NEUROBIOLOGY OF LEARNING AND MEMORY **65,** 65–72 (1996)
Article No. 0007

Inactivation of Hippocampus or Caudate Nucleus with Lidocaine Differentially Affects Expression of Place and Response Learning

MARK G. PACKARD* AND JAMES L. MCGAUGH†,[1]

**Department of Psychology, University of New Orleans 70148; and †Center for the Neurobiology of Learning and Memory and Department of Psychobiology, University of California, Irvine 92717*

Involvement of the hippocampus and caudate nucleus in place and response learning was examined by functionally inactivating these brain regions bilaterally with infusions of lidocaine. Rats were trained to approach a consistently baited arm in a cross-maze from the same start box (four trials/day/14 total days). On Days 8 and 16 a single probe trial was given, in which rats were placed in the start box opposite that used in training and allowed to approach a maze arm. Three minutes prior to the probe trial, rats received bilateral injections of either saline or a 2% lidocaine solution (in order to produce neural inactivation) into either the dorsal hippocampus or dorsolateral caudate nucleus. On the probe trials, rats which entered the baited maze arm (i.e., approached the *place* where food was located during training) were designated place learners, and rats which entered the unbaited maze arm (i.e., made the same turning *response* as during training) were designated response learners. Saline-treated rats displayed place learning on the Day 8 probe trial and response learning on the Day 16 probe trial, indicating that with extended training there is a shift in learning mechanisms controlling behavior. Rats given lidocaine injections into the hippocampus showed no preference for place or response learning on the Day 8 probe trial, but displayed response learning on the Day 16 probe trial, indicating a blockade of place learning following inactivation of the hippocampus. Rats given lidocaine injections into the caudate nucleus displayed place learning on both the Day 8 and the Day 16 probe trials, indicating a blockade of response learning following inactivation of the caudate nucleus. The findings indicate: (1) the hippocampus and caudate nucleus selectively mediate expression of place and response learning, respectively (2), in a visually cued extramaze environment, hippocampal-dependent place learning is acquired faster than caudate-dependent response learning, and (3) when animals shift to caudate-dependent response learning with extended training, the hippocampal-based place representation remains intact.

INTRODUCTION

Throughout the history of research on animal learning there have been conflicting views concerning the fundamental issue of what animals learn. Cognitive theorists such as Tolman (1932; 1948) proposed that animals acquire knowledge of "what-leads-to-what" that result in expectations of the consequences of their behavior. In contrast, following the pioneering work of Thorndike (1898; 1933) and Pavlov (1927), other theorists proposed that animal learning consists of the formation of stimulus–response (S-R) habits (Hull, 1943; Guthrie, 1935) or, simply, the learning of motor responses.

In experiments addressing this issue, rats were trained in mazes and subsequently tested in a variety of ways in an attempt to discover whether the learning was based on acquisition of knowledge or learning of responses (e.g., Tolman, Ritchie, & Kalish, 1946, 1947; Blodgett & McCutchan, 1947, 1948; Blodgett, McCutchan, & Matthews, 1949; Thompson & Thompson, 1949; Hill & Thune, 1952; Scharlock, 1955). For example, after animals were trained to enter one arm of a T-maze where they were rewarded with food in a goal box, had they learned a *turning response* or, alternatively, had they learned *where* food was located? In order to examine this question, Tolman and colleagues introduced the cross-maze paradigm (Tolman et al., 1946, 1947). The cross-maze is essentially a T-maze built such

[1] This research was supported by NRSA Grant 1 F32NS08973-01 (M.G.P.) and USPHS Grant MH12526 from NIDA and NIMH (J.L.M.). The authors thank Norman White, Norman Wienberger, and Richard Thompson for helpful comments on an earlier version of the manuscript. Address correspondence and reprint requests to Mark G. Packard, Department of Psychology, University of New Orleans, New Orleans, LA 70148.

1074-7427/96 $12.00

that the choice point connecting the two goal boxes (e.g., east–west), can be approached from start boxes located on either side of the maze (e.g., north–south). During an initial training period, animals are placed in the same start box and trained on several trials to obtain a food pellet from the same goal box. Following this training period, a critical probe trial is given in which animals are placed in the start box opposite the one used during training and allowed to approach either goal box. According to *cognitive* theory, animals should approach the goal box which was baited during training, since they acquired information concerning the spatial location of the food reward. Animals displaying this behavior on the probe trial are designated "place learners." In contrast, S-R theory predicts that animals should approach the goal box which was unbaited during training, since they have learned a response tendency (i.e., a specific body turn at the choice point). Animals displaying this behavior are designated "response learners." Although the cross-maze paradigm provides a procedure to contrast cognitive and S-R learning theories, the findings of many experiments using this task were inconclusive. Under some conditions animals indicated knowledge of the location of rewards (i.e., place learning), and under other conditions they made specific body turn responses on the probe trial (for review see Restle, 1957).

Findings indicating that both place and response learning occurred raises the possibility that these two forms of learning might be mediated by distinct neural mechanisms. This hypothesis is consistent with extensive evidence suggesting that different forms of learning and memory are mediated by different neural systems in humans (e.g., Milner, 1962; Corkin, 1965; Weiskrantz & Warrington, 1979; Cohen & Squire, 1980; Schacter, 1992), monkeys (e.g., Gaffan, 1974; Zola-Morgan, Squire, & Mishkin, 1982; Mahut & Moss, 1984), and rats (e.g., Hirsh, 1974; O'Keefe & Nadel, 1978; Olton, Becker, & Handelmann, 1979; Sutherland & Rudy, 1989). Within the context of the debate between cognitive and S-R learning theorists, it has been suggested that the hippocampal system may selectively mediate "cognitive" memory (Hirsh, 1974; Mishkin & Petri, 1984), and that the caudate nucleus may selectively mediate "S-R habit" formation (Mishkin & Petri, 1984; Packard and White, 1987; Packard, Hirsh, & White, 1989). Similarly, Kesner and colleagues hypothesized that the hippocampus selectively mediates allocentric spatial behavior within a "data-based" memory system, while the caudate nucleus selectively mediates egocentric learning within an "expectancy-based" memory system (Kesner & DiMattia, 1987).

Findings of double dissociations of the effects of brain lesions and intracerebral drug treatments on memory strongly support the hypothesis that the hippocampal system and caudate nucleus mediate different forms of memory. Lesions of the hippocampal system (Packard, Hirsh, & White, 1989; Packard & McGaugh, 1992; McDonald & White, 1993; Kesner, Bolland, & Dakis, 1993), and posttraining injections of drugs into the hippocampus (Packard & White, 1991; Packard, Cahill, & McGaugh, 1994), alter cognitive learning but do not affect response learning. Conversely, lesions of the caudate nucleus (Packard et al., 1989; Packard & McGaugh, 1992; McDonald & White, 1993; Kesner et al., 1993), and posttraining injections of drugs into the caudate (Packard & White, 1991; Packard et al., 1994), alter response learning but do not affect cognitive learning.

The present study was designed to determine whether the evidence suggesting differential roles of the hippocampus and caudate nucleus in memory might provide a resolution of the place versus response learning question. Rats implanted bilaterally with cannulae in either the hippocampus or caudate nucleus were first trained (four trials per day) using one starting alley of a cross-maze (e.g., south) and consistently rewarded in the goal box of one alley (e.g., west). On Days 8 and 16 the rats were given a single test trial using the other starting alley (e.g., north) to determine whether they made the same turning response made in training or made a different turning response and went to the place where food was located during the training. Prior to the test trials lidocaine or saline was infused bilaterally into either the caudate nucleus or hippocampus. Lidocaine produces a temporary functional blockade of neural activity following local administration in the brain and has been used in studies examining brain function and memory (e.g., Perez-Ruiz & Prado-Alcala, 1989; Salinas, Packard, & McGaugh, 1993). If cognitive and response learning occur in parallel and are mediated by different neural systems, selective temporary inactivation of one of these neural systems prior to testing should influence the type of learning, i.e., place or response learning expressed by the animal on the test trials.

METHODS

Subjects

The subjects were 50 male Sprague–Dawley rats (275–300 g). Animals were individually housed in a temperature-controlled environment on a 12-h light/

dark cycle with the lights on from 7 AM to 7 PM. All animals were given *ad lib.* access to water.

Apparatus

The apparatus was a wooden cross maze painted flat gray. The maze consisted of four arms (north, south, east, and west) of an eight-arm radial maze (other maze arms were removed). The arms of the cross maze measured 60 × 9 cm. The center platform of the maze connecting the four arms measured 40 cm in diameter. A clear Plexiglas cross-shaped alleyway structure placed on the center platform of the modified radial maze connected the four arms of the cross-maze. The alleyways measured 20 × 9 × 15 cm. A recessed food well was present at the end of the west arm of the maze. The maze was located in a testing room that contained many extramaze cues including wall posters, a lamp, table, animal cage rack, and the seated experimenter.

Surgery

Animals were anesthetized with sodium pentobarbital (50 mg/kg) and implanted with bilateral guide cannula in the dorsal hippocampus (10 mm length) or dorsolateral caudate nucleus (15 mm length) using standard stereotaxic techniques. The cannulae (23 gauge) were anchored to the skull with jewelers screws and dental acrylic. Coordinates for the dorsal hippocampal placements were AP = −3.1 mm, ML = ±2.5 mm, and DV = −2.0 mm from bregma. Coordinates for the dorsolateral caudate nucleus placements were AP = −.26 mm, ML = ±4.2 mm, DV = −4.0 mm. After surgery, stylets (30 gauge) were inserted and left in place to ensure cannulae patency until injections were made. Behavioral testing began 1 week after surgery.

Injection Procedures

A 2% lidocaine hydrochloride solution (Western Medical Supply, Inc.) was used to produce reversible inactivation of brain sites. Injections (0.5 μl) were administered intracerebrally using 30-gauge injection needles inserted into the guide cannulae. The needles were connected by polyethylene tubing to 10-μl Hamilton microsyringes (Hamilton Co., Reno, NV). The volume of 2% lidocaine solution used was chosen on the basis of previous evidence indicating that this volume produces functional inactivation of the caudate nucleus (Perez-Ruiz & Prado-Alcala, 1989) and amygdala (Salinas et al., 1993) sufficient to cause memory impairment. Other findings indicate that volumes of 2% lidocaine solution as low as 0.25 μl can produce memory impairment following intracerebral administration (Parent & McGaugh, 1993). The injections were delivered over a period of 37 s using a syringe pump (Sage Instruments), and the injection needles (extending 1 mm from the end of the guide cannulae) were left in place an additional 60 s to allow for diffusion of the solution away from the needle tip. Lidocaine injections were administered approximately 2–3 min prior to the probe trial tests on Days 8 and 16 of training. Saline injections were administered using procedures identical to those used for lidocaine injections.

Histology

At the completion of behavioral training, animals were deeply anesthetized with a 1.0-ml injection of sodium pentobarbital and perfused with saline followed by 10% formal-saline. The brains were removed and subsequently sectioned at 20-μm sections through the cannula tract region and stained with Cresyl violet. Cannula placements were examined for verification of needle tip location using the atlas of Paxinos and Watson (1986).

Cannulae placements for both dorsolateral caudate nucleus and dorsal hippocampus are shown in Fig. 1 (left, right, respectively). Caudate nucleus placements were located in the dorsolateral caudate, ranging from 0.20 mm to −0.30 mm from bregma (Fig. 1, left). Hippocampal placements were located in the dorsal hippocampus, ranging from −2.8 mm to −3.3 mm from bregma (Fig. 1, right).

Behavioral Procedures

Prior to training, all rats were reduced to 85% of *ad lib.* body weights over 7 days and maintained at this weight throughout the experiment. On 2 consecutive days, rats were placed into the cross-maze in the start box (south arm) and allowed to explore the maze for 5 min. No food was present in the maze on either of these 2 habituation days. Access to the north arm of the cross-maze was blocked during habituation sessions and the subsequent food rewarded training trials with a clear Plexiglas shield. Following habituation on both days, the animals were allowed to consume ten 45-mg Noyes food pellets in their home cage. Food trials began on Day 3. On each food trial rats were placed into the start box and allowed to traverse the maze and consume a single Noyes food pellet located in the food cup at the end of the goal arm of the cross maze (west arm). On the initial food trial only, a trail of four pellets leading to the food cup was placed along the length of the goal arm. Each rat received four food rewarded trials per day. Entries into the unbaited arm of the

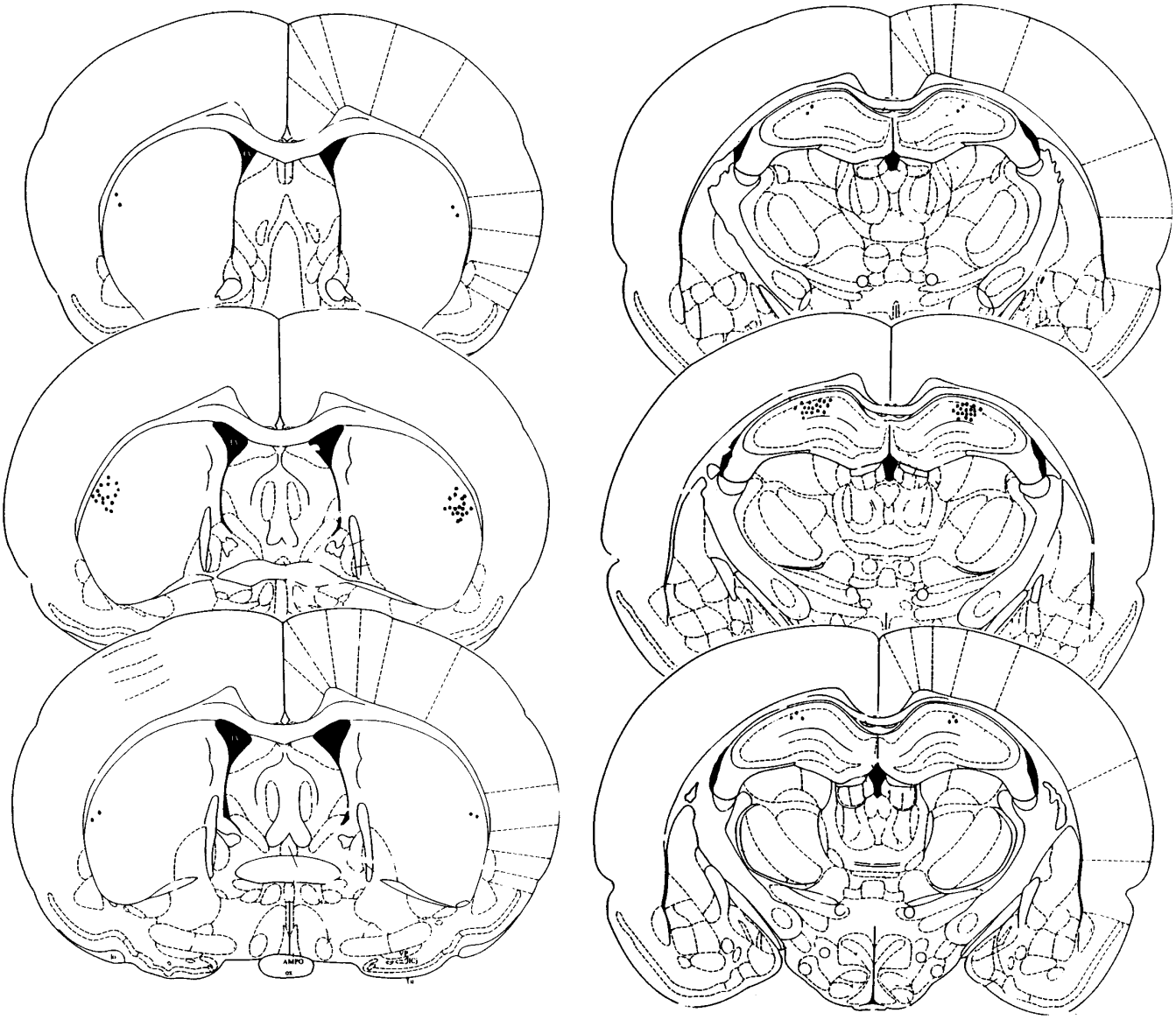

FIG. 1. Dorsolateral caudate nucleus (left) and dorsal hippocampus (right) cannulae placements showing the anterior/posterior extent of needle tip locations at 0.5-mm sections. Caudate nucleus placements ranged from 0.20 to −.30 mm from bregma. Hippocampal placements ranged from −2.8 to −3.0 mm from bregma. (Plates adapted from atlas of Paxionos and Watson, 1986).

cross-maze (east) were scored as incorrect responses during the training trials, and entries into the baited arm of the cross-maze (west) were scored as correct responses. A correction procedure was used such that rats making an incorrect response were allowed to trace back to the baited maze arm and consume the food pellet. If a rat failed to consume the food pellet within 2 min, the trial was terminated and the rat was manually placed in the goal box and allowed to consume the pellet. After consuming the pellet on a given trial, the rat was placed in a holding cage located directly behind the start arm for a 30-s intertrial interval.

On Day 8 of the food-rewarded trials, rats were assigned to experimental groups (n = 12–14 per group) in a rank-order method to assure that levels of learned performance (i.e., number of correct responses over the first 7 days of training) of the groups were comparable prior to treatment. On Day 8 a single probe trial was given. Three minutes prior to the probe trial, half of the animals with caudate nucleus implants received a saline injection and the other half received a lidocaine injection. Similarly, half of the animals with hippocampal implants received a saline injection prior to the probe trial, and half received an injection of lidocaine. On the probe trial, animals

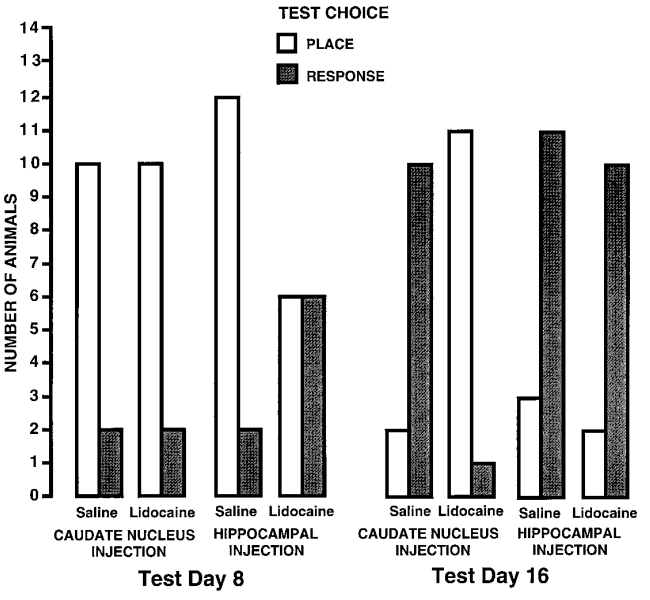

FIG. 2. Number of rats in each treatment group that exhibited *place* or *response* learning on both the Day 8 and Day 16 test trials.

were placed into the start box opposite that used during training (i.e., north arm) and were allowed to make a single entry into either the baited or the unbaited maze arm. The entrance to the south maze arm (i.e., the arm containing the start box used during training) was blocked by a clear Plexiglas shield on the probe trials. Animals entering the baited arm on the probe trial were designated "place" learners (i.e., animals going to the *place* where food was located during training), and animals entering the unbaited arm on the probe trial were designated "response" learners (i.e., animals making the same turning *response* as during training).

On Day 9 of training, food-rewarded training (four trials per day) was reinstated using procedures identical to those of Training Days 1–7. On Day 16, a second probe trial was given using procedures identical to the probe trial given on Day 8. Animals received the same intracerebral saline or lidocaine treatments given on the Day 8 probe trial and were again allowed to make a single entry into either the baited or unbaited maze arm.

RESULTS

Figure 2 shows the results of the test trials on Days 8 and 16. χ^2 analyses ($p < .05$ for all comparisons) were computed in order to determine whether groups showed a significant tendency to display place or response learning on the probe trials. On the Day 8 probe trial, animals given saline injections into either the hippocampus or caudate nucleus were predominantly place learners (hippocampus–saline $\chi^2 = 7.14$, $p < .05$; caudate nucleus–saline $\chi^2 = 5.34$, $p < .05$). Rats given intracaudate injections of lidocaine were also predominantly place learners ($\chi^2 = 5.34$, $p < .05$), while those receiving intrahippocampal injections of lidocaine did not show a significant trend toward either place or response learning ($\chi^2 = 0$, n.s.). These findings indicate that functional inactivation of the hippocampus, but not caudate nucleus, prevented the expression of place learning.

On the Day-16 probe trial, animals given saline injections into either the hippocampus or caudate nucleus were predominantly response learners (hippocampus–saline $\chi^2 = 4.58$, $p < .05$; caudate nucleus–saline $\chi^2 = 5.34$, $p < .05$). Rats receiving intrahippocampal injections of lidocaine were also predominantly response learners ($\chi^2 = 5.34$, $p < .05$), while those receiving intracaudate injections of lidocaine were predominantly place learners ($\chi^2 = 8.32$, $p < .05$). These findings indicate that with extended training, saline-treated rats switched from displaying place learning to response learning. Functional inactivation of the caudate nucleus, but not hippocampus, prevented the expression of response learning and, in fact, preserved place learning.

DISCUSSION

The results indicate that place and response learning occur concurrently and are mediated by different neural systems involving the hippocampus and caudate nucleus, respectively. The findings are consistent with previous studies using pretraining irreversible lesions of the caudate nucleus (Thompson, Guilford, & Hicks, 1980), and fimbria–fornix (Decastro, 1974), which reported that such lesions result in a predominant tendency toward place and response learning, respectively. Our findings indicate that in addition to acquisition, the functional integrity of the hippocampus and caudate nucleus are necessary for the expression of these two forms of learned behavior.

The finding that rats initially acquire place information and that the expression of such learning is blocked by inactivation of the hippocampus is consistent with extensive evidence implicating the hippocampus in spatial learning (e.g., O'Keefe & Nadel, 1978).

The hippocampal injection sites in the present study were located along the dorsal edge of the hippocampus, and areas of parietal cortex located dorsolateral to the lidocaine injection sites may also be

involved in acquisition of spatial information. For example, large lesions of parietal cortex selectively impair acquisition of a spatial cheese-board task (Kesner, Farnsworth, & DiMattia, 1989) and produce deficits in acquisition and retention of spatial behavior in the Morris water maze (DiMattia & Kesner, 1988). However, the posterior extent of the large parietal cortex lesions reported to impair spatial behavior (Kesner, Farnsworth, & DiMattia, 1989) is approximately 0.5–0.8 mm anterior and 1.0–1.2 mm lateral to our effective injection sites in dorsal hippocampus. Furthermore, small lesions of parietal cortex which may more closely mimic the behavioral effects of any limited spread of lidocaine from hippocampus in the present study do not impair acquisition of spatial behavior in the Morris water maze or the radial maze (Kolb, Sutherland, & Whishaw, 1983). Thus, although the possibility that the spread of lidocaine to adjacent parietal cortex influenced the expression of place learning cannot be completely ruled out, the effect of lidocaine injections on place learning observed in the present study was likely due to neural inactivation of the hippocampus.

The finding that the expression of response learning is blocked by functional inactivation of the caudate nucleus is consistent with the view that the caudate nucleus selectively mediates learning involving the use of "egocentric" cues to guide navigation (Potegal, 1972; Kesner & DiMattia, 1987). For example, lesions of the caudate nucleus impair acquisition of left–right maze discrimination tasks (Cook and Kesner, 1988; Kesner et al., 1993). As the region of the caudate targeted by the lidocaine injections (dorsolateral) receives cortical input from the somatosensory cortex (Heimer, Alheid, & Zarbosky, 1985) such input may be critical for establishing an association between the maze cues and the egocentric cues mediating the specific body turn required for response learning. However, it is important to note that egocentric learning may be but one example of a class of stimulus-response learning functions mediated by the caudate (Packard et al., 1989; Packard and McGaugh, 1992; Viaud & White, 1989), each of which is hypothesized (White, 1989) to be organized on the basis of the sensory cortical input the caudate receives (Heimer et al., 1985).

Rats given saline injections into the hippocampus or caudate nucleus displayed a strong place learning tendency on the Day 8 probe trial. However, animals with the hippocampus inactivated with lidocaine prior to the Day 8 probe trial did not display either place *or* response learning tendencies. Although the caudate nucleus was presumably functional in these rats, a response learning tendency had apparently not been acquired by this system prior to the eighth day of training. Thus, one difference between the operating characteristics of the hippocampal-based and caudate-based memory systems is that the former system appears to be involved in the rapid acquisition of new information, while the latter system acquires information in a slower, incremental fashion.

With extended training in the cross-maze, animals acquired a response learning tendency (i.e., on the Day 16 probe trial control rats made the same turning response as during training). The finding that the animals shifted from place learning to response learning with increased training is consistent with that of previous research (e.g., Ritchie, Aeschliman, & Pierce, 1950; Hicks, 1964). Importantly, selective functional inactivation of the caudate nucleus prevented the expression of the acquired response and revealed *preserved* place learning. Thus, the predominance of response learning expressed after extensive training is not due to elimination of the place representation. These findings provide strong evidence that the two memory systems are functioning independently.

In 1957, Restle proposed a resolution of the place versus response learning debate based on findings suggesting that either type of learning could be predicted based on the availability of various extramaze/intramaze cues present (Restle, 1957). Thus, in open mazes located in visually heterogeneous environments place learning is dominant (Blodgett & McCutchan, 1947; Blodgett, McCutchan, & Matthews, 1949; Tolman et al., 1946, 1947), while in closed mazes or visually homogeneous environments response learning is dominant (Blodgett & McCutchan, 1948; Thompson & Tompson, 1949; Hill & Thune, 1952; Scharlock, 1955). According to Restle's multiple-cue theory, a single learning mechanism was responsible for both place and response learning, and this mechanism was "tuned" to produce either type of learning by the nature of the extramaze/intramaze environment. However, although evidence indicates that the nature of the testing environment contributes to the relative expression of place and response learning, Restle's resolution of the debate is, at least, incomplete. The nature of the environment appears to interact with separate learning systems in determining the expression of place or response learning. Consistent with this suggestion, acquisition of a caudate nucleus-mediated win–stay radial maze task by intact rats is facilitated when extramaze cues are reduced by surrounding the maze with curtains (Packard & White,

1987). Future studies are necessary to determine what other factors in addition to the nature of the testing environment contribute to the use of a given memory system in a particular task.

Finally, these results indicate that the place versus response controversy was based on a false premise: The debate was primarily based on the assumption that there is only one kind of learning and that the appropriate test would reveal the nature of that learning (but see Tolman, 1949). Evidence that the brain uses different neural systems for acquiring and expressing different kinds of learning would appear to resolve this long-lasting controversy.

REFERENCES

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

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

Blodgett, H. C., McCutchan, K., & Matthews, R. (1949). Spatial learning in the T-maze: The influence of direction, turn, and food location. *Journal of Experimental Psychology,* **39,** 800–809.

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

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

Corkin, S. (1965). Tactually-guided maze learning in man: Effect of unilateral cortical excision and bilateral hippocampal lesions. *Neuropsychologia,* **3,** 339–351.

DeCastro, J. M. (1974). A selective spatial discrimination deficit after fornicotomy in the rat. *Behavioral Biology,* **12,** 373–382.

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

Gaffan, D. (1974). Recognition impaired and association intact in the memory of monkeys after transsection of the fornix. *Journal of Comparative and Physiological Psychology,* **86,** 1110–1109.

Galanter, E. H., & Shaw, W. A. (1954). "Cue" vs. "reactive inhibition" in place and response learning. *Journal of Comparative and Physiological Psychology,* **47,** 395–398.

Guthrie, E. R. (1935). *The Psychology of Learning.* Harper and Row, New York.

Heimer, L., Alheid, G. F., & Zaborsky, L. (1985). Basial Ganglia. *In* G. Paxinos, (Ed.) *The Rat Nervous System* (pp. 37–87). New York: Academic Press.

Hicks, L. H. (1964). Effects of overtraining on acquisition and reversal of place and response learning. *Psychological Reports,* **15,** 459–462.

Hill, C. W., & Thune, L. E. (1952). Place and response learning in the white rat under simplified and mutually isolated conditions. *Journal of Experimental Psychology,* **43,** 289–297.

Hirsh, R. (1974). The hippocampus and contextual retrevial of information from memory: A theory. *Behavioral Biology,* **12,** 421–442.

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

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

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

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

Kolb, B., Sutherland, R. J., and Whishaw, I. Q. (1983). A comparison of the contributions of the frontal and parietal association cortex to spatial localization in rats. *Behavioral Neuroscience,* **97,** 13–27.

Mahut, H., & Moss, M. (1984). Consolidation of memory: The hippocampus revisited. *In* N. Butters and L. R. Squire (Eds.), *Neuropsychology of Memory* (pp. 297–315). New York: Guilford.

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

Milner, B. (1962). Les troubles de la memoire accompagnant des lesions hippocampiques bilaterales. *In* P. Passant (Ed.), *Psysiologie de l'Hippocampae* (pp. 257–272). Paris: Centre de la Recherche Scientifique.

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

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

O'Keefe, J., & Nadel, L. (1978). *The Hippocampus as a Cognitive Map.* New York: Oxford University Press.

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

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

Packard, M. G., & White, N. M. (1987). Differential roles of the hippocampus and caudate nucleus in memory: Selective mediation of "cognitive" and "associative" learning. *Society for Neuroscience Abstracts,* **13,** 1005.

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

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

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

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

Parent, M. B., & McGaugh, J. L. (1993). Time-dependent retrograde impairment produced by lidocaine injections into the basolateral complex of the amygdala. *Society for Neuroscience Abstracts,* Vol. 19, 1227.

Pavlov, I. P. (1927). *Conditioned Reflexes.* Clarendon Press, London.

Paxinos, G., & Watson, C. (1986). *The Rat Brain in Stereotaxic Coordinates.* New York: Academic Press.

Perez-Ruiz, C., & Prado-Alcala, R. A. (1989). Retrograde amnesia induced by lidocaine injection into the striatum: protective effect of the negative reinforcer. *Brain Research Bulletin,* **22,** 599–603.

Potegal, M. (1972). The caudate nucleus egocentric localization system. *Acta Neurobiologica Experimentia,* **32,** 379–494.

Restle, F. (1957). Discrimination of cues in mazes: A resolution of the place vs. response controversy. *Psychological Review,* **64,** 217–228.

Ritchie, B. F., Aeschliman, B., & Pierce, P. (1950). Studies in spatial learning: VIII. Place performance and the acquisition of place dispositions. *Journal of Comparative and Physiological Psychology,* **43,** 73–85.

Salinas, J. A., Packard, M. G., & McGaugh, J. L. (1993). Amygdala modulates memory for changes in reward magnitude: Reversible post-training inactivation with lidocaine attenuates the response to a reduction in reward. *Behavioral Brain Research,* **59,** 153–159.

Schacter, D. L. (1992). Priming and multiple memory systems: Perceptual mechanisms of implicit memory. *Journal of Cognitive Neuroscience,* **4,** 244–256.

Scharlock, D. P. (1955). The role of extramaze cues in place and response learning. *Journal of Experimental Psychology,* **50,** 249–254.

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.

Thompson, M. E., & Thompson, J. P. (1949). Reactive inhibition as a factor in maze learning: II. The role of reactive inhibition in studies of place learning versus response learning. *Journal of Experimental Psychology,* **39,** 883–891.

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

Thorndike, E. L. (1898). Animal Intelligence: An experimental study of the associative processes in animals. *Psychological Review,* **8,** 28–31.

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

Tolman, E. C. (1932). *Purposive Behavior in Animals and Men.* New York: Appleton-Century Crofts.

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

Tolman, E. C. (1949). There is more than one kind of learning. *Psychological Review,* **55,** 189–208.

Tolman, E. C., & Gleitman, H. (1949). Studies in spatial learning: VII. Place and response learning under different degrees of motivation. *Journal of Experimental Psychology,* **39,** 633–659.

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

Tolman, E. C., Ritchie, B. F., & Kalish, D. (1947). Studies in spatial learning: V. Response versus place learning by the noncorrection method. *Journal of Experimental Psychology,* **37,** 285–292.

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

Weiskrantz, L., and Warrington, E. K. (1979). Conditioning in amnesic patients. *Neuropsychologia,* **17,** 187–194.

White, N. M. (1989). A functional hypothesis concerning the striatal matrix and patches: Mediation of S-R memory and reward. *Life Sciences,* **45,** 1943–1947.

Zola-Morgan, S., Squire, L., & Mishkin, M. (1982). The neuroanatomy of amnesia: Amygdala–hippocampus versus temporal stem. *Science,* **218,** 1337–1339.