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RESEARCH NOTE

Katharine E. Ragozzino · Stefan Leutgeb
Sheri J. Y. Mizumori

Dorsal striatal head direction and hippocampal place representations during spatial navigation

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Abstract Several theories of basal ganglia function describe a striatal contribution to learning that is independent of hippocampal function. This study examined the question of whether the striatum should be regarded as functioning independently of or acting in concert with limbic structures. Dorsal striatal head direction cells and hippocampal place cells were recorded in parallel while rats performed a hippocampal-dependent radial maze task. Changes in the directional preference of head direction cells and the location of place fields were compared following alterations of the sensory environment. When familiar visual cues were presented in new spatial arrangements, or when new visual cues were placed in a familiar environment, rotations of directional preferences were consistent with the mean place-field response. When familiar visual and nonvisual cues were presented in conflict, or when rats were exposed to novel environments, the responses of the two cell types were inconsistent relative to each other. This pattern suggests that current perceptions and expectations of familiar spatial contexts may dynamically modulate the relationship between hippocampus and dorsal striatum.

Keywords Basal ganglia · Limbic system · Navigation · Rat

Introduction

Recent evidence suggests that multiple brain systems contribute to spatial learning. Spatial deficits result from damage to cortical and subcortical structures including hippocampus (HPC; Morris et al. 1982) and dorsal striatum (DS; Devan et al. 1999). Also, both HPC and DS neurons exhibit spatial codes such as location-specific firing (place fields) or head direction (HD) firing that is consistent with an animal's heading direction independent of its location (O'Keefe and Dostrovsky 1971; Wiener 1993; Mizumori et al. 1999, 2000; Leutgeb et al. 2000). Other data suggest that HPC and DS make independent contributions to learning, with only HPC being selectively involved in spatial processing (McDonald and White 1993; Packard and McGaugh 1996). Here we tested whether the HPC and DS should be considered as functioning independently during spatial learning by recording simultaneously DS HD cells and HPC place cells as rats performed a spatial maze task. Unit responses to various environmental manipulations were compared.

Methods

All methods described here were approved by the University of Utah IACUC. Male rats were individually housed on a 12-h light/dark cycle and reduced to 80% of ad libitum weights. Behavioral testing and unit recording took place within a black-curtained, square environment (158 cm×158 cm×305 cm) while rats performed on an eight-arm, remote-controlled radial maze (Mizumori and Williams 1993). The maze arms (58 cm×5.5 cm) radiated from a round central platform (19-cm diameter). Symmetrical lighting was provided within the curtained arena. For standard testing situations, visual cues were attached to the curtains. The computer and recording equipment were located in a room adjacent to the maze room.

Six rats were recorded during asymptotic performance levels in which a different sequence of maze arms had to be recalled each trial (Mizumori and Williams 1993). The first four arms in the sequence was randomly selected and individually presented to the rat (forced choice procedure). All eight arms were then made available to the rat. Re-entries into maze arms already entered on that trial constituted working memory errors.

When rats completed eight trials within 1 h, they were anesthetized for stereotaxic surgery. Four stereotrodes, two per hemisphere, were implanted (DS: AP +0.2–1.2 mm, L ±1.5 mm, DV 2.0 mm; HPC: AP –3.5–4.5 mm, L ±2.5 mm, DV 1.5 mm). In accordance with previously described methodologies (Leutgeb and Mizumori 1999; Mizumori and Williams 1993), neural activity de-

K.E. Ragozzino · S. Leutgeb
Psychology Department and Program in Neuroscience,
390E. 1530S., Rm 502, University of Utah, Salt Lake City,
Utah 84112, USA

S.J.Y. Mizumori (✉)
Psychology Department, Box 351525, University of Washington,
Seattle, WA 98195, USA
e-mail: mizumori@u.washington.edu
Tel.: +1-206-5432699, Fax: +1-206-6853157

tected on the eight channels was recorded simultaneously and independently with a Datawave Workstation. Each spike occupied a distinct location in a parametric space that took into account numerous waveform properties. Spikes from a given cell tend to form a cluster of spikes. These clusters were matched across days on the basis of similarity of cluster boundaries and waveform characteristics. HD cells were recorded using either single-diode or double-diode tracking. Consistent with previous comparisons of HD responses recorded with either single- or double-diode methods (Leutgeb et al. 2000), changes in directional preferences following experimental manipulations were identical when recorded with either tracking method. Note, however, a possible difference in the maximum amplitude of response in the preferred direction. This apparent difference may be due to the different resolutions of directional movement offered by the two tracking methods. All recording sites were verified histologically.

The following manipulations were performed to test (a) the relative contribution of visual and nonvisual information to the spatial correlates (lights off manipulation), (b) responses to cue conflict situations (maze and cue rotation manipulations), and (c) sensitivity to changes in visual cue reliability (novel/altered environment conditions).

Lights off

Rats performed 5 trials with the lights on (2-min intertrial interval), followed by 5 trials with the lights turned off, and 5 trials with the lights restored (light-dark-light, or LDL condition). Rats were not removed from the maze while lights were turned off and on.

Maze rotation

Rats were brought into the maze room in darkness with the maze rotated 45° or 90° counterclockwise (CCW). They performed 5 trials in darkness, then 5 trials with the lights on. Animals initially entered the test area through one of four entrances (randomly determined). The maze remained rotated throughout the test.

Cue rotation

Rats first performed 5 trials with the visual cues in standard configurations and locations (baseline condition), 5 trials with all cues rotated 180°, then 5 trials with cues restored. The animals were removed from the room while the cues were rotated.

Novel room/altered familiar room

HD and place cells were recorded in the familiar environment, then recorded (1) when rats performed in a structurally similar but different maze room that contained novel visual cues (novel environment condition), or (2) following exposure to novel visual cues or novel visual cue arrangement in the familiar environment (altered familiar environment condition). For the altered familiar environment condition, the curtains surrounding the maze were raised (providing rats with a larger visual environment and new cues), or the distal cues were scrambled (providing new spatial relationships between familiar cues). In both conditions, the rat was removed temporarily from the maze room during the cue manipulations.

Behavioral correlations

For spatial memory recording sessions with unique cell pairs, we tested for correlations (during the manipulated conditions) between HD tuning and errors, and between place cell specificity/reliability and errors. Location specificity reflected the relative difference between in-field and out-field firing rates, and reliability measures reflected the proportion of trials in which the maximum firing occurred within the defined place field (McNaughton et al. 1983). HD cell directional specificity (tuning) was determined by first calculating the firing rates as the rat moved in the preferred direction, then dividing by the mean rate as the rat moved in the remaining seven directions offered by the maze arms. For sessions recorded with a single diode, only outbound rates were used because, as verified in offline analysis, they represent the longest uninterrupted bout of the same behavior in each of the eight directions.

Spatial correlation analysis

To compare the responses of HD and place cells, we calculated the angular deviation between baseline and each manipulated condition. Since space was sampled in 45° steps, we restricted the resolution of the analysis to these increments. For HD cells, the directional tuning was estimated by first calculating the discharge rate for each of the eight directions in baseline and manipulated conditions. These conditions were compared by calculating pairwise correlation coefficients while shifting the maze orientations in 45° steps with respect to each other. The angular deviation that corresponded to the maximum pairwise correlation coefficient was defined as the characteristic response for each recording session. The angular deviation of HPC place fields was measured with a similar algorithm but with a polar coordinate system. When more than one HD cell or more than one place cell was recorded, correlation coefficients were averaged for each cell type.

Results

Thirty-four recording sessions are described in which one or two DS HD cells and one to five hippocampal place cells were recorded simultaneously. Seven sessions included two simultaneously recorded HD cells and 15 sessions included more than one place cell. A total of 11 HD cells were recorded with 20 place cells. Within each manipulation condition, the recording sessions were of unique cell pairs. Many of the same cell pairs were tested across several manipulations. The following description of changes in the directional preferences of HD cells reflects a change in the preferred direction, and not elevated firing during movements in many directions.

Altered illumination

Thirteen HPC place cells and nine DS HD cells were recorded in eight LDL recording sessions. In seven sessions, HD and place cell responses were similar in that they were not significantly altered by changes in room illumination (Fig. 1A). The persistence of spatial correlates in darkness was observed when rats performed the spatial memory task in a familiar environment, when rats had minimal exposure (less than 5 days) to the environment, and when rats performed in novel or altered familiar environments. In one session, both HD (*n*=1) and place cell (*n*=1) changed their response properties in darkness.

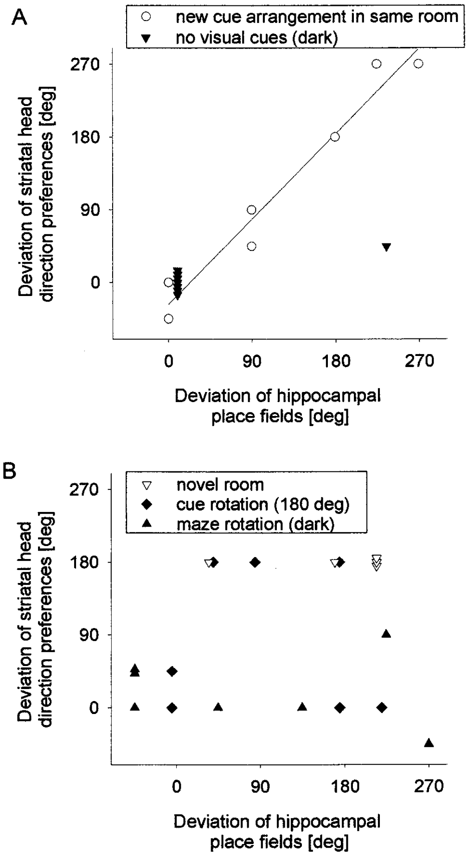

Fig. 1A, B Scattergrams comparing the angular deviation of hippocampus (HPC) place fields or head direction (HD) preferences (relative to baseline trials) following different experimental manipulations. Each point is the mean response of all place fields or all HD preferences recorded in a single recording session. **A** A significant correlation was found between dorsal striatal HD and hippocampal place cell responses following changes in the constellation or spatial arrangement of distal visual cues in an otherwise familiar environment, indicating that both cell types tended to respond in parallel. In addition, most HD and place cells remained unchanged during the light-dark-light (LDL) manipulation. In one session, place fields reorganized during darkness, then returned to baseline locations after the restoration of lights. **B** Manipulations that presented conflicts with familiar cues or a novel environment resulted in uncorrelated responses by HD and place cells

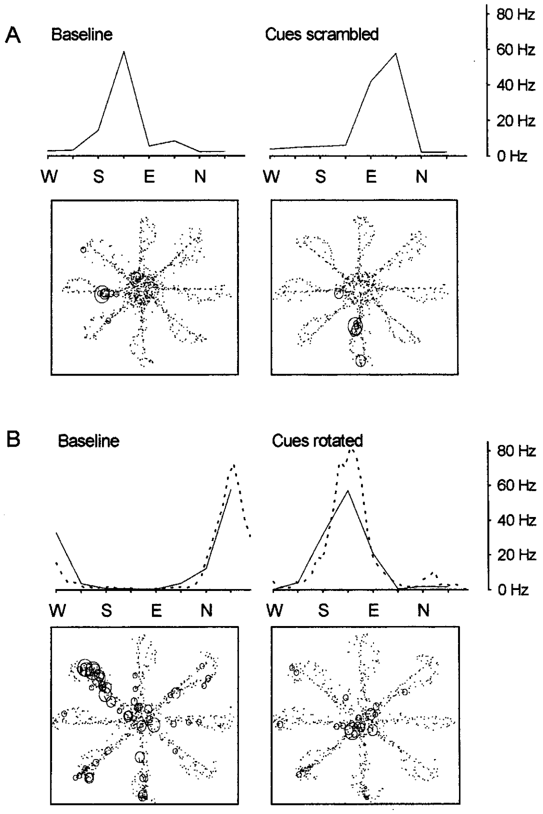

Fig. 2A, B Directional tuning curves for HD cells and spatial distribution plots of simultaneously recorded place fields. **A** Both correlate types showed a similar degree of change following a cue scramble manipulation. Peak firing rate of the HD cell and the location of the place field shifted by about 90°. (*Circles* identify locations of high firing; *overlapping circles* occur with repeated entries into the place field; visited locations are shown by *dots*) **B** When familiar cues were rotated, HD cells tended to respond independently of place fields. The tuning curves illustrate similar shifts in directional preference regardless of whether the data were subject to single (*solid lines*) or double (*dashed lines*) diode analysis

Maze rotation

Twelve HPC place cells and nine DS HD cells were recorded in seven maze rotation sessions (Fig. 1B). A variety of responses were observed. In some cases, place and HD preferences were found to both rotate either along with or independent of the maze (four sessions; *n*=1 or 2 HD cells/session; *n*=1–5 place cells/session). In other sessions either place fields or HD preferences rotated while the other cell response type did not (three sessions; *n*=1 HD cell/session; *n*=1 place cell/session).

Cue rotation of 180°

Following 180° visual cue rotations (seven sessions involving 7 HD cells and 15 place cells), four patterns of results were observed (see Fig. 1B): (1) both place (*n*=1) and HD cell (*n*=1) rotated their spatial preferences by 180° (one session); (2) neither cell type rotated with the cues (one session; *n*=1 HD cell; *n*=3 place cells); (3) HD cells rotated with the cues while place cells ceased firing or fired in new locations (two sessions; *n*=1 HD cell/session; *n*=1 to 3 place cells/session); (4) HD cells did not rotate, and place cells ceased firing or fired in new locations (two sessions; *n*=1 HD cell/session; *n*=1 place cell/session; also see Fig. 2B); or (5) the HD cell (*n*=1) rotated its directional preference slightly while the place field (*n*=1) did not change (one session).

Novel environment

In the novel environment (Fig. 1B), all eight HD cells tested (five recording sessions) rotated 180° in absolute compass direction relative to their orientation in the familiar environment (e.g., if the cell fired magnetic north in the familiar environment, it would fire due south in the novel environment). For novel and familiar recording rooms, the maze is located in the same place relative to an adjacent computer room and the room entrance. Importantly, however, in the familiar room, the room entrance and computer room are north of the maze, while in the novel room they are located south of the maze. Rats were not disoriented upon entering the room. Thus, the HD cells could have relied on either static background cues (e.g., auditory cues) or self-motion cues.

HPC place cell responses (*n*=10) to a novel room were more diverse. For example, in one session, a place cell (*n*=1) from one animal rotated 180° along with the HD cells' (*n*=2) directional preferences. However, for a second animal in which four place cells were recorded simultaneously, one place cell developed a different field and three place fields rotated 180° along with the HD cell's (*n*=1) preferred direction. Two of the rotated place fields remained as such over days. One other place field that initially rotated with the HD preference developed a different and distinct field on the second exposure to the novel environment even though the HD cell's preferred directions remained the same. This mixture of rotating and nonrotating place fields is reflected in mean rotation values other than 180°. In two other sessions, the single place cell recorded did not change in concordance with the single HD cell recorded. Thus, HD cell responses were not consistent with all place cell responses.

Altered environment

Changing either the spatial relationship of familiar cues or adding new visual cues in an otherwise familiar room resulted in similar rotations of place fields and HD preferences (Fig. 1A; r=0.98, P<0.001). For two sessions tested in the cue scramble condition and one session in which all visual cues were removed, the four HD and nine place cells tested showed comparable degrees of change in terms of displacement of HD preferences or place field location. The changed location of the place fields or the change in directional preferences were not associated with the new location of specific cues. The spatial firing returned to their baseline correlate when the distal visual cues were repositioned to their familiar configuration. When the familiar test room was altered by raising the black curtains surrounding the maze (four sessions from two rats), again the place fields (*n*=14) and HD cells' (*n*=5) preferred direction rotated in alignment with each other.

Correspondence between spatial firing and choice accuracy

A significant correlation between the number of errors and HD cell directionality was found (r=–0.277, P<0.025), indicating a tendency for errors to increase when the tuning of HD cells was less specific. The correlation for place-field specificity/reliability and errors was not significant, nor was there a statistical correlation between choice accuracy and times when HD preferences and place fields responded similarly or differently. As described in previous investigations of rat performance in darkness (Brown and Bing 1997; Save 1997), rats in the present study were relatively undisturbed in terms of choice accuracy during dark trials.

Discussion

Spatial representations in DS and HPC responded similarly during the LDL and the altered familiar environment conditions. In these situations, visual aspects of a familiar environment underwent such dramatic changes that previously reliable visual information became unreliable. That both HD preferences and place fields remained aligned when visual cues became unreliable suggests that these cells were dependent upon a common nonvisual spatial coordinate system. That is, they may have become coupled in the absence of external visual cues that served to align the spatial correlates in light conditions. One interpretation of this pattern of results is that current perceptions and expectations of familiar spatial contexts modulate the relationship between hippocampal and dorsal striatal representations.

One of two conditions that frequently led to *different* patterns of change for HD and place cells presented a cue conflict situation (by cue or maze rotation) in which the expected relationship between extramaze and intramaze sensory conditions was disrupted. Consistent with the literature on place field reorganization phenomena, place fields reorganized during cue conflict situations. The proportion of place cells that rotated with the visual cues was lower than previously reported (Muller and Kubie 1987; Bostock et al. 1991), perhaps due to a difference in the behavioral history of the animals. The cue rotation sessions of this study occurred in well-trained animals and after other visual manipulations, a situation that may result in less cue control over place fields (Knierim et al. 1995). HD cells, on the other hand, tended to either not change or follow salient landmarks even when recorded simultaneously with place cells.

The second condition that led to different responses for HD and place cells was exposure to a novel room with novel cues. All HD cells tested rotated their directional preferences by 180°, while the place fields reorganized in unpredictable ways. HD cells probably used common static background cues to align directional preferences. In contrast place cells appeared to have greater reliance on unique distal cues, showing near complete reorganization when animals were placed in a novel environment (Bostock et al. 1991; Knierim et al. 1995).

The degree of conditional alignment of HD and place cells observed in this study can be compared with the coupling reported for HD cells of the anterior nucleus of the thalamus (ATN) and HPC place cells (Knierim et al. 1995). Differences in the behavioral testing history of

ATN and DS HD cells may give the appearance of a functional distinction when none exist. That is, the fact that this study found a greater proportion of HD and place cell pairs that did not respond in a similar fashion may be due to the more drastic environmental manipulations used in the present experiment. In the future, simultaneous recordings of DS and ATN HD cells are needed to resolve this issue.

If it is the case that there is no significant difference in the response of ATN and DS HD cells, an interesting question to ask is why a similar neural code is needed for two brain structures that are considered to make different contributions to learning. The ATN seems important for understanding one's directional sense during navigation (Taube 1998), and the DS is typically considered important for mediating procedural or habit learning (McDonald and White 1993; Knowlton et al 1996; Packard and McGaugh 1996). It is possible that there are multiple component processes required for accurate performance of a working memory task on a radial maze. As animals solve the task, knowledge about the spatial context must be integrated with knowledge about the current and expected reinforcement conditions and response options. Perhaps, HD signals are useful in multiple neural systems because they provide a common reference frame within which to interpret different kinds of information. That is, depending on one's orientation in an environment, there may be a different meaning to current spatial context, reinforcement, or response option information. In this way, both HPC and DS may make complementary, not completely independent, contributions to learning.

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