

Effects of medial and dorsal cortex lesions on spatial memory in lizards

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Abstract

In mammals and birds, the hippocampus is a major learning and memory center that plays a prominent role in spatial memory, the use of distal cues to guide navigation. The role of reptilian hippocampal homologues, the medial and dorsal cortex, in spatial memory has not been thoroughly investigated. The medial and dorsal cortex of reptiles is known to play a role in learning both tasks that are hippocampally dependent and tasks that are not hippocampally dependent in mammals and birds. In order to examine the specific role of the medial and dorsal cortex in spatial memory, we trained medial cortex, dorsal cortex, and sham lesioned *Cnemidophorus inornatus* lizards to locate the one heated rock of four identical rocks spaced evenly around the perimeter of a circular, sand filled, arena in a cool room. We used probe trials to examine the strategies used by lizards to locate the goal. Medial cortex lesions and dorsal cortex lesions slowed acquisition and altered the strategies used to locate the goal. However, none of the lizards adopted a spatial strategy to locate the goal suggesting that the dorsal cortex and medial cortex are involved in using non-spatial strategies for navigation. © 2001 Elsevier Science B.V. All rights reserved.

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1. Introduction

The medial cortex (MC) and dorsal cortex (DC), reptilian forebrain regions, are putative homologues of the avian and mammalian hippocampal formation [10–12,21,34,35]. The MC is believed to be most similar to the mammalian dentate gyrus and Ammon's horn, while the DC has greatest similarities to entorhinal cortex, subiculum, and parts of surrounding isocortex [11,21,34,35,45]. In addition to these structural homologies, it appears that the mammalian and avian hippocampus share with the reptilian MC and DC a relationship between the relative size of these neuroanatomical regions and niches that demand intensive search for resources [17]. For example, the hippocampus appears to be larger in food storing birds [3,15,33,41] and in certain polygynous mammals [26],

than in closely related species that do not search for scattered resources. Similarly, in an active foraging lizard (*Acanthodactylus boskianus*) the MC and DC are larger than in a sit-and-wait predator (*A. scutellatus*) [17]. Given these similarities across taxa one might predict that the MC and DC and the hippocampus would have similar functions.

The deficits resulting from hippocampal lesions in a variety of mammals and birds suggest that the hippocampus plays an important role in spatial learning [5,36,38,49,60–62,65,66] as well as a variety of non-spatial tasks [1,13,22,27–30,40,43,51,56–58,64,68]. Direct tests of the function of the MC and DC of reptiles in solving spatial tasks of the variety that are impaired by hippocampal lesions in birds and mammals apparently have not been done but see [24]. However, the DC and MC appear to share some non-spatial functions with the hippocampus. Lesions of the DC in turtles produce deficits in a variety of non-spatial tasks [6,31,32,47,55], some that are hippocampally-dependent in mammals and birds, others that are not. Lesions of

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the DC in the lizard *Dipsosaurus dorsalis* disrupts retention of a Lashley maze and serial position reversals [53] similar to deficits in long term memory and reversal learning in rats with hippocampal lesions [30]. In contrast, lesions of the MC in turtles do not produce deficits in a number of tasks that are known to be hippocampally-dependent in mammals [30] and birds [56] such as the acquisition or reversal of a right-left discrimination [32], reversal of a brightness discrimination [32], and acquisition or reversal of a go–no go discrimination [31]. However, MC lesions in the lizard *Ophisaurus apodus* have been shown to interfere with reversal and extinction of a conditioned response [37]. Rats with hippocampal lesions similarly demonstrate deficits in extinction, and reversal learning [30].

Although direct test of MC or DC involvement in mammal-like spatial cognition have, to our knowledge, not been published but see [24] correlational evidence suggests that these brain regions may not play a major role in spatial learning. Mammals adapted to searching for resources and having a relatively large hippocampus appear to do better on spatial tasks than closely related species with a relatively small hippocampus [26]. Active foraging (*A. boskianus*) lizards have a larger MC and DC than sit-and-wait predators (*A. scutellatus*) [17], but were not found to be better at locating a goal in a spatial maze [18]. In addition, neither of the *Acanthodactylus* lizard species tested learned the task using distal cues to guide them to the location of the goal [18] as mammals [14] and birds [62] apparently do. Although this negative evidence for spatial memory differences between species should not be construed as conformational, these results suggested that the MC and DC were involved in some aspect of learning, but not in using distal cues to solve a spatial maze [18]. In support of MC and DC involvement in other forms of learning, the active foraging lizard was better than the sit-and-wait predator on a non-spatial task [17].

There has been much debate over the mechanisms involved in spatial behavior and the definition of spatial learning. To avoid becoming mired in such debates, we present our results as testing whether lizards perform as though they are using distal cues or one of a discrete set of defined alternative strategies to determine the location of a goal. Spatial memory or spatial ability in this context refers to the apparent use of distal cues rather than local cues to navigate to a reward. We refer to distal cues as stimuli not spatially contiguous with the goal and to local cues as objects that are spatially contiguous or nearly spatially contiguous with the goal sensu Morris [48]. In order to determine whether the MC and DC are involved in using distal cues to solve a spatial task, we tested lizards with lesions of the DC or MC on their ability to locate a warm rock in a cool arena. In addition to a spatial strategy using distal cues, there are a variety of other strategies that do not

depend on use of distal cues alone or at all that can be used to improve the ability to reach a goal in a spatial task [18,19,69,70]. Praxis relies on learning a series of stereotyped motor patterns such as ‘move towards wall and circle’. Taxis is the association between one prominent local or distal cue used as a beacon to guide search directly to a goal. Trial-and-error search can also be used to locate a reward with improvements in trail-and-error methods across training. In addition, the association between compounds of cue types may be important to locating a goal. The use of such compounds may be referred to as a configural strategy [57,58]. Though tests of configural abilities typically employ compounds made up of cue types in different modalities such as visual and auditory [16,57], tactile and olfactory [72] or tactile and visual [73] we will refer to compounds made up of distal and local cues. A configural strategy differs from a spatial strategy in that attention to multiple, distal cues may not be as important as attention to a combination of specific local cues in conjunction with specific distal cues. A configural strategy would allow one to locate the goal as long as the configuration of local and distal cues in the room has not been disrupted. Displacing one set of cues relative to another set would disrupt a configural strategy of this type [18], but not a spatial strategy using distal cues alone. Previous studies have suggested that compounds of local and distal cues might be important in lizard navigation [18].

In order to assess whether spatial learning or another one of these strategies was used to solve the spatial task we ran probe trials [18,49] at the end of training that involved manipulation of local and distal cues. Thus, we were able to examine whether MC and DC lesions impaired general performance in acquisition of a spatial task, and we were able to discriminate between strategies intact and lesioned lizards used to locate the warm rock.

2. Methods

2.1. Subjects

Cnemidophorus inornatus males ($n = 26$) were caught in west Texas between May and June of 1996. Lizards were housed individually on a controlled light cycle (14 h light/10 h dark). Cages were maintained at an ambient temperature of $\sim 30^{\circ}\text{C}$ with additional heat supplied by 50 W incandescent bulbs during light hours and an ambient temperature of $\sim 25^{\circ}\text{C}$ during dark hours. Lizards were tested from the third hour of light to the eighth hour of light, between 0800 and 1400 h. This approximates the lizards’ activity period in the field (personal observation). Lizards were randomly assigned to DC, MC, and sham lesion groups. Prior to

surgery, the average snout-vent-length of lizards that completed the study was 56.58 ± 0.48 mm (mean \pm SEM). After completion of the study, the average snout-vent-length of these lizards was 58 ± 0.57 mm (mean \pm SEM).

2.2. Apparatus

Lizards were tested in a circular arena (1.5 m diameter and 0.4 m height) with a 1.25 cm thick plywood floor and walls made out of flashing that were painted tan to provide a homogenous field. Four insulated hot rocks (Junior Sizzle Stones by Tetra Terrafuna[®], $16 \times 9.8 \times 5.5$ cm with insulation) were placed at equal intervals along the perimeter of the arena. The insulated hot rocks (heat gradient negligible, 2 cm horizontal, 3 cm vertical) are heated by internal coils and reached a substrate temperature between 39 and 45°C. For each batch of lizards tested, one rock was chosen as the goal rock and only this rock was heated during training. The arena was filled with sand (5.5 cm high) so that the sand and hot rocks were level with each other.

We positioned a blue triangle and a green geometric shape on the walls of the maze (Fig. 1), such that direct approach or avoidance of either one would not lead to contact with the goal. Although these distal cues are intramaze cues, they cue the goal rock indirectly by providing information about the spatial arrangement of the arena but not providing local information about the goal. Cues were not placed outside the arena as previous experiments with other species [18] and pilot studies with *C. inornatus* have shown that lizards do not attend

to cues placed outside the arena but are able to use local cues inside the arena to navigate to a goal [18]. Although *C. inornatus* have not been tested on ability to discriminate the particular shapes and colors used as distal cues in this experiment, we know *C. inornatus* can discriminate a variety of other shapes and colors (unpublished observations) and that other lizard species have been shown to make fine distinctions between shapes and colors [4,7].

The testing room was cooled to between 22 and 24°C. During the experiment, lizards were held in tubular cages (30 cm height and 15 cm diameter) with hinged tops opened so that the cages could be heated by lamps to between 29 and 32°C. To release lizards into the center of the arena the lid of the holding cage was closed then the cage was turned upside down and placed in the center of the arena. The holding cage was then pulled up by a handle, releasing the hinged top and freeing the lizard. Each lizard's performance was videotaped from above and monitored on-line from another room to minimize observer effects.

3. Procedures

Animal care and treatment followed guidelines established by the Institutional Animal Care and Use Committee of the University of Texas, Austin (Protocol No. 03952301).

3.1. Surgery

Lizards were anesthetized using ice for 10 min and kept chilled throughout surgery. Lizards were placed in a Kopf stereotaxic device modified for lizard brain surgery. The frontoparietal scale and underlying skull were excised to expose the brain and, with the exception of the lizards receiving a sham lesion, a series of 6 radiofrequency lesions were made on each lizard. Lesions were made bilaterally at coordinates lateral to the central sinus, ventral to the surface of the brain, and rostral to the intersection between the frontal and frontoparietal scales. DC coordinates were respectively ± 0.65 , -0.25 , $+0.7$; ± 0.75 , -0.3 , $+0.9$; and ± 0.85 , -0.35 , $+1$. MC coordinates were ± 0.25 , -0.35 , $+0.5$; ± 0.25 , -0.5 , $+1$; and ± 0.25 , -0.7 , $+1.5$, respectively. After surgery, the frontoparietal skin and scale were replaced, and lizards were allowed 10 days to recover before behavioral testing.

3.2. Behavioral testing

Lizards were tested in four batches with six or seven lizards in each batch. One of the four rocks was randomly assigned to be the goal rock for each batch to reduce any biases that might occur with innate prefer-

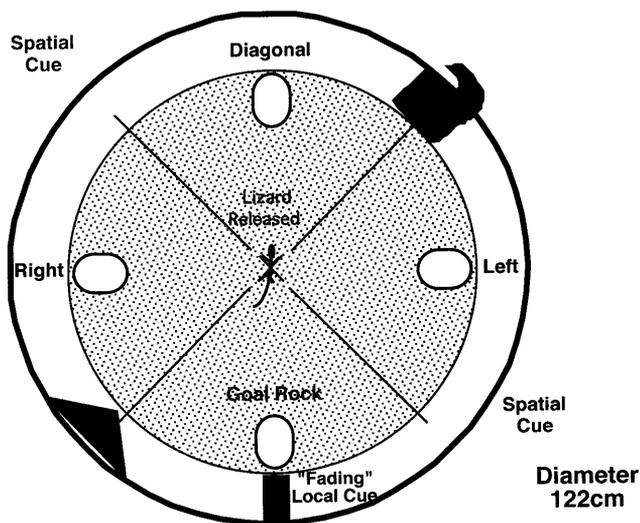


Fig. 1. Illustration of arena and cues. Training began with a local cue that was reduced in size and then removed in four steps. The spatial cues remained throughout testing. The maze was divided into four quadrants relative to the quadrant containing the goal rock for analysis of activity during training and probe trials.

ences for particular directions in the arena. Testing ran from April 1997 to December 1997 with each testing period lasting 53 days.

3.2.1. Acquisition trials

On the first trial of training, lizards were placed on the goal rock for 3 min. All other trials began when lizards were released from the holding cage into the center of the arena and ended when the lizard reached or was placed on the goal rock. Lizards were allowed to remain on the goal rock for 3 min. Latency was defined as the time beginning with the lizards initial directed movement after release from the holding cage to the time the lizards contacted the goal, at which time a trial ended. During initial trials a lizard would frequently remain motionless after release or dash from the holding cage to the wall and then remain motionless for a few seconds to several minutes. This time was not included in the total latency. If the lizard remained motionless for 5 min, we would tap the sand next to the lizard with a clear rod. This was usually sufficient to start the lizard moving. If the lizard remained motionless for another 10 min after this, the lizard was placed on the goal rock for 3 min and latency was recorded as 10 + , and the trial ended.

Once the goal was located, lizards rarely moved from the goal during the 3 min reinforcement period. If the lizard briefly touched the goal rock but did not remain there for more than one minute, the trial was not ended until the lizard returned to the goal rock and remained there for more than 1 min. If the lizard paused near the goal rock, but did not make contact with the rock with any body part, the trial was not ended. The lizard was given 10 min to make bodily contact with the rock and remain touching the rock for > 1 min. If the lizard did not locate and remain on the rock in 10 min, it was captured and placed on the rock for the 3 min reinforcement period and latency was recorded as 10 + and the trial ended.

The lizard's path to the rock was drawn on a scaled map of the arena with reference made to video recordings as necessary for accuracy. Path distance was measured using Sigma Plot software and a bit map pad. We assessed total path distance and the percentage of total path distance in four pie-shaped quadrants of the maze, each centered on one of the rocks. Learning was defined as a decrease across trials in one or more of the following: latency, total distance traveled, and distance traveled in non-goal quadrants.

After each trial we swept sand from the surface of the rocks, cleaned each rock with alcohol, and swept the rest of the sand in the arena to conceal any paths in the sand and obscure olfactory cues. After a single trial for each lizard, we tested a different lizard. Lizards were tested in squads of three or four lizards, thus intertrial

intervals ranged from ~ 6–20 min depending on the performance of intervening lizards.

One block of three trials was conducted daily for 52 days. During the first 24 blocks we used a shaping procedure to promote the use of experimenter-supplied cues. This procedure was similar in concept to one that has helped rats with drug-induced [19] and lesion-induced [20] hippocampal deficits and impaired spatial abilities to select efficient spatial strategies. In addition to the distal intramaze cues, a prominent local cue (10 × 45 cm) was placed directly behind the goal for 24 testing blocks. This cue was reduced in size (10 × 28 cm) before testing block 12, and again (10 × 15 cm) before block 19, and then removed before testing block 24. We conducted all remaining testing blocks without the local cue.

3.2.2. Probe trials

After the lizards first reached asymptotic performance, we began to conduct Probe Trials to explore the lizards' learning strategies. Although a reduction in latency or distance to the goal or an increase in the percentage of total path distance in the goal quadrant implies learning, it does not necessarily indicate that a spatial strategy is being used to locate the rock. Four probe trials of two types were conducted in the following order: None-Hot-1; None-Hot-and-Turn-1; None-Hot-2; and None-Hot-and-Turn-2. The first set was meant to capture strategies on early trials when the lesion groups differed maximally and the second set was meant to capture strategies after all groups had demonstrated learning in the maze. During what we are calling None-Hot probe trials conducted on days 30 (None-Hot-1) and 47 (None-Hot-2), we simply unplugged the goal rock so that no rocks in the arena were heated. None-Hot and Turn probe trials were run on days 35 (None-Hot-and-Turn-1) and 53 (None-Hot-and-Turn-2). During these probe trials, all rocks were unheated and the maze was turned 180°. Intramaze cues were left in the same spatial location with respect to the room so that local feature cues such as slight aberrations on the walls and any peculiarities of the goal rock were now diagonally opposite their original position whereas the relationship between the previous spatial location of the goal rock and the distal cues remained the same.

During probe trials lizards were released into the center of the arena and allowed to explore for 5 min. At the end of trials they were placed back in their holding cages. We recorded latency to reach the previous position of the goal rock with respect to distal cues and latency to reach the rock on the opposite side of the arena as well as latency to reach the other two rocks. We measured path distance as in acquisition trials and assessed the percentage of total distance in each quadrant of the maze. We also measured the number of

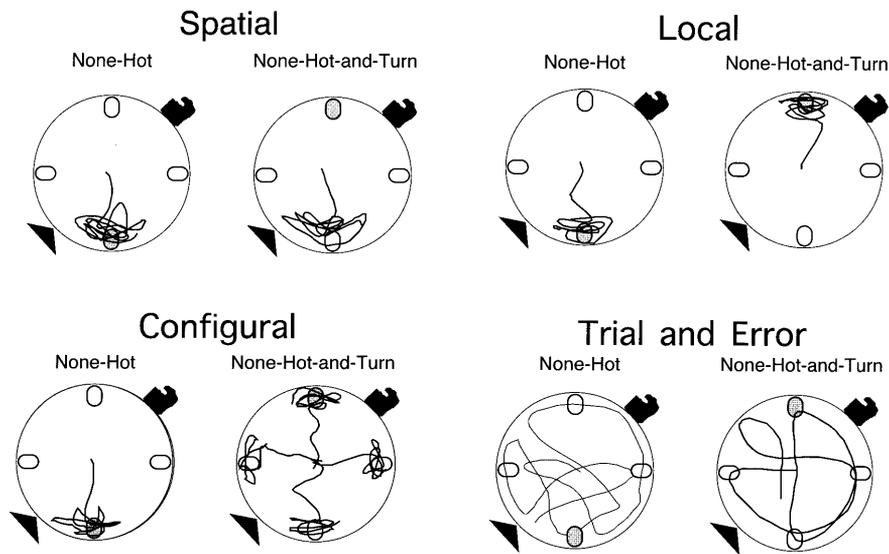


Fig. 2. Paths of movement during the two probe trial types, none-hot and none-hot-and-turn, that would typify each of the navigation strategies tested, spatial, local, configural, and trial-and-error. The wall behind the goal rock travels with the rock when it turns. The original goal rock is shaded gray. Black geometric shapes outside of the large circles represent distal cues. Black lines drawn within the larger circles represent prototypical paths taken by a lizard following the appropriate strategy. The four paths shown for the none-hot-and-turn probe trial of the configural strategy represent possible paths taken by four different lizards as there is no group bias predicted for this probe trial.

times lizards crossed each rock. If a group of lizards is quicker to contact the rock in a particular quadrant, traverses a greater percentage of total path distance in that quadrant, or crosses a rock in a particular quadrant more than other rocks, it suggests that the lizards have a bias for searching in that quadrant. Searching biases in a particular quadrant imply that the lizards expected a reward in that quadrant.

On the basis of performance on the two types of probe trials, we could discriminate between four different strategies the lizards might have been using to locate the goal rock (Table 1, Fig. 2). If the lizards located the rock during acquisition by trial-and-error search or praxis (rules for stereotyped motor patterns such as ‘search towards wall’), we would not expect them to have an expectation of reward in any particular quadrant and would thus anticipate little bias for any quadrant of the maze on None-Hot or None-Hot-and-Turn probe trials. If the lizards have a group bias for the goal quadrant during both None-Hot and None-Hot-and-Turn probe trials, this suggests that the lizards were attending to the distal cues and thus using a spatial search strategy. A bias to the goal quadrant on None-Hot probe trials does not necessarily indicate a spatial search strategy. In these situations lizards could have been using local features of the wall or the goal rock, alone or in combination, with distal cues to identify the goal quadrant. If lizards use local feature cues to identify the goal during acquisition, we expect them to search for the goal in the original goal quadrant during None-Hot probe trials, but to search for the goal in the diagonally opposite quadrant during

None-Hot-and-Turn probe trials because the walls of the maze and the original goal rock are now in this position. The last acquisition strategy we can identify by probe trial performance is a configural strategy. This strategy involves using a combination of local feature cues and distal cues to locate the goal. During None-Hot probe trials lizards using a configural strategy to locate the goal would be biased to search in the goal quadrant. During None-Hot-and-Turn probe trials, local feature cues and distal cues are put into conflict with each other. The quadrant that any particular lizard is biased to search will depend on the individual lizard’s reliance on particular local feature cues and particular distal cues and how the individual lizard reacts to the conflicting cues. For example, a lizard might define the location of the goal by associating the following, moving away from a distal cue between the right and diagonal quadrants, moving towards some local cue (such as a minor scratch on the wall behind

Table 1
Strategies discriminated by probe trial performance^a

| Strategy | None Hot | None Hot and Turn |
|-----------------|--------------------|------------------------|
| Spatial | Group bias to goal | Group bias to goal |
| Configural | Group bias to goal | Individual bias |
| Local | Group bias to goal | Group bias to diagonal |
| Trial and error | Little group bias | Little group bias |

^a None Hot refers to the first and third probe trials when none of the rocks were heated. None Hot and Turn refers to the second and fourth probe trials when none of the rocks were heated and the arena was rotated 180° while distal spatial cues were left in the same position in relation to the room as they had been in during training.

the goal rock), and arriving at the goal. A conflict in the original arrangement of these cues should lead to biased search, because the lizard has learned to orient to particular cues to navigate, but the search should be in a novel location because the cues no longer exhibit the same spatial arrangement. Thus, each lizard should have a quadrant that is preferred over other quadrants but there may not be a group bias to any particular quadrant as different lizards may have been using different cues to navigate.

3.3. Histology

Approximately 24 h after behavioral testing was completed lizards were sacrificed by rapid decapitation under cold anesthesia. Heads were placed in 10% neutral buffered formalin for 1 week. Brains were removed from skulls, paraffin embedded, sliced coronally at 12 μ m, and stained with cresyl violet.

3.4. Data analysis

Performance on acquisition trials was analyzed by two way (lesion group \times block) repeated measures analysis of variance (ANOVA) followed by Fishers LSD for comparisons between lesion groups. To examine block effects for each lesion group one way ANOVAs for each lesion group were followed by Linear Contrast. To further examine the effects of lesions on initial acquisition and final training we analyzed performance between the probe trial sessions independently using two-way (lesion group \times block) ANOVAs.

To analyze probe trials, we ran separate two way (lesion group \times quadrant) ANOVAs for each dependent measure for each of the four probe trials. When significant main effects or interactions were found, performance was further analyzed by one way ANOVAs for each lesion group followed by planned comparisons to contrast behavior in the goal quadrant with behavior in the three other quadrants of the maze.

These planned comparisons allowed us to determine whether a group bias for the goal quadrant existed. When a group bias on None-Hot probe trials was followed by no bias on None-Hot-and-Turn probe trials it was necessary to determine whether individual lizards in this group had a bias for non-goal quadrants on None-Hot-and-Turn probe trials as characterized by a configural strategy. The completion of such analyses are noted where appropriate.

Previous experiments with lizards in a similar spatial maze were not able to detect use of a spatial strategy [18]. Thus, although we fully realize that performance on each probe trial and our dependent measures are not entirely independent variables, we have analyzed each probe trial and each dependent measure separately and have not corrected alpha for multiple comparisons on

follow up tests. Thus we have a greater chance of Type I errors. We are willing to accept this conformational bias in order to allow ourselves the greatest chance of detecting spatial strategies where we had not been able to find them before.

4. Results

4.1. Histology

Lesion placement was confirmed by viewing sections with a light microscope. Any lizards with more than minimal intrusions into brain regions other than that intended were excluded from the study. Any lizards that were sickly and died of unknown causes during the study were also excluded. One lizard with a DC lesion was killed in an accident prior to the second probe trial. This lizard's data are included in the analysis up to the first probe trial. Final numbers in each group were: Medial cortex lesioned (MCL) = 7, Dorsal cortex lesioned (DCL) = 5 (4 after first probe trial), Sham lesioned controls = 6. Representative sections showing lesions are given in Fig. 3.

Lesioned regions did not necessarily appear devoid of tissue, but rather often appeared to have discombobulated cell layers and abnormal cells as can be seen in Fig. 3. We believe this was due to disorganized re-growth of lesioned tissue [25,44,50]. Because the proportion of abnormal tissue and areas devoid of tissue varied between lizards we did not feel comfortable quantifying lesions by typical measurements of tissue

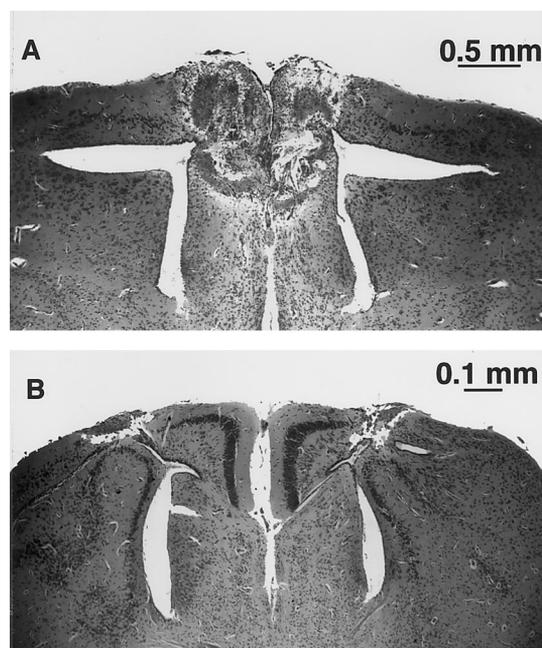


Fig. 3. Representative sections showing medial cortex (A) and dorsal cortex (B) lesions.

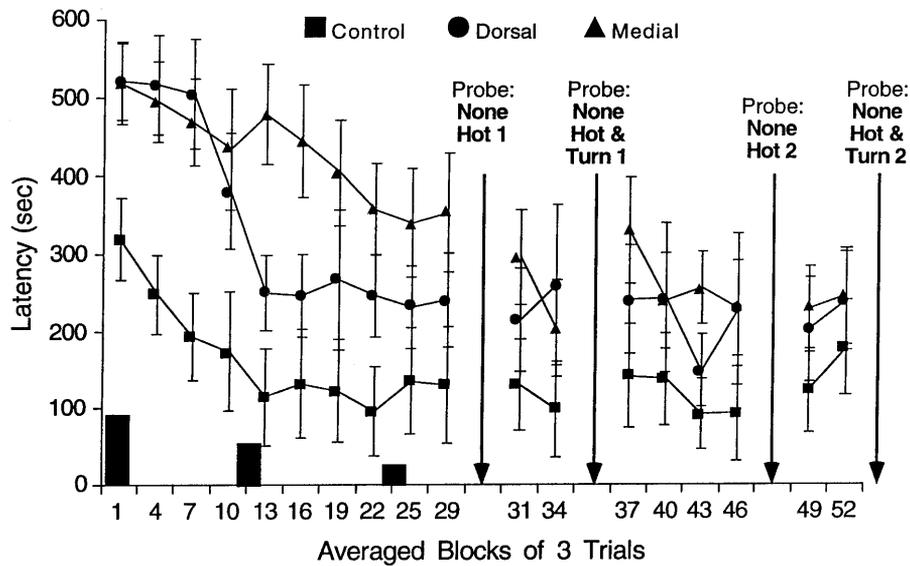


Fig. 4. Latency to the goal for sham lesioned control, dorsal cortex lesioned, and medial cortex lesioned lizards during acquisition. The reduction and removal of the local cue is indicated by the rectangles along the X-axis. The labels and black arrows along the X-axis indicate the timing and type of probe trials. All statistics were performed on single blocks of three trials each. For better presentation, points on the graph are averages of three blocks (nine trials) except when total blocks prior to probe were not divisible by three, then the last blocks prior to probe trial are averages of two blocks (eight trials). Numbers on the X-axis indicate ending block in the computation of averages.

absence. Instead, we give qualitative descriptions of lesions below.

A small portion of the focal tissue appeared intact in most lizards. In MC lesioned animals, the caudal MC was typically spared. The majority of rostral MC tissue was destroyed with slight sparing of more lateral cells. Minimal intrusions into DC appeared in three of the seven MC lesioned lizards and minimal dorsal ventricular ridge (DVR) intrusions appeared in four of the seven MCL lizards. DVR intrusions in two of these four lizards consisted of nothing more than a puckering of tissue without any absence of DVR tissue. In DC lesioned lizards, rostral tissue of the DC prior to when the DC obtains its most dorsal position was typically spared. The most lateral portions of DC were also typically spared. Of the five DC lesions, one had a slight intrusion into DVR rostrally, one had slight intrusions into MC caudally, and one had slight intrusions into MC and DVR in a few middle sections from rostral to caudal. As can be seen in Fig. 3, intrusions into DVR mostly involved puckering of tissue with few cells lost and intrusions into MC typically damaged small portions of the large celled lateral region of the MC.

4.2. Acquisition

4.2.1. Latency

Controls had shorter latencies to the goal rock (Fig. 4) than DCL and MCL lizards (ANOVA: Lesion effect: $F(2,14) = 10.96$, $P < 0.001$; Fishers LSD: controls versus DCL $t(9) = 142.23$, $P < 0.02$; controls versus MCL

$t(11) = 210.82$, $P < 0.0004$). Across all blocks control performance differed from DCL and MCL lizards, and DCL lizards performance differed from MCL lizards (Full Interaction: $F(98, 686) = 1.73$, $P < 0.0001$; Simple effects controls versus DCL $F(49, 392) = 1.58$, $P < 0.01$; controls versus MCL $F(49, 539) = 2.03$, $P < 0.001$; DCL versus MCL $F(49, 441) = 1.53$, $P < 0.02$) (Fig. 4). There was a significant block effect across groups $F(49, 686) = 8.195$, $P < 0.0001$ and each lesion group demonstrated a reduction in latency across trials (Block Effect: Controls $F(49, 245) = 2.8$, $P < 0.0001$, MC $F(49, 294) = 4.74$, $P < 0.0001$, DC $F(49, 147) = 3.63$, $P < 0.0001$; Linear Contrast: Controls $F(1) = 40.04$, $P < 0.0001$, MC $F(1) = 182.27$, $P < 0.0001$, DC $F(1) = 99.74$, $P < 0.0001$).

It appeared that the differences between lesion groups diminished as training went on (Fig. 4). Prior to the first probe trial, controls performed better than DCL and MCL lizards and DCL lizards performed better than MCL lizards ($F(2,15) = 15.23$, $P < 0.0002$; Fishers LSD: controls versus DCL $t(9) = 153.61$, $P < 0.01$; controls versus MCL $t(11) = 266.78$, $P < 0.0001$; DCL versus MCL $t(10) = 113.18$, $P < 0.04$). Between the first and second probe trial there was no significant difference between the groups, principally due to high variability on these few trials. Prior to the third probe trial, controls performed better than MCL lizards ($F(2,14) = 4.04$, $P < 0.04$; Fishers LSD: $t(11) = 149.13$, $P < 0.01$) but did not differ from DCL lizards. All three groups had similar performance at the end of training prior to the fourth probe trial suggesting all three groups acquired the task.

To determine whether the shaping procedure using the local fading cue had influenced undue reliance on this cue, we compared performance between the last block of training prior to the removal of the local fading cue and the first block after the cue had been removed. There was no decrement in performance across lesion groups ($F(1,15) = 0.85$, $P < 0.05$) when the local cue was removed and there was no interaction ($F(2,15) = 1.9$, $P < 0.05$) suggesting that the lizards were not relying on this cue to locate the goal.

4.3. Probe trials

For comparison with statistical results, examples of actual paths taken by lizards during probe trials are shown in Fig. 5.

4.3.1. Total distance

Poor performance by lizards with DCL or MCL lesions can not be attributed to reduced activity levels compared to controls. There was no significant difference between lesion groups in the total distance covered during the first three probe trials. In fact, there was a trend for the controls to cover less distance during None-Hot-and-Turn-1 ($F(2,14) = 4.21$, $P < 0.08$) and None-Hot-2 ($F(2,14) = 3.12$, $P < 0.09$) probe trials and this difference was significant for None-Hot-and-Turn-2 ($F(2, 14) = 4.21$, $P < 0.04$). Controls traversed less total distance than both DCL lizards (Fishers LSD: $t(8) = 547.48$, $P < 0.05$) and MCL lizards (Fishers LSD: $t(11) = 585.89$, $P < 0.02$) during the None-Hot-and-Turn-2 probe trial (Fig. 6).

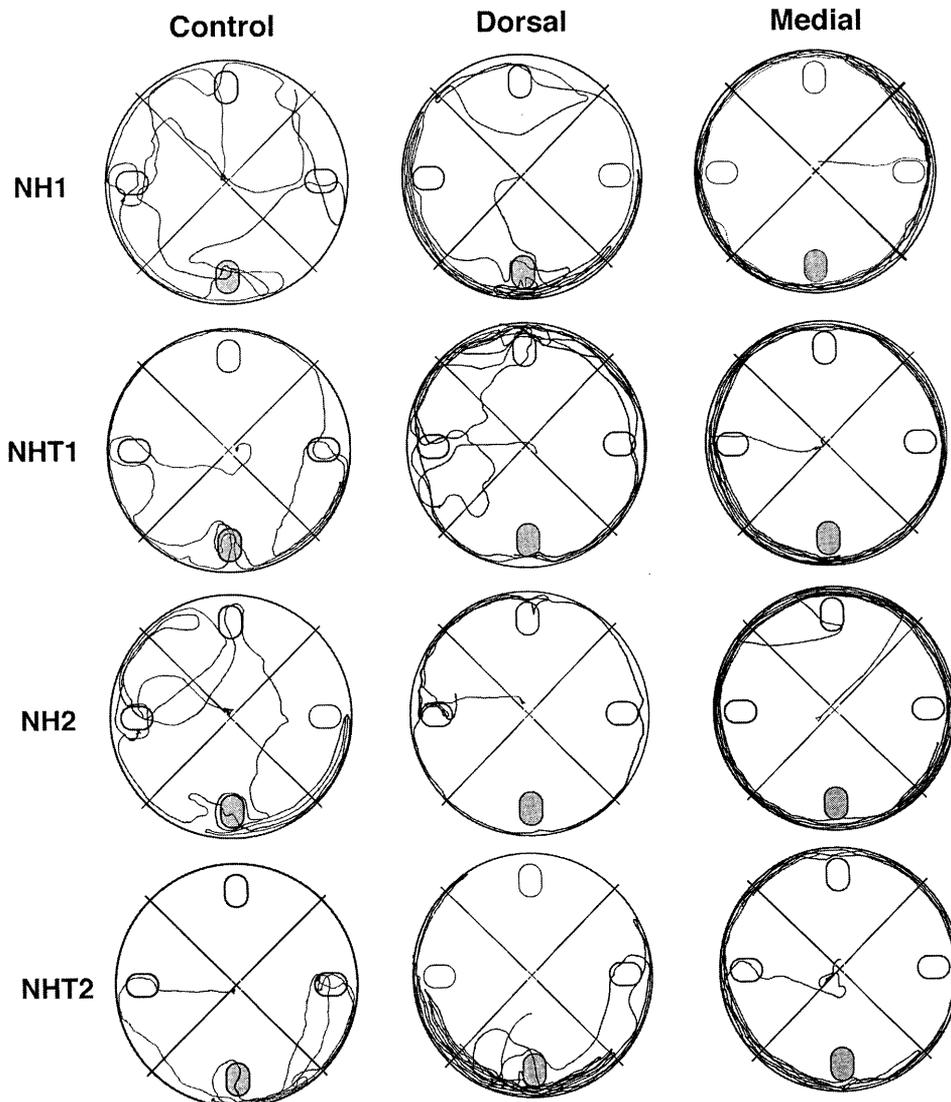


Fig. 5. Representative paths taken by sham lesioned control, dorsal cortex lesioned and medial cortex lesioned lizards during each of the four probe trials. Lizards were released in the center of the maze. The goal rock is at the bottom of the arena and is shaded gray. NH1 = None Hot 1, NHT1 = None Hot and Turn 1, NH2 = None Hot 2, NHT2 = None Hot and Turn 2. During None Hot trials, the hot rock was turned off. During None Hot and Turn trials, the hot rock was turned off and the walls of the maze were rotated 180°.

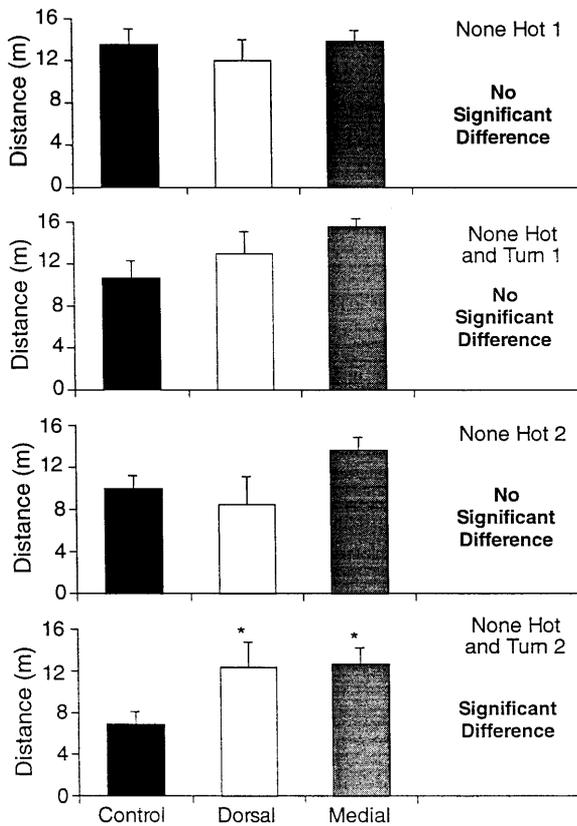


Fig. 6. Total path distance for sham lesioned control, medial cortex lesioned, and dorsal cortex lesioned lizards for each of the four probe trials. Asterisks indicate means that are significantly different from means for control lizards.

4.3.2. Percent distance in quadrants

Controls showed a biased search of the goal quadrant during None-Hot-and-Turn-1. DCL lizards showed a biased search of the goal quadrant during None-Hot-1 (Fig. 7).

4.3.2.1. None-Hot-1. Across lesion groups the quadrants were not searched equally ($F(3,45) = 6.3, P < 0.001$). The difference between quadrants was significant for DCL lizards only ($F(3,12) = 8.07, P < 0.003$). DCL lizards searched the goal quadrant more than the diagonal ($F(1) = 14.88, P < 0.002$), right ($F(1) = 5, P < 0.05$), or left ($F(1) = 20.32, P < 0.0007$) quadrants.

4.3.2.2. None-Hot-and-Turn-1. The quadrants were not searched equally across groups ($F(3,42) = 3.67, P < 0.02$) and lesion groups were not similarly biased ($F(6,42) = 2.61, P < 0.03$). Only controls showed a biased search ($F(3,15) = 5.36, P < 0.001$) of the quadrants with a greater amount of total distance in the goal quadrant than the other three quadrants (goal versus diagonal $F(1) = 15.43, P < 0.0013$; goal versus right $F(1) = 5.31, P < 0.04$; goal versus left $F(1) = 7.06, P < 0.02$).

Because DCL lizards preferred to search the goal

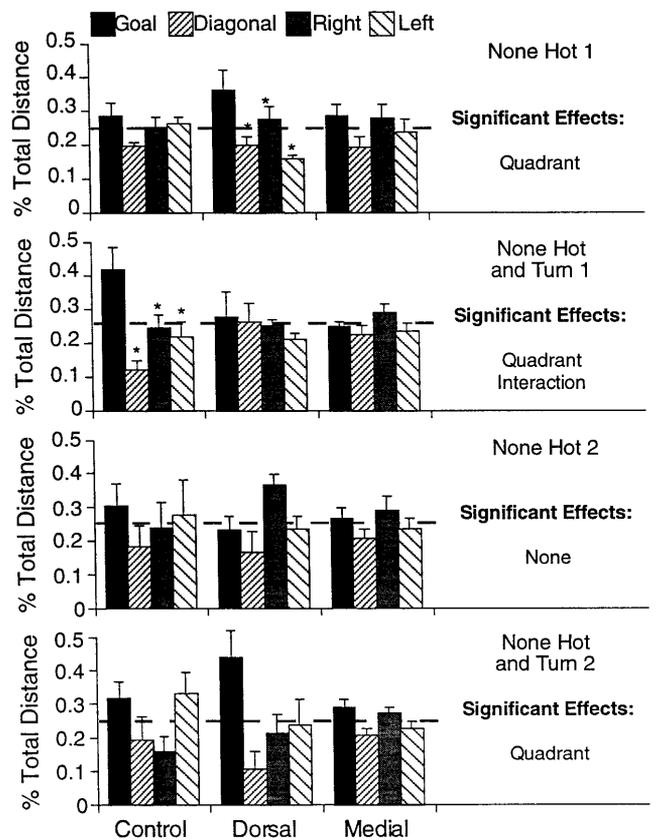


Fig. 7. Percent of total distance explored during the probe trial in each quadrant of the maze for the four probe trials. The dashed line indicates chance performance. Asterisks indicate means that are significantly different from those for the goal quadrant.

quadrant in the None-Hot-1 probe trial but not in the None-Hot-and-Turn-1 probe trial, there was a possibility that they were using a configural strategy [18] (Table 1, Fig. 2). However, further test suggests this was not the case. Biased search is indicated by deviation from a chance value of 25% in that quadrant most preferred by the lizard. If we examine the percentage of total path distance traversed in the most preferred quadrant for each lizard, the group should show a biased search if the individuals had biased search. This was not the case. We ran a one sample t -test comparing the group mean of the total percent path distance traversed in each individual's most preferred quadrant to the chance value of 25%. It did not appear that there was biased search ($t(3) = 2.4, P > 0.05$).

4.3.2.3. None-Hot-2. There were no significant differences between lesion groups in the percentage of total path distance in each quadrant, and the interaction was not significant.

4.3.2.4. None-Hot-and-Turn-2. Across lesion groups, the quadrants were not searched equally ($F(3,42) =$

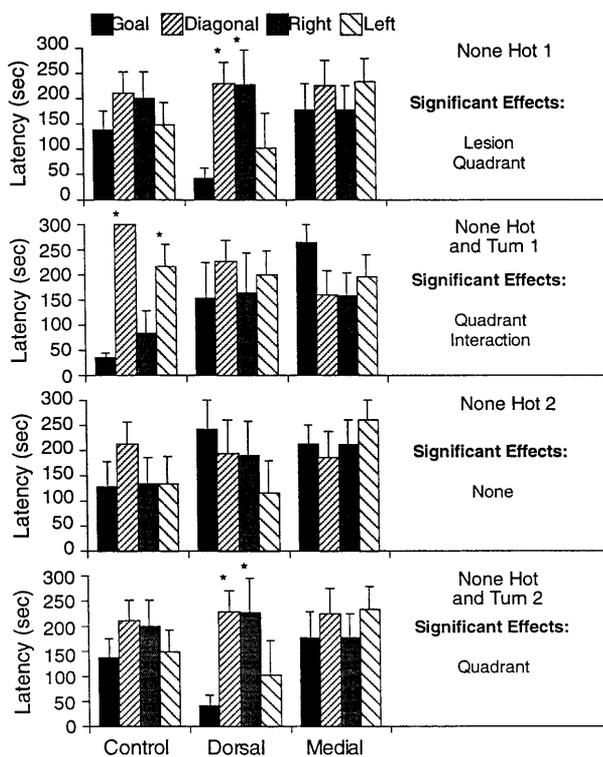


Fig. 8. Latency to reach rocks for sham lesioned control, medial cortex lesioned, and dorsal cortex lesioned lizards for each of the four probe trials. Asterisks indicate means that are significantly different from those for the goal rock.

5.98, $P < 0.002$) but no treatment group had a significant bias to search a particular quadrant.

4.3.3. Latency to rocks

On the first None-Hot probe trial, controls and DCL lizards had significantly shorter latencies to reach the rocks than MCL lizards. The goal rock was reached faster than other rocks during one of the None-Hot-and-Turn-1 for controls and during None-Hot-1 and None-Hot-and-Turn-2 for DCL lizards (Fig. 8).

4.3.3.1. None-Hot-1. Controls and DCL lizards had shorter latencies to rocks than MCL lizards ($F(2,15) = 5.72$, $P < 0.01$; Fishers LSD: controls versus MCL $t(11) = 117$, $P < 0.005$; DCL versus MCL $t(9) = 79.71$, $P < 0.05$). The quadrant effect across groups ($F(3,45) = 3.53$, $P < 0.02$) was significant for DCL lizards only ($F(3,12) = 8.07$, $P < 0.003$), which reached the goal rock faster than the diagonal ($F(1) = 10.21$, $P < 0.008$) or right rock ($F(1) = 6.43$, $P < 0.03$).

4.3.3.2. None-Hot-and-Turn-1. Latencies to the rocks in each quadrant were not equivalent ($F(3,42) = 2.99$, $P < 0.04$) and lesion groups were not similarly biased ($F(6,42) = 3.83$, $P < 0.004$). Controls showed a biased search ($F(3,15) = 16.81$, $P < 0.0001$), reaching the goal rock prior to the rock in either the diagonal ($F(1) =$

40.08, $P < 0.0001$) or left quadrant ($F(1) = 18.68$, $P < 0.0006$).

Because DCL lizards preferred to search the goal quadrant in the None-Hot-1 probe trial but not in the None-Hot-and-Turn-1 probe trial, they may have been using a configural strategy (Table 1, Fig. 2), but tests for biased search of quadrants by individual lizards did not confirm this possibility. To examine individual preferences, we ran a preferred quadrant analyses [18]. The pattern of performance did not suggest individual lizards had a biased search during the probe trial. Latency to the goal rock on the last trial of training was not significantly different from latency to non-preferred rocks during the probe trial ($t(3) = 1.915$, $P > 0.05$). This suggests that strategies guiding behavior to the goal on the last trial of training were not significantly different from behaviors guiding lizards to non-preferred rocks, indicating their strategy was not biased by preference for a particular quadrant.

4.3.3.3. None-Hot-2. There were no significant differences between lesion groups in latency to reach the rocks, and the interaction was not significant.

4.3.3.4. None-Hot-and-Turn-2. Across lesion groups latencies to reach the rocks were not equivalent ($F(3,42) = 2.78$, $P < 0.05$). DCL lizards ($F(3,9) = 3.9$, $P < 0.05$) reached the goal rock faster than the rocks in the diagonal ($F(1) = 7.81$, $P < 0.02$) or right quadrant ($F(1) = 7.54$, $P < 0.02$). No other lesion group reached one rock faster than the other rocks.

4.3.4. Rock crossings

During the None-Hot-1 probe trial controls crossed the goal rock and other rocks more often than MCL lizards. The controls showed a bias for the goal during None-Hot-1 and None-Hot-and-Turn-1 but not during None-Hot-2 or None-Hot-and-Turn-2. MCL lizards showed biased search during None-Hot-and-Turn-1 but this was to a non-goal quadrant (Fig. 9).

4.3.4.1. None-Hot-1. Controls crossed the rocks more than MCL lizards ($F(2,15) = 4.24$, $P < 0.035$, Fishers LSD: $t(11) = 1.49$, $P < 0.01$). The rocks in each quadrant were not traversed to the same extent across lesion groups ($F(3,45) = 6.41$, $P < 0.001$). The difference between rock crossings was significant for controls only ($F(3,15) = 3.45$, $P < 0.04$). Controls crossed the goal rock more than the diagonally opposite rock ($F(1) = 9.32$, $P < 0.02$) but not more than the rock to the left or right side of the goal rock.

4.3.4.2. None-Hot-and-Turn-1. The lesion groups did not have a similar bias for rock crossings ($F(6,42) = 3.77$, $P < 0.0043$). Controls were biased towards the goal rock ($F(3,15) = 11.63$, $P < 0.003$; goal versus diag-

onal $F(1) = 34.08, P < 0.0001$; goal versus right $F(1) = 13.31, P < 0.002$; goal versus left $F(1) = 11.6, P < 0.004$). MCL lizards showed a slight bias for the right rock ($F(3,18) = 3.21, P < 0.047$, goal versus right $F(1) = 9.64, P < 0.006$). DCL lizards did not show a bias for any rock.

4.3.4.3. *None-Hot-2*. There were no significant differences between lesion groups or the number of crossings for each rock and the interaction was not significant.

4.3.4.4. *None-Hot-and-Turn-2*. Across lesion groups, the rocks were not crossed an equivalent number of times ($F(3,42) = 2.79, P < 0.05$), but no treatment group had a significant bias for the goal.

5. Discussion

Our results show that sham-lesioned control lizards readily acquire a spatial maze using non-spatial navigation strategies but do not adopt a spatial strategy even with extended training. Lizards with lesions to DC or MC exhibited deficits in acquisition of a spatial maze.

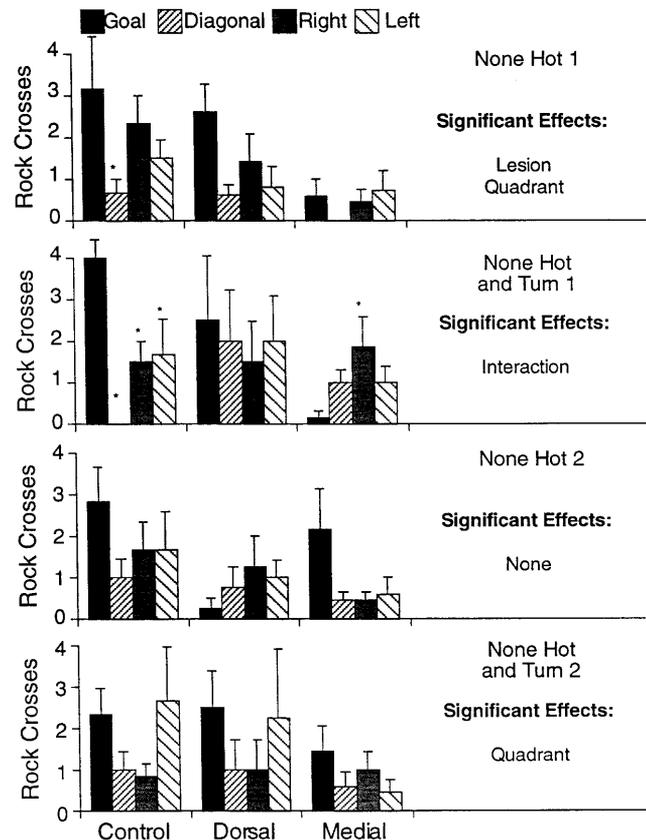


Fig. 9. Number of times rocks were crossed for sham lesioned control, dorsal cortex lesioned, and medial cortex lesioned lizards for each of the four probe trials. Asterisks indicate means that were significantly different from those for the goal rock.

Lesions of the DC slow acquisition of learning and appear to interfere slightly with formation of control-like strategies for the solution of the maze. Lesions of the MC slow acquisition of learning in the spatial maze and severely impair efficient navigation apparently by interfering with the transition from prepotent thigmotaxis to alternative strategies (Fig. 5).

5.1. Acquisition

Both MC lesions and DC lesions significantly affected acquisition of our spatial task. Across all acquisition trials, controls had shorter latencies to reach the goal rock. The impairments of DCL lizards did not appear to be as severe as MCL lizards. During initial training trials, prior to the first probe trial, MCL lizards were impaired compared to DCL lizards and controls while DCL lizards were impaired compared to controls. As training progressed, DCL lizards improved faster than MCL lizards. Although both lesion groups still had longer latencies than controls prior to the third probe trial, only MCL lizards were significantly different from controls at this time. At the end of training, all three groups had shown improvements in performance and there were no significant differences between groups suggesting all three groups eventually learned the task.

5.2. Probe trials

Lesions affected performance on the probe trials. In general, controls and DCL lizards had shorter latencies to explore rocks, crossed rocks more frequently, and traversed a greater amount of total distance in the goal quadrant than MCL lizards suggesting less efficient exploratory strategies by MCL lizards than either DCL lizards or controls. Controls and DCL lizards appeared to use different strategies to solve the spatial task, but we have no convenient method to identify these differences. Although both controls and DCL lizards had a bias for the goal for some of the probe trials for each dependent measure, these instances were inconsistent and did not wholly fit the pattern of performance for any of the four strategies we could discriminate.

5.3. Comparison across lesion groups

There was a significant effect of lesions on probe trial performance for both latency to rocks and number of rock crossings during the None-Hot-1 probe trial. Both controls and DCL lizards reached rocks significantly faster than MCL lizards. Controls crossed significantly more rocks than MCL lizards. By examining the actual paths taken by MCL lizards in Fig. 5, it can readily be seen that these impairments are the result of thigmotaxis. MCL lizards rarely left the walls of the arena and

thus took longer to reach rocks and they did not cross rocks frequently during probe trials.

During None-Hot-and-Turn-1 probe trials controls were biased towards the goal quadrant for each of the dependent measures while neither MCL or DCL lizards showed such a bias. Although qualitative differences between the paths taken by control lizards and lizards in the two lesion groups during the second set of probe trials can be seen in Fig. 5, there were no significant effects of lesions or interactions for any of the dependent measures of quadrant bias for this set of probe trials.

5.4. Strategies used to solve the spatial maze

The strategy used by the MCL lizards to solve the spatial maze can be easily identified. These animals did not show a bias to the goal quadrant for any of the probe trials for any of the dependent measures (Figs. 7–9). Thus, it appears that MCL lizards used a trial-and-error search strategy to locate the rock during acquisition trials. Looking at Fig. 5, this is readily apparent. MCL lizards searched quadrants randomly. They show a praxis strategy of thigmotaxis, simply circling the arena and moving away from the walls only slightly to contact rocks. MC lesions appear to limit the lizards' ability to exercise flexibility in moving from the prepotent strategy of thigmotaxis used by all lizards during initial training to a biased search of the maze.

Unlike MCL lizards, both controls and DCL lizards appeared to have a slight bias for exploration of the goal rock or goal quadrant. Control and DCL lizards' superior performance cannot be attributed to lower activity levels by MCL lizards. The total distance traveled during probe trials was, in general, lowest for controls, slightly higher for DCL lizards and highest for MCL lizards (Fig. 6).

Performance of controls and DCL lizards was not identical, but it is difficult to discern their particular differences in strategy because neither group performed in a manner consistent with one of the four strategies we could identify. Neither controls nor DCL lizards appeared to rely totally on trial-and-error because both groups had some bias to the goal. Neither controls nor DCL lizards showed a bias for the diagonal quadrant on None-Hot-and-Turn probe trials, which would indicate that local cues were being used to guide them to the location of the goal rock during training.

Neither group fit the pattern for a configural or a spatial strategy. DCL lizards had a greater percentage of total path distance in the goal quadrant and reached the goal rock faster than other rocks during the None-Hot-1 probe trial. During None-Hot-and-Turn-1 they did not show a group bias to the goal as required for a spatial strategy nor demonstrate that individuals had a preference for other quadrants of the maze as required for a configural strategy.

Control lizards were biased to the goal only during the first None-Hot probe trial and only for number of rock crossings. This bias on the None-Hot-1 probe trial was not indicative of a configural strategy because it was followed by a group bias for the goal on the None-Hot-and-Turn-1 probe trial rather than individual preference for non-goal quadrants. Instead, this pattern, seen only for rock crossings and only for the first set of probe trials, is indicative of a spatial strategy. Although this one instance appears like a spatial strategy, we hesitate to suggest that lizards had learned a spatial strategy during acquisition. For lizards to have learned a spatial strategy but show it in only this instance, we would have to assume that the number of rock crossings is the most appropriate dependent measure of spatial bias and that controls had a spatial bias during early acquisition that was somehow disrupted by conducting the probe trials or by continued training. Rock crossings appears not to be the only appropriate dependent measure as latency to reach the goal rock clearly decreased over acquisition trials. Latency to reach the goal during acquisition also suggests that performance was not disrupted immediately prior to the second set of probe trials (Fig. 4). Although latency increased slightly after the None-Hot-and-Turn-1 probe trial, prior to the None-Hot-2 probe trial latency to the goal rock was at the lowest in training. If lizards were using a spatial strategy to locate the goal rock during training, latency to the goal rock during the None-Hot-2 probe trial should have been similar to that immediately prior to the probe trial. A comparison of Figs. 4 and 8 show that the control lizards took longer to reach the goal rock during the probe than during training, suggesting a spatial strategy was not being used. In addition, we hesitate to suggest a spatial strategy based on rock crossings during the None-Hot-1 probe trial because goal rock crossings differed only from diagonal rock crossings and not from right or left rock crossings suggesting spatial bias was weak at best.

Thus, it is clear that DCL and control lizards were not using trial-and-error search, local cues, a configuration of cues, or spatial cues to guide them to the goal rock during acquisition. Although bias to the goal was not always significant for controls, the tendency for controls to spend more time in the goal quadrant, to approach the goal rock faster, and to cross the goal rock more during probe trials is admittedly intriguing (Figs. 7–9). It suggests that controls were using some type of cues to guide them to the goal, but that the use of these cues did not provide highly accurate or efficient means by which to identify the location of the goal. DCL lizards also had some bias towards the location of the goal rock but their performance was far more inconsistent than controls, suggesting that the lesion affected their ability to perform with the precision of sham lesioned control lizards. DCL lizards appeared to

be less affected than MCL lizards. MCL lizards appeared to be incapable of using any strategy other than trial-and-error or praxis search to locate the goal rock.

5.5. Comparison with MC and DC function in other reptiles

Previous studies in lizards have found, as we did, that the MC and DC play a role in learning. Lesions of the DC have been shown to impair retention of Lashley mazes and serial reversals while initial reversals were not impaired [53]. Lesions of the MC have been shown to impair reversal learning and extinction [37]. In addition, the habit of intact lizards to use non-spatial strategies to solve a spatial task has been seen in two other lizard species (*A. boskianus* and *A. scutellatus*) in a task nearly identical to this one [18].

Our results are in contrast to those in turtles that do not show a deficit in learning as a result of lesions of the MC [31,32]. This could be due to the specifics of the tasks or slightly different neuroanatomical connections in turtles and lizards [55]. The DC appears to share at least some functions between turtles and lizards. As in lizards [52] DC lesions in turtles produce deficits in reversal learning but also in acquisition of simple stimulus-response associations such as a key press response for a food reward [31]. The similarity between DC function in lizards and turtles is particularly interesting because the DC has distinctly different anatomical connections in turtles and lizards. In turtles, the path from the retina to the lateral geniculate nucleus of the thalamus terminates in both DC and pallial thickening, whereas in lizards it terminates only in the pallial thickening [10,11,55]. Our DC lesions did not include ablation of the pallial thickening.

5.6. Comparison with hippocampal function

The MC and DC of lizards apparently does not share with the avian and mammalian hippocampus a role in spatial learning using distal cues. However, MC and DC lesions do affect the lizards' ability to use non-spatial strategies to efficiently solve a spatial task and thus share with the hippocampus a role in navigation. In addition, rats with hippocampal lesions demonstrate behaviors quite similar to our MCL lizards when tested in the Morris Water Maze. Rats with hippocampal lesions have a tendency to thigmotaxis and take more trials than intact rats to switch from this prepotent behavior to more efficient strategies [20]. Because rats with hippocampal lesions appear to have trouble switching from one strategy for the solution of the Morris Water Maze to another strategy, the role of the hippocampus in spatial learning has been characterized as allowing for pliancy [20]. We believe the MC plays a similar role in pliancy in lizards, allowing for selection of appropriate strategies.

Unlike our MCL lizards, rats with hippocampal lesions tested in the Morris Water Maze can acquire a spatial strategy with extended training or under special training regimes [20,70,71]. Despite extensive training, MCL lizards never adopted control-like strategies for the solution of the spatial maze, although their efficiency in using thigmotaxis and trial-and-error search to locate the hot rock did improve across training trials. The more extensive deficits of MCL lizards compared to rats with hippocampal lesions may be due in part to the greater difficulty lizards in general have acquiring the spatial task [18] or to the fact that lizards have fewer extrahippocampal brain regions to take over the functions of the MC when this region is lesioned.

Lizards with DCL also show some similarity to rats with hippocampal lesions [20] in that acquisition in a spatial maze is slowed but with extensive training their behavior begins to resemble controls. Because DCL lizards did not use one of the four strategies we could discriminate to solve the spatial maze, it is difficult to be certain how similar their behaviors are to intact lizards. We cannot therefore characterize their impairment specifically. These lizards are slower than controls to switch from initial thigmotaxis to more complex strategies, but they eventually show some indication that they expect the goal to be in a particular location, a behavior that is contrary to trial-and-error search (Figs. 4, 7–9). Thus, the DC, like the MC and hippocampus, appears to be related to pliancy but does not appear as crucial to this ability as the MC. Further testing in other behavioral tasks will be necessary to elucidate the function of this reptilian cortical region.

The differential function of the MC and DC may share some similarity with the differential function of their putative homologues. The MC is thought to be more similar to the dentate gyrus and Ammon's horn while the DC is thought to be more similar to entorhinal cortex and subiculum [11,21,34,35,45]. In rats, lesions of the dentate gyrus produce severe deficits in spatial learning [66] and lesions of the medial perforant path that activate the dentate gyrus also appear essential for spatial learning [23]. Entorhinal cortex lesions were not found to interfere with rats' performance in a variable start location Morris Water Maze [36]. However, entorhinal cortex lesions are thought to disrupt reference memory for external cues [36,42] as they disrupt performance in a single start Morris Water Maze [36]. Although MC lesions do not interfere with spatial ability per se, they, like dentate gyrus lesions compared to lesions of other parts of the hippocampal formation, do produce more pronounced deficits in our spatial task than do DC lesions. The reference memory for external cues believed to be a function of the entorhinal cortex is a skill that would be useful during the initial training trials of our spatial maze when the local cue was present and, interestingly, when our DCL

lizards appeared to have the greatest learning impairments (Fig. 4). Thus, structural homologies between MC and DC and parts of the mammalian hippocampal formation may translate into functional similarities with their mammalian counterparts.

5.7. Comparative notes

Because the ability to use distal cues appears to exist in other non-mammal, non-bird species such as the corn snake (*Elaphe guttata guttata*), the gobiid fish (*Bathygobius soporator*), the gold fish (*Carassius auratus*) [2,59] and the cockroach (*Periplaneta americana*) [46], it may seem surprising that our lizards did not readily use distal cues to navigate in a spatial maze. However, the adaptations of a particular species may not indicate the condition for an entire class of organisms. For example, some avian species are clearly specialized to take advantage of spatial information while others are not biased towards the use of spatial cues to locate rewards [8,9,63]. In addition, traits seen in species thought of as 'lower' vertebrates need not appear in those thought of as 'higher' vertebrates and vice versa. In this vein, it is interesting to note that the Brazilian short-tailed opossum (*Monodelphis domestica*) does not use a spatial search strategy in the Morris Water maze [39]. Without appropriate phylogenetic comparisons we can not really gauge how unusual it is for any particular species to exhibit a particular behavior.

Be that as it may, we do believe definitive answers about the existence of spatial memory in lizards should await further testing. Perhaps lizards would show use of distal cues if our maze was easier. However, in comparison to similar mazes used to test spatial learning in mammals [19,39,48,49,65–67,70] our maze was not overly difficult by design. The size of the arena and the size of the goal in relation to the size of the animal can alter the difficulty of a spatial localization task. We compared the ratio of arena size to goal size standardized by the typical length of the animal for our lizard arena to the average pool and platform size in eight randomly chosen Morris water maze experiments using rats. We set the standard length of a rat at 210 cm. This ratio was 206.43 ± 58.22 for the rat experiments and 112.7 for our experiment showing that the lizard spatial arena is easier by this measure than the typical Morris Water Maze.

Although size of the maze did not seem to make our maze more difficult than others, perhaps lizards would perform better with reinforcers or cues that are more ecologically relevant. Heat rewards and stationary visual cues may not be the most appropriate for lizards. We have used escape from high heat as an effective reinforcer in other experiments (unpublished results) with lizards and believe examination of this reinforcer in the spatial arena would be useful. Alternative distal

cues such as olfactory, vibratory, or moving visual stimuli should also be tried.

6. Conclusion

Performance of sham-lesioned *C. inornatus* lizards suggests these lizards, similar to *A. boskianus* and *A. scutellatus* [18], do not readily adopt a spatial strategy to navigate to a goal. Our lesion results support the growing body of evidence showing that the reptilian MC and DC are involved in learning. These two brain regions appear to have slightly different functions. The MC, like the dentate gyrus, appears to be necessary for the flexible behavior important for learning navigation strategies in a spatial maze. The DC may be involved in learning about unchanging external cues, similar to the entorhinal cortex, or may be involved more generally in learning as is suggested by work on DC function in turtles [6,31,32,47,54]. DC lesions in lizards impair acquisition of our spatial task but do not appear to prevent the formation of strategies for its solution similar to, but less consistent than, sham-lesioned controls. These characterizations of DC and MC function are necessarily simplistic and incomplete as they are based on performance deficits in only one task. Considerably more behavioral tests must be done before the discrete functional properties of these brain regions can be isolated.

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