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Lesions of the hippocampus or dorsolateral striatum disrupt distinct aspects of spatial navigation strategies based on proximal and distal information in a cued variant of the Morris water task

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Abstract

The hippocampus and dorsolateral striatum are critically involved in spatial navigation based on extra-maze and intra-maze cues, respectively. Previous reports from our laboratory suggest that behavior in the Morris water task may be guided by both cue types, and rats appear to switch from extra-pool to intra-pool cues to guide navigation in a sequential manner within a given trial. In two experiments, rats with hippocampal or dorsolateral striatal lesions were trained and tested in water task paradigms that involved translation and removal of a cued platform within the pool and translations of the pool itself with respect to the extra-pool cue reference frame. In the first experiment, moment-to-moment analyses of swim behavior indicate that hippocampal lesions disrupt initial trajectories based on extra-pool cues at the beginning of the trial, while dorsolateral striatal lesions disrupt subsequent swim trajectories based on the location of the cued platform at the end of the trial. In the second experiment lesions of the hippocampus, but not the dorsolateral striatum, impaired directional responding in situations where the pool was shifted within the extra-pool cue array. These results are important for understanding the cooperative interactions between the hippocampus and dorsolateral striatum in spatial learning and memory, and establish that these brain areas are continuously involved in goal-directed spatial navigation. These results also highlight the importance of the hippocampus in directional responding in addition to place navigation.

Keywords

spatial navigation; Morris water task; hippocampus; striatum; cued navigation

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1. Introduction

Manipulations of the Morris water task (MWT; [1, 2]) and virtual MWT (VMWT; [3]) have been studied extensively to elucidate specific strategies used by rodents and humans to navigate to an escape platform based on a constellation of cues located both within and beyond the pool [4]. More recently these manipulations have been used to describe the neurocircuitry that is engaged during these specific behaviors as they relate to learning and memory processes [5].

Of particular interest is the extent to which different brain regions are involved in the processing of extra- and intra-apparatus cues during active navigation. With regard to the MWT, several studies have demonstrated a double dissociation between the hippocampus (HPC) and dorsolateral striatum (DLS) with respect to place navigation based on extra-pool cues and intra-pool cue responding (i.e. a cue marking the platform location). It has been consistently reported that the HPC is critically involved in place navigation based on extra pool-cues, but not cued-responding, whereas the DLS is engaged during intra-pool cue responding, but not place navigation [6, 7]. The extent to which these brain areas interact has been the focus of several research reports [6–11], but remain unclear.

Based on these results in the MWT and other land-based tasks (i.e. the radial arm maze), it has been suggested that the HPC and DLS interact in a competitive manner, such that the region with greater activation is expressed behaviorally based on the demands of the task [6]. It has also been posited that shifts between the HPC and DLS occur in a serial time-dependent manner wherein one (HPC) is behaviorally expressed early in training and the other (DLS) later in training, with a shift between systems occurring over multiple training sessions [10]. It is also possible that such an interaction is cooperative in nature, with the animal actively switching between HPC and DLS based systems while navigating an environment within a given trial, but this has yet to be evaluated experimentally.

Work in our laboratory using moment-to-moment analysis of swim behavior has demonstrated that rats switch from extra-pool to intra-pool cue use when navigating to a submerged platform in the MWT when the platform is marked by a distinct cue [12]. It is hypothesized that rats initially use extra-pool cues (i.e. posters, cabinets, and/or doors) to orient themselves to their location within the pool when released and then switch to using the platform cue to navigate to the goal location. In normal rats, there appears to be a specific “shift point” early in trials where a distinct deceleration in swim speed coincides with a dramatic reduction in heading error to the platform. This is believed to be a behavioral expression of a shift from extra- to intra-pool cue use to guide spatial navigation. Similar results have also been described in humans using the VMWT and eye-tracking equipment [13], which suggests such behaviors generalize across species.

With these behavioral results in mind, the current set of experiments were carried out to determine the role of the HPC and DLS in within-trial shifts in strategy in the MWT using moment-to-moment analysis of heading error and swim velocity to a cued escape platform (Experiment 1), as well as how these brain areas interact when the intra- and extra-pool cues are put into competition by translating the pool within the task environment. The use of this

type of kinematic behavioral analysis has not been reported previously in rats with HPC or DLS lesions. Prior research has focused on describing molar behavior after a set number of trials [7]. It was hypothesized that rats with lesions of the HPC would rely solely on the platform cue to guide behavior, regardless of the location of the pool or the alignment of the platform cue with the extra-pool cues. Rats with lesions of the DLS, on the other hand, were expected to rely on the extra-pool cues to guide behavior regardless of the pool location or the cued platform location within the pool. If damage to these brain areas renders these rats unable to actively switch from one type of navigation strategy to the other, there would also be a lack of shift point head scanning behavior in the rats with lesions.

2. Experiment 1

2.1 Materials and methods

2.1.1 Subjects—Subjects were 25 naïve male and female hooded Long-Evans rats bred at the Psychology Department Animal Research Facility at the University of New Mexico, originally from Charles River Laboratories stock (Charles River Laboratories, Wilmington, MA). All rats were at least 90 days old at the beginning of training and individually housed in plastic cages and maintained on a reverse 12-hour light/dark cycle with food and water available *ad libitum*. All behavioral testing was conducted during the dark phase, and all procedures were approved by the Institutional Animal Care and Use Committee (IACUC) at the University of New Mexico.

2.2.2 Surgery—Rats were randomly assigned to one of three surgical conditions: HPC lesion, DLS lesion, or sham lesion surgeries. All animals were anesthetized with Isoflurane (Phoenix Pharmaceuticals, St. Joseph, MO) and mounted into a stereotaxic frame (David Kopf Instruments, Tujunga, CA). All flat skull stereotaxic coordinates are derived from the atlas of Paxinos and Watson [14] using bregma of the skull surface as the reference point. Neurotoxic lesions were produced in the HPC by injecting a 7.5mg/mL solution of N-methyl-D-aspartate (NMDA) in phosphate buffered saline (PBS) through a 30-gauge cannula attached to a Harvard mini-pump (Harvard Apparatus, Holliston, MA). Ten total infusions were made in each rat, five per hemisphere. The coordinates in millimeters for each are AP: -3.1, -4.1, -5.0, -5.3, -6.0; ML: ± 1.5 , ± 3.0 , ± 3.0 , ± 5.2 , ± 5.0 ; DV: -3.6, -4.0, -4.0, -7.3, -7.3, respectively. Injections were infused at 0.15 $\mu\text{L}/\text{min}$ for two minutes and forty seconds and the cannula was left in the brain for three minutes to allow diffusion of the solution. After surgery, all rats were given 0.1 mL of buprenorphine s.c. as an analgesic, and diazepam (1 mL/kg) was administered by i.p. injection at the first sign of wakefulness.

Neurotoxic lesions were produced in the DLS by injecting a 7.5mg/mL solution of NMDA in the same manner as with the HPC lesions. Four total infusions were made in each rat, two per hemisphere. The coordinates in millimeters for each are AP: +1.5, +2.0; ML: ± 3.2 , ± 4.0 ; DV: -4.4, -4.8, respectively. Sham rats received identical surgical procedures, but no cannula was lowered into the brain. Animals were allowed at least 14 days to recover from surgery before behavioral testing began.

2.2.3 Histology—Following the completion of all behavioral testing rats with HPC and DLS lesions were deeply anesthetized with an i.p. injection of sodium pentobarbital (55

mL/kg) and perfused transcardially with 0.9% saline followed by 4% paraformaldehyde. Brains were removed from the skull and stored in a 20% sucrose solution for at least seven days and then frozen. Coronal sections were cut with a cryostat at 40 μ m through the regions of interest; every fifth section was mounted and stained with cresyl violet. Stained sections were examined microscopically and digitally photographed to verify the extent of lesion damage.

2.2.4 Apparatus—A circular pool measuring 1.5 m in diameter and 48 cm high was placed on a 48 cm tall wooden frame that was mounted on appliance rollers, allowing the pool to be moved laterally while full of water. The escape platform was constructed of plastic and was 25 cm high with a 16 cm $\times$ 16 cm top surface that was covered with wire mesh so that it could be grasped easily by the rats. The platform cue was a black sphere (9 cm in diameter, 11.5 cm in height) attached to a metal rod that extends 11.5 cm above the platform surface. The pool was filled to a depth of 26 cm with cold ($\sim$ 21 C $^{\circ}$) water so that the platform surface was $\sim$ 1 cm below the water surface. The water was made opaque by adding approximately 2 oz. of powdered white tempura paint. The testing room contained several distinct distal visual cues that formed a complex geometry. All behavior was videotaped via a ceiling mounted camera and digital camcorder. The digital video was then transferred to a Linux workstation for analysis.

2.2.5 Behavioral analysis—Video recordings were used to analyze swim paths and latency to the platform location using in-house designed software. Separate analyses of variance (ANOVAs) were used to analyze critical measures for the probe and test trials with lesion (HPC, DLS, and sham) as a between-subjects factor. Significant main effects were followed up using appropriate *post hoc* Fisher's LSD tests. Where appropriate, planned comparisons using one-way ANOVA or the Helmert contrast were used to test differences between sham, DLS, and HPC groups.

2.2.6 Kinematic analysis—Moment-to-moment heading error was determined by digitizing video footage of probe and test trials, as well as the training trials that took place immediately beforehand. These videos were sampled at a rate of 30 frames per second, from the release of the rat into the pool until it grasped the escape platform. For each frame, a line was drawn from the tip of the snout to a point at the midline between the ears. This was used as a measure of heading error relative to the platform location and were calculated for each rat and normalized across 34 time points for each trial so that between-groups comparisons could be made. Heading to the platform was calculated at the determined "shift point" for each rat, or where the shift point head scanning behavior was not evident, the average shift point for control rats. In addition, heading error was computed 37.5 cm and 75 cm (corresponding to half of both the radius and diameter of the pool, respectively) beyond the shift point. This allowed for comparisons of heading error for training vs. probe trials and training vs. platform relocation test trials for all groups.

2.3 Procedure

2.3.1 Cued-platform removal and relocation—Experiment 1 was divided into an initial training period and a probe trial, followed by retraining and a test trial. During initial

training, all rats received two trials per day with the cued platform located in the middle of the eastern quadrant of the pool for half of the rats in each lesion condition, and in the western quadrant for the other half. During each daily session rats were released one time each from one release point closest to the platform (either NE or SE for the eastern platform location, NW or SW for the western location) on trial 1 and one release point far from the platform (either NW or SW for the eastern platform location, NE or SE for the western location) on trial 2. The particular release points were selected randomly so that each rat was released an approximately equal number of times from each of the four possible release points over the course of training. Each rat was released into the pool facing the pool wall and given 60 s to navigate to the platform. Once the rat reached the platform, it was given 5 s to remain on the platform before being returned to the holding cage. If a rat failed to navigate to the platform in 60 s, it was placed on the platform by the experimenter for 5 s and then returned to the holding cage. This training continued until all rats had reached a criterion of three consecutive days of direct swim paths to the platform from the far release points.

After criterion was met, all rats were given a brief probe trial in which the platform and cue were removed from the pool (Figure 1). Rats were released from the same point used in the training trial that preceded the probe trial. Comparisons were made within subjects on this probe trial and the last training trial to determine kinematic differences and heading error at the shift point and corresponding points 37.5 cm and 75 cm beyond the shift point. Three additional days of training were administered after the probe trial, at which time rats were given a single test trial with the cued platform moved to a new location near the pool wall opposite the trained platform location (Figure 1). All rats were released from the same release points as the training trial that preceded the test trial in order to analyze within subject change in trajectory and heading error to the trained and relocated platform locations.

2.4 Results

2.4.1 Histology—The minimal and maximal extent of HPC and DLS lesions are presented in Figure 2. In general, the minimal extent of damage presented is representative of the lesions in the animals included in the results below. HPC rats exhibited near-complete damage to the entire hippocampal formation, including Ammon's Horn (CA1-3) and the dentate gyrus (DG). DLS lesions were small and limited to the dorsolateral region of the striatum. Four rats (2 HPC and 2 DLS) were excluded due to incomplete or excessive lesion damage, resulting in the following group sizes: Sham ($n = 8$), DLS ($n = 6$), and HPC ($n = 7$). Preliminary analyses found no significant main effects or interactions for sex or training platform location; therefore these factors were not included in the results reported below.

2.4.2 Training—Results for the number of trials to criterion are presented in Figure 3A. HPC rats took longer to reach criterion compared to DLS and sham rats, while DLS and sham rats learned the task in a similar number of trials. The number of trials to reach a criterion of three consecutive direct swims from the long release points was recorded. A one-way ANOVA revealed a significant effect of lesion [$F(2,18) = 17.2$, $p < 0.001$, $\eta^2 = 0.66$]. Planned comparisons revealed that HPC rats took longer to reach criterion than DLS

[$F(1,11) = 34.02$, $p < 0.001$, $\eta^2 = 0.76$] and sham rats [$F(1,13) = 39.06$, $p < 0.001$, $\eta^2 = 0.75$], while the DLS and sham rats did not differ in number of trials to criterion [$F(1,12) = 0.17$, $p = 0.94$, $\eta^2 = 0.01$].

2.4.3 No-platform probe trials—Immediately after reaching criterion, rats were given a brief (~5 s) probe trial from the last release point used during training with the platform and cue removed from the pool. Representative swim paths for the last training trial and probe trial are presented in the top row of Figure 4. HPC rats were impaired in the absence of the cued platform, while DLS and sham rats navigated toward the platform location despite the absence of the cue. Swim distance and the minimum distance to the trained platform location (Figure 3B) were analyzed using separate ANOVAs. No significant differences between groups were found for distance traveled [$F(2,18) = 2.31$, $p = 0.13$, $\eta^2 = 0.20$]. There was a significant effect of lesion group for the minimum distance measure [$F(2,18) = 3.64$, $p = 0.047$, $\eta^2 = 0.29$]. Planned comparisons indicate that sham [$F(1,13) = 82.9$, $p < 0.001$, $\eta^2 = 0.86$] and DLS [$F(1,11) = 78.34$, $p < 0.001$, $\eta^2 = 0.88$] rats swam closer to the trained platform location compared to HPC rats, while no significant differences between sham and DLS rats were noted [$F(1,12) = 0.06$, $p = 0.95$, $\eta^2 = 0.01$].

2.4.4 Platform relocation test trials—Following the no-platform probe trials, three additional days of training were carried out before rats received a platform relocation test trial (Figure 1). Results for average latency and path length to the new platform location are presented in Figure 3C and 3D, and representative swim paths are plotted in the bottom row of Figure 4. Although DLS rats took longer and had increased distance traveled while navigating to the new platform location compared to HPC and sham rats, measures of mean latency [$F(2,18) = 1.70$, $p = 0.21$, $\eta^2 = 0.16$] and path length [$F(2,18) = 1.85$, $p = 0.19$, $\eta^2 = 0.17$] failed to detect a significant difference. For a more specific analysis of swim behavior, the number of times each rat entered a circular region (30 cm in diameter) immediately surrounding the old platform location were recorded, as well as the total time spent within this region during the test trial. Contrasts comparing the combination of sham and HPC rats to DLS rats were carried out for these measures. While HPC and sham rats swam more or less directly to the relocated platform, DLS rats spent more time in (Helmert contrast; $p = 0.042$), and navigated closer to (Helmert contrast; $p = 0.038$) the old platform location.

2.4.5 Kinematic analysis—For a more detailed description of within-trial behavior in situations where the cued platform was removed from the pool or shifted to the adjacent quadrant within the pool, moment-to-moment analyses of heading error were carried out at three distinct points during the swim path during both the no platform probe trials and the platform relocation test trials. The shift point, where head-scanning behavior is evident, is hypothesized to correspond to a shift in navigational strategies from extra- to intra-pool cues. We compared heading errors for both the last training trial and the subsequent probe and relocation test trials at the shift point (or the average shift point for individual rats that did not display the behavior), 37.5 cm, and 75 cm beyond the shift point. These distances are based on the radius and diameter of the pool, respectively. Results for these analyses are summarized in Figure 5. Separate ANOVAs were carried out for the no platform probe trials and the platform relocation test trials with lesion as a between-subjects factor and trial type

(train vs. probe/test) and distance from the shift point (0, 37.5, and 75 cm) as within-subjects factors. Discernable shift point head scans were found during the last training trial in sham rats (7/8), but not DLS (1/6) or HPC (1/7) [$\chi^2(2) = 10.52$, $p = .005$]. For the probe trials, there was a significant main effect of lesion where HPC rats had higher heading errors during both the training and probe trials at each distance from the shift point than DLS and sham rats [$F(2,18) = 9.51$, $p = 0.002$, $\eta^2 = 0.51$]. In particular, HPC lesions led to disrupted trajectories at the shift point [$F(2,18) = 4.13$, $p = 0.03$, $\eta^2 = 0.31$], which in turn led to significant increases in heading error at 37.5 cm [$F(2,18) = 12.91$, $p < 0.001$, $\eta^2 = 0.59$] and 75 cm [$F(2,18) = 4.18$, $p = 0.03$, $\eta^2 = 0.32$] beyond the shift point relative to sham and DLS rats.

Planned comparisons between the last training trial and the probe trial at each distance from the shift point revealed that sham rats (Figure 5A) had similar heading errors during both the training trial and probe trial at 0 cm [$F(1,7) = 1.70$, $p = 0.52$, $\eta^2 = 0.06$] and 37.5 cm [$F(1,7) = 1.0$, $p = 0.35$, $\eta^2 = 0.13$] from the shift point, but the lower error during the training trial compared to the probe trial at 75 cm from the shift point approached significance [$F(1,7) = 4.50$, $p = 0.07$, $\eta^2 = 0.39$], consistent with the hypothesis that removal of the cued platform disrupts terminal, but not initial, swim trajectories. For DLS rats (Figure 5C), no differences between the last training trial and the probe trial were revealed 0 [$F(1,5) = 3.55$, $p = 0.12$, $\eta^2 = 0.42$], 37.5 cm [$F(1,5) = 1.85$, $p = 0.23$, $\eta^2 = 0.27$], or 75 cm [$F(1,5) = 1.29$, $p = 0.31$, $\eta^2 = 0.21$] from the shift point. Similar outcomes were noted for HPC rats (Figure 5E) at 0 cm [$F(1,6) = 0.27$, $p = 0.62$, $\eta^2 = 0.04$], 37.5 cm [$F(1,6) = 0.15$, $p = 0.71$, $\eta^2 = 0.03$], and 75 cm [$F(1,6) = 0.78$, $p = 0.41$, $\eta^2 = 0.12$] from the shift point.

For the platform relocation test trials, again there was a significant main effect of lesion [$F(2,18) = 8.22$, $p = 0.003$, $\eta^2 = 0.48$] with HPC rats having increased heading error compared to sham and DLS rats across all trials and distances from the shift point. The main effect of trial was also significant [$F(1,18) = 7.23$, $p = 0.02$, $\eta^2 = 0.29$], with lower heading error observed for the last training trial compared to the platform relocation trial. The main effect of distance from the shift point was also significant [$F(2,36) = 39.24$, $p < 0.001$, $\eta^2 = 0.69$], as heading error to the platform decreased as the distance from the shift point increased for all groups. The lesion X trial X distance [$F(4,36) = 1.24$, $p = 0.31$, $\eta^2 = 0.67$], lesion X distance [$F(4,36) = 2.01$, $p = 0.11$, $\eta^2 = 0.18$], and the trial X distance interactions were not significant [$F(2,36) = 0.26$, $p = 0.78$, $\eta^2 = 0.14$]; the lesion X trial interaction approached significance [$F(2,18) = 3.49$, $p = 0.052$, $\eta^2 = 0.28$].

An analysis of the differences between the last training trial and the subsequent platform relocation trial at each distance from the shift point found no significant differences at 0 cm [$F(1,7) = 0.53$, $p = 0.49$, $\eta^2 = 0.07$], 37.5 cm [$F(1,7) = 2.69$, $p = 0.15$, $\eta^2 = 0.28$], or 75 cm [$F(1,7) = 3.38$, $p = 0.11$, $\eta^2 = 0.33$] from the shift point between the last training trial and the platform relocation test trial for sham rats (Figure 5B). A similar pattern of results was revealed for HPC rats (Figure 5F) at 0 cm [$F(1,6) = 0.04$, $p = 0.84$, $\eta^2 = 0.01$], 37.5 cm [$F(1,6) = 0.09$, $p = 0.77$, $\eta^2 = 0.02$], or 75 cm [$F(1,6) = 0.36$, $p = 0.57$, $\eta^2 = 0.06$] from the shift point. DLS rats, on the other hand, had significant increases in heading error to the new platform location than to the trained platform location (Figure 5D) at 0 cm [$F(1,5) = 928.1$, $p < 0.001$, $\eta^2 = 0.99$], 37.5 cm [$F(1,5) = 927.7$, $p < 0.001$, $\eta^2 = 0.99$], or 75 cm [$F(1,5) =$

93.32, $p < 0.001$, $\eta^2 = 0.95$]. This result supports the hypothesis that DLS lesions disrupt proximal cue navigation.

2.4.6 Discussion—In Experiment 1, manipulations of the cued platform within the pool differentially disrupted spatial navigation in sham, DLS, and HPC rats. On probe trials where the cued platform was removed from the pool, Sham and DLS rats swam closer to the platform location than HPC rats, presumably because HPC rats had learned to use the cued platform to guide their swim behavior during training. On test trials where the platform was relocated to another quadrant of the pool equidistant from the start location used during the previous training trial, DLS rats had longer latencies and path lengths to the new platform location. Although these effects were not statistically significant, additional analyses revealed that the increases in latency and path length coincided with increased time spent in and around the old trained platform location compared to sham and HPC rats.

Analysis of moment-to-moment heading error during test trials further lend support to the hypothesis that HPC lesions disrupt initial trajectories while DLS lesions disrupt subsequent swim segments to a cued platform. In the probe and test trials, as well as the training trials that preceded them, HPC rats had higher heading errors than sham or DLS rats at the point in the swim path where sham rats had initiated head scanning behavior, which is believed to coincide with a shift from extra- to intra-pool cue use to successfully navigate to the escape platform [12]. That HPC rats had increased errors at this point compared to sham and DLS rats suggests that initial trajectories were disrupted in these animals, given that shift point head scans occurred early on during swim trials (usually within 1–2 s after being released into the pool). On no-platform probe trials, there was a slight increase in heading error for sham and DLS for the probe trial compared to the preceding training trial, although these differences were not statistically significant. This was expected for sham rats but not DLS rats. One possible explanation is that the platform cue had become part of the overall constellation of cues used by the DLS rats. This difference could also account for the less drastic effect of the platform removal compared to previous studies using a visible platform [12].

DLS rats had dramatically increased heading errors to the new platform location compared to the trained location when the cued platform was moved to a novel location within the pool. This again shows that DLS rats swam to, and persisted in searching at, the old platform location before navigating to the relocated platform. This effect was not evident in sham and HPC rats, and is consistent with the more general findings based on measures of latency and path length, as well as time spent near the platform location. Additionally, shift point head scanning behavior was robust in sham animals, but almost completely absent in HPC and DLS rats. This would indicate a lack of a strategy shift as a result of lesions to these brain areas, as each had utilized different strategies to locate the escape platform. With the changes in intra-pool cues producing differential deficits in rats with lesions of the HPC and DLS, Experiment 2 was carried out to determine how these lesions might alter navigation when the pool itself was shifted within the extra-pool cue reference frame.

3. Experiment 2

3.1 Materials and methods

3.1.1 Subjects—Subjects were 50 naïve male and female hooded Long-Evans rats bred at the Psychology Department Animal Research Facility. The origin and handling of these animals are identical to those used in Experiment 1.

3.1.2 Surgery, histology, apparatus, and behavioral analysis—The surgical and histological procedures, as well as the apparatus, environment, and behavioral analyses, are the same as described in Experiment 1.

3.2 Procedure

3.2.1 Pool shift test and probe trials—In the second experiment, rats received cued-platform training in three blocks of four trials per day for four days. Two pool positions were used and the escape platform was always located in the same overlap position of these pool positions (location B in Figure 6). Half of the rats from each lesion condition were trained with the pool in position 1 and the other half trained with the pool in position 2 (Figure 6). At the end of the eighth block of training trials on day three, a competition test trial was administered. In this test trial the pool was shifted 75 cm (the radius of the pool) laterally from the trained position for all rats, so that the rats trained in pool position 1 were tested with the pool in position 2, and vice versa. Half of the rats in each lesion condition were assigned to the *absolute* shift condition where the cued platform was in the same location relative to the distal room cues (location B), but in the opposite quadrant of the pool than where training occurred. The other half of the rats from each lesion condition were assigned to the *relative* condition where the cued platform shifted along with the pool so that it was in the same quadrant of the pool as it was during training (location C for rats trained in pool position 1, location A for rats trained in pool position 2), but shifted away from the absolute location relative to the distal room cues. Rats were released from novel release points for these test trials (N or S, counterbalanced). At the end of the ninth block of trials on day 3, a 60 s probe trial was administered with the cued platform removed from the pool. The pool remained in the same location within the room for half of the rats in each condition, and for the other half the pool was shifted as in the test trial. Again, rats were released from the N or S so that each rat experienced each release point in the test and probe trials.

On day four rats received the same training, test, and probe trials as on day three with each rat receiving the opposite conditions. Thus, rats that were given the pool shift test trial with the platform in the absolute location on day three received the test trial with the platform in the relative location on day four. Likewise, rats that received the no shift probe trials on day three were given the shift probe trial on day four. Again, release points (either N or S) were counterbalanced so that each rat experienced each release point across the test and probe trials.

3.3 Results

3.3.1 Histology—Lesion extent for HPC and DLS rats are included in Figure 2. As in Experiment 1, the minimal extent of the lesions is representative of the subjects included below. Two rats with incomplete DLS lesions and 3 rats with incomplete HPC lesions were excluded from the results presented here resulting in the following group sizes; sham ($n = 16$), DLS ($n = 15$), and HPC ($n = 14$).

3.3.2 Pool shift training—Group performance across training trial blocks is presented in Figure 7. Sham and DLS rats improved performance rapidly across trial blocks. HPC rats also improved across days of training, but did not reach the levels of the other groups. A repeated measures ANOVA with lesion as a between-subjects factor and the 12 trial blocks as a within-subjects factor found significant main effects for lesion [$F(2,42) = 18.3$, $p < 0.001$, $\eta^2 = 0.47$] and trial block [$F(11,462) = 76.0$, $p < 0.001$, $\eta^2 = 0.64$], as well as a significant lesion X trial block interaction [$F(22,462) = 3.84$, $p < 0.001$, $\eta^2 = 0.16$]. *Post hoc* Fisher's LSD analyses of the significant interaction revealed that HPC rats had greater latencies on all trial blocks compared to DLS and sham rats (all p 's < 0.045), while no differences were found between sham and DLS rats on any trial blocks (all p 's > 0.48).

3.3.3 Pool shift test trials—Results for the lesion groups, as well as representative trials for each condition, are presented in Figure 8. Sham and DLS rats swam quickly to the cued platform when it was in the relative location, but typically navigated in the direction of the relative location in the pool when the platform was in the absolute location. HPC rats, on the other hand, navigated to the cued platform regardless of whether it was in the absolute or relative location. A repeated measures ANOVA with lesion as a between-subjects factor and latencies to the absolute and relative platform location as a within-subjects factor (Figure 8A) revealed a significant main effect of platform location [$F(1,42) = 13.89$, $p = 0.001$, $\eta^2 = 0.25$], indicating that there were, in general, longer latencies for the absolute location compared to the relative location. The main effect of lesion [$F(2,42) = 0.41$, $p = 0.67$, $\eta^2 = 0.02$] and the lesion X location interaction [$F(2,42) = 1.63$, $p = 0.21$, $\eta^2 = 0.07$] were not significant. Planned comparisons within each lesion condition indicated that sham [$F(1,15) = 4.59$, $p = 0.049$, $\eta^2 = 0.23$] and DLS [$F(1,14) = 17.17$, $p = 0.001$, $\eta^2 = 0.55$] rats had longer latencies to the absolute location than to the relative location, whereas HPC rats demonstrated no preference for either location [$F(1,13) = 3.52$, $p = 0.084$, $\eta^2 = 0.21$].

Similar results for path length are reported in Figure 8B. A repeated measures ANOVA with lesion as a between-subjects factor and path length to the absolute and relative platform location as a within-subjects factor revealed a significant main effect of platform location [$F(1,42) = 10.81$, $p = 0.002$, $\eta^2 = 0.21$], indicating that there were longer swim paths to the absolute location than to the relative location for all groups. The main effect of lesion [$F(2,42) = 0.54$, $p = 0.59$, $\eta^2 = 0.03$] and the lesion X location interaction [$F(2,42) = 1.29$, $p = 0.29$, $\eta^2 = 0.06$] were not significant. Planned comparisons within each lesion condition indicated that sham [$F(1,15) = 4.39$, $p = 0.05$, $\eta^2 = 0.23$] and DLS [$F(1,14) = 7.64$, $p = 0.02$, $\eta^2 = 0.35$] rats had longer swim paths to the absolute location than to the relative location, whereas HPC rats demonstrated no preference for either location [$F(1,13) = 3.84$, $p = 0.072$, $\eta^2 = 0.23$].

3.3.4 Shift and no-shift probe trials—Representative swim paths for each lesion condition for shift and no-shift probe trials are presented in Figure 9. For the no-platform probe trials, a repeated measures ANOVA with lesion as a between-subjects factor and with pool (shift and no-shift) and location of interest (absolute vs. other/relative) as within-subjects factors was conducted with latency to region, time spent in region, number of region crosses, and proximity to region as dependent variables (Figure 10). Significant lesion X shift X location interactions were found for latency [$F(2,42) = 6.77$, $p = 0.003$, $\eta^2 = 0.24$], time in region [$F(2,42) = 8.54$, $p = 0.001$, $\eta^2 = 0.29$], region crosses [$F(2,42) = 7.81$, $p = 0.001$, $\eta^2 = 0.27$], and proximity to region [$F(2,42) = 7.15$, $p = 0.002$, $\eta^2 = 0.25$]. To further evaluate the pool shift X location interactions, the data were analyzed separately for each lesion group.

3.3.4.1 Sham rats: Sham rats showed preferences for the absolute location during the no-shift probe trials and for the relative location during the shift probe trials (Figure 9). Within the sham group, there were significant pool shift X location interactions for latency to region [$F(1,15) = 38.91$, $p < 0.001$, $\eta^2 = 0.72$], time in region [$F(1,15) = 68.57$, $p < 0.001$, $\eta^2 = 0.82$], region crosses [$F(1,15) = 17.44$, $p = 0.001$, $\eta^2 = 0.54$], and proximity to region [$F(1,15) = 32.05$, $p < 0.001$, $\eta^2 = 0.68$]. Simple effects tests indicate that during the no-shift probe trials, sham rats navigated faster to [$F(1,15) = 17.92$, $p = 0.001$, $\eta^2 = 0.54$], spent more time in [$F(1,15) = 22.39$, $p < 0.001$, $\eta^2 = 0.60$], crossed [$F(1,15) = 7.74$, $p = 0.01$, $\eta^2 = 0.34$], and navigated closer to [$F(1,15) = 12.87$, $p = 0.003$, $\eta^2 = 0.46$] the absolute location compared to a location in the opposite quadrant of the pool. During the pool-shift probe trials, sham rats navigated faster to [$F(1,15) = 40.76$, $p < 0.001$, $\eta^2 = 0.73$], spent more time in [$F(1,15) = 22.64$, $p < 0.001$, $\eta^2 = 0.60$], crossed [$F(1,15) = 9.83$, $p = 0.007$, $\eta^2 = 0.40$], and swam closer to [$F(1,15) = 25.33$, $p < 0.001$, $\eta^2 = 0.63$] the relative location compared to the absolute location.

3.3.4.2 DLS rats: DLS rats displayed preferences similar to shams for the absolute location during the no-shift probe trials and for the relative location during the shift probe trials (Figure 9 and Figure 10). Significant pool shift X location interactions were found for latency to region [$F(1,14) = 55.36$, $p < 0.001$, $\eta^2 = 0.80$], time in region [$F(1,14) = 133.26$, $p < 0.001$, $\eta^2 = 0.91$], region crosses [$F(1,14) = 32.19$, $p < 0.001$, $\eta^2 = 0.70$], and proximity to region [$F(1,14) = 53.07$, $p < 0.001$, $\eta^2 = 0.79$]. Simple effects tests show that during the no-platform probe trials, DLS rats swam faster to [$F(1,14) = 16.24$, $p = 0.001$, $\eta^2 = 0.54$], spent more time in [$F(1,14) = 40.77$, $p < 0.001$, $\eta^2 = 0.74$], crossed [$F(1,14) = 16.44$, $p = 0.001$, $\eta^2 = 0.54$], and swam closer to [$F(1,14) = 22.44$, $p < 0.001$, $\eta^2 = 0.62$] the absolute location compared to a similar region in the opposite quadrant of the pool. During the shift probe trials, DLS rats swam faster to [$F(1,14) = 24.58$, $p < 0.001$, $\eta^2 = 0.64$], spent more time in [$F(1,14) = 29.87$, $p < 0.001$, $\eta^2 = 0.68$], crossed [$F(1,14) = 14.69$, $p = 0.002$, $\eta^2 = 0.51$], and navigated closer to [$F(1,14) = 23.61$, $p < 0.001$, $\eta^2 = 0.63$] the relative location compared to the absolute location.

3.3.4.3 HPC rats: In contrast to the sham and DLS rats, HPC rats did not show any preferences for either the absolute or comparison location in the no-shift probe trials (Figure 9 and Figure 10). On the shift probe trials, HPC rats displayed similar, but less striking,

preferences for the relative location as sham and DLS rats. Analysis of the pool shift X location interaction revealed significant effects for latency to region [$F(1,13) = 5.14$, $p = 0.04$, $\eta^2 = 0.28$] and time in region [$F(1,13) = 11.83$, $p = 0.004$, $\eta^2 = 0.48$], while the proximity to region measure approached significance [$F(1,13) = 4.31$, $p = 0.058$, $\eta^2 = 0.25$]. No significant effect for regional crosses were noted [$F(1,13) = 1.54$, $p = 0.236$, $\eta^2 = 0.11$]. Simple effects analysis reveal that during the no-shift probe trials, HPC rats did not show any preference for either the absolute or comparison location based on latency to region [$F(1,13) = 0.76$, $p = 0.40$, $\eta^2 = 0.06$], region crosses [$F(1,13) = 2.32$, $p = 0.15$, $\eta^2 = 0.15$], or proximity to region [$F(1,13) = 1.42$, $p = 0.25$, $\eta^2 = 0.10$] measures. The time in region measure approached significance [$F(1,13) = 4.56$, $p = 0.052$, $\eta^2 = 0.26$], with HPC rats showing a trend for increased time in the absolute location. For the shift probe trial, HPC rats demonstrated a preference for the relative location based on the latency to location [$F(1,13) = 7.70$, $p = 0.02$, $\eta^2 = 0.37$] and time in region [$F(1,13) = 13.09$, $p = 0.003$, $\eta^2 = 0.50$] measures. No significant effects were found for region crosses [$F(1,13) = 1.00$, $p = 0.336$, $\eta^2 = 0.07$] or proximity to region [$F(1,13) = 3.42$, $p = 0.09$, $\eta^2 = 0.21$].

3.4 Discussion

When the intra-pool cues were put into competition with the extra-pool distal cue array by shifting the pool within the room prior to test and probe trials, sham and DLS rats overwhelmingly demonstrated a directional response to the relative platform location within the pool whether the cued-platform was in this location or the absolute location, or removed from the pool altogether [15]. HPC rats had a similar, albeit weaker preference for the relative platform location, but only in probe trials where the cued platform was not present in the pool. In test trials where the cued platform was either in the absolute or relative platform location, sham and DLS rats had clear preferences for the relative location compared to the absolute location. HPC rats had nearly identical measures of latency and path length to the platform regardless of whether the cued platform was in the relative or absolute location.

Recent studies have shown that directional responding, as opposed to true place navigation, is learned faster and the preferred navigational strategy for mice [16] and rats in both land [17] and water based tasks [15, 18]. Based on the results of Experiment 2, DLS lesions did not appear to have any effect on this preference for the relative platform location during cued- and no- platform probe trials. Based on findings that suggest DLS rats neglect intra-pool cues in favor of extra-pool cues in navigating to a goal [7, 19] and the presence of head direction cells in the dorsal striatum [20], it was predicted that DLS lesions would disrupt directional responding to the relative location or that these rats would become hyper sensitive to the shift of the pool within the extra-pool cue set, resulting in a preference for the absolute location (or a lack of preference for either platform location). These hypotheses were not supported by the results of Experiment 2. It could be that the pool shift was not dramatic enough of a change in the distal cue view to be detected by the DLS rats, or that the medial aspect of the dorsal striatum (DMS) might be involved in guiding directional responding. Indeed, previous reports have found that lesions of the DMS disrupt navigation in a manner similar to that of HPC lesions [8, 9].

Interestingly, HPC rats demonstrated similar preferences for directional responding during no-platform pool shift probe trials, but not when the cued-platform was located in the relative or absolute location during pool shift test trials. This is in contrast to results reported by Stringer et al [21] where HPC lesions disrupted directional responding in a land-based T-maze task. One possible explanation for this discrepancy is the fact that Stringer et al [21] utilized an appetitive dry land task, while the results described here and elsewhere (i.e. [15, 18, 22]) involved the MWT. Prior research reports have noted differences in shifts in navigation strategy and disruption of behavior as a result of disorientation between dry land and water tasks. One recent study using a T maze found that rats demonstrated an initial response strategy that shifted to place navigation after multiple days of training [23], in contrast to findings in the MWT [22]. Other reports have noted that disorienting rats by rotating holding cages prior to training resulted in impaired navigation in a radial arm maze, but not the MWT [24, 25], even when the task was simplified by using a T maze [26].

For the pool shift test trials, these results support the findings of Experiment 1 in that HPC rats use intra-pool cues to guide behavior regardless of where it is in the pool relative to training, and in this case, to where it is relative to the distal cues. When the cue is absent, however, it appears that directional responding, to some extent, remains intact after HPC lesions. This could be due to spared HPC tissue from incomplete lesions, or that head direction (HD) cells that code for directional orientation have been found in several structures outside the HPC [27]. It is possible that this HD circuit might guide behavior in HPC rats, indeed such a result has been reported recently in mice [16].

4. General Discussion

4.1 Distal vs. proximal cue navigation effects

The results of the current experiments support the hypothesis that the HPC is critically involved in establishing initial trajectories based on extra-pool cues while the DLS is required during subsequent swim trajectories based on intra-pool cues, and that in intact animals these learning systems interact in a cooperative manner where both cue types are available in the MWT. In the absence of the cued platform in the no-platform probe trials, rats with lesions of the HPC were impaired compared to sham and DLS rats. Whereas rats with lesions of the DLS and controls swam closely to the platform location, HPC rats displayed greater minimum distances to the location. On the cued platform relocation trials, DLS rats were disrupted relative to HPC and sham rats. HPC rats overwhelmingly navigated to the new platform location, while sham rats displayed initial trajectories to the old location that were quickly corrected to the new location. Occasionally sham rats would navigate near the old location first; however their persistence and location crosses were reduced compared to the DLS rats. DLS rats spent more time persisting at the old platform location, as evidenced by the number of crosses of the region surrounding the old platform location and the amount of time spent in this region.

These findings indicate that initial trajectories in the MWT are dependent on the extra-pool cues, while subsequent swim paths to the platform are dependent on more intra-pool cues, in this case the cued platform [13]. Given the findings that an intact HPC is necessary for navigation based on a constellation of extra-pool cues [28, 29] and the role of the DLS in

navigating to a cued or visible platform [9], it appears that these two memory systems interact in a cooperative manner within trials in the MWT. Although these results are in accordance with theories of HPC function, it should be noted that this effect may not generalize across different navigation tasks. Recently it has been demonstrated that lesions of the dorsal HPC did not disrupt return trips to a home base in an open field foraging task where the room was illuminated, but did cause a disruption when the room was dark [30]. This result suggests that dorsal HPC lesions do not disrupt navigation to a start location based on a constellation of distal cues. There are several possibilities for reconciling this finding with the results presented here. The MWT involves swimming to a specific goal location from various starting points, while the food foraging task involves learning to return to a single start point from various goal locations. The foraging task also takes place on a flat apparatus that does not contain a conspicuous boundary, which could impact navigational strategies. For example, previous work in our lab has shown that when the prominence of the pool was reduced to a minimal level, rats demonstrated a preference for true place navigation, as opposed to the directional responding reported here and elsewhere [22]. Lastly, the basic differences between dry land and water tasks have been documented previously. The act of swimming vs. walking has also been shown to alter spatial navigation strategies and could change the way in which neural representations of the environment are processed. Specifically, Whishaw and Pasztor [31] found that rats tended to return to reinforced locations in a water task, but not in a dry land task. The stress produced by being forced to swim to find an escape platform as opposed to exploring the environment at will could also bias navigational strategies as well.

4.2 Kinematic Analysis

Results from moment-to-moment behavior analysis provide evidence for the shift point head scanning that was first reported by Hamilton and colleagues [12]. In the present study, sham rats did appear to show discernable shift-point head scans during training trials where the platform was reached quickly and reliably. This behavior was almost completely abolished in rats with HPC or DLS lesions, suggesting that sham rats shift between hippocampal- and striatal-based strategies while navigating to the platform, while HPC rats rely primarily on the intra-pool cues while DLS rats rely primarily on the extra-pool cues.

Analysis of the no-platform probe trials and platform relocation test trials indicate that all groups were reliably navigating to the platform on the last training trial, but HPC rats still had significantly higher measures of heading error at the three distances measured from the shift point. This deficit may be due to impaired initial trajectories. Such a disruption as a function of damage to the HPC could disrupt navigation throughout a given trial, without a detectable impairment on the ability to swim to the platform on a molar level. HPC rats were similarly impaired with regard to heading errors during the probe and test trials in the absence of the cued platform or when the cued platform was moved to a novel location. DLS rats were impaired compared to sham rats, albeit to a lesser degree than HPC rats during no-platform probe trials. DLS rats were even more impaired when the platform was moved to a novel location, resulting in elevated heading errors at all distances from the shift point compared to heading errors during the training trial. These results, along with the minimum-distance measures results, show a disruption in HPC rats compared to DLS or sham rats

when the cued platform is removed from the pool, and a disruption in DLS rats when the platform was relocated to a novel location equidistant from the release point. It is important to note that many of these effects may not have been detected based on traditional analyses of behavior often employed in the MWT [12]. Thus moment-to-moment behavioral analyses may be a more sensitive approach to describing deficits in the MWT.

It is important to note that DLS rats were able to locate the new platform location (often relatively quickly) after searching for the platform at the trained location. This may indicate that DLS rats did not have neglect for the cue that marked the platform location, but that the cued navigation strategy was not the preferred method in these rats for solving the task. This would fit with previous work indicating that rats with damage to the dorsal striatum are able to use intra-pool cues to guide behavior, but only when forced to do so [19].

In contrast to previous studies, HPC rats took longer to reach criterion than DLS and sham rats in Experiment 1. This was unexpected result given the fact that other reports found no deficits in acquisition for HPC rats in visible or cued platform versions of the MWT [7]. One possible explanation is that the extent of the hippocampal lesions in the current study involved almost complete damage to the hippocampus, while other studies have focused on the dorsal hippocampus [32] or the fimbria/fornix [6]. It may also be the case that excessive damage to the overlying cortex might also explain this defect (See Figure 2). This does not seem likely, however, given that only one HPC rat had the most extensive cortical damage and did not differ significantly from other HPC rats on any behavioral measures. In addition, previous reports (i.e. [28]) have found that such extensive cortical damage does not impair performance in similar MWT experiments. Alternatively, the training protocol employed here (two trials per day) could also explain the increased trials to criterion for HPC rats, given the finding that cued learning is incremental. Thus, giving rats reduced training across sessions could intensify the effects of HPC lesions. Likewise, cued training might be enhanced in sham and DLS rats, thus driving the significant effect of the trials to criterion measure. With the results of this experiment indicating that sham and DLS rats use extra-pool cues to learn the platform location, this could also explain the superior training performance of these groups. Given the fact that HPC rats in the current study were able to eventually reach criterion, and were able to navigate directly to the new location during platform relocation trials, there is no reason to suspect that these rats had deficiencies in motivation or sensory processes involved in solving the MWT. Although HPC rats received more training than DLS or sham rats due to the increased number of trials to reach criterion, the results of the test and probe trials were in line with the expected outcomes based on prior research [7].

4.3 Directional responding

When the pool was translated within the extra-pool cue array, sham and DLS rats demonstrated similar preferences for the relative location within the pool, as opposed to the absolute location based on the extra-pool cues. This was the case regardless of the presence or absence of the cued platform [15, 18]. For HPC rats, the presence of the cued platform was important. When the platform was left in the pool for the pool shift test trials, HPC rats swam directly towards it regardless of whether it was in the relative or absolute location.

However, when the cued platform was removed for pool shift probe trials, HPC rats did appear to demonstrate a preference for the relative location similar to that of sham and DLS rats. Although the effect sizes were smaller than those found in sham and DLS rats, this result was unexpected and deserves further consideration. It is possible that circuitry beyond the hippocampus might be critical for directional responding and shifts in intra- and extra-pool cue sets. Indeed, studies of the head direction system have found that thalamic cells that code for specific heading within an environment are important for spatial navigation [27], and lesions of the dorsal tegmental nuclei (DTN) in which these head direction cells are generated disrupt navigation to a cued platform in a similar fashion as those demonstrated in the current set of experiments [33]. In studies using mice, Stackman et al [16] found that inactivation of the anterior thalamic nuclei, a region rich in head direction cells downstream of the DTN, resulted in a preference for place responding as opposed to directional responding. In addition, inactivation of the CA1 region failed to disrupt directional responding in mice when the pool was shifted as in the current experiment. Therefore it is possible that directional responding, to some extent, is intact in rats with HPC lesions. Similarly, as the pool shift experiments involve pitting changes in the intra-pool cue reference frame into competition with the extra-pool cue frame, the entorhinal cortex (EC) may be important for tracking such shifts as opposed to the HPC. Neunuebel and colleagues [34] have recently reported that cells of the medial EC track changes in the extra-maze cue array, while cells in the lateral EC track changes in the intra-maze reference frame in a dry land task. Lastly, the presence of boundary cells in the EC [35] may also be important to directional responding, as it appears that the pool wall is the primary reference frame for the directional responding found here and previously [15, 18, 22, 36, 37]. The extent to which the EC is involved in directional responding, as opposed to true place responding, remains to be determined.

There are limitations related to the experimental design reported here that need to be considered when interpreting these results. In the current experiments, naïve rats with lesions were trained in the MWT. Although the case can be made that pre-training might have reduced some of the differences between lesion groups with regard to training in the task, we were interested in describing the emergence of learning in rats with HPC or DLS lesions. Another limitation was the sample size. Although the trends for the platform relocation test trials were in the expected direction for latency and path length, these effects were not statistically significant. More subjects could have helped to reduce error and increase the power to detect DLS disruptions.

The results reported here prompt several questions to be addressed in future studies. In order to solidify the sequential nature of the interactions between HPC and DLS, studies involving pharmacological inactivation of these brain regions [11] could yield more convincing results using rats that are well trained in the MWT. For example, if these interactions operate in normal rats trained in a similar manner as described here, then immediate inactivation of the HPC should disrupt initial trajectories, while subsequent navigation remained intact. The opposite effect would be expected for DLS inactivation. Since no delay between training and test trials would be necessary for infusion studies like this, a more specific analysis of the nature of these interactions could be possible. Similarly, studies using functional neuroimaging (fMRI, MEG, or EEG) in humans and/or single-unit recordings in rodents

offer the temporal resolution to observe activity in the HPC and DLS while the subject is actively navigating in an environment. Although studies using these techniques have been previously reported in humans [38] and animals [39], questions regarding cooperative interactions within a single trial have not been addressed.

Another consideration to be addressed in future studies is an expansion of the nature of the “shift” from HPC- to DLS- based navigation strategies. The nature of this shift has been described behaviorally in the present study in rodents and using eye tracking in humans [13]. The neural basis of such a shift remains to be described. Recent findings using single-unit recordings in rats indicate that this could be an attention-related process mediated by the medial prefrontal cortex [40]. Again, inactivation studies targeting this brain region in rats, or imaging studies in humans could examine this hypothesis.

In demonstrating the cooperative nature of interactions between HPC and DLS, the experiments presented here provide significant opportunities to further the understanding systems-level cooperation between brain regions involved in learning and memory, and how these interactions shape behavior during goal-directed navigation. From these results, we conclude that HPC lesions disrupt initial trajectories based on extra-pool cues, but not subsequent navigation based on intra-pool cues. In contrast, DLS lesions do not disrupt initial trajectories based on extra-pool cues, but do result in the disruption in the use of intra-pool cues to guide subsequent navigation to the cued platform. It also appears that lesions of the HPC, at least to some extent, disrupt directional responding while DLS lesions do not. In demonstrating the cooperative nature of interactions between HPC and DLS, these experiments present important factors to be considered in understanding systems-level cooperation between brain regions involved in learning and memory, and how these interactions shape behavior.

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Research Highlights

- Rats with hippocampus or striatum lesions were tested in the Morris water task.
- Moment to moment swim behavior was analyzed during shifts in swim behavior.
- Initial trajectories and directional responding required hippocampal activity.
- Subsequent swim behavior was guided by the dorsolateral striatum.
- Behavioral shifts within trials appear to be related to shifts between brain areas.

Figure 1.

Representative procedures for Experiment 1. Small dot indicates release point, dashed box indicates trained platform location with platform removed or relocated.

Figure 2. Coronal sections representing the minimum (Grey) and maximum (Black) extent of HPC (Left) and DLS (Right) lesions in rats included for all experiments. Digital images of the rat brain adapted from Paxinos & Watson [10].

Figure 3.

Results from no-platform probe trials and platform relocation trials in Experiment 1. Average trials to criterion during initial training (A), average minimum distance from the platform location during no-platform probe trials (B), average latency (C) and path length (D) to the new location during relocation test trials.

Figure 4.

Representative swim paths for each lesion condition for no-platform probe trials (Top) and platform relocation test trials (Bottom) in Experiment 1. Black paths indicate the swim paths for the training trial preceding the platform removal/relocation, red paths indicate distance traveled equated to black paths during probe/test trials, and blue paths indicate distance traveled beyond black paths. Grey box indicates platform location during training; black box indicates new location of relocated platform during test trials.

Figure 5.

Summary of results for kinematic analysis of heading error to the platform for each lesion condition at the shift point and 50 cm beyond the shift point. The shift point was determined for each animal that demonstrated a clear deceleration point early in the trial that coincided with a dramatic reduction in heading error to the platform. The average timing of the shift point for sham animals was applied to all other animals for quantitative analysis purposes.

Figure 6.

Layout of the MWT environment used in Experiment 2. Two pool positions were used during training with the platform always in location B. During Test trials, locations A and C served as relative platform locations. Small circles indicate release points used during training, small squares represent release points used during test and probe trials.

Figure 7.
Average latencies for each lesion condition across training trial blocks (4 days, 3 blocks per day) for Experiment 2.

Figure 8. Results for the lesion groups on the cued-platform pool shift test trials. Latency (A) and path length data (B) are on the left, representative trials for each group in each condition are presented on the right.

Figure 9.

Representative swim paths for the no-shift (right) and shift (left) conditions for each lesion condition. For no-shift trials, the darker circle indicates the trained absolute location, while the lighter circle indicates the comparison region in the opposite quadrant. For the shift trials, the dark circle indicates the absolute trained location, while the lighter circle indicates the relative platform location. The large circles indicate the pool boundaries.

Figure 10.

Results for the no-shift (NS) and shift (SH) probe trials for the lesion groups. The measures taken include latency to (A), time in (B), number of crosses of (C), and proximity to (D) region.