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Dorsal and ventral hippocampus: Same or different?

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Dorsal and ventral hippocampus: Same or different?

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Previous work has suggested that the hippocampus (HPC) is not a functionally homogenous structure, because lesions of the septal pole have been found to produce more of a deficit in spatial navigation. To investigate whether this dissociation extends to configural-relational learning, we tested rats with dorsal or ventral HPC lesions in a modified version of the Morris water task and in a discriminative context-conditioning paradigm. Results indicated that dorsal HPC lesions were more efficient in impairing performance in the spatial navigation task but that ventral HPC lesions also had some effect. However, no differences between groups were found in the nonspatial context-conditioning task. Both lesion groups acquired discriminative freezing at a rate identical to that of the controls, but lesioned animals could not acquire preference for the safe environment even after three pairings with shock. Thus, comparison of multiple cues with different emotional valence requires integration along the septotemporal axis of the HPC. Reviewing previous studies, we conclude that although the dorsal HPC pole is more efficient than the ventral in supporting spatial navigation, the dissociation is not absolute. We also hypothesize that physiological activity along the longitudinal axis of the HPC might have particular behavioral relevance. Theoretical implications of this hypothesis are considered.

The hippocampus (HPC) is a brain structure that has been the focus of memory research for the past 30 years. Despite these efforts, the debate around its exact function is still far from resolution (Cohen & Eichenbaum, 1994; Gloor, 1997; Schacter & Tulving, 1994). Hippocampal involvement in spatial learning has long been argued for (O'Keefe & Nadel, 1978) and demonstrated repeatedly (Morris, Garrud, Rawlins, & O'Keefe, 1982; Morris, Schenk, Tweedie, & Jarrard, 1990; Sutherland, Kolb, & Whishaw, 1982; Sutherland & Rudy, 1988). More recent theories have been emphasizing relational-configural aspects of hippocampal function (Eichenbaum, Otto, & Cohen, 1992; Rudy & Sutherland, 1995; Sutherland & Rudy, 1989). Part of the reason for the controversy present in the literature is not only the vast array of behavioral tasks employed, but also the variation in size and type of lesions. Anatomical data (Amaral, Dolorfo, & Alvarez-Royo, 1991; Canteras & Swanson, 1992; Ottersen, 1982; Room & Groenewegen, 1986; Ruth, Collier, & Routtenberg, 1982, 1988; Siegel & Tassoni, 1971; van Groen & Wyss, 1990; Van Haeften, Wouterlood, Jorritsma-Byham, & Witter, 1997; Witter & Groenewegen, 1984), as well as electrophysiological data (Alonso & Garcia-Austt, 1987; Buzsáki, Chen, & Gage, 1990; Edinger, Siegel, & Troiano, 1973; Jung, Wiener, & McNaughton, 1994; McNaughton et al., 1996; Poucet, Thinus-Blanc, &

Muller, 1994), indicate that the HPC is not a homogenous structure along its dorsal/ventral axis.

Early evidence (Lanier & Isaacson, 1975; Nadel, 1968; Sinnamon, Freniere, & Kootz, 1978; Stevens & Cowey, 1973) has suggested that dissociation along the dorso-ventral hippocampal axis has behavioral relevance. However, these studies were not formulated within the more modern theoretical frame of hippocampal function, and they did not test configural-relational learning. In addition, in some cases, the lesions were incomplete or encompassed such areas as the entorhinal and perirhinal cortices. More recently, it has been demonstrated (E. [I.] Moser, M.-B. Moser, & Andersen, 1993; M.-B. Moser, E. I. Moser, Forrest, Andersen, & Morris, 1995) that the dorsal, but not the ventral, HPC is essential for learning in a spatial navigation task. Hock and Bunsey (1998) also reported a deficit following dorsal, but not ventral, HPC lesions in a spatial delayed alternation T-maze task and impairment for both lesion groups in an internal state-shock association test. The results of the latter task were interpreted as evidence that the ventral HPC is particularly involved in using internal states as conditional cues. However, because the learning deficit is present following *both* types of lesions, this conclusion is not well supported.

Although past work focused on the role of the dorsal and ventral HPC in spatial tasks, no similar studies have been undertaken in the case of discriminative context conditioning. Configural-relational theories postulate that the HPC memory system forms representations of relationships among a constellation of cues. From this perspective, spatial learning and context conditioning are both particular examples of a general category of tasks relevant to hippocampal function. The present study used neuro-

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toxic localized lesions of either dorsal or ventral HPC to test whether these two areas have different roles in context conditioning. In addition, we tested the same animals with a water task designed to help overcome thigmotaxic behavior. This paradigm was different than the classical version previously used (E. [I.] Moser et al., 1993; M.-B. Moser et al., 1995).

METHOD

Subjects

Thirty-nine Long-Evans male rats (Charles River Colonies) were used in this experiment. The animals were individually housed in clear plastic cages, were given food and water ad lib, and were kept on a 12:12-h light:dark cycle. All behavioral testing occurred during the dark cycle. The animals were randomly assigned to three groups: control ($n = 13$), dorsal HPC lesion ($n = 13$), and ventral HPC lesion ($n = 13$). No surgical procedures were performed on the control group.

Surgery

The rats were anesthetized with 65 mg/kg of sodium pentobarbital (Penlong, MTC Pharmaceuticals) and placed in a stereotaxic apparatus. The skin of the scalp was cut on the midline and deflected. Each rat received a total of 10 injections (5 per side) of *N*-methyl-D-aspartate (NMDA) in phosphate buffer (5 mg/ml), pH 7.4, at the locations indicated in Table 1, using a 10- μ l Hamilton syringe connected to a cannula (30 Ga). An interval of 3 min was allowed at the end of each injection before the cannula was retracted. The rats were given an interval of 5–7 days for recovery.

Behavioral Testing

The animals were tested in three tasks: conditioned place preference, spatial navigation in the water task, and discriminative context conditioning. The results of the conditioned place preference task will not be reported here. The experiment was run in stages, so that the rats whose data were included for final analysis (following the lesion assessment, see below) were assigned to counterbalanced groups in the context discrimination task.

Water task. This procedure has been previously used by McDonald and White (1994) and is constituted by an alternation of visible and invisible platform training. In this experiment, this paradigm served two purposes: (1) to control for motivational, motor, or other impairments that might have occurred in the lesion groups and (2) to provide an alternative to the classical Morris water task that probably places less computational demand on the HPC.

A white plastic pool 180 cm in diameter was filled with water (temperature, 21°C) mixed with nontoxic white paint. A Plexiglas platform with a 12 \times 12 cm rectangular top was submerged in the southwest quadrant of the pool. A second, wooden platform painted black on the sides and white on the top could be attached to this. All

the testing was conducted using a tracking system (VP118, HVS Image) controlled by an air-operated device used to start and end each trial.

The platform was maintained in the same position during the first 12 days of the procedure. During Days 1–3, the rats were trained to the visible platform, whereas during Day 4, the visible top was removed, and the animals were required to find the invisible platform. This cycle was repeated three times. During Day 13, the platform with the visible top attached was placed in the northeast quadrant in a position diametrically opposed to the one used during Days 1–12. Thus, during Days 4, 8, and 12, the task required spatial navigation; during Days 1–3, 5–7, and 9–12, the animals swam to a visible platform; and during Day 13, an option between a response to the visible cue and a response to location was available.

For Days 1–12, training consisted of four individual trials, each starting at a different cardinal compass point of the room. The sequence of starting points was pseudorandom and was the same for all the subjects. All the subjects were kept in the testing room in individual wire cages mounted in a cage rack. Each animal was removed from the cage and placed in the pool facing the wall. The recording of the swim started when the rat was released and ended either 30 sec later or when the rat found the platform, whichever came first. Regardless of whether he found the platform or not, the rat was allowed to spend a 10-sec interval on the top of the platform (visible or invisible) before being returned to his assigned cage. The animals were all given their first trial, then all given their second trial, and so forth; therefore, the intertrial interval varied with type of task (visible vs. invisible platform) and with level of training. During Day 13, only two trials were run, starting equidistantly between the old and the new platform positions.

Four parameters were calculated on each trial: (1) latency to find the platform, (2) length of trajectory traversed in the water, (3) time spent in the platform quadrant (as a percentage of latency), and (4) heading angle deviation. The latter was defined as the angle between a straight line connecting the starting position and the platform, on the one hand, and a line connecting the starting position and a point located 36 cm on the trajectory, on the other hand. For each day, an average for the four trials was calculated for heading, trajectory length, and platform quadrant preference and reported as one data point. For the heading angle, the data resulting from the starting position closest to the platform were excluded because the distance between these two points was shorter than 36 cm this resulted in a large bias, particularly for the visible platform data.

Context discrimination. The apparatus used for this task has been described in detail elsewhere (Ferbinteanu, Holsinger, & McDonald, 1999). Briefly, two large chambers connected by a middle alley (16.5 \times 11 \times 11 cm) were used. One of the chambers was a black triangular prism (61-cm edge, 30 cm in height) associated with one particular odor (amyloacetate). The other chamber was a white rectangular prism (41-cm edge, 30 cm in height) associated with a second, different odor (eucalyptus). Both chambers and the middle alley were covered with translucent plastic, which blocked access to cues in the testing room. The apparatus was mounted on a

Table 1
Injection Coordinates and Volumes

Dorsal	Ventral
1. AP -3.1; L \pm 1.0; V -3.6 0.25 μ l	1. AP -5.0; L \pm 5.2; V -5.0 0.25 μ l
2. AP -3.1; L \pm 2.0; V -3.6 0.25 μ l	2. AP -5.0; L \pm 5.2; V -7.3 0.25 μ l
3. AP -4.1; L \pm 2.0; V -4.0 0.25 μ l	3. AP -5.8; L \pm 4.4; V -4.4 0.25 μ l
4. AP -4.1; L \pm 3.5; V -4.0 0.25 μ l	4. AP -5.8; L \pm 5.1; V -6.2 0.40 μ l
5. AP -5.0; L \pm 3.0; V -4.1 0.25 μ l	5. AP -5.8; L \pm 5.1; V -7.5 0.40 μ l

Note—AP, anteroposterior from bregma; L, lateral from bregma; V, ventral from bregma. All coordinates are given in millimeters.

transparent tabletop, underneath which an angled mirror (45°) was placed. This set-up allowed monitoring of the animal's movements within the apparatus.

During the whole procedure, the rats were kept on a cart in their home cages and were not allowed to see the room except when introduced and removed from the apparatus. During Day 1, each rat was introduced into the middle alley and allowed to freely explore the two chambers for 10 min (habituation). On Days 2 and 3 (training days), the openings of the middle alley were obstructed. Each rat was assigned a particular combination of room identity (black vs. white), order of pairing (shock on Day 2 or Day 3), and order of testing (paired chamber on Day 4 or Day 5; see below). The animal was introduced into its assigned box and confined there for 5 min. On shock days, 0.6 mA of current (scrambled shock) was delivered for 2 sec at minutes 2, 3, and 4. In each case, signs of distress (flinch, vocalization, defecation) were recorded. On no-shock days, no shock was delivered. During Days 4 and 5 (testing days), freezing (defined as absence of any movement except breathing) was measured upon introduction and confinement (5 min) in a chamber (exposure to both paired and unpaired chambers, but on different days). During Day 6, the middle alley openings were freed and the animals were allowed to explore the apparatus for 20 min (preference). Following this test, there were two more training sessions (Days 7 and 8, second shock; Days 11 and 12, third shock), two more testing sessions (Days 9 and 10, second shock; Days 13 and 14, third shock), and one more final preference test (Day 15). To summarize, the sequence of events was the following: Day 1, habituation; Days 2 and 3, training shock 1; Days 4 and 5, testing 1; Day 6, preference after first shock; Days 7 and 8, training shock 2; Days 9 and 10, testing 2; Days 11 and 12, training shock 3; Days 13 and 14, testing 3; Day 15, final preference. This is illustrated in the following flow chart:

Day 1: habituation ⇒
Days 2 and 3: training I ⇒ Days 4 and 5: freezing I ⇒
Day 6: preference I ⇒
Days 7 and 8: training II ⇒ Days 9 and 10: freezing II ⇒
Days 11 and 12: training III ⇒ Days 13 and 14: freezing III ⇒
Day 15: preference II.

Histology

At the end of behavioral testing, the lesioned animals were deeply anesthetized and perfused intracardially first with 0.9% saline and then with a 10% formalin solution. The brains were removed and placed in 10% formalin for a minimum of 24 h, then moved in a 15% sucrose solution. Following crioprotection, the brains were sectioned in the coronal plane (40 μ) and stained with a metachromatic thionin stain.

Each lesion was assessed by marking the damaged tissue onto histological plates showing the HPC in coronal sections. The area of the lesion was measured in each case (Scion software), and the total volume of the lesion was calculated, using the formula

$$\text{volume lesion} = \sum [(area_i + area_j) / 2 * \text{distance}(area_i, area_j)],$$

where $area_i$ and $area_j$ were the areas of the lesion as measured on two successive histological plates. Total HPC volume was calculated in a similar way. Finally, the volume of the lesion was expressed as a percentage of the total volume of the HPC.

RESULTS

Histology

Figure 1 shows the extent of the smallest (black) and largest (hatched) lesions for both dorsal and ventral HPC

lesion groups. In this study, we attempted to produce a lesion of medium size (40%–60% of total hippocampal volume, as described by M.-B. Moser et al., 1995). Our measurements indicated that the dorsal lesions encompassed an average of 38.83% ($\pm 2.73\%$) of total hippocampal volume, whereas ventral lesions were slightly larger, at 48.12% ($\pm 3.64\%$). Lesion size was not correlated with the results of the behavioral tests for either lesion group, but this is not surprising, given the consistency of the lesion sizes and the restricted number of data points (8 subjects/group).

Dorsal hippocampal lesions. Of the 13 rats that underwent this type of surgery, 5 were eliminated because the lesions were incomplete. Thus, 8 animals were included in this group. All but one of these rats had some cortical damage at the cannula insertion site. The dentate gyrus was completely destroyed bilaterally in all cases. Some small bilateral sparing in the CA3 field at the anterior pole was present in three cases. CA2 sparing, found in 5 animals, was restricted only to the most posterior areas (close to the splenial region) of the dorsal HPC. Partial bilateral CA1 sparing was observed in 1 rat at posterior levels. Small unilateral damage to the dorsal thalamus occurred in two cases, one of which was selected as the smallest lesion. Bilateral damage of the same structure was found in 1 rat; this animal was selected as showing the largest lesion.

Ventral hippocampal lesions. As in the case of the dorsal lesion group, of the total 13 rats, 5 were eliminated because of incomplete lesions. Thus, data from 8 animals were included in the final analysis. In all cases, some cortical damage was present at the cannula insertion point. Sparing of the most ventral tip of the dentate gyrus, similar to the one shown by E. [I.] Moser et al. (1993), M.-B. Moser et al. (1995), and Hock and Bunsey (1998), occurred in all cases. Fields CA3 and CA2 were completely damaged bilaterally in all 8 animals. Unilateral sparing in field CA1 was found in two instances, whereas 2 other animals showed very limited bilateral sparing of this field in the most posterior regions. Some subicular damage occurred only at the most anterior levels of the field (at the border with CA1). Partial damage to the pre- and parasubiculum was found in three cases. Of these, the one encompassing the most extensive portions of these two structures was selected to represent the largest lesion.

The technical means we had available did not allow us to perform a computerized volumetric analysis of lesion size similar to the one presented by M.-B. Moser et al. (1995). However, based on a comparison between our plates and the plates the Moser laboratory presented previously (E. [I.] Moser et al., 1993), as well as on the volumetric lesion reconstruction and on the position of the sections presented by M.-B. Moser et al. (1995), we estimated that our dorsal and ventral lesions would most likely be similar to medium size lesions (40%–60%) presented by this group.

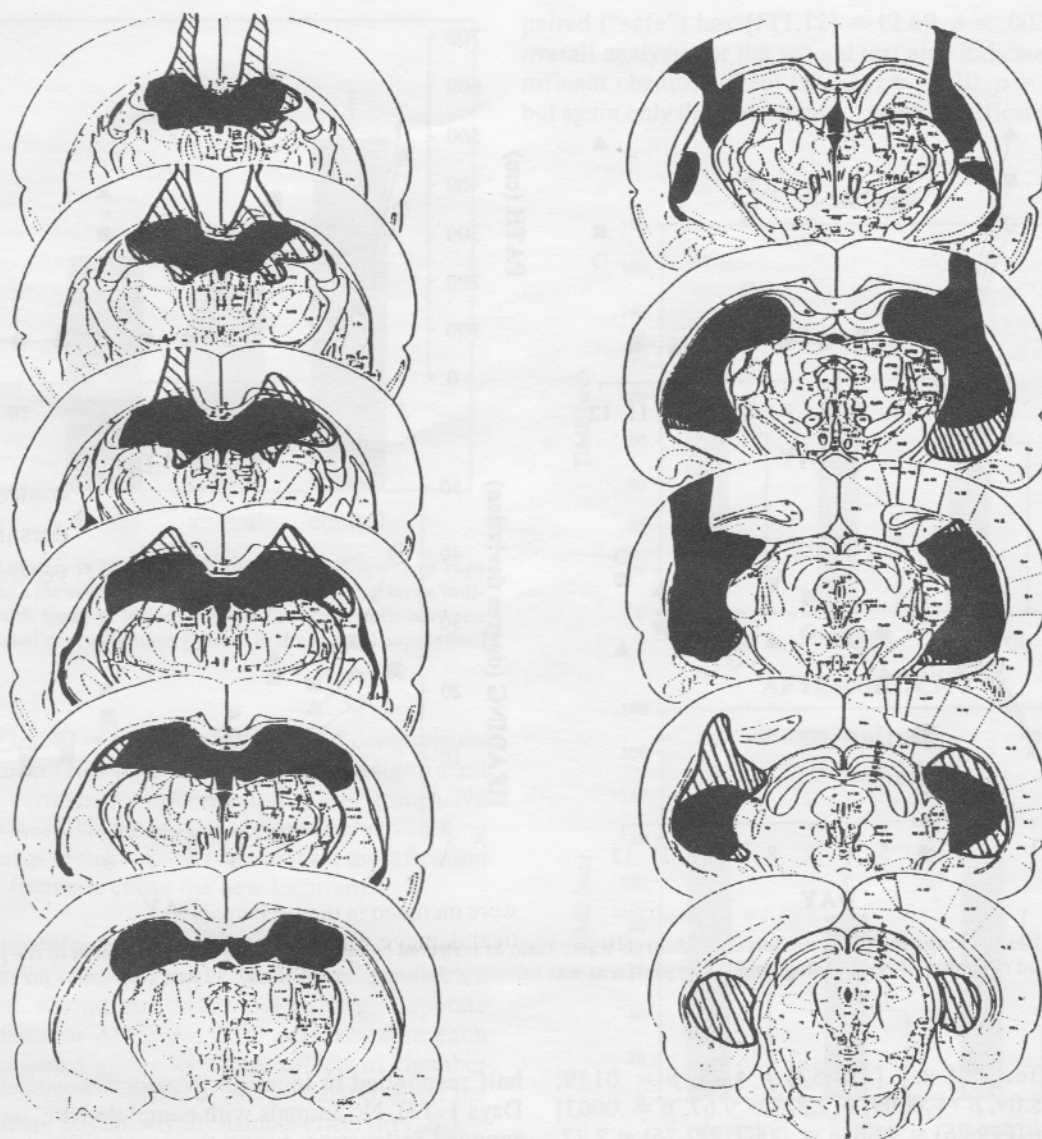


Figure 1. Reconstruction of dorsal (left) and ventral (right) hippocampal lesions. The largest lesion is shown in hatches, and the smallest in solid black. The results of the quantification procedure indicated that dorsal hippocampal lesions were close to 40% and ventral hippocampal lesions close to 50% of the total hippocampal volume.

Water Task

Results from both visible and invisible platform testing are shown in Figure 2.

Visible platform test. Overall lesion \times day analyses of variance (ANOVAs) on the latency, trajectory, quadrant preference, and heading angle indicated, in all cases, a significant effect of day [$F(8,208) = 57.84, p < .0001$; $F(8,208) = 48.68, p < .0001$; $F(8,208) = 10.79, p < .0001$; and $F(8,208) = 16.63, p < .0001$, respectively] but no significant effects of lesion. The analysis also revealed a significant day \times lesion interaction [$F(16,208) = 1.95, p = .0181$] for latency only. Because the data indicated no differences for Days 5–7 or 9–11 for latency and no signif-

icant interactions for the other measurements were found, no further investigations were performed. The results were interpreted as indicating no differences between the groups in motivation, motor ability, or ability to associate a visible cue with a motor response (dorsal striatum type of task).

Invisible platform test. The dorsal HPC group showed longer latencies in finding the platform, swam longer distances, and spent less time in the platform quadrant, as compared with the controls and the ventral HPC group. These differences diminished toward the end of testing. Thus, overall lesion \times day ANOVAs on latency, trajectory, and quadrant preference showed, in all cases, sig-

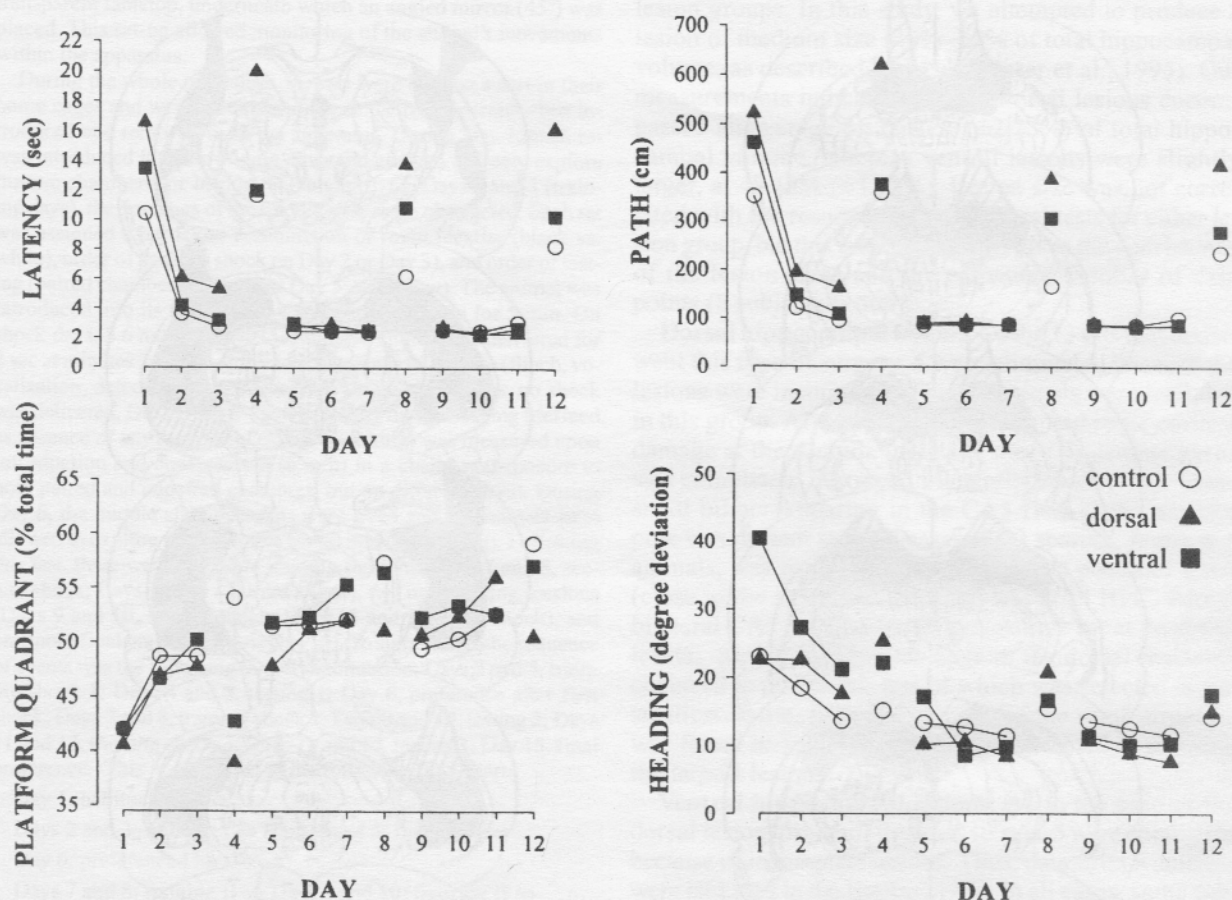


Figure 2. Results of the modified version of the Morris water task, as reflected by latency, path length, time spent in the platform quadrant, and deviation of the heading angle. The platform was submerged during Days 4, 8, and 12 and was visible for the rest of the testing.

nificant effects of day [$F(2,52) = 4.65, p = .0139$; $F(2,52) = 8.09, p = .0009$; $F(2,52) = 9.67, p = .0003$] and of lesion [$F(2,26) = 9.66, p = .0007$; $F(2,26) = 7.77, p = .0023$; $F(2,26) = 6.14, p = .0065$]. Comparisons using the Student–Newman–Keuls post hoc test indicated that, for latency, there were significant differences between the dorsal HPC lesion group and the other two groups during both the first and the last day of spatial learning. The same test run on trajectory showed dorsal HPC versus control and ventral HPC differences during Day 4, but no differences during Day 12. Quadrant preference was significantly higher for controls than for both lesion groups during Day 4, but there were no differences during Day 12. Heading angle measurement showed an overall day effect that approached significance [$F(2,26) = 3.10, p = .0533$], but no significant lesion \times day effect. The data for this last parameter did not suggest any differences between groups during any of the invisible platform tests.

Probe trial, Day 13. Previous results (McDonald & White, 1994) indicated that in a group of normal animals, half responded to the cue (visible platform), and

half responded to location (platform position during Days 1–12). No animals with complete HPC lesions responded to location during the competition test. Thus, whereas some normal animals show strong association between cue and motor response, some others respond better to location. HPC lesion abolishes the response to location. Figure 3 shows the latency data obtained with all three groups in this experiment. Eight out of 13 control animals had latencies longer than 6 sec (a typical latency to reach the visible platform is about 3 sec). Of these 8, 7 animals actually crossed into the quadrant where the platform had been placed during the previous days. The animals with short latencies (2.4–4.3 sec) did not cross this quadrant at all. In the dorsal HPC group, 1 out of 8 animals had latencies longer than 6 sec. This rat did not enter the quadrant previously containing the platform, but 2 others, with latencies of 5.1 and 5.9 sec, respectively, did. In the ventral HPC group, 3 animals had latencies longer than 6 sec, and 2 of them entered the location quadrant. A 3rd animal, which had a latency of 5.2 sec, also crossed the same quadrant. An ANOVA on the latency data revealed a significant lesion effect for the

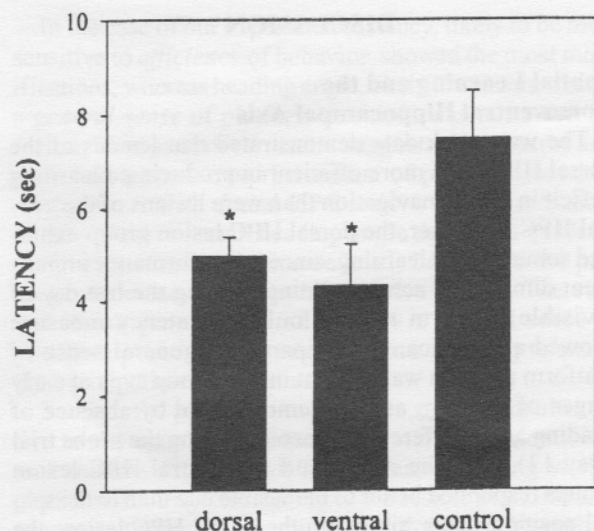


Figure 3. Latency in the competition trial. Both lesion groups were faster than the controls in reaching the visible platform, indicating that both types of lesions altered the equal split between spatial and visual cue responders present in the normal population.

first trial [$F(2,26) = 5.90, p = .0077$], and comparisons using the Student Newman-Keuls test showed significant differences between controls and both lesion groups. No differences were found for the second trial, indicating that one trial was sufficient to introduce a modification in behavior (animals chose the new location).

Context Conditioning Task

Freezing. Figure 4 shows the freezing data collected after the first, second, and third shock pairings. Separate lesion \times chamber ANOVAs were performed in each case, and an investigation of simple effects of chamber was run, using an adjusted α of $.05/3 = .0166$. After the first shock, there was an overall chamber effect [$F(1,26) = 6.55, p = .0167$], but no individual group showed significantly higher freezing in the paired condition. After the second shock, there was an overall chamber effect [$F(1,26) = 28.62, p < .0001$], and all the groups froze significantly higher in the paired chamber [$F(1,12) = 9.23, p = .0103$, for controls; $F(1,7) = 4.57, p = .0156$, for the dorsal HPC lesion group; and $F(1,7) = 12.37, p = .0098$, for the ventral HPC lesion group]. After the third shock, there was an overall chamber effect [$F(1,26) = 37.82, p < .0001$] and significant differences for all groups [$F(1,12) = 18.15, p = .0011$, for controls; $F(1,7) = 12.86, p = .0089$, for the dorsal HPC lesion group; $F(1,7) = 9.97, p = .0160$, for the ventral HPC lesion group].

Preference. The preference data were analyzed in a similar way (Figure 5). There was no overall significant preference for any of the groups during habituation. After the first shock, a significant overall chamber effect [$F(1,26) = 5.41, p = .0289$] was found, but only the control group showed a significant preference for the un-

paired ("safe") box [$F(1,12) = 12.69, p = .0039$]. The overall analysis for the second test also indicated a significant chamber effect [$F(1,26) = 13.30, p = .0012$], but again only the control group spent significantly more

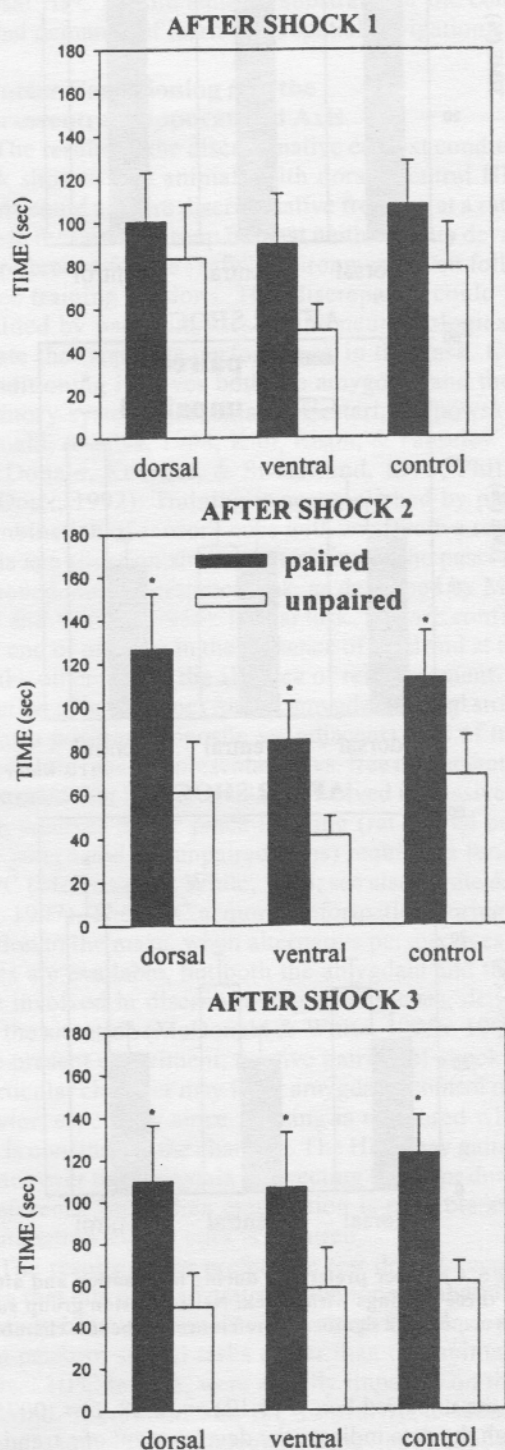


Figure 4. Acquisition of discriminative freezing following successive pairings with shock. Neither lesion group was different from the controls.

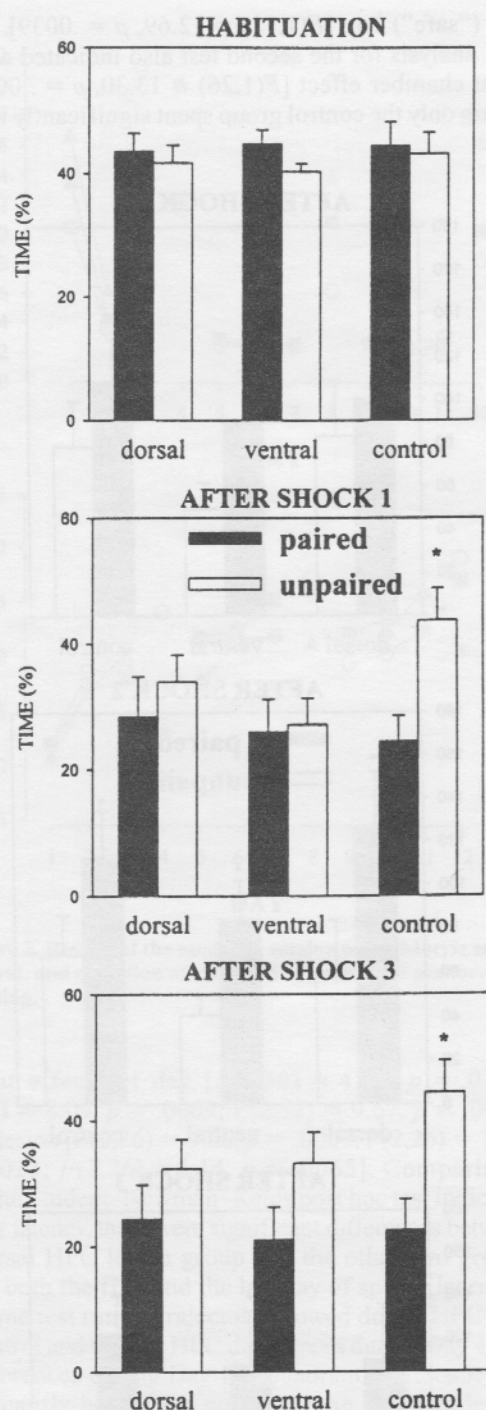


Figure 5. Chamber preference during habituation and after one and three pairings with shock. Neither lesion group succeeded in acquiring a significant preference for the safe chamber.

time in the unpaired box [$F(1,12) = 10.28, p = .0075$]. Although the data indicate the development of a trend in the same direction for the lesion groups, the preference was not statistically significant.

DISCUSSION

Spatial Learning and the Dorsoventral Hippocampal Axis

The water task data demonstrated that lesions of the dorsal HPC were more efficient in producing a learning deficit in spatial navigation than were lesions of the ventral HPC. However, the dorsal HPC lesion group exhibited some limited learning, since its performance impairment diminished across training. During the last day of invisible platform testing, only the latency measure showed a significant discrepancy. A general sense of platform position was present in this group even at early stages of training, as was demonstrated by absence of heading angle differences. Second, during the probe trial (Day 13), both the dorsal and the ventral HPC lesion groups responded better to the visible cue than to the spatial position. Thus, similar to the dorsal HPC lesion, the ventral HPC lesion altered the normal equal split (McDonald & White, 1994) between *place learners* and *cue learners*. Together, these results demonstrate that the ventral HPC can support some spatial learning in the water maze and damage in this area interferes with the processing of spatial information. Therefore, although there is a clear quantitative difference between the dorsal and the ventral HPC functions regarding spatial navigation, our data do not argue for an absolute dissociation.

Our interpretation is more in line with the earlier position of E. [I.] Moser et al. (1993), ventral HPC that has a limited role in spatial learning, and is more compatible with the newest data reported by this group, which show involvement of the ventral HPC in the retrieval of information (M.-B. Moser & E. I. Moser, 1998a). We disagree with the latest position of M.-B. Moser and E. I. Moser (1998b), who argue for a strict dissociation between the functions of dorsal and the ventral HPC. The reasons for our position are multiple.

First, we investigated four different measurements of spatial navigation. It is important to notice that *if only latency is considered*, our data replicate the results of M.-B. Moser et al. (1995) obtained with neurotoxic lesions. However, when other parameters are included in the analysis, the lesion effects prove to be more complicated. In our view, the information provided by these multiple measurements has to be considered in an integrative fashion. Thus, an animal that has some, but limited representation of the platform position within the room may swim in the right direction (small heading angle deviation) and circle around the right position (high preference for the platform quadrant), but the latency for reaching the platform may be high. The path length may vary, depending on whether the animal is searching for the platform slowly or not. Alternatively, a rat that has a very precise representation of platform position will probably show short latency and path length, but his preference for the platform quadrant may be low, because he will not spend a long time searching for the platform.

In the case of our experiment, latency, likely to be most sensitive to *efficiency* of behavior, showed the most modifications, whereas heading angle, likely to concern mainly a *general sense* of platform position, was not much affected. This pattern of results suggests that control animals had a precise representation of platform location, whereas rats with dorsal HPC lesions started searching in the right area (small heading angle deviation, quadrant preference much over chance level) but lacked the precision necessary to make this search efficient. The ventral lesion group acquired quickly a general sense of platform position, but needed more training to make their navigation efficient as well.

Second, the paradigm used in this study is an alternative to the classical, submerged platform version. Normal animals acquire spatial information during visible platform training. Swimming to the visible platform also promotes procedural learning and does not favor thigmotaxic behavior, possibly present in the lesion groups. Third, in this experiment, the rats were allowed an interval of 24 h (as opposed to 4 h, reported by E. [I.] Moser et al., 1993, and M.-B. Moser et al., 1995) between blocks of testing, time during which memory consolidation processes are likely to have occurred (Wilson & McNaughton, 1994). Fourth, there are discrepancies between the results of previously published studies. Thus, E. [I.] Moser et al. (1993) found learning deficits with dorsal HPC lesions larger than 20% and ventral HPC lesions larger than 39% of the total HPC tissue. The more recent study (M.-B. Moser et al., 1995), employing a similar task, indicated that dorsal HPC lesions of 20%–40% and ventral HPC lesions larger than 40% (and up to 80%) of the total HPC had no effect. It is difficult to speculate what the cause of this discrepancy may be, but possibilities are differences in lesion technique (aspiration vs. neurotoxin) and inconsistencies in lesion size assessment.

Our conclusion is that the HPC is heterogeneous in its efficiency of supporting spatial navigation: The gradient is maximal at the dorsal tip and decreases progressively toward the ventral tip. The substrate of this discrepancy is not clear. Particularities of anatomical connections (see Amaral & Witter, 1995, and Witter, Groenewegen, Lopes Da Silva, & Lohman, 1989, for extensive reviews) suggest that the dorsal HPC would receive predominantly exteroceptive information, whereas the ventral HPC is involved mostly in processing internal/emotional input (Amaral & Witter, 1995). Septotemporal connections of pyramidal cells in the distal (bordering subiculum) CA1 tend to run predominantly in the dorsal direction, whereas connections of proximal CA1 run mainly toward the ventral tip of the HPC (Amaral et al., 1991). Second, Buzsáki et al. (1990) reported maximum activation in CA1 located in a more dorsal (or anterior) position, as compared with maximum activation of the dentate gyrus, and a maximum density of interneurons (whose activity has been linked to coherence of the theta and gamma oscillations; Buzsáki & Chrobak, 1995) at the septal end. It is also known that the place cells, more

numerous in the dorsal HPC, have more specific fields than do their counterparts in the ventral HPC (Jung et al., 1994; McNaughton et al., 1996; Poucet et al., 1994). Although details are far from being understood, it is conceivable that the specifics of the local circuitry make the dorsal HPC a more suitable substrate for the computational demands of learning in spatial navigation.

Context Conditioning and the Dorsoventral Hippocampal Axis

The results of the discriminative context conditioning task showed that animals with dorsal ventral HPC lesions could acquire discriminative freezing at a rate similar to the control group but that neither group developed a preference for the "safe" environment, even following three training sessions. This discrepancy could be explained by particularities of the neurobiological substrate that supports performance in this task. Context conditioning involves both the amygdala and the HPC memory systems (Frankland, Cestari, Filipowski, McDonald, & Silva, 1998; Kim, Rison, & Fanselow, 1993; McDonald, Koerner, & Sutherland, 1995; Phillips & LeDoux, 1992). Training is accomplished by pairing a combination of sensory cues with an affective response. This is a situation similar to training in the passive conditioned place preference task, as described by McDonald and White (1995a). In that task, rats are confined at the end of one arm in the presence of food and at the end of the other arm in the absence of reinforcement. Investigation of lesion type (fornix, amygdala, dorsal striatum), of arm position (opposite vs. adjacent), and of training procedure (passive presentation vs. free movement) demonstrated that the amygdala is involved in passive learning, whereas active place learning (rat moved between the paired and the unpaired arms) required a functional HPC (McDonald & White, 1993; see also White & Ouellet, 1997). The HPC acquires information during habituation to the maze, when alternative perspectives on the cues are available, but both the amygdala and the HPC are involved in discriminating among cues, depending on the situation (McDonald & White, 1995a, 1995b). In the present experiment, passive pairing of shock with a particular chamber may favor amygdalar control over behavior, especially since freezing is measured while the rat is confined in the chamber. The HPC may gain precedence over the amygdala in directing behavior during the preference test, when exploration is possible and discrimination among cues is required.

The results of the preference test do not support the idea that rats use a spatial solution for chamber discrimination, because animals with ventral HPC lesions, who can perform spatial tasks easier than can animals with dorsal HPC lesions, were equally impaired on this test. Second, the dorsal and the ventral HPC seem to be equally important for adequate behavior in choosing the "safe" environment, suggesting that discrimination between two sets of cues with conflicting emotional valence *requires* extensive integration along the dorsoven-

tral axis of the HPC. This is different than in the case of spatial navigation, which although it uses a large subset of the hippocampal network in normal conditions (M.-B. Moser & E. I. Moser, 1998a), *requires* functional integrity in only limited portions of the HPC network (E. [I.] Moser et al., 1993; M.-B. Moser et al., 1995; present report). The implications of this finding are discussed below.

Dorsal and Ventral—Same or Different? Hippocampal Function—Spatial or Configural-Relational?

On the basis of differences in anatomical connections, Amaral and Witter (1995) proposed that differences in the content of information input to different poles of the HPC (exteroceptive to the dorsal HPC, interoceptive/emotional to the ventral HPC) may result in differences in behavioral function. Since spatial information is related to exteroceptive input, the conclusion that the dorsal HPC is more efficient in supporting spatial learning agrees with this statement. That the ventral HPC can support some limited acquisition of spatial information (present report), which it probably does in normal conditions (M.-B. Moser & E. I. Moser, 1998a), is also within the interpretation proposed by Amaral and Witter, because the dissociation in anatomical connections is relative, rather than absolute. However, the anatomy also predicts a predominant involvement of the ventral HPC in tasks that require processing of interoceptive information. Presently, there is no evidence to support this view. Hock and Bunsey (1998) found that *both* dorsal and ventral HPC lesion groups were impaired in associating an internal state (hunger/satiety) with shock. (In fact, if anything, the *p* values indicate that the difference between the dorsal lesion group and the controls was more reliable than the difference between the ventral lesion group and the controls.) Many of the earlier reports (e.g., Lanier & Isaacson, 1975; Nadel, 1968; Sinnamon et al., 1978) are difficult to interpret because the lesions are not sufficiently inclusive or restrictive. A different problem is that in other cases (e.g., Stevens & Cowey, 1973), the paradigms employed are difficult to interpret in light of the evidence regarding HPC function accumulated since then. Thus, the data available presently do not provide any indication regarding a possible specialization of function for the ventral HPC.

Our results showed different patterns in the spatial navigation versus context-conditioning tasks. There are three possible explanations that we can envision. First, ventral HPC lesions may be associated with behavioral impairment in a more difficult water task. Such a test in fact does exist, and it consists in navigation to an invisible platform whose position is changed daily (Whishaw, 1985). Direct comparison between normal animal groups (M.-B. Moser et al., 1995) show that rats need 12 training sessions to reach a performance level similar to that of rats tested with the classical paradigm. In contrast, normal animals acquire chamber preference after only 1

training session. This indicates that the *moving platform* and discriminative context-conditioning tasks are not comparable in terms of acquisition rate. The classical water task paradigm requires about 3 (M.-B. Moser et al., 1995), and our modified version 2, training sessions for the control animals to attain efficient navigation. Thus, from the general perspective of acquisition rate, discriminative conditioning to context is more similar to the version of the water task employed in this experiment than to the moving platform version.

A second explanation for the difference obtained between the results of the two tasks is that information acquisition in discriminative context conditioning requires a more extended neural network than is required in the case of spatial navigation. That both lesion groups could learn discriminative freezing at the same rate as control animals argues against this explanation. The data indicate that the lesioned groups were able to form a functional representation of the testing apparatus but that they were unable to use it in particular circumstances.

A third possibility is that although the formation of representations is not different between the two lesion groups, their utilization in the larger context of behavior is. It might be the case that performance in at least some configural-relational, nonspatial tasks requires extended integration along the septotemporal hippocampal axis, whereas spatial navigation tasks can be supported by restricted segments of the HPC. Anatomical (Amaral et al., 1991) and physiological (Buzsáki et al., 1990; Jung et al., 1994; Poucet et al., 1994) data suggest the possibility that activity along the longitudinal hippocampal axis may be necessary for some behaviors, but not for others. If true, this view implies that the spatial task is not simply a subset of the nonspatial, configural task. This is in the sense that spatial navigation would not be equivalent to configural-relational processing applied to spatial input but would be supported by spatial-specific processing applied to spatial information. The converse would be true of configural-relational learning: Input regarding a constellation of cues would undergo a configural-specific type of processing. Because performance in the two types of paradigms is supported partially by a shared network, the spatial-specific and configural-specific memory processes would probably not be completely distinct. On the other hand, they would not be identical either.

The idea that spatial and configural learning are not the same is, of course, not new. O'Keefe and Nadel (1978) and Nadel (1991, 1994) have long argued that there are two memory systems: the locale, which is hippocampally based, and the taxon, which is hippocampally independent. One difference between them is that the locale system has exploration as the motivational drive, whereas the taxon system is based on "standard motivations" (e.g., hunger; Nadel, 1994). Indeed, the configural-relational tasks currently employed are based on associations of a stimulus with some affective response, and thus are likely to involve the amygdala memory system, or of a stimulus with a motor response, and thus are likely to involve

the dorsal striatum memory system (see McDonald & White, 1993, for a synthesis). Second, anatomical evidence indicates that the dorsal and the ventral HPC have different outputs to the nucleus accumbens (see Pennartz, Groenewegen, & Lopes Da Silva, 1994, for a review), a structure that participates in the neural circuits through which the HPC controls motor output. It is thus possible that configural-relational tasks involve a neural network that straddles on the HPC as well as on other memory-related structures, whereas learning in spatial navigational tasks requires only the hippocampal memory system, particularly its dorsal area. In agreement with the position advocated by Nadel (1991, 1994), spatial learning would not be a subset of configural-relational learning. Rather, the two paradigms may involve some common memory processes supported by the common anatomical substrate and some separate, specific memory processes that take place in dedicated networks. Spatial and configural-relational learning would therefore be neither disjunctive nor identical sets, nor would one be a subset of the other, but rather they would be conjunctive sets, with some common and some specific elements. It is, thus, conceivable that the HPC could be the anatomical site of more than one type of memory process.

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