numbered sessions and no access to food on odd numbered sessions; the pattern was reversed for the remaining rats.

On the pairing trials, each rat was placed into the appropriate arm, the curtain was closed, and the rat was left in the arm for 30 min. The room lights were dimmed to increase the salience of the intramaze lights.

The final session was a test session. No food was placed in the maze, and the entrances to both arms were open. For each rat, the light at the entrance of the arm that had been illuminated during the training sessions was on; the other arm was dark. Each rat was placed in the maze for 20 min, and the amount of time spent in each arm was recorded.

Results

The top panel of Figure 7 shows the results for the animals with fornix lesions. The rats in all groups acquired a CCP, with the fornix group (n = 8) showing the largest CCP. An ANOVA with repeated measures and planned comparisons revealed significant differences between the amounts of time spent in the paired and unpaired arms for the lesion, $F(2, 21) = 13.4$, $p < .01$, sham, $F(2, 21) = 3.72$, $p < .05$, and control groups, $F(2, 21) = 6.41$, $p < .01$.

The middle panel of Figure 7 shows that rats in the sham and control groups acquired a CCP, whereas rats with damage to the lateral nucleus of the amygdala (n = 8) failed to acquire a CCP. An ANOVA with repeated measures and planned comparisons indicated that there were significant differences in time spent in the two arms for the sham, $F(2, 21) = 17.5$, $p < .01$, and control groups, $F(2, 21) = 14.8$, $p < .01$. There was no significant difference between the amounts of time spent in the paired and unpaired arms for the lesion group, $F(2, 21) = 0.31$, $p < .05$.

The bottom panel of Figure 7 shows that rats in all groups acquired a CCP, with the dorsal striatum group (n = 8) showing the largest difference. An ANOVA with repeated measures and planned comparisons revealed significant differences between the amounts of time spent in the paired and unpaired arms for the lesion, $F(2, 21) = 20.7$, $p < .01$, sham, $F(2, 21) = 10.3$, $p < .01$, and control groups, $F(2, 21) = 5.2$, $p < .05$.

Discussion

Electrolytic lesions of the fornix–fimbria did not impair acquisition or expression of a CCP. In fact, the rats with these lesions exhibited larger CCPs than did the rats in the other groups. This result is consistent with Hiroi and White's (1991) demonstration that lesions of the fornix–fimbria or ventral hippocampus do not affect an amphetamine conditioned place preference (also see Flaherty et al., 1989).

This finding is consistent with the results of Experiment 1 because the CCP task does not require the animal to learn about the relationships among cues for accurate performance, merely to make a simple stimulus (light)–reward (food) association.

The results of this second experiment demonstrate that electrolytic lesions of the lateral nucleus of the amygdala impair acquisition or expression (or both) of a CCP based on an association between food and a visual stimulus. This result is consistent with Hiroi and White's (1991) report that damage to the lateral amygdala attenuates acquisition and expression of an amphetamine CPP. Everitt et al. (1991) showed that lesions of the basolateral amygdala disrupt a sucrose CPP, which illustrates the role of the amygdala in associating neutral cues with natural rewards.

Rats with damage to the dorsal striatum acquired and expressed a CCP. This result suggests that the dorsal striatum is not necessary for acquisition of a stimulus–reward association.

Experiment 3: Win–Stay Task

Materials and Method

Subjects For each lesion type, 26 rats were randomly assigned to one of three groups: lesion (n = 10), sham (n = 8), or control (n = 8).

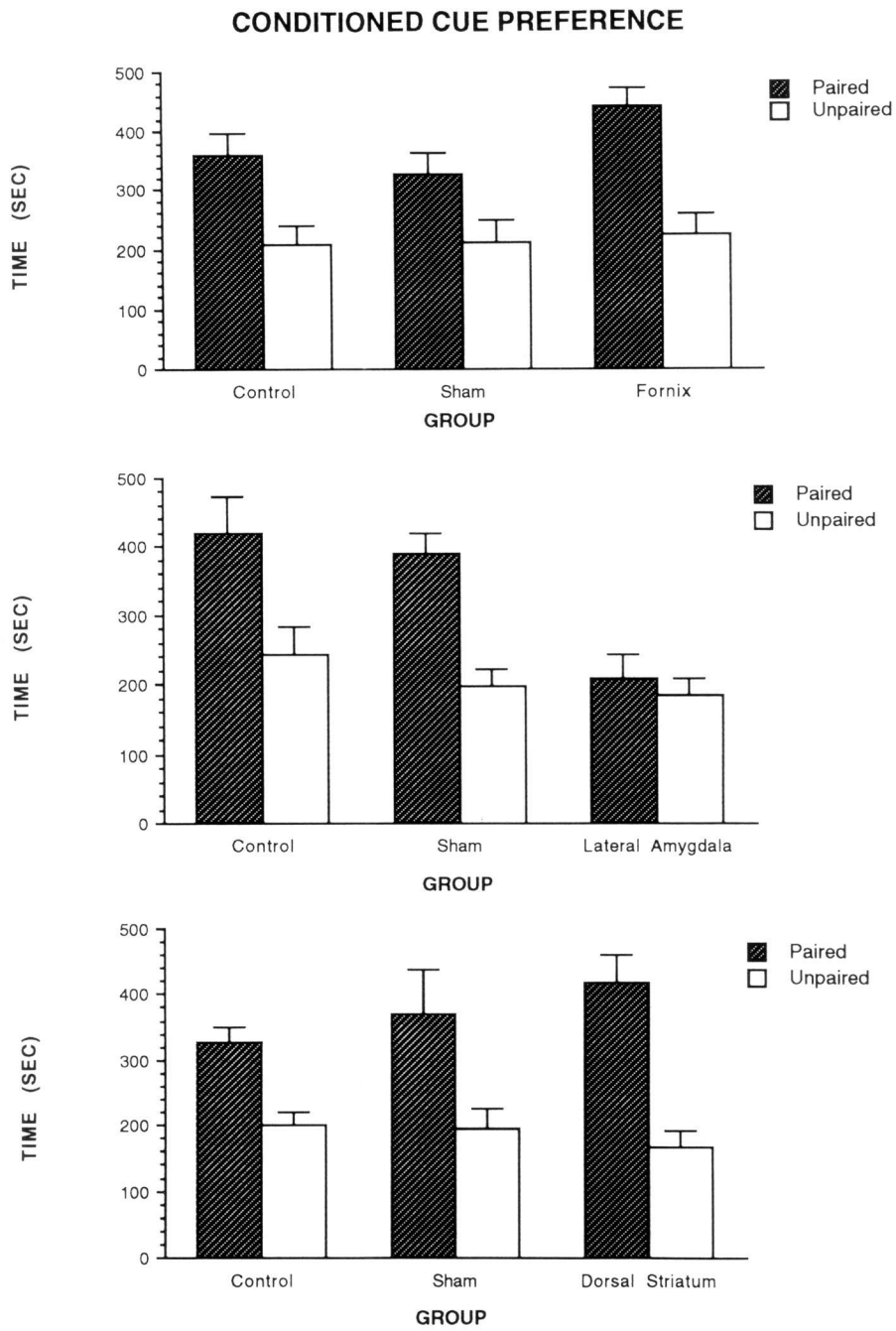

Figure 7. Mean amount of time (±*SE*; in seconds) spent in the paired and unpaired arms by groups of rats with radio-frequency lesions of the fornix (top panel), electrolytic lateral amygdala lesions (middle panel), or electrolytic dorsal striatal lesions (bottom panel) and their respective sham and control groups on the conditioned cue preference task.

Apparatus. The radial maze that was described in the General Method section was used with minor modifications. A system for rebaiting arms was added to the configuration used for the CCP task. Tubes were connected at one end to the food wells of each arm and at the other end to a point outside the enclosure where the experimenter stood. When rebaiting was required, the experimenter merely dropped food pellets into the appropriate tube.

Procedure. All rats were placed on a food-deprivation schedule and handled daily on 4 successive days for 5 min each. Rats were then individually habituated to the radial maze for 5 min each on 2 consecutive days. During this period, the rats were habituated to the food pellets (Noyes' Improved Formula A) in a glass dish that was placed in their home cages. After the habituation procedures, acquisition trials began. On each trial, four randomly selected arms were lit (with the exception that no more than two adjacent arms could be lit), and food was placed in their food wells. The lights in the room were dimmed to increase the salience of the lights in the maze. The rat was then placed, through an opening in the curtains, onto the center

platform, and the curtain was closed. Immediately after a rat left a lit arm having eaten the pellet located there, the well in that arm was rebaited. When the rat retrieved the second pellet from any arm, the light was turned off, and no further food was placed there. After 10 min had elapsed or 8 pellets had been retrieved, the curtain was opened, and the rat was removed from the maze. Records were kept of arms chosen. Entries into unlit arms were scored as errors. Choice accuracy (mean percentage of correct choices) was calculated by dividing the number of correct choices (always 8) by the total number of choices and multiplying this quotient by 100. The trials were run once a day until the control animals reached a choice accuracy of 80% or higher on 2 consecutive days.

Results

The effects of fornix lesions on this task are shown in the top panel of Figure 8. The data are presented in blocks of two. The rats with damage to the fornix ($n = 7$) acquired the win–stay task at a faster rate than did the sham ($n = 6$) and control ($n = 7$) rats, but eventually all groups reached similar levels of performance. An ANOVA with repeated measures computed on choice accuracy revealed a significant main effect of group, $F(2, 17) = 3.8, p > .04$, a significant effect of trial, $F(11, 187) = 46.4, p < .0001$, and no significant interaction between group and trial, $F(22, 187) = 1.6, p > .5$. Post hoc tests using Scheffe's method revealed, on the sixth and seventh trial blocks, significant differences between the lesion and sham groups (Fs = 5.0 and 6.2, respectively, ps $< .05$) and between lesion and control groups (Fs = 4.8 and 7.2, respectively, ps $< .05$. There was no significant difference between the sham and control groups on either of these trial blocks (Fs = 0.02 and 0.01, respectively, ps $< .05$).

The effects of amygdaloid lesions on this task are shown in the middle panel of Figure 8. Lesions of the lateral nucleus of the amygdala ($n = 8$) had no effect on acquisition of the win–stay task. The control group ($n = 7$) acquired the win–stay task at similar rates. An ANOVA with repeated measures computed on choice accuracy indicated no significant main effect of group, $F(1, 13) = .04, p > .8$, a significant effect of trial block, $F(23, 299) = 16.8, p < .0001$, and no significant interaction between group and trial block, $F(23,299) = 1.5, p > .05$.

The bottom panel of Figure 8 shows that compared with sham ($n = 7$) and control ($n = 7$) rats, the rats with damage to the dorsal striatum ($n = 7$) were impaired on the win–stay task. An ANOVA with repeated measures computed on choice accuracy indicated a significant main effect of group, $F(2, 18) = 10.4, p < .001$, a significant effect of trial block, $F(10, 180) = 44.3, p < .0001$, and a significant interaction effect between group and trial block, $F(20, 180) = 3.2, p < .0001$. Post hoc tests using Scheffe's method revealed, on the last trial of acquisition, significant differences between the lesion and sham groups ($F = 11.92, p < .05$) and between the lesion and control groups ($F = 10.37, p < .05$). There was no significant difference between the sham and control groups ($F = .02, p < .05$).

Discussion

Rats with damage to the fornix–fimbria were able to acquire this simple stimulus–response task. In fact, the lesions accelerated the rats' acquisition of the win–stay task. This result is consistent with Packard et al.'s (1989) finding that fornix lesions improve performance on the win–stay task. Improved acquisition after fornix lesions is commonly found on tasks that have a simple associative solution (Eichenbaum et al., in press; Hirsh, 1974; O'Keefe & Nadel, 1978; Sutherland & Rudy, 1989). Similar enhancement effects have been found in rats with fornix lesions on a variety of tasks including two-lever alternation (Jackson & Strong, 1969), single-lever go–no go alternation (Means, Walker, & Isaacson, 1970; Walker, Means, & Isaacson, 1970), brightness discriminations (Harley, 1972), single-cue guided alternation (Stevens & Cowey, 1972), cued radial maze performance (Winocur, 1980), olfactory discrimination reversal (Eichenbaum, Fagan, & Cohen, 1986; Fagan & Olton, 1988), two-way passive avoidance (Tonkiss, Feldon, & Rawlins, 1990), successive cue go–no go olfactory discrimination (Eichenbaum, Fagan, Matthews, & Cohen, 1988), and autoshaping of an operant response (Nanry, Mundy, & Tilson, 1989).

Damage to the lateral nucleus of the amygdala appeared to have no effect on acquisition of the win–stay task. This result is consistent with a large number of investigations demonstrating that an intact amygdala is not necessary for the acquisition of appetitive tasks that have a stimulus–response contingency during training (Eichenbaum et al., 1986; Goddard, 1964; Kemble & Beckman, 1970; Kentridge et al., 1991; Pellegrino, 1968; Schwartzbaum, 1960; Slotnick, 1985). Taken together with these findings, the present result clearly suggests that the lateral amygdala is not necessary for the acquisition of such simple stimulus–response tasks.

Rats with large electrolytic lesions of the dorsal striatum were impaired on acquisition of the win–stay task. This result is consistent with Packard et al.'s (1989) finding that an intact dorsal striatum is necessary for normal acquisition of the win–stay task in the radial arm maze. The present result is also consistent with those of a large number of other experiments on the role of the dorsal striatum in the acquisition of simple stimulus–response tasks (Allen et al., 1972; Allen & Davison, 1973; Chorover & Gross, 1963; Colombo, Davis, & Volpe, 1989; Green et al., 1967; Gross et al., 1965; Hannon & Bader, 1974; Kirkby & Polgar, 1974; Kirkby et al., 1981; Neill & Grossman, 1971; Packard & White, 1991; Potegal, 1969; Prado-Alcala et al., 1975; Viaud & White, 1989; Winocur, 1974).

Experiment 4: Neurotoxic Lesions

Materials and Method

Subjects For each lesion type, 26 rats were randomly assigned to one of three groups: lesion ($n = 10$), sham ($n = 8$), or control ($n = 8$).

Apparatus and procedure. The apparatus and procedures for each of the three tasks and lesions were identical to those described in Experiments 1–3.

Results

Win–shift: Hippocampus. The top panel of Figure 9 shows that rats in the sham and control groups quickly learned to avoid reentering arms in which food had been obtained within

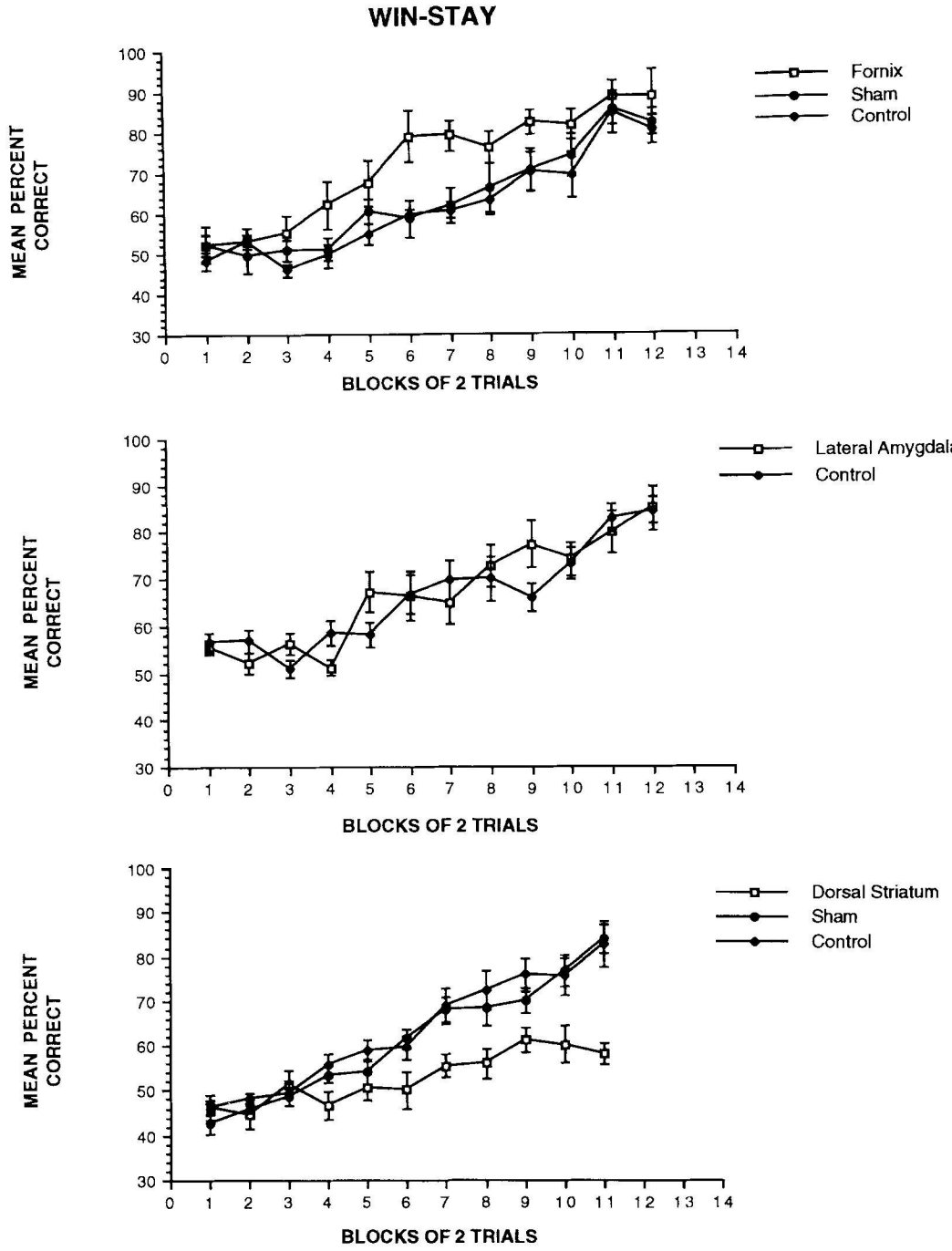

Figure 8. Mean percentage of lit arms (±*SE*) chosen by groups of rats with radio-frequency lesions of the fornix (top panel), electrolytic lateral amygdala lesions (middle panel), or electrolytic dorsal striatal lesions (bottom panel) and their respective sham and control groups on acquisition of the win–stay task (blocks of 2 days).

that trial. The rats in the hippocampal group (n = 8) made considerably more errors than did the rats in the control and sham groups. An ANOVA with repeated measures computed on the error measure indicated that there was a significant main effect of group, $F(2, 20) = 62.3, p < .0001$, a significant effect of trial, $F(9, 180) = 9.21, p < .0001$, and a significant interaction between group and trial, $F(18, 180) = 2.73, p < .001$.

The results of this experiment demonstrate that intrinsic neurons of the hippocampus are necessary for the acquisition of the win–shift version of the radial maze task.

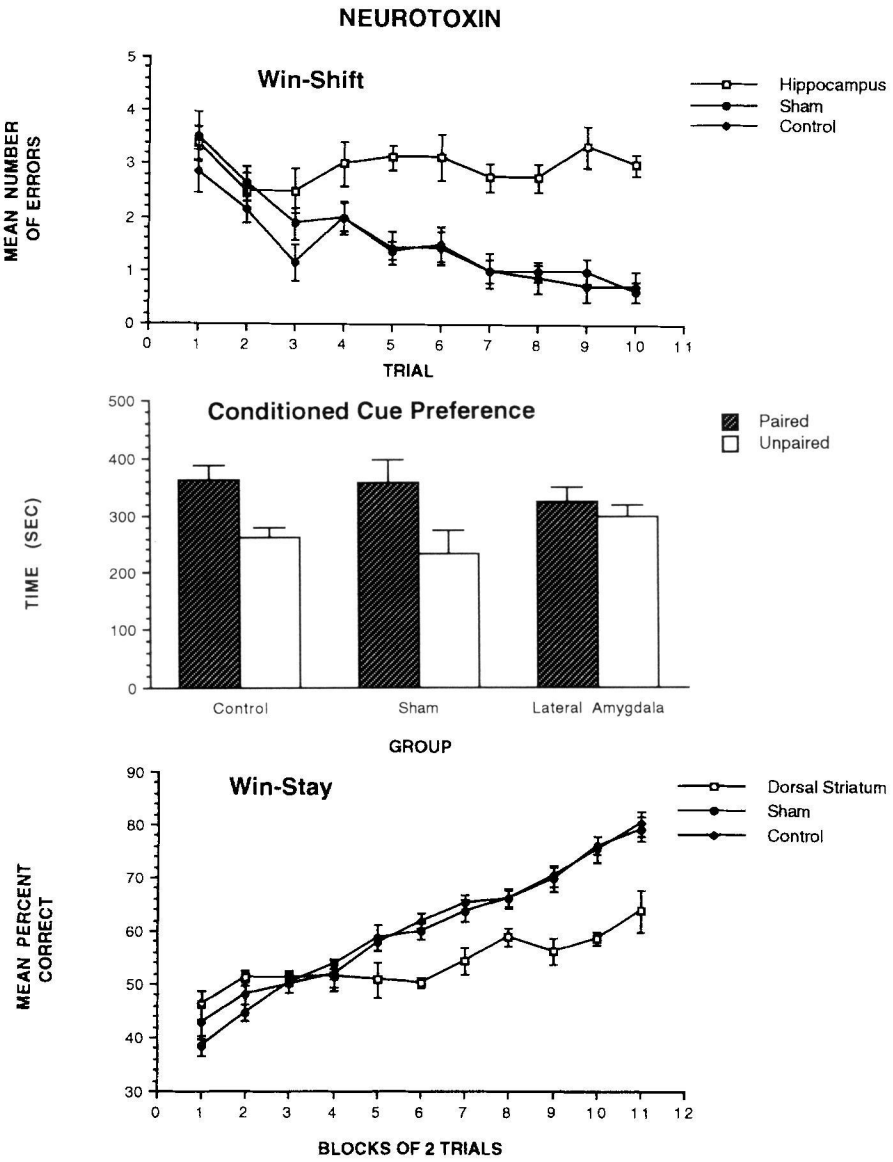

Figure 9. Mean number of errors (±*SE*) made by groups of rats with neurotoxic damage (colchicine + kainic acid) to the hippocampus, by groups of rats with sham lesions, or by groups of unoperated controls on acquisition of the win–shift task (top panel); mean amount of time (±*SE*; in seconds) spent in the paired and unpaired arms by groups of rats with neurotoxic damage (*N*-methyl-D-aspartate [NMDA]) directed at the lateral nucleus of the amygdala, by groups of rats with sham lesions, or by groups of unoperated controls on the conditioned cue preference (middle panel); mean percentage of lit arms chosen (±*SE*) by groups of rats with neurotoxic damage (NMDA) of the dorsal striatum, by groups of rats with sham lesions, or by groups of unoperated controls on acquisition of the win–stay task (bottom panel).

CCP: Amygdala. The results of this experiment are shown in the middle panel of Figure 9. The sham and control groups acquired a CCP, whereas neurotoxic damage to the lateral nucleus of the amygdala (n = 8) disrupted acquisition of the CCP. An ANOVA with repeated measures and a planned comparison revealed significant differences in time spent in the two arms for the sham, $F(2, 21) = 8.99, p < .01$, and control groups, $F(2, 21) = 5.7, p < .05$. There was no significant difference between the time spent in the paired and unpaired arms for the lesion group, $F(2, 21) = 0.4, p < .05$.

The results of this experiment demonstrate that intrinsic neurons of the lateral nucleus of the amygdala are necessary for the acquisition or expression (or both) of a CCP based on an association between food and a visual stimulus.

Win–stay: Dorsal striatum. The bottom panel of Figure 9 shows that compared with sham (n = 8) and control (n = 8) rats, the rats with neurotoxic damage to the dorsal striatum (n = 6) were impaired on the win–stay task. An ANOVA with repeated measures computed on the choice accuracy measure indicated a significant main effect of group, $F(2, 19) = 19.0$,

$p < .0001$, a significant effect of trial block, $F(10, 190) = 75.4$, $p < .0001$, and a significant interaction between group and trial block, $F(20, 190) = 4.8$, $p < .0001$. Post hoc tests using Scheffe's method revealed, on the last trial of acquisition, significant differences between the lesion and sham groups ($F = 7.28$, $p < .01$) and between the lesion and control groups ($F = 7.82$, $p < .01$). There was no significant difference between the sham and control groups on this trial block ($F = .01$, $p < .01$). The results of this experiment demonstrate that neurotoxic lesions of the dorsal striatum impair acquisition of the win–stay task.

This result suggests that intrinsic neurons of the dorsal striatum are necessary for the acquisition of stimulus–response task.

General Discussion

Using a set of three memory tasks developed for the radial arm maze, selective impairments in acquisition after damage to the hippocampal system, the dorsal striatum, or the lateral nucleus of the amygdala were observed. The acquisition rates of rats with radio-frequency-induced fornix damage were (a) severely impaired on the win–shift task, (b) normal on the CCP task, and (c) enhanced on the win–stay task. Rats with neurotoxic damage to the hippocampus exhibited deficits similar to those observed in fornix-damaged rats on acquisition of the win–shift task. The acquisition rates of rats with electrolytic damage to the lateral nucleus of the amygdala were (a) normal on the win–shift task, (b) impaired on the CCP task, and (c) normal on the win–stay task. Rats with neurotoxic damage to the lateral amygdala exhibited deficits similar to those observed in the electrolytic lesion group on acquisition of the CCP task. The acquisition rates of rats with electrolytic damage to the dorsal striatum were (a) normal on the win–shift task, (b) normal on the CCP, and (c) severely impaired on the win–stay task. Rats with neurotoxic damage to the dorsal striatum exhibited deficits similar to those observed in the electrolytic lesion group on acquisition of the win–stay task. This pattern of results represents a triple dissociation of function with respect to three learning tasks.

The triple dissociation suggests that a different neural system mediates learning in each of the three tasks. The fact that all three tasks use the same apparatus, sensory modality of the discriminative stimuli, and similar food reinforcers is good evidence that the specific deficits produced by the three lesions are not due to motor, sensory, or motivational deficits.

The results of the present study do not indicate whether the observed deficits are in acquisition or expression of the learned behavior. However, other evidence suggests that the hippocampus is necessary for both the acquisition and expression of spatial memory, although it should be noted that the dependence on the hippocampus for expression appears to be temporally limited (Sutherland, Arnold, & Rodriguez, 1987; Zola-Morgan & Squire, 1990). The lateral amygdala is also necessary for acquisition and expression of the amphetamine-conditioned place preference (Hiroi & White, 1991). In most previous investigations of the role of the dorsal striatum in mnemonic processes, animals were lesioned before training; therefore, it is difficult to determine whether this structure is necessary for the acquisition or expression (or both) of the win–stay task.

The pattern of impaired and spared performance on the radial maze tasks after damage to a specific brain region suggests that each of the three tasks has some unique feature or features that make it sensitive to the function of the particular neural system that when damaged impaired its acquisition.

Win–Shift Task: Hippocampus

In the win–shift task, each arm contains a food pellet. To obtain these pellets in the most efficient manner possible, a rat must visit each arm once without revisiting any arm. When the radial maze is in a room that contains extramaze cues, normal rats perform this task by remembering the extramaze stimuli associated with each arm and using this information to discriminate visited from unvisited arms (Olton & Collison, 1979; Olton & Samuelson, 1976).

This task cannot be solved in a simple associative manner (Hull, 1943; Rescorla & Wagner, 1972; Spence, 1936; Sutherland & Rudy, 1989). According to associative learning theory, an animal's sensory world is composed of a number of stimulus elements. Experience with these stimuli, including their history of reinforcement contingencies, alters the way an animal responds to them based on increases or decreases in the habit strength of the stimulus–response associations of the individual stimulus elements.

Two features inherent in the design of the win–shift task suggest that it cannot be acquired by a memory system that operates in this manner. First, within a trial, the habit strength of the approach response to a particular arm increases when the animal receives a reinforcer after entering that arm. If a simple associative learning system is guiding a rat's behavior, then the animal should return to the previously visited arms on that trial. The opposite behavior is required for correct win-shift performance. Second, the rat's local view from each arm entrance must contain combinations of visual stimuli, with adjacent arms almost certainly containing common elements. To identify the individual arms, an animal must learn about the relationship of each arm to a particular configuration of stimuli (O'Keefe & Nadel, 1978; Sutherland & Rudy, 1989). Because the configurations associated with adjacent arms contain common elements, animals must learn at least two different responses to these elements, a requirement that violates the basic assumption of associative learning that each stimulus can be associated with only a single response. In line with this assumption, when each arm of the eight-arm radial maze was distinguishable by a single cue, rats with damage to the hippocampal system were not impaired on the radial maze task (Jarrard, 1983; Nadel & McDonald, 1980; Rasmussen et al., 1989; Winocur, 1980). In contrast, evidence suggests that it is the fact that the rat must use information about the relationships among stimuli that makes the win–shift task sensitive to hippocampal damage (Barnes, 1988).

The results of the present study support this hypothesis and also suggest that, no matter what their functions are, the amygdala and dorsal striatum are not necessary for accurate performance on a task that requires the use of spatial relation-

ships to guide behavior (Becker et al., 1980; Packard et al., 1989; Parkinson et al., 1988; Sutherland & McDonald, 1990).

CCP: Amygdala

The CCP task assesses a rat's preference for two distinct cues after it has had previous experience with those cues in the presence or absence of a primary reward. In the present version of the CCP experiment, a visual cue acquired the ability to attract a rat in the absence of the reward.

The CCP differs from the win–shift task in that the item to be remembered is a single element instead of a configuration of stimuli. The CCP differs from the win–stay task in that the former has no response–reinforcer contingency. The rat is allowed to consume the food in the presence of a neutral stimulus without making approach responses toward the stimulus. For the rat to express a CCP, it must associate the sensory cue with the stimulus properties of the food (e.g., taste, smell) or the internal consequences of consumption of the food. In either case, this can be described as a "stimulus–reward" association (Cador et al., 1989; Everitt et al., 1989; Gaffan & Harrison, 1987; Hiroi & White, 1991). This type of learning has also been referred to as "conditioned reinforcement" (Jones & Mishkin, 1972), but in the present context, a more accurate term would be "conditioned reward."

The results of the present study provide evidence that intrinsic neurons of lateral nucleus of the amygdala are critical for the formation or expression of conditioned reward. The data also suggest that neither the hippocampal system nor the dorsal striatum is necessary for the acquisition of this type of association.

Similar effects of amygdaloid lesions have been previously reported (Everitt et al., 1991; Hiroi & White, 1991; Jones & Mishkin, 1972; Kentridge at al., 1991; Peinado-Manzano, 1989). It has also been suggested that simple stimulus–reward associations are left intact in animals with amygdaloid damage and that only second-order conditioning is disrupted by these lesions (Cador et al., 1989; Everitt et al., 1989; Gaffan & Harrison, 1987). In second-order conditioning, a neutral stimulus, because of its previous association with a reward, serves as a conditioned reward in the acquisition of a new behavior.

Given the results of the present study, it is interesting to consider the argument that the amygdala is not involved in simple associations in appetitive situations (Cador et al., 1989; Cahill & McGaugh, 1990; Everitt et al., 1989; Gaffan & Harrison, 1987). The lack of effect of amygdaloid lesions in some of these studies may be due to two factors. First, in some studies, the lesions may not have included the critical lateral nucleus (Hiroi & White, 1991). Second, in some experimental situations, it may have been possible to learn the particular task used by acquiring relationships of a type other than conditioned reward (e.g., relational information–reward or reinforced stimulus–response contingencies). According to the present multiple parallel memory systems hypothesis, in the presence of a nonfunctional amygdala, these tasks could have been learned by one of the other systems. Even animals with an appropriate amygdaloid lesion might not be impaired on such tasks. For example, if a first-order conditioning procedure has both a stimulus–response contingency and a stimulus–reward contingency, then either the amygdala or the dorsal striatum could acquire the information required for accurate performance.

In the second-order conditioning procedure, a neutral stimulus is associated with a conditioned reward but not with the primary reward. According to the present hypothesis, this type of learning is dependent on a memory of the stimulus–reward contingency and thus on an intact amygdala. Any other form of memory, such as a stimulus–response contingency, that might have allowed normal performance on the first-order conditioning task would not include the type of information necessary to involve the neural mechanisms of second-order conditioning.

Win–Stay Task: Dorsal Striatum

In the win–stay task, only arms that are lit contain food pellets. Rats are required to enter each baited arm twice per trial, thereby receiving a total of eight pellets. The rat receives a reinforcer every time it completes a specific stimulus (light)–response (approach) sequence. An important feature of the win–stay task is that the rat must enter lit arms regardless of their locations in space. Because a different set of arms is lit on each trial, attempting to use relationships among cues to identify the baited arms will impair performance on the win–stay task. However, this task can be learned in a simple associative manner. The habit strength of the light–approach association is repeatedly increased by reinforcement, whereas the habit strength of the dark–approach association is theoretically weakened by lack of reinforcement. Over many trials, a rat's tendency to approach lit arms increases until the rat almost exclusively enters lit arms.

The present study provides evidence that intrinsic neurons of the dorsal striatum are critical for the acquisition of the win–stay task. This is consistent with similar deficits found in rats with dorsal striatal damage on other tasks consisting primarily of a reinforced stimulus–response contingency (Cook & Kesner, 1988; Packard et al., 1989; Potegal, 1969; Schwartzbaum & Donovick, 1968).

The results of the present study also suggest that the hippocampus and amygdala are not necessary for the acquisition of a reinforced stimulus–response task (Cook & Kesner, 1988; Eichenbaum et al., 1989; Packard et al., 1989; Potegal, 1969).

The enhancement in acquisition rates found in rats with hippocampal system damage on the win–stay task is also consistent with other reports (Eichenbaum et al., 1986, 1989; Fagan & Olton, 1988; Harley, 1972; Jackson & Strong, 1969; Means et al., 1970; Stevens & Cowey, 1972; Tonkiss et al., 1990; Walker et al., 1970). This enhancement effect suggests that in the normal rat the hippocampal system may interfere with learning about simple stimulus–response contingencies. It may be that the hippocampal system is dominant in the mammalian brain and has the ability to somehow inhibit the other systems (O'Keefe & Nadel, 1978; Sutherland & Rudy, 1989). This may be because the hippocampal system acquires information more rapidly than the other memory systems and is therefore able to influence ongoing behavior as it occurs, in

an "on-line" manner. If the hippocampal system processes information that is irrelevant to a particular task (e.g., learning irrelevant spatial information in the win–stay task), then this processing may interfere with correct performance of the task. Damage to the hippocampal system would remove this interference with performance of the correct response as it is acquired by the dorsal striatal associative system.

Support for this hypothesis comes from an experiment in which a radial maze was placed in a relatively homogeneous environment to discourage the rats from attending to extramaze cues. Normal rats attained correct performance on the win–stay task faster than when the extramaze cues were present (Packard, 1987). Thus, the effect of removal of the information thought to be used by the hippocampal system was essentially similar to the effect of a lesion of the hippocampal system on acquisition of the win–stay task.

Differences in Reinforcer Function

The food reinforcer was common to all three memory tasks, so it is interesting to examine the implications of our hypotheses for its role in the types of learning thought to be mediated in each of the three memory systems.

In the win–shift task, the hippocampal memory system treats the food as one of many stimulus elements in the situation and on each trial learns about its unique relationship to the spatial and other elements of the situation. Knowledge about the presence or absence of food in the arms is a critical feature of the task because this differentiates among the visited and unvisited arms.

In the CCP task, the lateral amygdala may acquire information about the food through projections it receives from areas of the brain representing unconditioned responses to the food (Bystrzycka & Nail, 1985; De Olmos, Alheid, & Beltramino, 1985). This may include information about the magnitude and quality (taste, smell) of the food based on the size of the unconditioned response (its rewarding properties). This information converges with sensory information that the amygdala receives from areas of the brain representing the stimulus features of the environment (De Olmos et al., 1985). So the amygdala acquires information about the relationships between neutral stimuli and the rewarding properties of stimuli that have them.

In the win–stay task, the dorsal striatum acquires no information about the food. Rather, the food acts to reinforce or strengthen the stimulus–response association involving approach to the lit arm. The consumption of food following performance of a specific stimulus–response sequence acts to "stamp in" (Thorndike, 1898) the association between the stimulus and the response. This association may be represented in the dorsal striatum. Any stimulus–response sequences (such as approaching dark arms) that are not followed by consumption of food are not reinforced and are therefore (theoretically) weakened.

Interactions Among Memory Systems

If the three suggested memory systems work in parallel in intact animals, then it is interesting to consider how they might interact to influence behavior. Our analysis suggests that it is the demands of the tasks that make them sensitive to particular memory systems. Three major types of interactions could occur and depend on the demands of particular tasks; for descriptive purposes, we can define these in terms of three major types of tasks. Tasks in category A fit precisely the mnemonic function of a single system, and the other systems may interfere with or have no influence on the acquisition of category A tasks. Tasks in category B can be acquired by more than one of the memory systems, with each system acting alone. Tasks in category C may require the function of two or more of the systems for accurate performance.

According to this scheme, each of the three tasks used in the present study belong to category A. The fact that each was impaired by only one of the three lesions suggests that each could be acquired by only one of the three hypothesized memory systems that we studied. This makes them good representatives of the types of tasks that can be acquired by each system and allows the formation of hypotheses about the types of memory mediated by each system.

Another example of a category A hippocampal system task is a configural association task developed for a Y maze (Sutherland et al., 1989). In this task, rats chose between black and white goal arms regardless of their spatial locations. When the start box was illuminated, the white arm contained food; when the start box was dark, food was in the black arm. Rats with damage to the hippocampal formation were impaired in acquiring this task. Because both the white and black boxes were reinforced 50% of the time, there were no stimulus–response or stimulus–reward contingencies that could support accurate performance on this task.

Kemble and Beckman (1970) used a runway task that might be an example of a category B task. Rats were placed in a start box and allowed to traverse a straight runway to a goal box that contained food. Normal rats quickly learned to run to the goal box. Kemble and Beckman reported that rats with damage to the amygdala were impaired at the initial phases of acquisition on this task compared with controls. However, this impairment was temporary; after a number of trials, the performance of the lesioned animals was indistinguishable from that of control rats.

According to the present hypothesis, this task could have been acquired by either the amygdaloid or dorsal striatal memory systems. The amygdaloid memory system could have learned that the stimulus features of the box were associated with the rewarding properties of the food. Because of the rapid acquisition properties of this system (LeDoux et al., 1990), the behavior was acquired in relatively few trials. The dorsal striatal system could acquire a response tendency associated with some feature of the maze. However, because the dorsal striatal system requires that the stimulus–response association be reinforced repeatedly before it becomes a behavioral tendency, numerous postlesion trials were required before this system could influence behavior.

According to the present analysis, another possible category B task would be a conditional task identical to the previously described Y-maze experiment except that the goal boxes remain in the same positions throughout training. This "conditional task" has both a configural and simple associative

solution. A simple stimulus–response contingency (lit start box, left turn; dark start box, right turn) exists in this paradigm that would allow a rat with hippocampal damage to solve this task, further suggesting that the dorsal striatum would also be able to acquire it. According to our analysis, it is not surprising that rats with hippocampal damage (Winocur, 1991) are not impaired at these "conditional discrimination" tasks.

An example of a category C task may be the negative patterning paradigm (Rudy & Sutherland, 1989; Sutherland & McDonald, 1990; Woodbury, 1943). The task consists of random presentations of a tone that is always reinforced (T+), a light cue that is always reinforced (L+), and a compound that is never reinforced (TL−). Normal rats learn to barpress for food during presentations of the single elements and withhold responding during presentations of the compound. Hippocampal lesions impair the animals' ability to withhold responding to the compound but have no effect on their ability to learn to respond to the single elements. Although the experiment has not been done, it seems likely that lesions of the dorsal striatum would impair responding to the elements, further suggesting that acquisition of the negative patterning task involves at least two memory systems acting together.

Conclusion

The current experiments emphasize (a) the dissociable functions of the hippocampus, amygdala, and the dorsal striatum in memory tasks; (b) the importance of the hippocampus to memory tasks that require information about the relationships among stimuli; (c) the importance of the lateral nucleus of the amygdala in memory tasks that require information about stimulus–reward contingencies in the absence of a response; (d) the importance of the dorsal striatum to memory tasks that require reinforced stimulus–response associations; and (e) the importance, in studies of the neural basis of learning and memory, of the use of tasks that are selectively sensitive to the function of the structure under investigation. The present data suggest that this can be done by understanding the various contingencies available to an animal in a given learning situation. If it is true that there are multiple memory systems in the mammalian nervous system and that they work in parallel, then animals can learn various things simultaneously about a particular situation, and information in these various modules (Nadel & Wexler, 1985) may all be capable of producing accurate behavior in different ways.

References

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.

Allen, J. D., & Davison, C. S. (1973). Effects of caudate lesions on signalled and non-signalled Sidman avoidance in the rat. *Behavioral Biology, 8,* 239–250.

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

Alvarado, M., & Rudy, J. W. (1989). The transverse patterning problem: Configural processing in the hippocampal formation. *Society for Neuroscience Abstracts, 15,* 610.

Bagshaw, M. H., & Benzies, S. (1968). Multiple measures of the orienting reaction 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.

Baylis, L. L., & Gaffan, D. (1991). Amygdalectomy and ventromedial prefrontal ablation produce similar deficits in food choice and in simple object discrimination learning for an unseen reward. *Experimental Brain Research, 86,* 617–622.

Becker, J. T., Walker, J. A., & Olton, D. S. (1980). Neuroanatomical basis of spatial memory. *Brain Research, 200,* 307–320.

Best, P. J., & Orr, T. (1973). Effects of hippocampal lesions on passive avoidance and taste aversion conditioning. *Physiology and Behavior, 10,* 193–196.

Black, A. H., Nadel, L., & O'Keefe, J. (1977). Hippocampal function in avoidance learning and punishment. *Psychological Bulletin, 84,* 1107–1129.

Blanchard, D. C., & Blanchard, R. J. (1972). Innate and conditioned reactions to threat in rats with amygdaloid lesions. *Journal of Comparative and Physiological Psychology, 81,* 281–290.

Blanchard, R. J., Blanchard, C. D., & Fial, R. A. (1970). Hippocampal lesions in rats and their effect on activity, avoidance, and aggression. *Journal of Comparative and Physiological Psychology, 72,* 92–102.

Bouffard, J. P., & Jarrard, L. E. (1988). Acquisition of a complex place task in rats with selective ibotenate lesions of hippocampal formation: Combined lesions of subiculum and entorhinal cortex versus hippocampus. *Behavioral Neuroscience, 102,* 828–834.

Bresnahan, E., & Routtenberg, A. (1972). Memory disruption by unilateral low level sub-seizure stimulation of the medial amygdaloid nucleus. *Physiology and Behavior, 9,* 513–525.

Brown, S., & Schaeffer, E. A. (1888). An investigation into the functions of the occipital and temporal lobes of the monkey's brain [abstract]. *Philosophical Transactions of the Royal Society of London. Series B. Biological Sciences, 179,* 303–327.

Bruner, J. S. (1969). Modalities of memory. In G. A. Talland & N. C. Waugh (Eds.), *Pathology of memory* (pp. 253–259). San Diego, CA: Academic Press.

Bystrzycka, E. K., & Nail, B. S. (1985). Brain stem nuclei associated with respiratory, cardiovascular and other autonomic functions. In G. Paxinos (Ed.), *The rat nervous system: Volume 2. Hindbrain and spinal cord* (pp. 95–110). San Diego, CA: Academic Press.

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.

Cahill, L., & McGaugh, J. L. (1990). Amygdaloid complex lesions differentially affect retention of tasks using appetitive and aversive reinforcement. *Behavioral Neuroscience, 104,* 532–543.

Chorover, S. L., & Gross, C. G. (1963). Caudate nucleus lesions: Behavioral effects in rats. *Science, 141,* 826–827.

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

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

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 and Neural Biology, 49,* 332–343.

Cormier, S. M. (1981). A match-mismatch theory of limbic system function. *Physiological Psychology, 9,* 3–36.

Dafters, R. I. (1976). Effect of medial archistriatal lesions on the conditioned emotional response and on auditory discrimination performance of the pigeon. *Physiology and Behavior, 17,* 659–665.

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

Davis, M., Gendelman, D. S., Tischler, M. D., & Gendelman, P. M. (1982). A primary acoustic startle circuit: Lesion and stimulation studies. *Journal of Neuroscience, 6,* 791–805.

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

Douglas, R. J. (1967). The hippocampus and behavior. *Psychological Bulletin, 67,* 416–442.

Dunn, L. T., & Everitt, B. J. (1988). Double dissociation of the effects of amygdala and insular cortex lesions on conditioned taste aversion, passive avoidance, and neophobia in the rat using the excitotoxin ibotenic acid. *Behavioral Neuroscience, 102,* 3–23.

Eichenbaum, H., Cohen, N. J., Otto, T., & Wible, C. (in press). Memory representation in the hippocampus: Functional domain and functional organization. In L. R. Squire, G. Lynch, N. M. Weinberger, & J. L. McGaugh (Eds.), *Memory organization and locus of change. London: Oxford University Press.*

Eichenbaum, H., Fagan, A., & Cohen, N. J. (1986). Normal olfactory discrimination learning set and facilitation of reversal learning after medial-temporal damage in rats: Implications for an account of preserved learning in amnesia. *Journal of Neuroscience, 6,* 1876–1884.

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., Matthews, P., & Cohen, N. J. (1989). Further studies of hippocampal representation during odor discrimination learning. *Behavioral Neuroscience, 103,* 1207–1216.

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.

Fagan, A. M., & Olton, D. S. (1988). Learning sets, discrimination reversal, and hippocampal function. *Behavioural Brain Research, 21,* 13–20.

Fitzgerald, R. E., & Burton, M. J. (1981). Effects of small basolateral amygdaloid lesions on ingestion in the rat. *Physiology and Behavior, 27,* 431–437.

Flaherty, C. F., Rowan, G. A., Emerich, D. F., & Walsh, T. J. (1989) Effects of intrahippocampal administration of colchicine on incentive contrast and on radial maze performance. *Behavioral Neuroscience, 103,* 319–328.

Gabriel, M., Foster, K., Orona, E., Saltwick, S. E., & Stanton, M. (1980). Neuronal activity of cingulate cortex, anteroventral thalamus, and hippocampal formation in discriminative conditioning: Encoding and extraction of the significance of conditional stimuli. *Progress in Psychobiology and Psychology, 9,* 125–231.

Gaffan, D. (1974). Recognition impaired and association intact in the memory of monkeys after transection of the fornix. *Journal of Comparative and Physiological Psychology, 86,* 1100–1109.

Gaffan, D., Gaffan, E. A., & Harrison, S. (1989). Visual–visual associative learning and reward-association learning in monkeys: The role of the amygdala. *Journal of Neuroscience, 9,* 558–564.

Gaffan, D., & Harrison, S. (1987). Amygdalectomy and disconnection in visual learning for auditory secondary reinforcement by monkeys. *Journal of Neuroscience, 7,* 2285–2292.

Gallagher, M., Graham, P. W., & Holland, P. C. (1990). The amygdala central nucleus and appetitive pavlovian conditioning: Lesions impair one class of conditioned behavior. *Journal of Neuroscience, 10,* 1906–1911.

Goddard, G. V. (1964). Functions of the amygdala. *Psychological Bulletin, 62,* 89–109.

Good, M., & Honey, R. C. (1991). Conditioning and contextual retrieval in hippocampal rats. *Behavioral Neuroscience, 105,* 499–509.

Goomas, D. T., & Steele, M. K. (1980). The collapse effect and delay of reinforcement with amygdalectomized rats. *Physiological Psychology, 8,* 463–466.

Graf, P., Mandler, G., & Haden, P. E. (1982). Simulating amnesic symptoms in normal subjects. *Science, 218,* 1243–1244.

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

Gross, C. G., Chorover, S. L., & Cohen, S. M. (1965). Caudate, cortical, hippocampal, and dorsal thalamic lesions in rats: Alternation and Hebb-Williams maze performance. *Neuropsychologia, 3,* 53–68.

Hannon, R., & Bader, A. (1974). A comparison of frontal pole, anterior median and caudate nucleus lesions in the rat. *Physiology and Behavior, 13,* 513–521.

Harley, C. W. (1972). Hippocampal lesions and two cue discrimination in the rat. *Physiology and Behavior, 9,* 343–348.

Harley, C. W. (1979). Arm choices in a sunburst maze: Effects of hippocampectomy in the rat. *Physiology and Behavior, 23,* 283–290.

Henke, P. G., Allen, J. D., & Davison, C. (1972). Effects of lesions in the amygdala on behavioral contrast. *Physiology and Behavior, 8,* 173–176.

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

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

Hirst, W. (1982). The amnesic syndrome: Descriptions and explanations. *Psychological Bulletin, 91,* 435–460.

Horvath, F. E. (1963). Effects of basolateral amygdalectomy on three types of avoidance in cats. *Journal of Comparative and Physiological Psychology, 56,* 380–389.

Hsaio, S., & Isaacson, R. L. (1971). Learning of food and water position by hippocampus damaged rats. *Physiology and Behavior, 6,* 81–83.

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

Huppert, F. A., & Piercy, M. (1976). Recognition memory in amnesic patients: Effect of temporal context and familiarity of material. *Cortex, 12,* 3–20.

Isaacson, R. L., Douglas, R. J., & Moore, R. Y. (1961). The effect of radical hippocampal ablation on acquisition of avoidance response. *Journal of Comparative and Physiological Psychology, 54,* 625–635.

Jackson, W. J., & Strong, P. N. (1969). Differential effects of hippocampal lesions upon sequential tasks and maze learning by the rat. *Journal of Comparative and Physiological Psychology, 68,* 442–450.

Jarrard, L. E. (1983). Selective hippocampal lesions and behavior: Effects of kainic acid lesions on performance of place and cue tasks. *Behavioral Neuroscience, 97,* 873–889.

Jarrard, L. E., Okaichi, H., Goldschmidt, R., & Stewart, O. (1984). On the role of the hippocampus connections in the performance of place and cue tasks: Comparison with damage to the hippocampus. *Behavioral Neuroscience, 98,* 946–954.

Jellestad, F. K., Markowska, A., Bakke, H. K., & Walther, B. (1986) Behavioral effects after ibotenic acid, 6-OHDA and electrolytic lesions in the central amygdala nucleus of the rat. *Physiology and Behavior, 37,* 835–862.

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

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

Kaye, H., & Pearce, J. M. (1987). Hippocampal lesions attenuate latent inhibition and the decline of the orienting response in rats. *Quarterly Journal of Experimental Psychology, 39B,* 107–125.

Kemble, E. D., & Beckman, G. J. (1970). Runway performance of rats following amygdaloid lesions. *Physiology and Behavior, 5,* 45–47.

Kemble, E. D., & Tapp, J. T. (1968). Passive and active avoidance performance following small amygdaloid lesions in rats. *Physiology and Behavior, 3,* 713–718.

Kentridge, R. W., Shaw, C., & Aggleton, J. P. (1991). Amygdaloid lesion and stimulus–reward associations in the rat. *Behavioural Brain Research, 42,* 57–66.

Kesner, R. P., & DiMiattia, B. V. (1987). Neurobiology of an attribute model of memory. *Progress in Psychobiology and Physiological Psychology, 12,* 207–277.

Kesner, R. P., & Wilburn, M. W. (1974). A review of electrical stimulation of the brain in context of learning and retention. *Behavioral Biology, 10,* 259–293.

Kimble, D. P. (1963). The effects of bilateral hippocampal lesions in rats. *Journal of Comparative and Physiological Psychology, 56,* 273–283.

Kinsbourne, M., & Wood, F. (1975). Short-term memory processes and the amnesic syndrome. In D. Deutsch & J. A. Deutsch (Eds.), *Short term memory* (pp. 258–291). New York: Wiley.

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.

Kirkby, R. J., Polgar, S., & Coyle, I. R. (1981). Caudate nucleus lesions impair the ability of rats to learn a simple straight-alley task. *Perceptual and Motor Skills, 52,* 499–502.

Kluver, H., & Bucy, P. C. (1939). Preliminary analysis of functions of the temporal lobes in monkeys. *Archives of Neurology and Psychiatry, 42,* 979–1000.

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

Lidsky, A., & Slotnick, B. M. (1970). Electrical stimulation of the hippocampus and electroconvulsive shock produce similar amnestic effects in mice. *Neuropsychologia, 8,* 363–369.

Mahut, H. (1971). Spatial and object learning in monkeys with partial temporal lobe ablations. *Neuropsychologia, 9,* 409–424.

Mahut, H. (1972). A selective spatial deficit in monkeys after transection of the fornix. *Neuropsychologia, 10,* 65–74.

McGleary, P. A. (1966). Response-modulating functions of the limbic system: Initiation and suppression. *Progress in Physiological Psychology, 77,* 171–178.

Means, L. W., Walker, D. W., & Isaacson, R. L. (1970). Facilitated single-alternation go/no go acquisition following hippocampectomy in the rat. *Journal of Comparative and Physiological Psychology, 72,* 278–285.

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

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.

Nachman, M., & Ashe, J. H. (1974). Effects of bilateral amygdala lesions on neophobia, learned taste aversions, and sodium appetite in rats. *Journal of Comparative and Physiological Psychology, 80,* 622–643.

Nadel, L., & McDonald, L. (1980). Hippocampus: Cognitive map or working memory? *Behavioral and Neural Biology, 29,* 405–409.

Nadel, L., & Wexler, K. (1985). Neurobiology, representations, and memory. In G. Lynch, J. L. McGaugh, & N. M. Weinberger (Eds.), *Neurobiology of learning and memory* (pp. 125–134). New York: Guilford Press.

Nanry, K. P., Mundy, W. R., & Tilson, H. A. (1989). Colchicine-induced alterations of reference memory in rats: Role of spatial versus non-spatial task components. *Behavioural Brain Research, 35,* 45–53.

Neill, D. B., & Grossman, S. P. (1971). Behavioral effects of lesions or cholinergic blockade of the dorsal and ventral caudate of rats. *Journal of Comparative and Physiological Psychology, 71,* 311–317.

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

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

Okaichi, H. (1987). Performance and dominant strategies on place and cue tasks following hippocampal lesions in rats. *Psychobiology, 15,* 58–63.

Olton, D. S., Becker, J. T., & Handelmann, G. E. (1979). Hippocampus, space, and memory. *Behavioral and Brain Sciences, 2,* 313–365.

Olton, D. S., & Collison, C. (1979). Intra-maze cues and "odor trails" fail to direct choice behavior on an elevated maze. *Animal Learning and Behavior, 7,* 221–223.

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.

Olton, D. S., Walker, J. A., & Gage, F. H. (1978). Hippocampal connections and spatial discrimination. *Brain Research, 139,* 295–308.

Packard, M. G. (1987). *Differential roles of hippocampus and caudate nucleus in memory: Selective mediation of "cognitive" and "associative" learning.* Unpublished master's thesis, McGill University, Montréal, Québec, Canada.

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

Parkinson, J. K., Murray, E. A., & Mishkin, M. (1988). A selective mnemonic role for the hippocampus in monkeys: Memory for the location of objects. *Journal of Neuroscience, 8,* 4159–4169.

Paxinos, G., & Watson, C. (1982). *The rat brain in stereotaxic coordinates.* San Diego, CA: Academic Press.

Peeke, H. V. S., & Herz, M. J. (1971). Caudate nucleus stimulation retroactively impairs complex maze learning in the rat. *Science, 173,* 80–82.

Peinado-Manzano, A. (1989). Intervention of the lateral and central

amygdala on the association of visual stimuli with different magnitudes of reinforcement. *Behavioural Brain Research, 32,* 289–295.

Pellegrino, L. (1968). Amygdaloid lesions and behavioral inhibition in the rat. *Journal of Comparative and Physiological Psychology, 65,* 483–491.

Potegal, M. (1969). Role of the caudate nucleus in spatial orientation of rats. *Journal of Physiological and Physiological Psychology, 69,* 756–764.

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 and Behavior, 15,* 283–287.

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

Rawlins, J. N. P. (1985). Associations across time: The hippocampus as a temporary memory store. *Behavioral and Brain Sciences, 8,* 479–496.

Rescorla, R. A., & Wagner, A. R. (1972). A theory of Pavlovian conditioning: Variations in the effectiveness of reinforcement and nonreinforcment. In A. H. Black & W. F. Prokasy (Eds.), *Classical conditioning: II. Current research and theory* (pp. 64–99). New York: Appleton-Century-Crofts.

Rickert, E. J., Lorden, J. F., Dawson, R., Smyly, E., & Callahan, M. F. (1979). Stimulus processing and stimulus selection in rats with hippocampal lesions. *Behavioral and Neural Biology, 27,* 454–465.

Ridley, R. M., Aitken, D. M., & Baker, H. F. (1989). Learning about rules but not about reward is impaired following lesions of the cholinergic projection to the hippocampus. *Brain Research, 502,* 306–318.

Rolls, E. T., & Rolls, B. J. (1973). Altered food preferences after lesions in the basolateral region of the amygdala in the rat. *Journal of Comparative Physiological Psychology, 83,* 248–259.

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.

Ryle, G. (1949). *The concept of mind.* San Francisco: Hutchinson.

Sanares, C. B., & Campbell, B. A. (1989). Role of the central nucleus of the amygdala in olfactory heart rate conditioning. *Behavioral Neuroscience, 103,* 519–525.

Saunders, R. C., & Weiskrantz, L. (1989). The effects of fornix transection and combined fornix transection, mamilliary body lesions and hippocampal ablations on object-pair association memory in the rhesus monkey. *Behavioural Brain Research, 35,* 85–94.

Schacter, D., & Tulving, E. (1982). Memory, amnesia, and the episodic/semantic distinction. In R. L. Isaacson & N. E. Spear (Eds.), *The expression of knowledge* (pp. 33–65). New York: Plenum.

Schwartzbaum, J. S. (1960). Changes in reinforcing properties of stimuli following ablation of the amygdaloid complex in monkeys. *Journal of Comparative and Physiological Psychology, 53,* 388–395.

Schwartzbaum, J. S., & Donovick, P. J. (1968). Discrimination reversal and spatial alternation associated with septal and caudate dysfunction in rats. *Journal of Comparative and Physiological Psychology, 65,* 83–92.

Scoville, W. B., & Milner, B. (1957). Loss of recent memory after bilateral hippocampal lesions. *Journal of Neurobiology, 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.

Sherry, D. F., & Vaccarino, A. L. (1989). Hippocampus and memory for food caches in black-capped chickadees. *Behavioral Neurosciences, 103,* 308–318.

Slotnick, B. M. (1973). Fear behavior and passive avoidance deficits in mice with amygdala lesions. *Physiology and Behavior, 11,* 717–720.

Slotnick, B. M. (1985). Olfactory discrimination in rats with anterior amygdala lesions. *Behavioral Neuroscience, 99,* 956–963.

Solomon, P. R., & Moore, J. W. (1975). Latent inhibition and stimulus generalization of the classically conditioned nictitating membrane response in rabbits (*Oryctolagus cuniculus*) following dorsal hippocampal ablation. *Journal of Comparative and Physiological Psychology, 89,* 1192–1203.

Speigler, 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.

Spence, K. W. (1936). The nature of discrimination learning. *Psychological Review, 43,* 427–449.

Spevack, A. A., Campbell, C. T., & Drake, L. (1975). Effect of amygdalectomy on habituation and CER in rats. *Physiology and Behavior, 15,* 199–207.

Squire, L. R. (1987). *Memory and brain.* New York: Oxford University Press.

Stern, L. D. (1981). A review of theories of human amnesia. *Memory and Cognition, 247–262.*

Stevens, R., & Cowey, A. (1972). Enhanced alternation learning in hippocampectomized rats by means of added light cues. *Brain Research, 46,* 1–22.

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

Sutherland, R. J., Arnold, K., & Rodriguez, A. (1987). Anterograde and retrograde effects on place memory after limbic or diencephalic damage. *Society for Neuroscience Abstracts, 13,* 1066.

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. *Behavioural Brain Research, 34,* 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 and Neural Biology, 52,* 331–356.

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 behavioral analysis of spatial localization following electrolytic, kainate, or colchicine-induced damage to the hippocampal formation in the rat. *Behavioural Brain Research, 7,* 133–153.

Thorndike, E. I. (1898). *Animal intelligence: Experimental studies.* New York: Macmillan.

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

Tonkiss, J., Feldon, J., & Rawlins, J. N. P. (1990). Section of the descending columns of the fornix produces delay- and interference-dependent working memory deficits. *Behavioural Brain Research, 36,* 113–126.

Tulving, E. (1972). Episodic and semantic memory. In E. Tulving & W. Donaldson (Eds.), *Organization of memory* (pp. 381–403). San Diego, CA: Academic Press.

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.

Viaud, M. D., & White, N. M. (1989). Dissociation of visual and

olfactory conditioning in the neostriatum of rats. *Behavioural Brain Research, 32,* 31–42.

Walker, D. W., Means, L. W., & Isaacson, R. l. (1970). The effects of hippocampal and cortical lesions on single alternation go/no go acquisition in rats. *Psychonomic Science, 21,* 29–31.

Walker, J. A., & Olton, D. S. (1979). Spatial memory deficit following fimbria/fornix lesions: Independent of time for stimulus processing. *Physiology and Behavior, 23,* 11–15.

Warrington, E. K., & Weiskrantz, L. (1982). Amnesia: A disconnection syndrome? *Neuropsychologia, 20,* 233–248.

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

Wickelgren, W. A. (1979). Chunking and consolidation: A theoretical synthesis of semantic networks, configuring, S-R versus cognitive learning, normal forgetting, the amnesic syndrome, and the hippocampal arousal system. *Psychological Review, 86,* 44–60.

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

Winocur, G. (1980). The hippocampus and cue utilization. *Physiological Psychology, 8,* 280–288.

Winocur, G. (1991). Functional dissociation of the hippocampus and prefrontal cortex in learning and memory. *Psychobiology, 19,* 11–20.

Woodbury, C. B. (1943). The learning of stimulus patterns by dogs. *Journal of Comparative and Physiological Psychology, 35,* 29–40.

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

Zola-Morgan, S., & Squire, L. R. (1990). The primate hippocampal formation: Evidence for a time-limited role in memory storage. *Science, 250,* 288–290.

Zola-Morgan, S., Squire, L. R., Alvarez-Royo, P., & Clower, R. P. (1991). Independence of memory functions and emotional behavior: Separate contributions of the hippocampal formation and the amygdala. *Hippocampus, 1,* 207–220.

Received April 13, 1992
Revision received July 21, 1992
Accepted July 23, 1992 ■