

Context-Dependent Reorganization of Spatial and Movement Representations by Simultaneously Recorded Hippocampal and Striatal Neurons During Performance of Allocentric and Egocentric Tasks

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Hippocampal and striatal place- and movement-correlated cell firing was recorded as rats performed place or response tasks in a familiar environment, and then after cue manipulation. In a familiar environment, place field properties did not differ across brain structures or task conditions. Movement correlates were stronger during place task performance only in hippocampal neurons. After cue manipulations, place- and movement-sensitive hippocampal and striatal neurons changed their correlate strength, regardless of behavioral strategy. Thus, for both structures, place-correlated cells may encode spatial context information, whereas movement-correlated cells may represent both egocentric movement and learned behavioral responses. The striking overall similarity between hippocampal and striatal neural responses to context manipulation (regardless of strategy) suggests that these structures operate continuously, and in parallel, during multiple forms of learning.

The hippocampus may process context information (Barrientos, O'Reilly, & Rudy, 2002; Frankland, Cestari, Filipkowski, McDonald, & Silva, 1998; Jeffery, Gilbert, Burton, & Strudwick, 2003; Mizumori, Ragozzino, Cooper, & Leutgeb, 1999; Nadel & Payne, 2002) by automatically recording and storing conjunctive representations of stimulus features (Eichenbaum, Dudchenko, Wood, Shapiro, & Tanila, 1999; O'Reilly & Rudy, 2001). During active navigation, physiological evidence supports a more broad definition of context to include not only the external sensory surround, but also behaviors relevant to the learned significance of a particular sensory environment (referred to as *spatial context*; Mizumori, Cooper, Leutgeb, & Pratt, 2001; Mizumori, Ragozzino, et al., 1999; Nadel & Wilner, 1980). The principal hippocampal cells (pyramidal neurons) preferentially discharge when rats occupy circumscribed locations in an environment (O'Keefe &

Dostrovsky, 1971). These hippocampal place cells are controlled by various sources of visual-based sensory information, including local and distal landmarks (Knierim, 2002; Muller & Kubie, 1987; O'Keefe & Nadel, 1978); idiothetic and proprioceptive cues (Knierim, Kudrimoti, & McNaughton, 1998; Shapiro, Tanila, & Eichenbaum, 1997); as well as nonspatial sensory, movement sequence, and temporal information (Frank, Brown, & Wilson, 2000; Huxter, Burgess, & O'Keefe, 2003; Wiener & Korshunov, 1995; Wood, Dudchenko, & Eichenbaum, 1999; Young, Fox, & Eichenbaum, 1994; Zinyuk, Kubik, Kaminsky, Fenton, & Bures, 2000). The firing rates of hippocampal interneurons (so-called "theta cells"), on the other hand, appear to be modulated primarily by variables related to an animal's movement, such as velocity (Czurkó, Hirase, Csicsvari, & Buzsáki, 1999; Muir & Bilkey, 2003). In addition, theta cells may exhibit modest location-specific firing (Kubie, Muller, & Bostock, 1990), as well as auditory-evoked increases in firing during fear conditioning (Moita et al., 2003). When combined, the spatial and movement cells of hippocampus may form the elements of a computation that evaluates the status of the current spatial context (Mizumori, Ragozzino, et al., 1999).

Neuropsychological and neurophysiological evidence suggest that hippocampus is not likely to be the only brain structure that processes context-related information. Although the striatum is traditionally viewed in terms of its contribution to motor function or response learning, there is growing evidence that striatum processes information that does not appear to be directly related to motor output. For example, patients with basal ganglia dysfunction reveal significant and striking cognitive deficits within the domains of working memory and attention (R. Cools, Barker, Saha-

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kian, & Robbins, 2001). Furthermore, Parkinson's disease patients often show impairments in context-based behavioral planning and selective attention, leading to difficulty reorganizing behavior according to new task requirements (e.g., A. Cools, Van den Bercken, Horstink, Spaendonck, & Berger, 1984).

Neural recordings from animals support the view that striatum processes contextual information. Striatal neurons exhibit egocentric movement-related discharge (e.g., Graybiel, 1995; Jog, Kubota, Connolly, Hillegaart, & Graybiel, 1999) that is context-dependent (Hikosaka, Sakamoto, & Usui, 1989; Rolls, Thorpe, & Maddison, 1983; Tremblay, Hollerman, & Schultz, 1998). In primates, striatal neurons become engaged in processing information about learned events that have not yet occurred; their discharge seems to be evoked by the "expectation" of events (Schultz, 2000). Factors that contribute to the (neural) expectation response include not only whether an event is going to occur, but also the location of the event or target stimulus (Hikosaka et al., 1989), as well as the direction of impending movement (Alexander & Crutcher, 1990). Strikingly similar neural responses have been described for striatal neurons of freely navigating rats: These cells discharge in anticipation of expected rewards and egocentric movement, as well as the location and orientation of the animal (Lavoie & Mizumori, 1994; Mizumori, Pratt, & Ragozzino, 1999; Mizumori, Ragozzino, & Cooper, 2000). It appears, then, that multiple contextual factors contribute to the response profile of striatal neuron discharge (Rolls, 1994; Wise, Murray, & Gerfen, 1996).

Differential use of context information by striatum and hippocampus may contribute to their allegedly unique roles in response and place learning (Mizumori, Ragozzino, & Cooper, 2000; Mizumori, Ragozzino, Cooper, & Leutgeb, 1999). Initial investigations of this hypothesis compared the context sensitivity of striatal place cells with known context-relevant properties of hippocampal place cells (Mizumori et al., 2000; Mizumori, Ragozzino, & Cooper, 1999; Mizumori, Ragozzino, et al., 1999; Ragozzino, Leutgeb, & Mizumori, 2001). In these studies, striatal place cells were recorded as rats performed a spatial memory task on a radial maze. In contrast to the partial reorganization of hippocampal place fields that is typically observed after imposed darkness (e.g., Mizumori, Ragozzino, et al., 1999), striatal place fields almost always showed complete reorganization after the same visual manipulation. This difference between hippocampal and striatal place field responses suggests that the two structures may differentially use visual-based context information during spatial performance.

The present study further tested the hypothesis that differential use of context information by striatum and hippocampus contributes to their unique roles in response and spatial learning, respectively. We recorded hippocampal and striatal single unit activity while rats performed either a place or response task on a plus-maze. The plus-maze was used so that the locomotor requirements, external sensory cues, and motivational state would be identical for rats performing according to place or response strategies. We were particularly interested in the context sensitivity of the two most frequently encountered types of neural representation in striatum and hippocampus, place and egocentric movement.

Method

Subjects

Male Long-Evans rats ($n = 11$) were obtained from Charles River Laboratories, then housed individually and kept in a temperature-controlled room (21 °C) that was maintained on a 12-hr light–dark cycle (lights on at 8 a.m.). The rats were food restricted to maintain their weights at approximately 80% of their ad-lib weights, but they had free access to water throughout the experiment. Prior to training, all rats were handled and habituated to the laboratory environment. All methods described were in compliance with the University of Washington Institutional Animal Care and Use Committee and National Institutes of Health guidelines for the care and use of animals in research.

Apparatus

Rats were tested on an elevated plus-maze. The plus-maze was configured by using four arms of an elevated (79 cm above the floor) eight-arm radial maze (Mizumori & Williams, 1993). Black Plexiglas runways (58.0 × 5.5 cm) extended from a center platform (19.5 cm diameter). Chocolate milk reward (0.5–0.7 ml) was placed at the end of goal arms. Two small plastic cages without lids were located next to the start arms and served as holding bins for rats during the intertrial interval. Black curtains surrounded the maze; several distinct visual cue cards were fixed onto the curtains. The experimenter's location was constant relative to the maze and could thus serve as a cue. Illumination was provided by four 15-W bulbs that were placed in the upper north, south, east, and west locations within the curtained area. The recording hardware was installed in a room adjacent to the experimental environment.

Training Procedure

During pretraining, rats were first made accustomed to chocolate milk that was placed in their home cages. The rats were then allowed to traverse a linear track that was located in a different room from the plus-maze room. Next, the rats were trained on either place or response versions of a plus-maze task. Both versions included the same two start locations at the distal ends of opposite arms (e.g., north and south). The sequence of start locations was selected at random for each training session. Three maze arms were available in any given trial. The rat was taken from an intertrial holding bin and placed on a start location facing the curtains. It was required to make a 180° turn, approach the central platform, and then make a 90° turn in order to get chocolate milk at the end of the goal arm. A rat was allowed to correct for an error if it initially went to a nonrewarded arm. After the rat finished drinking, the experimenter placed the rat into the intertrial holding bin for 10–20 s.

For the place task, the reward location was fixed. Depending on the start location, rats had to make either a right or left turn on the central platform in order to reach the reward. For the response task, the start and reward locations were paired such that rats had to make the same turn on the central platform (i.e., only right or only left) to obtain reward, regardless of the start location. During the training period, 10 trials (5 from each start location) were presented in pseudorandom order each day until choice accuracy was 90% or above. Then, recording electrodes were surgically implanted.

After postsurgical recovery, rats were retrained until they reached asymptotic performance, after which recording sessions started. Each recording session consisted of 20 trials (10 trials from each start location); during the first 10 trials (Block 1, or baseline phase), the rat ran the task in the standard experimental environment (in which the locations of visual cues were similar to those of the task acquisition phase). Then, the rat was removed from the maze room while visual cues were relocated. During the next 10 trials (Block 2, or manipulation phase), rats performed the same task in the visually modified environment. Cellular responses to visual

context changes appear to diminish with continued testing (Knierim et al., 1998). Therefore, in order to minimize habituation to a particular type of visual cue rearrangement, and to maximize neuronal responses to a context change, we presented rats with a variety of cue manipulations in an unpredictable order. The following types of cue manipulations were used: clockwise or counterclockwise 90° cue rotations, 180° cue rotations, a new configuration of the familiar set of cues, and the removal of all major visual cues (except the experimenter).

After a series of test sessions (one type of cue manipulation per session), rats were trained to perform a different task with the standard arrangement of visual cues. Rats initially trained according to the place strategy were now trained according to the response procedure, and vice versa. After rats reached asymptotic performance on the alternate task, a series of recording sessions with visual cue manipulations were conducted. After these tests were completed, the same rat was then trained according to the initial strategy, and additional cells were tested. However, the reward location differed on alternate sequences of place sessions, and the required behavioral response (right turn or left turn) differed on alternate sequences of response sessions. An example of a task switch sequence for rats initially trained to perform a response task is shown in Figure 1. The task switch sequence for these rats was as follows: Response 1 (e.g., turn right) → Place 1 (e.g., west) → Response 2 (e.g., turn left) → Place 2 (e.g., east) → . . . and so on. Individual rats experienced two to six task switches.

Surgery

Rats were anesthetized with sodium pentobarbital (40 mg/kg initial dose, with 0.05 cc supplements given as needed) and fixed in a stereotaxic apparatus (David Kopf Instruments, Tujunga, CA). Atropine sulfate (0.2 mg/kg) was administered to minimize respiratory distress. Burr holes were drilled through the skull, and four stereotrodes per hemisphere were implanted: two above dorsal striatum (0.2–1.2 mm anterior to bregma, 1.5 mm lateral, 1.7 mm ventral to the brain surface) and two above dorsal hippocampus (3.5–4.5 mm posterior to bregma, 2.5 mm lateral, 1.7 mm ventral to the brain surface). A reference electrode (constructed from 114- μ m Teflon-coated stainless steel wire) was inserted into the corpus callosum, and a ground screw (a jeweler's screw soldered to 250- μ m Teflon-coated stainless steel wire) was fastened to the skull. Rats were injected with antibiotic (0.1 cc Bicillin L-A, 600 units/ml) intramuscularly after surgery. Rats were allowed 1 week of recovery, during which time they were allowed free access to food. After this period, food access was again restricted for retraining on the maze and for unit recording.

Recording Technique and Behavioral Tracking

The stereotrode and microdrive construction of McNaughton and colleagues (McNaughton, Barnes, Meltzer, & Sutherland, 1989; McNaughton, O'Keefe, & Barnes, 1983; Mizumori & Williams, 1993) was used. Two lacquer-coated tungsten wires (20 μ m diameter each) were twisted together, coated with Epoxylite, and threaded through 30-gauge cannulas. Two cannulas were placed on each microdrive, with approximately 1 mm separating the pair of stereotrodes. Before surgery, the stereotrode tips

were cut at an angle of 45° and gold plated to impedances of 50–100 k Ω (tested at 1 kHz). Amphenol pins connected the recording electrodes and ground wire to a plastic 18-pin connector, which served as the interface between the rat and the recording equipment.

After postsurgical recovery, the electrodes were checked daily for spontaneous cellular activity. Rats were connected to the recording equipment by a preamplification head stage (NB Labs, Denison, TX). Signals from each stereotrode were sampled at a frequency of 26–32 kHz, depending on the number of stereotrodes simultaneously recorded. The stereotrodes were lowered in 22- μ m increments (no more than about 250 μ m/day) until single-unit activity was reliably detected and isolated. To be accepted for recording, cell signals had to be at least three times greater than the background activity. A given cell contributed only once to each manipulation condition. If cells remained stable across days, they were tested across different cue manipulations.

Electrophysiological data were recorded and analyzed on a DataWave Neuroscience Workstation (DataWave Technologies, Longmont, CO). Incoming signals were amplified 4,000 to 10,000 times and filtered (600 Hz–6 kHz). Impulses that exceeded a user-defined threshold initiated a 1-ms sampling period. The entire waveform was recorded by DataWave's Discovery software package. Units were isolated by means of an interactive cluster-cutting routine that processed waveforms on the basis of numerous spike parameters. Additional refinement of the cluster definition took place after recording. Once units were isolated, they were subjected to analysis for behavioral correlates. A rat's position was monitored and recorded by an automatic tracking system (Dragon Tracker, Model SA-2, Boulder, CO) that sampled the position of the anterior diode array located about 5 cm above the rat's head. A second, smaller diode array was located about 5 cm above the back of the rat and, when considered together with the location of the front diode array, was used to determine the orientation of the rat's head. The diodes were sampled at a frequency of 20 Hz (resolution = 1.5–2.0 cm). The DataWave Neuroscience Station logged the time of each position sample and unit activity.

Data Analysis

Various analysis routines (DataWave Technologies, as well as custom software; Leutgeb, Guazzelli, & Higginson, 1997) were used to analyze unit characteristics and behavioral data. Before unit and behavior analysis, position data were first viewed offline. Flags were entered into the data stream at the beginning of each trial (i.e., when the rat was placed on a start location) and at the end of each trial (i.e., when the rat finished drinking the reward). Flags also marked the beginning and end of trial blocks: Block 1 (baseline) refers to the first 10 trials, and Block 2 (manipulation) refers to the 10 trials after cue rearrangement. Spike width (latency difference between the maximum and minimum voltage points of the analog signal) was calculated for each cell. Also, average firing rates across the entire session and for each block of trials were calculated for each neuron. The behavior of the rat was measured in terms of the percent correct choices per phase of test (i.e., baseline or cue manipulation phase) and the average duration of each trial.

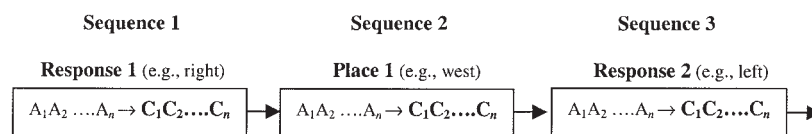


Figure 1. Example of a task switch sequence for rats initially trained as response learners. Subscript refers to session number. A = acquisition sessions; C = recording sessions with cue manipulation trials; west or east = location of reward arms for the place task condition; right or left = correct turn on the central platform for the response task condition.

Classification and Analysis of Location-Specific Neurons

For each cell, separate spatial plots were generated that reflected the firing rate distribution across the portion of the environment visited by a rat during baseline and manipulation trials. The maze area was divided into pixels of constant size (2.8×2.8 cm), and the average firing rate was calculated for each pixel. If the average firing rate within a pixel exceeded threshold (20% of the maximum firing rate), the pixel was highlighted on the plot. A cell's spatial correlate was defined on the basis of baseline trials. The following criteria were used to define a place field: (a) There were at least four adjacent highlighted pixels. The largest area of adjacent highlighted pixels was considered the cell's principal field. (b) The firing rate within the place field had to exceed the out-of-field rate by at least a factor of 2. (c) The cell's principal field had to be considered reliable. That is, above-threshold firing had to occur during more than 50% of the total number of visits that the rat made to the location of the principal field. All neurons that satisfied the above location-specific firing criteria were categorized as place cells and subjected to further analysis. In order to directly compare hippocampal and striatal spatial codes, we applied the same criteria for selecting neurons in both structures.

A spatial (Pearson's) correlation analysis was used to quantify place field reorganization across the two blocks of baseline and manipulation trials (Cooper & Mizumori, 2001; Leutgeb & Mizumori, 2002). The maze area was divided into squares (12.9×12.9 cm). The average firing rate within each square during baseline trials was correlated with the firing rate of the same cell recorded for the identical locations during manipulation trials. Only squares visited by the rat in both blocks of trials were analyzed. In addition to the spatial correlation analysis, field reorganization was evaluated by first calculating the firing rate within the principal field, and the field size for baseline and manipulation trial blocks. The percent change from baseline for field size and within-field rate measures was used to estimate the magnitude of neuronal response to a context change. Also, a difference index (*DI*) between blocks was calculated for each measure of each neuron according to the following formula: $DI = (b_2 - b_1) \div (b_2 + b_1)$, where b_1 and b_2 are average values of the corresponding parameters during the two blocks of baseline and manipulation trials, respectively. This index varies from -1.0 to $+1.0$ and is negative for parameter averages that were reduced during manipulation trials; $DI = 0$ would indicate no change.

Classification and Analysis of Movement-Specific Neurons

In addition to spatial attributes, egocentric movement variables are frequently correlated with hippocampal and striatal neural discharge in rats (e.g., Buzsáki, Leung, & Vanderwolf, 1983; Mizumori et al., 2000; Vanderwolf, 1969). In hippocampus, movement-related firing is typically observed for the theta cell (i.e., interneuron) population of cells. The movement relatedness is often characterized in terms of the correlation between cell firing rates and velocity or acceleration of movement. Therefore, in this study, the following analysis was restricted to neurons with average firing rates greater than 1 Hz, and to cells that did not show significant location-selective firing. That is, the firing rate of these neurons conformed to the classic definition of hippocampal theta-non-complex spike cells (e.g., Ranck, 1973), and the populations of spatial- and movement-sensitive neurons reported in this study did not overlap. Significant (linear) relationships between neural firing rates and velocity (2.24 cm/s bin size) or acceleration (2.24 cm/s² bin size) were identified on the basis of a 95% confidence interval ($\alpha = .05$). Correlation coefficients were calculated separately for trials within the baseline and manipulation phases of testing. Neurons that demonstrated significant relationships between firing rate and velocity or acceleration during at least one block of trials were selected for further analysis. The slope coefficient of the regression line was used to characterize the strength of the movement code. It should be noted that the selection of cells for this movement analysis was not meant to ignore the fact that hippocampal place cells are also known to be

velocity sensitive (Czurkó et al., 1999; McNaughton, Barnes, & O'Keefe, 1983; Wiener, Paul, & Eichenbaum, 1989). Rather, our intent was to evaluate cells that had as their primary correlate sensitivity to egocentric movement.

Analysis of variance (ANOVA) was used to identify differences between hippocampal and striatal neural responses to spatial and movement variables, and to compare neural responses between place and response task conditions. A paired *t* test was used to compare measures across baseline and manipulation phases within each group. A one-sample *t* test was used to analyze the normalized *DIs* (see above). All data were analyzed with the SPSS 11.0 statistical package (SPSS, Chicago, IL).

Histology

Once the electrodes were lowered 4.0 mm from the brain surface for hippocampus and 5.0 mm for striatum, rats were deeply anesthetized with sodium pentobarbital and perfused through the heart with a 0.9% (wt/vol) buffered NaCl solution, followed by 10% formalin. Electrodes were retracted, and the brain was removed and allowed to sink in a 30% sucrose-formalin solution. Forty-micron frozen sections were then sliced through the penetrated brain areas with a cryostat. Sections were stained with Cresyl violet, and the location of recorded cells were histologically verified by comparing the depth measurements at the time of recording with an electrode track reconstruction derived from examinations of the serial sections for each structure.

Results

Behavioral Performance

Six rats were initially trained according to the place task procedure, and 5 rats were initially trained according to the response task procedure. Behavioral data were collected from 73 sessions of place task performance and 52 sessions of response task performance. Many of the same rats contributed to both place and response conditions because they were switched between tasks during the course of the experiment. Asymptotic performance during the baseline test phases was stable across all recording sessions and did not differ significantly between place and response test conditions. The mean (\pm SEM) proportion of correct choices was 0.95 ± 0.01 and 0.96 ± 0.01 for place and response tasks, respectively, $F(1, 123) = 0.04$, $p > .05$. Overall, the different cue manipulations resulted in similar disturbances of behavioral performance in both tasks. The proportion of correct choices decreased significantly compared with baseline (0.88 ± 0.02 for both place and response tasks): place task, $t(72) = 3.35$, $p < .01$; response task, $t(51) = 4.10$, $p < .01$. The probability of making an error was highest during the first trial after a cue manipulation for both place and response task conditions, and it remained elevated throughout the manipulation phase (see Figure 2). The average time required to perform correct trials within a modified visual environment was significantly higher during place task performance (6.6 ± 0.6 s during baseline trials, 7.7 ± 1.0 s during manipulation trials), $t(10) = -2.36$, $p < .05$. The same tendency was observed during performance of the response task, although this was not statistically significant (6.3 ± 0.7 s vs. 7.2 ± 1.3 s), $t(8) = -0.72$, $p > .05$.

The amount of time spent at each velocity interval (up to 44.8 cm/s, the maximum velocity at which reliable data were obtained) and acceleration interval (up to 44.8 cm/s²) did not differ between baseline and manipulation trials. A repeated measures ANOVA

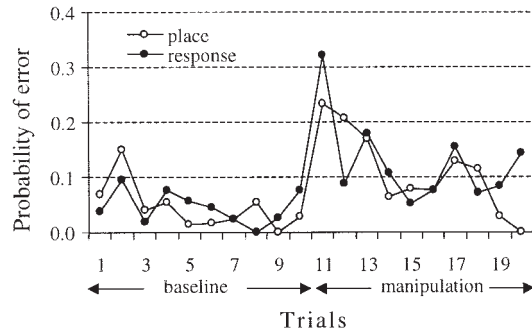


Figure 2. Behavioral accuracy during task performance. The average probability of making an error was calculated for each trial of the baseline and cue manipulation phases of testing. Included are data from all place or response task sessions performed by different rats. The maximum number of errors was observed at the onset of visual environment change (11th trial); the probability of errors remained elevated throughout the session regardless of the strategy condition.

did not reveal either manipulation or task effects for velocity: block effect, $F(1, 18) = 1.43, p > .05$; task effect, $F(1, 18) = 0.56, p > .05$, or acceleration: block effect, $F(1, 18) = 1.25, p > .05$; task effect, $F(1, 18) = 0.12, p > .05$. This result indicates that the overall behavior of the rat was similar before and after cue manipulation.

Baseline Firing Properties of Location-Specific Neurons Recorded During Place and Response Tasks

Hippocampus

Included for analyses are data from 56 hippocampal place cells that were recorded during 23 place task sessions ($n = 7$ rats; see Figure 3 for examples), and 63 place cells recorded during 20 response task sessions ($n = 4$ rats). Because the responses of CA1 and CA3 neurons were similar, the data were combined into one group for subsequent analysis.

All hippocampal place cells discharged at relatively low rates (place task: 0.91 ± 0.12 Hz, range = 0.09–4.07 Hz; response task:

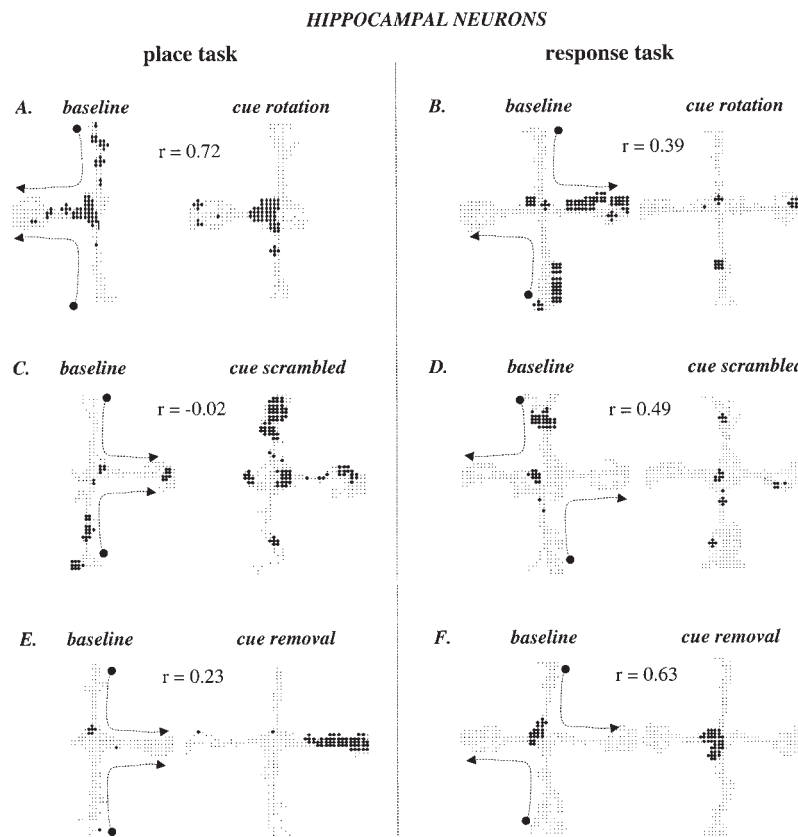


Figure 3. Examples of hippocampal place fields recorded before and after visual cue manipulations during place and response task performance. A and B: Cues rotated 90° or 180°; C and D: Cues scrambled; E and F: Cues removed. Small dots represent maze areas visited by the rat during the recording session; bold dots represent locations where neuronal firing was above the threshold (20% of the maximum firing rate; see Method section). The spatial correlation analysis compared the spatial distribution of firing across baseline and cue manipulation phases of place or response task performance. The values of the spatial correlation coefficient (r) are shown for each example. Each correlation analysis included firing above and below threshold. Arrows show the behavioral trajectories for a correct response. This trajectory remained the same during manipulation trials.

0.72 ± 0.08 Hz, range = 0.08–2.57 Hz); there was no significant difference in firing rate for cells recorded during the two task conditions, $F(1, 117) = 1.81, p > .05$. Neural signals recorded during place and response performance also did not differ in terms of spike width (place task: $366.8 \pm 14.4 \mu\text{s}$, response task: $357.6 \pm 7.4 \mu\text{s}$), $F(1, 117) = 0.35, p > .05$. These cell properties are consistent with those of hippocampal pyramidal neurons (Ranck, 1973).

The size of the principal field varied between cells recorded during the baseline condition (place task range = $46.5\text{--}844.8 \text{ cm}^2$, response task range = $46.5\text{--}1,402.8 \text{ cm}^2$); however, there was no statistically significant difference in average field size for the place and response groups ($224.2 \pm 24.6 \text{ cm}^2$ and $229.4 \pm 26.3 \text{ cm}^2$, respectively), $F(1, 117) = 0.02, p > .05$. The average firing rate within the principal field also did not differ (place task: 3.81 ± 0.34 Hz, range = 0.63–12.10 Hz; response task: 4.18 ± 0.31 Hz, range = 0.60–12.02 Hz), $F(1, 117) = 0.66, p > .05$. Cell firing within the principal field was highly reliable during performance of either place or response tasks ($81\% \pm 2.5\%$ and $86\% \pm 2.2\%$ for place and response groups, respectively). Thus, place cells that were recorded during place and response task conditions had similar baseline firing properties.

Striatum

Nineteen striatal neurons recorded during 12 place task sessions ($n = 5$ rats) and 15 neurons recorded during 10 response task sessions ($n = 4$ rats) satisfied our spatial criteria (see Figure 4 for examples). These neurons were characterized by a low average firing rate that was not significantly different between place (1.37 ± 0.35 Hz, range = 0.18–5.91 Hz) and response (1.15 ± 0.21 Hz, range = 0.24–3.39 Hz) groups, $F(1, 32) = 0.25, p > .05$.

The size of the principal field during the baseline condition varied for individual cells (place task range = $38.8\text{--}620.0 \text{ cm}^2$, response task range = $54.3\text{--}534.8 \text{ cm}^2$). However, group means were not significantly different between the place and response conditions, $F(1, 32) = 0.03, p > .05$. The within-field rate also did not differ as a function of the type of training (place task: 3.65 ± 0.60 Hz, range = 1.22–11.90 Hz; response task: 4.28 ± 0.58 Hz, range = 1.10–8.27 Hz), $F(1, 32) = 0.55, p > .05$. The neuronal firing within the principal field was highly reliable during baseline trials ($77\% \pm 4.5\%$ and $80\% \pm 3.8\%$ for neurons recorded during place and response tasks, respectively). Thus, there were no significant differences in striatal spatial coding during place and response performance.

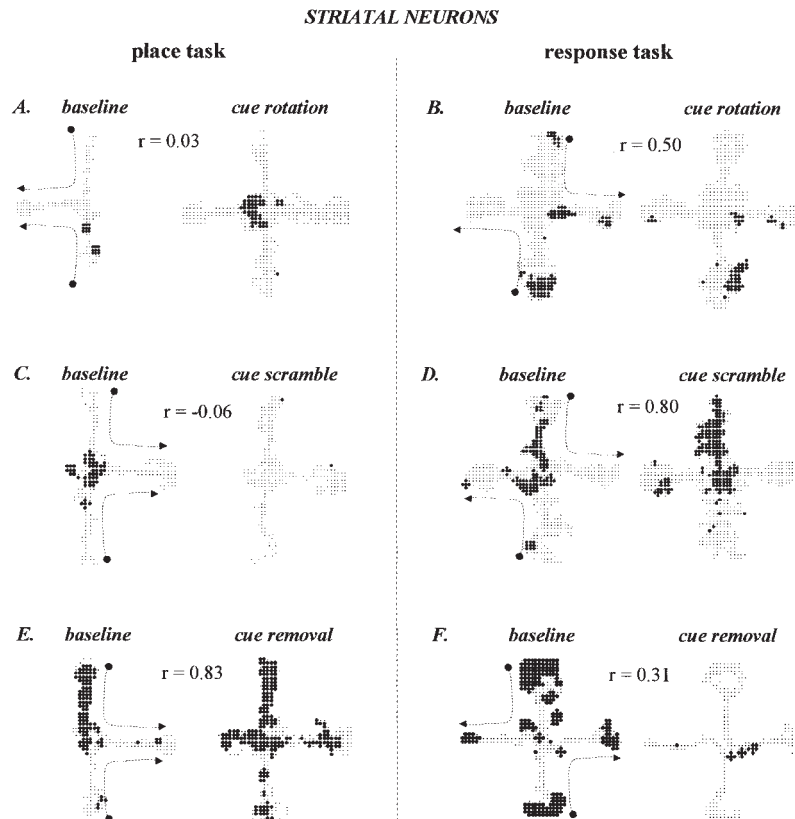


Figure 4. Examples of location-specific responses by striatal neurons before and after visual cue manipulations during place and response task performance. A and B: Cues rotated 90° or 180° ; C and D: Cues scrambled; E and F: Cues removed. Spatial firing patterns during baseline and manipulation trials of different neurons are shown. The analysis was as described for Figure 3. A variety of responses were observed, from very little change (Panels D and E), to reorganization of the spatial distribution of discharge (Panels A, B, and F), to elimination of firing (Panel C). It can be seen that a variety of changes in the place fields were observed for both hippocampal (Figure 3) and striatal cells.

Comparison of Baseline Firing Properties of Hippocampal and Dorsal Striatal Location-Selective Neurons

Hippocampal and striatal neurons with location-selective firing properties showed a number of brain region-specific features (see Table 1). A one-way ANOVA revealed that hippocampal cells exhibited lower average firing rates (0.81 ± 0.07 Hz vs. 1.27 ± 0.21 Hz in striatum), $F(1, 152) = 6.55, p < .05$ (Table 1), and wider spike widths ($361.9 \pm 7.8 \mu\text{s}$ vs. $308.4 \pm 19.1 \mu\text{s}$ in striatum), $F(1, 152) = 7.82, p < .01$. Despite statistically significant differences, it is worth noting that both hippocampal and striatal neurons had comparable ranges of rates and signal widths. Furthermore, there were no differences in principal field sizes or within-field rates for neurons recorded from the two brain regions. However, the within-field rate versus the out-of-field rate ratio was significantly higher in hippocampal neurons (9.1 ± 0.8 compared with 5.0 ± 0.6 for striatal neurons), $F(1, 152) = 6.34, p < .05$. This difference indicates that hippocampal location-specific neurons generated a higher signal-to-noise ratio than striatal location-specific neurons.

Sensitivity of Hippocampal and Striatal Spatial Codes to Visual Context Change During Place and Response Tasks

Context Sensitivity of Hippocampal Spatial Codes

Analysis of representational reorganization. A comparison of dependent measures across baseline and cue manipulation trials served as an index of the context sensitivity of unit activity. The spatial correlation between neuronal firing during baseline trials and neural firing during cue manipulation trials averaged $.37 \pm .05$ for place and $.46 \pm .04$ for response conditions. These did not differ significantly, $F(1, 117) = 1.90, p > .05$. The distribution of spatial correlation scores was broad for both place (minimum = $-.43$, maximum = $.94$) and response (minimum = $-.44$, maximum = $.98$) conditions, indicating a wide range of responses to the context change (Figure 5A). Figure 3 shows examples of different types of neuronal responses to cue manipulations during place and response task performance. It appears that cognitive strategy did not affect the degree of place field reorganization in response to visual context change.

Analysis of place field size and firing rate. Place field sizes and within-field rates were compared between blocks of baseline and cue manipulation trials. The average field size or within-field rate did not change after cue manipulations in the place group: field size, $t(55) = 0.42, p > .05$; field rate, $t(55) = 0.32, p > .05$. When rats performed the response task, the average size of the

principal field also remained stable across baseline and manipulation trials, $t(62) = 0.49, p > .05$, although the firing rate within the principal field was significantly reduced during the same set of trials, $t(62) = 3.09, p < .01$. This pattern of responses resulted in a lower signal-to-noise ratio after cue manipulation (11.2 ± 1.4 for Block 1 vs. 8.4 ± 1.2 for Block 2), $t(62) = 2.98, p < .01$. Thus, consistent with the spatial correlation result (above), hippocampal place neurons appear to be sensitive to visual context even during response task performance.

The distribution of normalized *DIs* revealed that cue manipulations could result in either increases or decreases in place field parameters during both place and response task performance (Figure 5C). ANOVAs did not reveal significant task effects on the *DIs*: field size change, $F(1, 117) = 1.81, p > .05$; within-field rate, $F(1, 117) = 0.88, p > .05$. Although no group differences were found, Figure 5C reveals that a broad range of responses were observed for all conditions. Indeed, the mean percent change for each parameter was significantly above zero (all $ps < .01$; see Table 2): place task, $t(55) = 6.82, p < .01$ and $t(55) = 6.57, p < .01$, for field size and field rate, respectively; response task, $t(62) = 7.52, p < .01$ and $t(62) = 9.28, p < .01$, for field size and field rate, respectively. Thus, cue manipulations provoked dramatic changes in the firing properties of a subpopulation of neurons during both place and response task performance, whereas other neurons showed no changes across conditions. ANOVAs did not reveal task-specific effects on the percent change in field size or within-field firing rate, $F(1, 117) = 3.67, p > .05$ and $F(1, 117) = 1.19, p > .05$, respectively (Figure 5B).

In summary, location-selective discharge by hippocampal neurons was observed during both place and response task performance. Hippocampal spatial codes appeared to be sensitive to visual environment change regardless of the cognitive strategy used; the magnitude of neuronal change was similar during performance of place and response tasks. The reorganization of the hippocampal spatial code was reflected in changed location-selective firing patterns (e.g., field relocation or the appearance of a new field) and/or a decrease or increase in place field size and within-field firing rates. A different subpopulation of hippocampal neurons showed preserved firing properties despite visual context change.

Context Sensitivity of Striatal Spatial Codes

Analysis of representational reorganization. The spatial correlation scores for comparisons of neuronal firing patterns between blocks of baseline and cue manipulation trials averaged $.32 \pm .08$ for place and $.44 \pm .07$ for response conditions, and these did not

Table 1
Mean (\pm SEM) Firing Properties of Hippocampal and Striatal Location- and Movement-Specific Neurons Independent of Strategy

Property	Hippocampus			Dorsal striatum		
	Location	Acceleration	Velocity	Location	Acceleration	Velocity
Average rate (Hz)	$0.81 \pm 0.07^*$	$9.38 \pm 1.34^*$	$5.18 \pm 0.68^*$	1.27 ± 0.21	10.92 ± 1.37	8.64 ± 1.05
Spike width (μs)	$361.9 \pm 7.8^*$	299.5 ± 18.0	318.2 ± 13.0	308.4 ± 19.1	272.9 ± 21.5	267.6 ± 21.1

* $p < .05$, for between-structures comparisons.

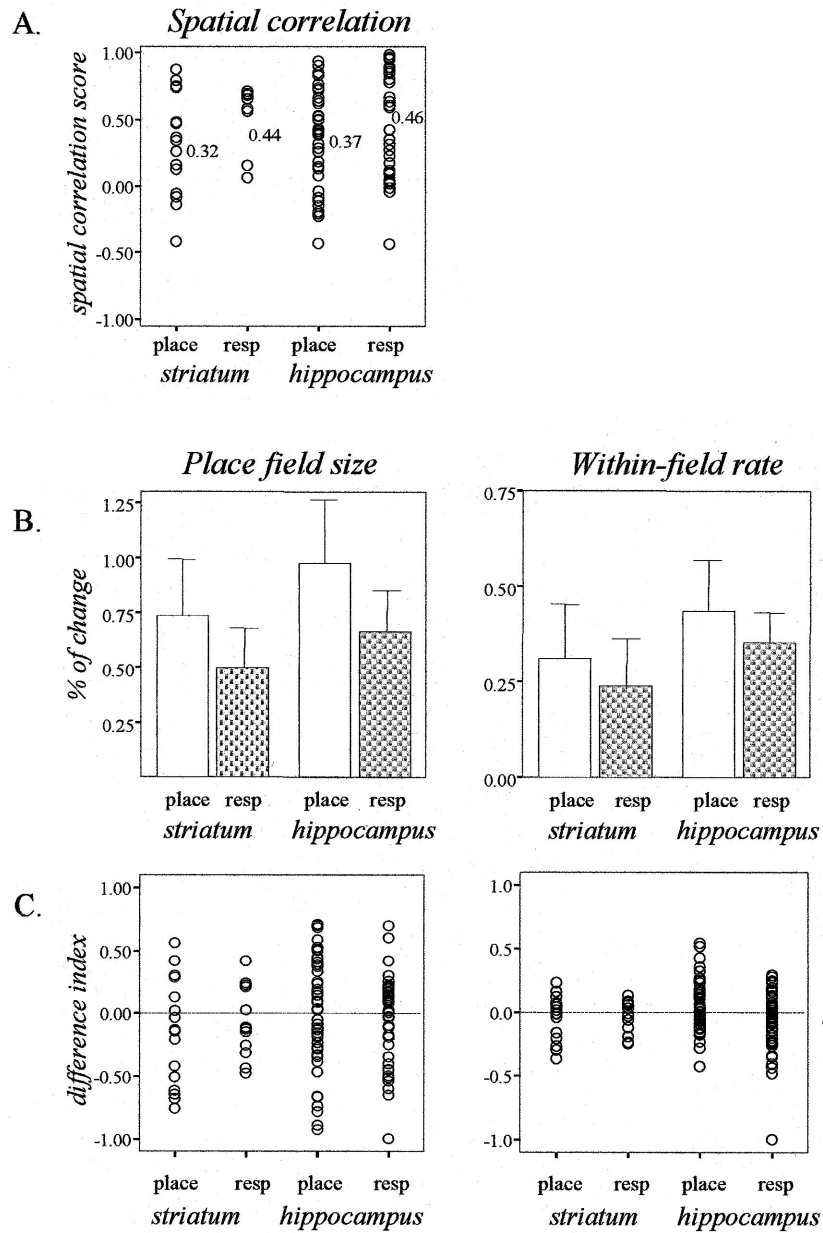


Figure 5. Summary of the reorganization of striatal and hippocampal location-specific information codes in response to visual context change. A: Distribution of the spatial correlation scores that compared spatial firing patterns during baseline and cue manipulation trials. Circles represent correlation scores of individual neurons, and these were grouped according to the brain structure and behavioral task. Cells with identical scores show up as a single circle. Numbers indicate the group means. B and C: Context-induced changes in place field size and within-field firing rates are shown as the percentage of change from baseline for each parameter (B), and in terms of the distribution of normalized difference indices calculated for individual neurons (C). There were no significant differences between task conditions in terms of mean change in place field sizes or within-field rates. Also, all cell groups included units that increased or decreased place field sizes and within-field firing rates. resp = response.

differ significantly, $F(1, 32) = 1.25, p > .05$. The range of correlation scores varied in both place (minimum = $-.42$, maximum = $.87$) and response (minimum = $-.15$, maximum = $.71$) conditions (Figure 5A), revealing a broad spectrum of place field reorganization, irrespective of the particular task. Examples of

individual striatal cell responses to context changes are shown in Figure 4.

Analysis of place field size and firing rate. The group averages of principal field size and mean within-field rate were compared between blocks of baseline and cue manipulation trials. These did

Table 2
Mean (\pm SEM) Cue Manipulation-Induced Changes in Place Field Size and In-Field Firing Rates for Hippocampal and Striatal Location-Specific Neurons

Measure	Hippocampus		Dorsal striatum	
	Place task	Response task	Place task	Response task
Spatial correlation score	0.37 \pm 0.05	0.46 \pm 0.04	0.32 \pm 0.08	0.44 \pm 0.07
% baseline field size	97.7 \pm 14.3	66.2 \pm 8.8	73.6 \pm 12.8	49.9 \pm 9.1
% change field rate	43.5 \pm 6.6	35.4 \pm 3.8	31.3 \pm 8.8	24.0 \pm 6.2

not differ for either place groups: field size, $t(18) = 2.02, p > .05$; field rate, $t(18) = 1.46, p > .05$, or response groups: field size, $t(14) = 1.90, p > .05$; field rate, $t(14) = 1.08, p > .05$. However, the analysis of normalized *DIs* revealed that cue manipulations resulted in differential responding by individual neurons (i.e., increases or decreases in field size or within-field firing rate, Figure 5C). When considered as a group, however, there was no task-related effect: field size change, $F(1, 32) = 0.76, p > .05$; within-field rate change, $F(1, 32) = 0.16, p > .05$.

Evaluation of the percent change from baseline revealed that the field size or within-field rates varied significantly from zero (Table 2), indicating neuronal sensitivity to visual context in some striatal neurons ($p < .01$ for all groups): place task, $t(18) = 5.73, p < .01$ and $t(18) = 4.50, p < .01$, for field size and field rate, respectively; response task, $t(14) = 5.46, p < .01$ and $t(14) = 3.87, p < .01$, for field size and field rate, respectively. However, there were no task-specific differences revealed in the magnitude of neuronal response to a visual environment change according to the parameters analyzed: field size, $F(1, 32) = 2.03, p > .05$; within-field rate, $F(1, 32) = 0.58, p > .05$ (see Figure 5B).

In summary, location-specific firing by medial dorsal striatal neurons was observed during both place and response task performance in familiar environments and after context change. Striatal neurons responded to changes in the visual environment by reorganizing the spatial distribution of firing, as well as by increasing or decreasing place field size and within-field firing rates. The magnitude of the neuronal response did not depend on the use of place or response behavioral strategy. Although some neurons were clearly context-sensitive, a subpopulation of striatal neurons showed preserved spatial codes when the visual context changed.

Comparison of Context Sensitivity of Hippocampal and Dorsal Striatal Location-Selective Firing

There were no statistically significant structure- or task-specific effects found for the place field parameters measured (i.e., spatial distribution of firing, size of the principal field, or within-field firing rate; Table 2). These neural measures were, however, sufficiently sensitive to detect changes in the visual environment for both hippocampal and striatal populations. For both groups of cells, only a subpopulation of cells showed representational reorganization. That is, partial reorganization was observed for both hippocampal and striatal neuron populations. Of those cells that responded to cue manipulations, a comparable range of individual cell responses (increased and decreased response) were observed in hippocampus and striatum (Figure 5).

In the following section, we first characterize the baseline neuronal properties of movement-sensitive hippocampal and striatal neurons. Then, we describe the consequences of visual context change on these movement-related neural codes.

Baseline Firing Properties of Movement-Related Hippocampal and Striatal Cells Recorded During Place and Response Tasks

Hippocampus

Overall, 72 hippocampal neurons with movement-related firing properties were recorded during 34 place task sessions. Examples of acceleration- and velocity-tuned hippocampal neurons can be found in Figure 6. The firing rates of 51 cells were significantly correlated with both acceleration and velocity components of movement, whereas the firing rates of 12 cells were related only to acceleration, and 9 cells were significantly related only to velocity. Fifty-three cells (including 5 cells tuned only to acceleration and 11 tuned only to velocity) were recorded during 25 response task sessions.

All hippocampal neurons that were significantly correlated with acceleration (either alone or in conjunction with velocity) were included in the following acceleration analysis. The absolute value of the correlation coefficient averaged $.66 \pm .02$ (range = $.47-.90$) and $.64 \pm .01$ (range = $.44-.95$) for place and response task groups, respectively, and these did not differ statistically, $F(1, 68) = 0.80, p > .05$. However, the relationship between acceleration and firing rate (as defined by the regression slope coefficient) was stronger during place task performance (0.056 ± 0.007 Hz/cm/s²) than during response task performance (0.033 ± 0.004 Hz/cm/s²), $F(1, 68) = 5.86, p < .05$ (see Figure 7). The firing rates of most (96%) acceleration-tuned cells were positively correlated with acceleration; the rest of the neurons showed negative correlations. Acceleration-tuned cells recorded during place and response task conditions did not differ according to spike width (place task: 293.3 ± 17.6 μ s; response task: 320.6 ± 16.6 μ s), $F(1, 68) = 1.20, p > .05$, or average firing rate (place task: 8.46 ± 1.08 Hz; response task: 6.68 ± 1.60), $F(1, 68) = 0.91, p > .05$.

All hippocampal neurons that were significantly correlated with velocity (either alone or in conjunction with acceleration) were included in the following velocity analysis. The absolute value of the correlation coefficient was nearly identical for the place group (average = $.61 \pm .02$; range = $.46-.78$) and the response group (average = $.61 \pm .02$; range = $.48-.83$). The absolute value of the linear regression slope coefficient was greater during place task

HIPPOCAMPUS

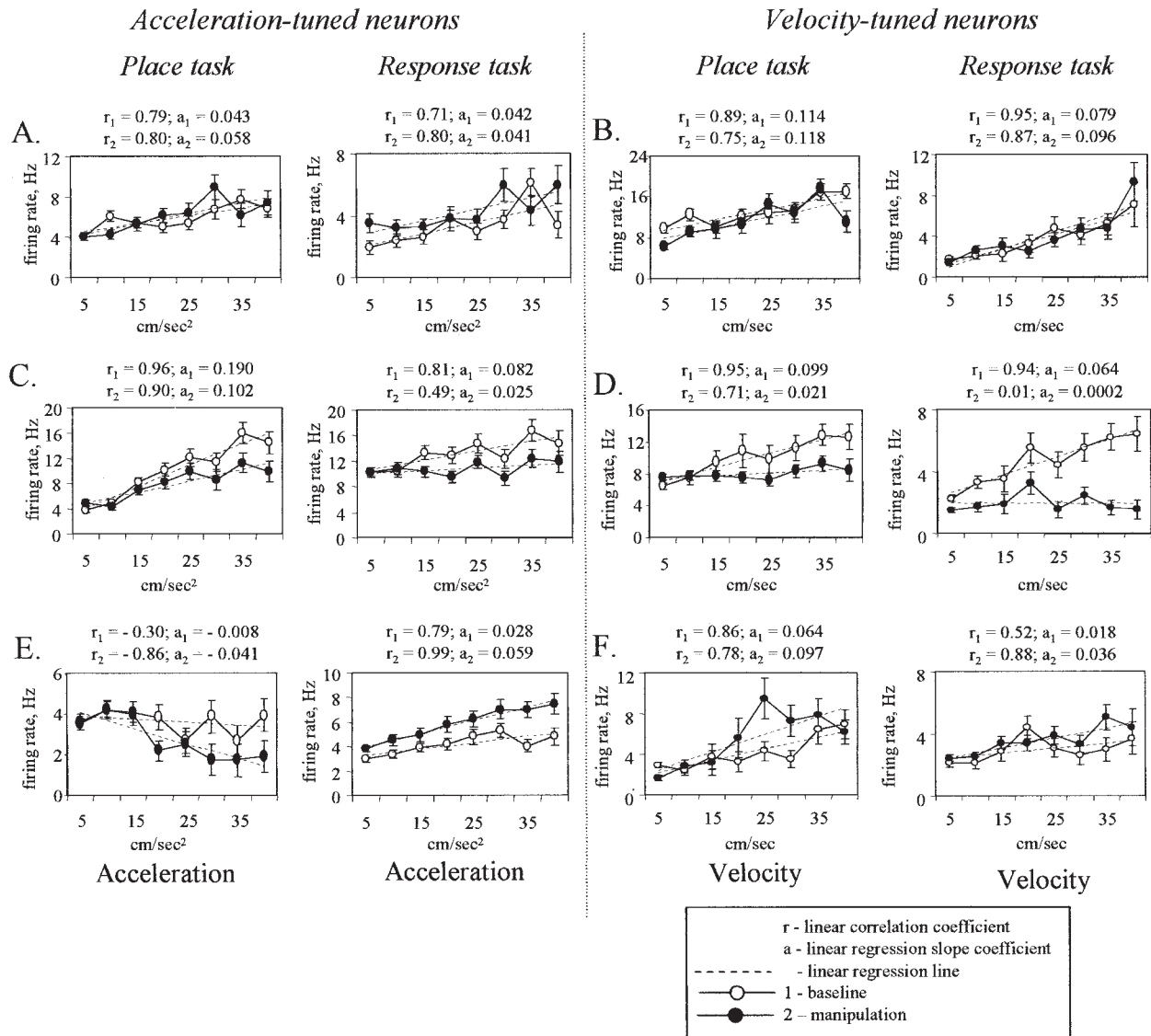


Figure 6. Examples of context-dependent responses of individual hippocampal acceleration- and velocity-tuned neurons recorded during place and response test conditions. The average firing rates are presented as a function of different velocities and acceleration. A and B: Movement-coding properties of individual cells that were stable across baseline and manipulation trials. C and D: Cells whose linear relations between firing rates and acceleration and velocity were weaker or lost after context change. E and F: Cells whose linear relations between firing rates and movement were stronger when tested in a new context. This change in strength of the relationship was true for both positively and negatively correlated neurons.

performance (0.099 ± 0.011 Hz/cm/s) than during response task performance (0.068 ± 0.007 Hz/cm/s), $F(1, 63) = 5.34$, $p < .05$ (Figure 7). The firing rates of most neurons (97%) were positively correlated with velocity; a small proportion of neurons (3%) displayed negative correlations. Hippocampal velocity-tuned cells recorded during place and response task performance did not differ according to spike width (place task: $293.2 \pm 18.7 \mu\text{s}$; response task: $338.3 \pm 14.6 \mu\text{s}$), $F(1, 63) = 3.52$, $p > .05$, or firing rate (place task: 7.00 ± 1.15 Hz; response task: 4.53 ± 0.58 Hz), $F(1, 63) = 3.50$, $p > .05$.

Striatum

Overall, 78 movement-sensitive striatal neurons were recorded during 34 place task sessions. Fifteen of these cells were correlated with acceleration only, 16 cells were tuned only to velocity, and 47 cells showed correlations with both acceleration and velocity. Twenty cells (4 tuned only to acceleration, and 16 with combined acceleration and velocity correlates) were recorded during 17 response task sessions. Examples of individual cell correlates can be found in Figure 8.

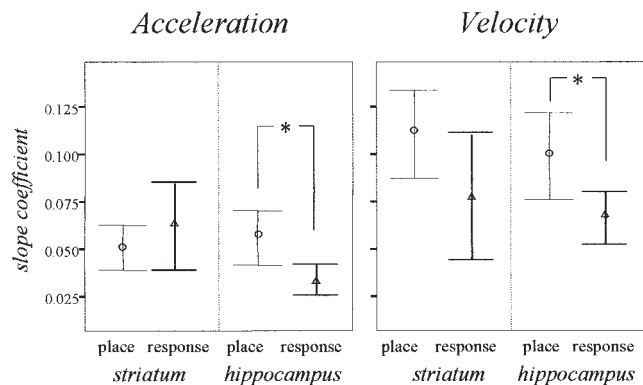


Figure 7. A comparison of baseline movement-coding properties of hippocampal and striatal place neurons. The mean (\pm SEM) values of the linear regression slope coefficient are shown according to the task and brain structure. It can be seen that there was no difference in this measure as a function of strategy condition for striatal neurons. Hippocampal neurons, in contrast, showed significantly stronger relationships during place performance than during response performance. * $p < .05$, for within-structure comparisons.

All striatal neurons that were significantly correlated with acceleration (either alone or in conjunction with velocity) were included in the following acceleration analysis. Striatal acceleration-tuned cells recorded during place and response task conditions did not differ on any parameter analyzed. The absolute value of the linear correlation coefficient averaged 0.62 ± 0.02 for the place group (range = 0.45–0.94) and 0.67 ± 0.04 for the response group (range = 0.47–0.85). The linear regression slope coefficients were similar regardless of the particular task performed (place task: $0.051 \text{ Hz/cm/s}^2 \pm 0.006 \text{ Hz/cm/s}^2$, response task: $0.062 \text{ Hz/cm/s}^2 \pm 0.011 \text{ Hz/cm/s}^2$), $F(1, 49) = 0.88$, $p > .05$ (Figure 7). Firing rates of 63% of neurons were positively correlated with acceleration; the firing rates of 37% of the neurons displayed the opposite relationship. The spike width averaged $283.0 \mu\text{s} \pm 22.3 \mu\text{s}$ for the place task group and $228.0 \mu\text{s} \pm 23.3 \mu\text{s}$ for response task group, $F(1, 49) = 1.72$, $p > .05$. The average firing rate was $10.67 \text{ Hz} \pm 1.27 \text{ Hz}$ and $11.16 \text{ Hz} \pm 1.81 \text{ Hz}$ during place and response task performance, respectively, $F(1, 49) = 0.04$, $p > .05$.

Baseline firing properties of striatal velocity-tuned cells also did not display task-specific effects. All striatal neurons that were significantly correlated with velocity (either alone or in conjunction with acceleration) were included in the following velocity analysis. The absolute value of the linear correlation coefficient averaged $.62 \pm .02$ for the place group (range = .46–.89) and $.60 \pm .03$ for the response group (range = .52–.88). The linear regression slope coefficients were similar regardless of the particular task performed (place: $0.111 \pm 0.012 \text{ Hz/cm/s}$; response: $0.078 \pm 0.013 \text{ Hz/cm/s}$), $F(1, 53) = 1.74$, $p > .05$ (Figure 7). The firing rates of 76% of the neurons were positively correlated with the rats' running velocity; the firing rates of 24% of the neurons were negatively correlated. The spike width averaged $282.9 \pm 21.4 \mu\text{s}$ for place task group and $272.1 \pm 37.4 \mu\text{s}$ for response task group, $F(1, 53) = 0.05$, $p > .05$. The average firing rate was $8.96 \pm 0.98 \text{ Hz}$ and $7.79 \pm$

1.68 Hz during place and response task performance, respectively, $F(1, 53) = 0.30$, $p > .05$.

Comparison of Baseline Characteristics of Hippocampal and Striatal Movement-Related Discharge During Place and Response Tasks

Comparisons of the linear correlation with acceleration for striatal and hippocampal neurons revealed no structure-specific effect during either place or response task performance. However, comparison of the slope coefficients showed that hippocampal cell discharge was more strongly related to acceleration during place task performance than during response task performance (Figure 7). No task effects were observed for striatal cells. Overall, striatal neurons showed higher firing rates than hippocampal neurons ($10.78 \pm 1.05 \text{ Hz}$ vs. $7.74 \pm 0.91 \text{ Hz}$; Table 1).

Comparison of the absolute correlation coefficients indicated that both hippocampal and striatal neurons showed strong linear relationships with movement velocity. When compared with response task performance, the relationship between cell firing and velocity was stronger during place task performance for hippocampal neurons (Figure 7). Such task relatedness was not observed for striatal velocity-tuned cells. Comparison of baseline firing rates of velocity-tuned neurons revealed that striatal cells discharged at higher rates than hippocampal cells, $F(1, 117) = 7.46$, $p < .01$ (Table 1).

Responses of Hippocampal and Striatal Movement-Related Neurons to Cue Manipulations

After visual cue manipulation, three types of responses were observed for hippocampal and striatal movement-related neurons:

1. Cells maintained a correlation with movement; however, there was a change in the degree to which cell firing was related to either velocity or acceleration.
2. There was a loss of the velocity or acceleration correlation with cell firing.
3. There was an acquisition of velocity or acceleration correlation with neuron discharge rate.

Table 3 presents the percentage of cells that showed these types of neural activity change after cue manipulation during place and response tests. Examples of individual neuron responses are shown in Figures 6 and 8.

In order to determine quantitatively the degree of reorganization of neuronal movement codes, we selected cells that displayed significant linear relations with velocity or acceleration during both baseline and cue manipulation phases. A comparison of the absolute values of the average correlation coefficient revealed no significant change in velocity or acceleration correlation for hippocampal and striatal neurons during manipulation trials (paired t test showed all $ps > .05$). When the neural responses were viewed in terms of the percent change in correlation scores, we observed a significant effect of task for hippocampal acceleration-tuned neurons: After cue manipulation, these cells showed a larger degree of change in acceleration tuning only during place task performance, $F(1, 45) = 4.48$, $p < .05$ (see Figure 9A). A similar

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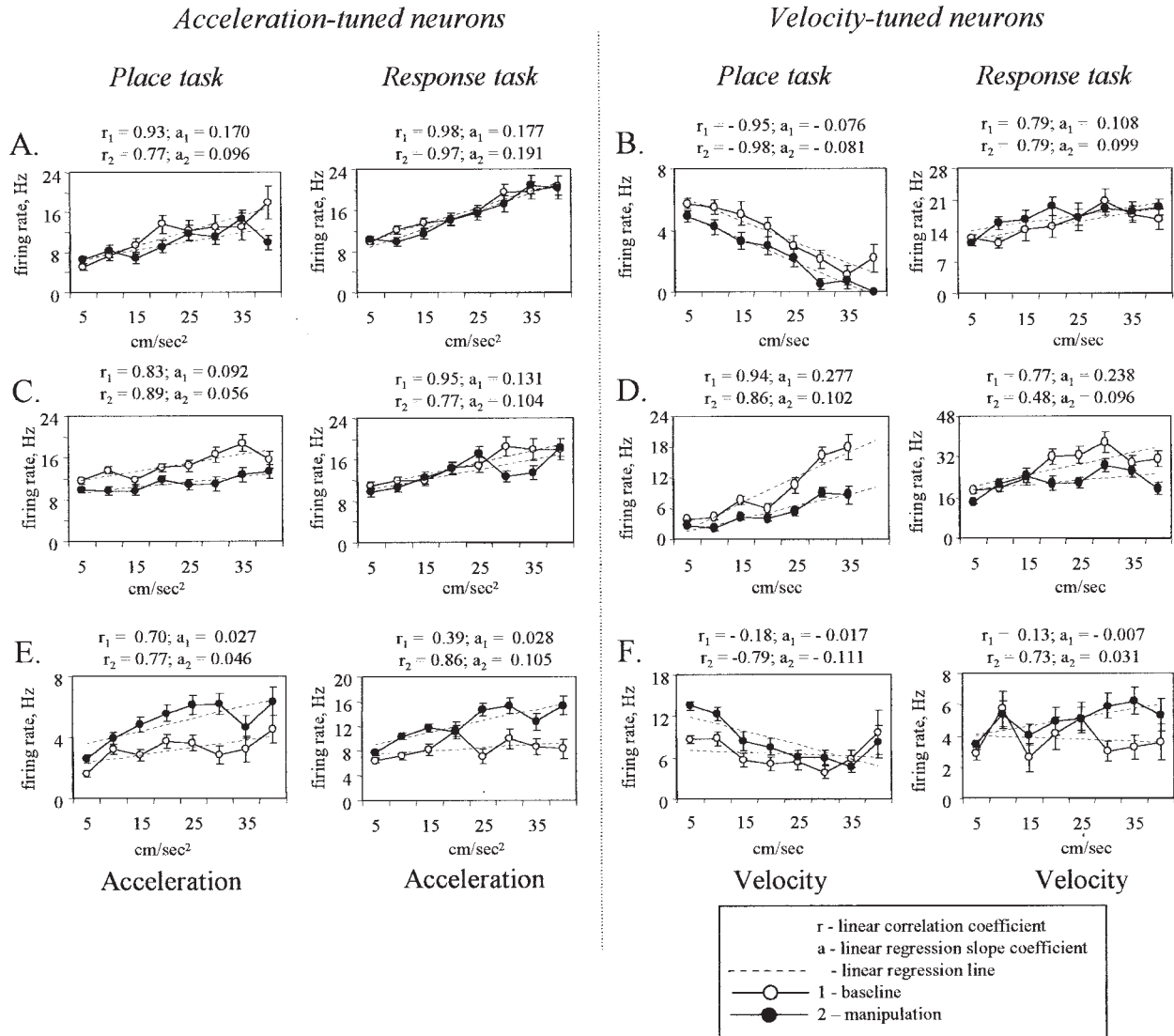


Figure 8. Examples of context-dependent responses of striatal acceleration- and velocity-tuned neurons during place and response conditions. The average firing rates for individual cells are presented relative to different values of acceleration and velocity. As in Figure 6, individual cell data exemplify movement-coding properties that were stable across baseline and manipulation trials (A and B), linear relations between firing rates and movement that became weaker or were lost after context change (C and D), or linear relations between firing rates and movement that were stronger when rats performed in a new context (E and F). As was observed for hippocampal neurons, a variety of striatal cell responses were found after cue manipulation.

trend was apparent for acceleration-tuned striatal neurons. However, this effect was not statistically significant, $F(1, 42) = 2.29$, $p > .05$ (Figure 9). There was no task-specific difference in the percent change of the correlation coefficient for velocity-tuned hippocampal or striatal neurons. Figure 9B shows the distribution of normalized *DIs* for acceleration and velocity correlation coefficients of individual cells from each group. It can be seen that the distribution is broad for all groups, indicating that some neurons did show changed relationships with acceleration or velocity after

visual context change, whereas others did not. Nevertheless, a manipulation effect was also confirmed by a one-sample *t* test showing that the mean values of the percent change in baseline were significantly different from zero for each group of neurons (all $ps < .05$).

A cue manipulation effect on acceleration- and velocity-tuned neurons was also evaluated by examining, for each neuron, the percent change in the linear regression slope coefficient. A one-sample *t* test confirmed that the absolute values of the percent change

Table 3
Types of Responses to Visual Context Changes for Hippocampal and Striatal Movement-Specific Neurons (Percentage of Cells Recorded)

Response	Hippocampus		Dorsal striatum	
	Place task	Response task	Place task	Response task
Acceleration-tuned neurons				
Stable correlate	53.4	41.0	39.3	52.6
Acquired correlate	29.3	28.2	30.4	36.8
Lost correlate	17.2	30.8	30.4	10.5
Velocity-tuned neurons				
Stable correlate	43.4	45.7	45.5	46.2
Acquired correlate	37.7	32.6	20.0	15.4
Lost correlate	18.9	21.7	34.6	38.5

scores were significantly higher than zero ($p < .01$ for all comparisons), except for striatal velocity-tuned neurons during the response task. A significant task effect was found for hippocampal velocity-tuned neurons, indicating that the magnitude of neuronal response to cue manipulation was significantly greater during response task performance, $F(1, 42) = 4.75, p < .05$ (Figure 9C). Hippocampal acceleration-tuned neurons showed a similar degree of slope coefficient change after cue manipulations, regardless of the particular task (Figure 9C). The tendency for a smaller percent change in the slope coefficient value during performance of the response task ($22.5\% \pm 4.5\%$ vs. $46.8\% \pm 8.5\%$ during performance of place task) was not significant, $F(1, 45) = 3.88, p > .05$. There were no task-specific effects on the percent change in slope coefficient for striatal acceleration- or velocity-tuned neurons (Figure 9C). The range of the percent change in *DIs* was similar for both brain structures and both behavioral tasks (Figure 9D). The firing rates of some neurons showed a greater magnitude of change with changing velocity (positive slope coefficient scores), whereas other neurons showed less sensitivity (negative slope coefficient scores).

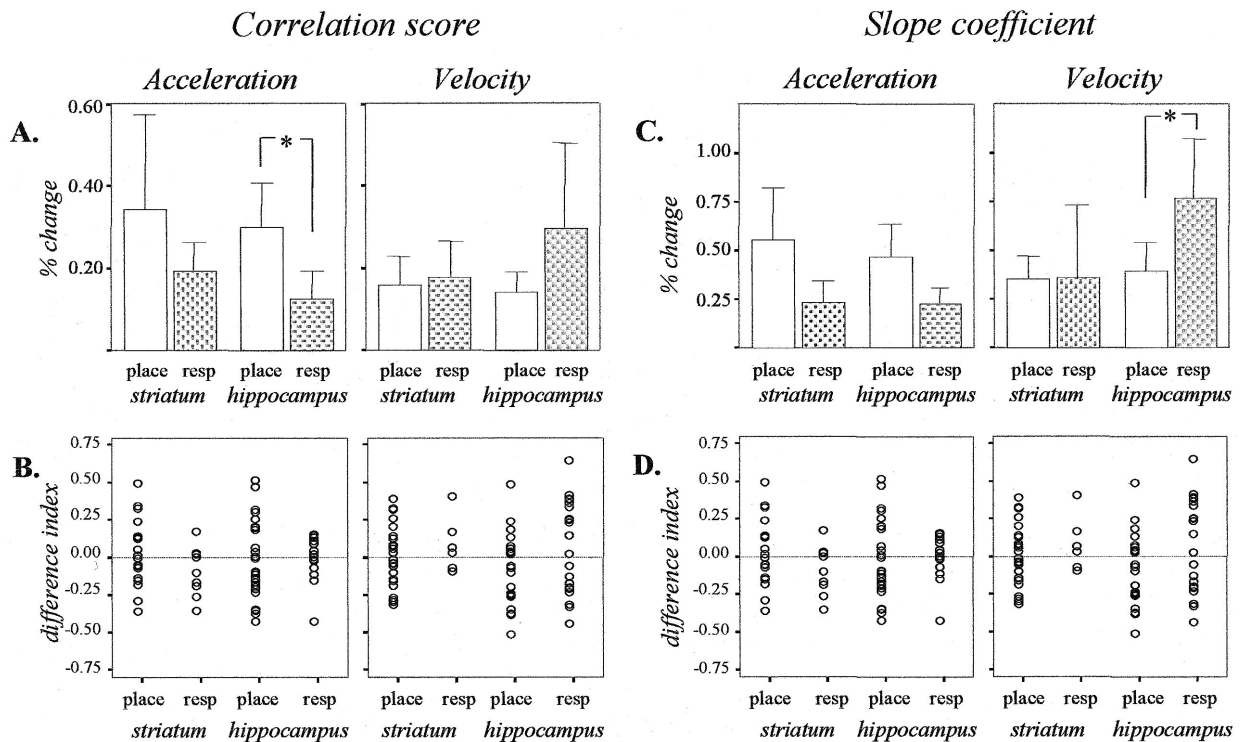


Figure 9. Context-dependent changes in movement sensitivity by hippocampal and striatal neurons as reflected by changes in the linear correlation (A and B) and linear regression slope coefficients (C and D). **A:** The percent change in correlation (r) values between baseline and cue manipulation phases. Hippocampal movement cells showed a larger change in correlation after cue manipulation during place performance than during response (resp) performance. The velocity measure did not distinguish hippocampal and striatal responses. **B:** The distribution of normalized difference shows that both enhanced and attenuated movement correlates were observed for hippocampal and striatal neurons recorded during place and response performance. **C:** When the movement correlate was measured according to the slope coefficient, it was observed that hippocampal neurons showed a stronger relationship to velocity during response performance than during place performance. **D:** As in B, the distribution of the normalized difference scores revealed a range of response types for hippocampal and striatal neurons. * $p < .05$, for within-structure comparisons.

Comparison of Striatal and Hippocampal Responses of Movement-Related Neurons

A two-way ANOVA (Brain Structure \times Task Design) revealed a significant task effect for acceleration-tuned neurons, $F(1, 78) = 6.31$, $p < .05$, in terms of the slope coefficient, indicating that these cells were more responsive to context change during the place task performance (Figure 9C). Both hippocampus and dorsal striatum showed a similar range of change, as there was no brain area effect, $F(1, 78) = 0.18$, $p > .05$, and no Brain Area \times Task interaction, $F(1, 78) = 0.13$, $p > .05$. No significant brain area, task, or interaction effects were found for velocity-tuned cells when percent change in correlation score, *DIs* for correlation scores, percent change in slope coefficient, or *DIs* for slope coefficient scores were compared (Figure 9).

In summary, reorganization of movement-related neuronal discharge was observed in hippocampus and dorsal striatum after visual context changes during place and response task performance. That is, the sensitivity of cells to changes in the rat's acceleration and/or velocity became more or less pronounced after visual cues were manipulated when rats performed either place or response tasks. However, the character of the neuronal response was specific to brain structure and neuronal correlate. Hippocampal acceleration-tuned neurons were more sensitive to visual context change during performance of the place task. Hippocampal velocity-tuned neurons appeared to be more sensitive during the response task condition, whereas responses of striatal velocity-tuned neurons were not task dependent. Thus, hippocampus movement-related firing was modulated by context information during both place and response tasks, albeit in different ways. In comparison, striatal movement-related firing (as a population) was not significantly affected by spatial context changes.

Discussion

Differential use of context information by striatum and hippocampus may contribute to their unique roles in response and place learning. The present study tested this hypothesis by comparing the relative impact of changes in the visual environment on spatial and movement representation by striatal and hippocampal neurons as rats performed either a place or response maze task. Hippocampal and striatal place fields exhibited context dependency by showing similar patterns and ranges of neuronal responses after visual cue manipulations, regardless of whether the rat was performing according to a place or response strategy. In contrast, the context sensitivity of hippocampal and striatal egocentric movement representation codes appeared to be dependent on brain structure and task. Baseline movement-related firing of hippocampal, but not striatal, neurons varied significantly depending on cognitive strategy: Hippocampal cell firing was more strongly related to velocity and acceleration during place task performance. Although many individual hippocampal and striatal cells responded to cue manipulations during place and response performance, as a group, movement-related firing was modulated by the cue changes to a greater extent in hippocampus than in striatum during both place and response task performance. Overall, the degree of similarity between hippocampal and striatal neural responses during place and response learning was striking and unpredictable by theories of distinct limbic and basal ganglia mem-

ory systems. Such a finding implies the existence of significant parallel processing across the different neural systems (in addition to distinct and specific neural codes), processing that continues regardless of the task requirements.

Because a goal of this study was to examine cognitive strategy effects on the visual context sensitivity of hippocampal and striatal neurons, we intentionally created a test situation in which only the cognitive strategy differed between tasks. The baseline sensory environment, motivation, and required behavioral acts were necessarily held constant for response and place learners. This similarity in baseline conditions may have biased the outcome so that neural codes in hippocampus and striatum responded similarly. However, because hippocampal, and not striatal, neural codes for movement velocity and acceleration showed context dependency based on cognitive strategy, such a bias was not likely present.

Context-Sensitive Spatial Codes in Hippocampus and Striatum

The current findings—that place cells in hippocampus and striatum changed their place field properties when the external environment changed—are consistent with the results of earlier studies. Hippocampal place fields are controlled by visual landmarks (e.g., Cressant, Muller, & Poucet, 2002; Muller & Kubie, 1987; O'Keefe & Conway, 1978); however, there are also cases of persistent field location (Mizumori et al., 2000; Mizumori, Ragozzino, et al., 1999; O'Keefe & Speakman, 1987; Quirk, Muller, & Kubie, 1990) as well as more complex relations between the topography of place fields and visual cues (Knierim, 2002; Lenck-Santini, Muller, Save, & Poucet, 2002; Lenck-Santini, Save, & Poucet, 2001; Muller, Poucet, Fenton, & Cressant, 1999; Shapiro et al., 1997; Tanila, Shapiro, & Eichenbaum, 1997). Context sensitivity has also been shown for spatial-correlated neurons in rat striatum during performance of a spatial working memory task (Mizumori et al., 2000). The results of this study extend these earlier findings by directly comparing the context sensitivity of simultaneously recorded hippocampal and striatal unit correlates as a function of cognitive strategy (i.e., place vs. response), a parameter often postulated to distinguish hippocampal and striatal contributions to learning. The fact that hippocampal and striatal place fields responded to context change regardless of cognitive strategy suggests that context information continually, and perhaps automatically, affects spatial neural representation in these structures.

It has been suggested that striatum and hippocampus differentially use context information (Mizumori et al., 2000). Most striatal place fields reorganized after imposed darkness (Mizumori et al., 2000), whereas only a portion of the hippocampal place fields reorganized when tested under similar conditions (Mizumori, Ragozzino, et al., 1999; Quirk et al., 1990). In the present study, no such structural differences were found in terms of the context sensitivity of place fields (Figure 5). Several differences between the studies are worth noting, however. Previously, rats were tested during spatial working memory tests on an eight-arm radial maze, and the cue manipulation was imposed darkness. Imposed darkness may induce a spontaneous change in strategy. In the present study, darkness was not used so that we could better control the strategy used by the rats.

Context-Sensitive Egocentric Movement Codes in Hippocampus and Striatum

The nature of the contribution to adaptive navigation by egocentric movement representations in hippocampus or striatum is not well understood. One possibility is that the movement codes reflect the current movement state of the animal. Certainly, the firing rates of these cells are significantly modulated by particular movements of the animal (e.g., turns, forward locomotion, velocity, and acceleration), providing strong support for this most parsimonious interpretation. Nevertheless, an alternative, or additional, interpretation is worth considering. That is, the movement correlates may reflect previously learned behavioral acts. If the latter hypothesis is correct, one would expect that changes in the visual context might affect the extent to which these cells demonstrate a movement correlate. Indeed, velocity- and/or acceleration-related firing by hippocampal neurons was modulated by cue manipulation regardless of cognitive strategy. In contrast, although individual striatal movement-related cells responded to visual manipulations (a result similar to what has been observed for primate response-sensitive striatal neurons; e.g., Hikosaka et al., 1989; Rolls et al., 1983; Tremblay et al., 1998), there was no consistent strategy-dependent effect on the population of striatal neurons.

The context sensitivity of hippocampal movement-related cell firing would not necessarily have been predicted by most current interpretations of hippocampal movement-related neural codes. Hippocampal interneurons are often referred to as *theta cells* because they discharge relative to the theta rhythm present in the hippocampal electroencephalogram. Theta appears in the electroencephalogram record when rats engage in voluntary movements (e.g., Ranck, 1973; Rose, 1983; Vanderwolf, 1969). Therefore, current theoretical models of hippocampal processing consider theta cell firing as reflecting the current movement state of the animal, or idiothetic information (Czurkó et al., 1999; Huxter et al., 2003; Kubie et al., 1990; McNaughton, Barnes, & O'Keefe, 1983; O'Keefe & Recce, 1993; Whishaw & Vanderwolf, 1973; Wiener et al., 1989). Specific movement information may ultimately arrive from perirhinal cortex (e.g., Muir & Bilkey, 2003) and/or subcortical theta generators (e.g., Bland & Oddie, 1998; Vertes & Kocsis, 1997).

Our data show not only that the movement codes of a number of hippocampal theta neurons reflect current idiothetic information, but also that the movement relatedness is modulated by spatial context. In this way, hippocampal interneurons may bring to intrahippocampal neurocomputations specific information about learned behavioral responses. Such a conclusion is consistent with past results indicating that, in addition to informing hippocampus about the current behavioral state, hippocampal interneuron discharge patterns may convey specific types of information (Kubie et al., 1990; Leutgeb, Ragozzino, & Mizumori, 2000; Mizumori & Leutgeb, 2001; Moita et al., 2003).

Relevant spatial context information may be transmitted to the interneurons from hippocampal pyramidal (place) neurons; the interneurons in turn may pass on to pyramidal neurons information about learned responses that apply to particular environmental contexts. According to this suggestion, then, hippocampus as a whole represents spatial context as an integrated construct of external and internal sensory information, together with behavioral responses appropriate to the sensory environment (Mizumori et al.,

2001; Mizumori, Ragozzino, et al., 1999). Motivational state information may also enter into hippocampal representations of context (Kennedy & Shapiro, 2003; Mizumori et al., 2001).

In contrast to the numerous primate studies showing context sensitivity of striatal response-correlated neurons, context sensitivity of response-related neurons in rats has not been consistently reported. In an earlier study, it was found that, as a group, movement-sensitive striatal cells did not show appreciable changes in firing when the room lights were turned off while rats performed a spatial working memory task on a radial maze (Mizumori et al., 2000). One explanation for the apparent discrepancy between these earlier findings and the present findings of numerous context-sensitive movement-related striatal cells is that these studies may have tested completely different populations of cells. Only those with significant velocity or acceleration correlates were included for context analysis in this study, whereas in the previous study, any cell that showed significant variation in firing rates relative to changes in behavioral state (based on perievent histogram analysis and regardless of the cell's correlation with velocity or acceleration) was included for analysis. Alternatively, the present study may have tested a subset of the type of cells tested in the previous study.

Relative Contributions of Hippocampus and Striatum to Adaptive Navigation

The overall pattern of hippocampal and striatal unit responses to context change is generally consistent with the proposed functions of hippocampus and striatum during adaptive navigation (Mizumori et al., 2000). If hippocampus determines the extent to which an expected spatial context has changed, it likely needs access to information that defines the elements of a training condition, or context. If the term *spatial context* refers to the constellation of inputs that uniquely define a particular environmental situation (Mizumori, Ragozzino, et al., 1999), then neural representations of its elements could be broad in type, including codes regarding the current sensory environment, context-relevant behavioral acts, reward expectancies, behavioral orientation, and an animal's location. If the discharge pattern of an individual hippocampal cell reflects the integration of these context elements, then alterations in any one of these elements could change the overall behavioral correlate of a given cell (Mizumori, Miya, & Ward, 1994). This is indeed what was observed for both spatial and nonspatial neural codes in hippocampus: Place and egocentric movement-related neural codes showed clear responses to changes in the visual cue environment. Similarly, in a previous study, removal of a source of orientation information (from lateral dorsal thalamus) resulted in dramatic hippocampal place field reorganization, and not just the elimination of the directional component of place cell discharge (Mizumori et al., 1994).

A common result of the cue manipulations was that a subset of hippocampal place fields did not reorganize after cue manipulation, whereas a different population of place fields did. These two patterns of responses are consistent with the view that hippocampus contains information about the expected spatial context as well as the current spatial context. Such data could enter into intrinsic neurocomputations that determine the extent to which the context has changed (Mizumori, Ragozzino, et al., 1999). Given that cognitive strategy did not differentially affect place cell responses

to cue manipulations, it appears that context evaluation takes place during more than just spatial learning for both striatum and hippocampus. One advantage of such parallel processing is that animals may more readily adapt to environmental change.

An ultimate contribution of striatal processing to experience-dependent navigation may be to update cortical memory representations regarding the consequence of behaviors performed within specific spatial contexts (Mizumori et al., 2000; Mizumori, Pratt, & Ragozzino, 1999). In this way, striatal computations may contribute to the selection of future responses (Houk, 1995; Schultz et al., 2003). These postulated striatal functions may require that ongoing context or stimulus information continually update striatal representations of the current context. Indeed, many striatal place fields were sensitive to changes in the visual environment. The finding that a portion of the movement-related cells in striatum also responded to context change suggests that, similar to hippocampus, striatum contains representations of learned, context-relevant behavioral responses. In addition, movement-related and location-specific cells were found that did not respond to context change, indicating that striatum also contains representations related to the current behaviors exhibited by the animal. Such a combination of representations may be used to analyze the extent to which the reinforcement consequences of learned behaviors are actually realized by ongoing acts (Mizumori et al., 2000; Mizumori, Pratt, & Ragozzino, 1999).

Because hippocampal movement cells were more responsive than striatal movement cells to cue manipulations during place performance, at least a portion of hippocampal computations may be more involved in context-dependent learning than striatal computations. Indeed, this conclusion is consistent with a number of behavioral investigations of hippocampal function (see below). The finding that striatal movement cells' sensitivity to cue manipulations did not differ depending on the task performed suggest that striatum continually evaluates, according to similar algorithms, the outcomes of context-specific responses during multiple types of learning. Such a result was predicted by our more general theory of striatal mnemonic functions (Mizumori et al., 2000; Mizumori, Pratt, & Ragozzino, 1999).

Implications for Theories of Multiple Memory Systems

Hippocampus is often considered to mediate allocentric learning (based on the use of distal cues), whereas striatum is thought to be selectively involved in egocentric learning (based on internally generated information; DeCoteau & Kesner, 2000; Kesner, Bolland, & Dakis, 1993; McDonald & White, 1993; Packard & Knowlton, 2002). The anatomical separation of different memory systems is supported by a number of studies showing structure-specific learning deficits in animals tested on allocentric or egocentric tasks after lesion or inactivation of either hippocampus or striatum (Devan, McDonald, & White, 1999; McDonald & White, 1994; Morris, Garrud, Rawlins, & O'Keefe, 1982; Oliveira, Bueno, Pomarico, & Gugliano, 1997; Packard, Hirsh, & White, 1989; Packard & McGaugh, 1996; Packard & Teather, 1999; Pearce, Roberts, & Good, 1998; White & McDonald, 2002).

Our data shed new light on the nature of the relationship between hippocampus and striatum during spatial and response learning. It is possible that the reported differential effects of hippocampal and striatal lesions on response and place learning

may relate to the different patterns of extrinsic connections of the two structures rather than the notion of one structure being active while the other is inhibited. In contrast to hippocampus, which is interconnected with many cortical and subcortical associational areas, striatum receives somatotopically organized input from primary motor and primary somatosensory cortex (Cho & West, 1997; Flaherty & Graybiel, 1993; Kemp & Powell, 1970). A second striatal afferent pattern is one in which diverse areas of cortex (e.g., frontal, parietal, and temporal cortices) converge onto restricted zones of striatum (McGeorge & Faull, 1989; Reep, Cheatwood, & Corwin, 2003). This convergent pattern allows for unique integration of a vast array of information. Wise et al. (1996) and Rolls (1994) suggest that the somatotopic pattern of striatal connections mediates stimulus-response learning, whereas the convergent pattern of inputs supports context-dependent learning. Thus, depending on whether learning requires stimulus-response associations or more flexible cognitive processing, different afferent patterns are activated. However, the different inputs may be subjected to similar neural processing within striatum because both types of inputs are thought to innervate the GABAergic, medium spiny projection neurons of striatum. The massive convergent input, bistable membrane potential (Wilson, 1995), and a dopamine-mediated training mechanism (Houk, 1995; Schultz, Apicella, Romo, & Scarnati, 1995) are consistent with the hypothesis that, regardless of the task requirements, striatum signals changes in the expected reward contingencies, and that such a signal incorporates information relevant to current egocentric movements, behavioral orientation, and spatial context (Mizumori et al., 2000; Mizumori, Pratt, & Ragozzino, 1999).

The unique striatal connections with sensory and motor cortex allow striatum to have critical and specialized input to stimulus-response learning. Although hippocampal processing likely continues during response training (as shown by the findings of this study), impaired response learning is not observed after hippocampal lesions, perhaps because other structures (e.g., striatum and neocortex) continue to process sufficient task-relevant information to support learning. Alternatively, the context evaluation by hippocampus may not be necessary for response learning to occur. During place learning, both striatum and hippocampus may normally contribute, albeit in different ways. An evaluation of changes in spatial context is likely essential for normal spatial learning. Thus, if hippocampus is damaged, spatial learning deficits are found. If, on the other hand, striatum is lesioned, one may not readily observe spatial deficits because of the existence of alternate neocortical routes for response evaluations (Mizumori, Pratt, Cooper, & Guazzelli, 2002).

Most (if not all) of the lesion studies report distinct hippocampal and striatal lesion effects in animals tested during task acquisition or soon after asymptotic performance was achieved. Cells that are reported in this study were recorded from rats performing at asymptotic performance levels, as a means of ensuring that rats clearly discriminated different reward contingencies and that their behavior reliably corresponded to the current task rule. It is possible that the influences of hippocampus and striatum are different during acquisition and asymptotic performance. Indeed, differential strategy-specific activation of these brain structures, as measured by acetylcholine release, was recently shown to take place during the early phase of learning, whereas comparable levels of activation were observed later in training (Chang & Gold, 2003).

In addition to entertaining the view that hippocampus and striatum act independently and competitively, others have suggested that there is significant interaction between different memory systems (Chang & Gold, 2003; Colombo, Brightwell, & Countryman, 2003; Gold, 2003; Kim & Baxter, 2001; Packard & Knowlton, 2002). Indeed, in addition to the present study, new evidence from rodent studies supports the view that parallel information processing by multiple memory systems may be more common than previously thought. For example, acetylcholine release is enhanced in hippocampus during learning of an amygdala-dependent task or a hippocampus-dependent task (McIntyre, Pal, Marriott, & Gold, 2002). Also, pCREB and c-Fos immunoreactivity are enhanced in both hippocampus and striatum immediately after training on a plus-maze, independent of response or place strategy use (Colombo et al., 2003). Increased firing of hippocampal pyramidal and theta neurons in response to conditioned stimuli during auditory fear conditioning (Moita et al., 2003) indicates that plastic changes in hippocampus might occur during learning of an amygdala-dependent (and allegedly hippocampus-independent) task.

Our data are consistent with the possibility that hippocampal and striatal computations occur in parallel, and that functional interaction between these neural systems may begin with the integration of hippocampal and striatal output. For the case of experience-dependent navigation, hippocampus may compare the current spatial context with that expected on the basis of past experience (Mizumori, Ragozzino, et al., 1999). Different output messages might be generated depending on the extent to which the expected and current contexts match. In contrast, striatum may compare the expected success of a learned behavior with the actual success experienced after the execution of behavior (Mizumori, Pratt, & Ragozzino, 1999). Thus, hippocampus might update cortical representations regarding changes in the expected spatial context, whereas striatum updates cortical representations based on the most recent reinforcement consequence of previously learned sensorimotor associations. Such functions should be important for multiple forms of learning, including stimulus–response and spatial learning. Optimal adaptive navigation may then be achieved when the hippocampus is allowed to continuously, and automatically, organize and update expectations about the spatial context, and striatum is allowed to update context-specific reinforcement expectations. Both systems may feed forward the results of their analysis to integrative response selection systems within the neocortex.

Summary

The findings of this study demonstrate a striking degree of parallel processing of spatial context and movement information in hippocampus and striatum during the performance of a spatial or response task. Therefore, these neural systems are continually engaged, regardless of the cognitive strategy being used. This finding suggests that a different contribution by hippocampus and striatum to place and response learning is determined by the pattern of extrinsic connections to behavioral control areas of the brain. A second important result of this study is that we provide the first evidence that movement-related firing by hippocampal and striatal neurons is frequently context dependent, suggesting that context determines the type of neural code observed. From this we

conclude that the movement codes in hippocampus and striatum represent learned behavioral responses, and not merely the current movement state. Such response information may continually refine the definition of spatial context encoded by the population of hippocampal and striatal neurons.

References

- Alexander, G. E., & Crutcher, M. D. (1990). Neural representations of the target (goal) of visually guided arm movements in three motor areas of the monkey. *Journal of Neurophysiology*, *64*, 164–178.
- Barrientos, R. M., O'Reilly, R. C., & Rudy, J. W. (2002). Memory for context is impaired by injecting anisomycin into dorsal hippocampus following context exploration. *Behavioural Brain Research*, *134*, 299–306.
- Bland, B. H., & Oddie, S. D. (1998). Anatomical, electrophysiological and pharmacological studies of ascending brainstem hippocampal synchronizing pathways. *Neuroscience & Biobehavioral Reviews*, *22*(2), 259–273.
- Buzsáki, G., Leung, L.-W., & Vanderwolf, C. H. (1983). Cellular basis of hippocampal EEG in the behaving rat. *Brain Research Reviews*, *6*, 139–171.
- Chang, Q., & Gold, P. E. (2003). Switching memory systems during learning: Changes in patterns of brain acetylcholine release in the hippocampus and striatum in rats. *Journal of Neuroscience*, *23*, 3001–3005.
- Cho, J., & West, M. O. (1997). Distributions of single neurons related to body parts in the lateral striatum of the rat. *Brain Research*, *756*, 241–246.
- Colombo, P. J., Brightwell, J. J., & Countryman, R. A. (2003). Cognitive strategy-specific increases in phosphorylated cAMP response element-binding protein and c-Fos in the hippocampus and dorsal striatum. *Journal of Neuroscience*, *23*, 3547–3554.
- Cools, A., Van den Bercken, J. H. L., Horstink, M. W. I., Spaendonck, K. P. M., & Berger, H. J. C. (1984). Cognitive and motor shifting aptitude disorder in Parkinson's disease. *Journal of Neurology, Neurosurgery, and Psychiatry*, *47*, 443–453.
- Cools, R., Barker, R. A., Sahakian, B. J., & Robbins, T. W. (2001). Enhanced or impaired cognitive function in Parkinson's disease as a function of dopaminergic medication and task demands. *Cerebral Cortex*, *11*, 1136–1143.
- Cooper, B. G., & Mizumori, S. J. Y. (2001). Temporary inactivation of retrosplenial cortex causes a transient reorganization of the spatial coding in hippocampus. *Journal of Neuroscience*, *21*, 3986–4001.
- Cressant, A., Muller, R. U., & Poucet, B. (2002). Remapping of place cell firing patterns after maze rotations. *Experimental Brain Research*, *143*, 470–479.
- Czurkó, A., Hirase, H., Csicsvari, J., & Buzsáki, G. (1999). Sustained activation of hippocampal pyramidal cells by “space clamping” in a running wheel. *European Journal of Neuroscience*, *11*, 344–352.
- DeCoteau, W. E., & Kesner, R. P. (2000). A double dissociation between the rat hippocampus and medial caudoputamen in processing two forms of knowledge. *Behavioral Neuroscience*, *114*, 1096–1108.
- Devan, B., McDonald, R. J., & White, N. M. (1999). Effects of medial and lateral caudate-putamen lesions on place- and cue-guided behavior in the water maze: Relation to thigmotaxis. *Behavioural Brain Research*, *100*, 5–14.
- Eichenbaum, H., Dudchenko, P., Wood, E., Shapiro, M., & Tanila, H. (1999). The hippocampus, memory, and place cells: Is it spatial memory or memory space? *Neuron*, *23*, 209–226.
- Flaherty, A. W., & Graybiel, A. M. (1993). Two input systems for body representations in the primate striatal matrix: Experimental evidence in the squirrel monkey. *Journal of Neuroscience*, *13*, 1120.

- Frank, L. M., Brown, E. N., & Wilson, M. (2000). Trajectory encoding in the hippocampus and entorhinal cortex. *Neuron*, *27*, 169–178.
- Frankland, P. W., Cestari, V., Filipkowski, R. K., McDonald, R. J., & Silva, A. J. (1998). The dorsal hippocampus is essential for context discrimination but not for contextual conditioning. *Behavioral Neuroscience*, *112*, 863–874.
- Gold, P. E. (2003). Acetylcholine modulation of neural systems involved in learning and memory. *Neurobiology of Learning and Memory*, *80*, 194–210.
- Graybiel, A. M. (1995). Building action repertoires: Memory and learning functions of the basal ganglia. *Current Opinion in Neurobiology*, *5*, 733–741.
- Hikosaka, O., Sakamoto, M., & Usui, S. (1989). Functional properties of monkey caudate neurons: III. Activities related to expectation of target and reward. *Journal of Neurophysiology*, *61*, 814–832.
- Houk, J. C. (1995). Information processing in modular circuits linking basal ganglia and cerebral cortex. In J. C. Houk, J. L. Davis, & D. G. Beiser (Eds.), *Models of information processing in the basal ganglia* (pp. 3–10). Cambridge, MA: MIT Press.
- Huxter, J., Burgess, N., & O'Keefe, J. (2003, October 23). Independent rate and temporal coding in hippocampal pyramidal cells. *Nature*, *425*, 828–832.
- Jeffery, K. J., Gilbert, A., Burton, S., & Strudwick, A. (2003). Preserved performance in a hippocampal-dependent spatial task despite complete place cell remapping. *Hippocampus*, *13*, 175–189.
- Jog, M. S., Kubota, Y., Connolly, C. I., Hillegaart, V., & Graybiel, A. M. (1999, November 26). Building neural representations of habits. *Science*, *286*, 1745–1749.
- Kemp, J. M., & Powell, T. P. S. (1970). The cortico-striate projection in the monkey. *Brain*, *93*, 525.
- Kennedy, P. J., & Shapiro, M. L. (2003, November). *Hippocampal lesions impair performance in a non-spatial, contextual retrieval task based on motivational state* (Poster session presented at the annual meeting of the Society for Neuroscience, Program No. 289.5). Retrieved from the 2003 Abstract Viewer and Itinerary Planner, <http://sfn.scholarone.com/itin2003/index.html>
- Kesner, R. P., Bolland, B. L., & Dakis, M. (1993). Memory for spatial locations, motor responses, and objects: Triple dissociation among the hippocampus, caudate nucleus, and extrastriate visual cortex. *Experimental Brain Research*, *93*, 462–470.
- Kim, J. J., & Baxter, M. G. (2001). Multiple brain-memory systems: The whole does not equal the sum of its parts. *Trends in Neuroscience*, *24*, 324–330.
- Knierim, J. J. (2002). Dynamic interactions between local surface cues, distal landmarks, and intrinsic circuitry in hippocampal place cells. *Journal of Neuroscience*, *22*, 6254–6264.
- Knierim, J. J., Kudrimoti, H. S., & McNaughton, B. L. (1998). Interactions between idiothetic cues and external landmarks in the control of place and head direction cells. *Journal of Neurophysiology*, *80*, 425–446.
- Kubie, J. L., Muller, R. U., & Bostock, E. (1990). Spatial firing properties of hippocampal theta cells. *Journal of Neuroscience*, *10*, 1110–1123.
- Lavoie, A. M., & Mizumori, S. J. Y. (1994). Spatial, movement-, and reward-sensitive discharge by medial ventral striatum neurons of rats. *Brain Research*, *638*, 157–168.
- Lenck-Santini, P.-P., Muller, R. U., Save, E., & Poucet, B. (2002). Relationships between place cell firing fields and navigational decisions by rats. *Journal of Neuroscience*, *22*, 9035–9047.
- Lenck-Santini, P.-P., Save, E., & Poucet, B. (2001). Evidence for relationship between place-cell spatial firing and spatial memory performance. *Hippocampus*, *11*, 377–390.
- Leutgeb, S., Guazzelli, A., & Higginson, C. (1997). *Single unit analysis package* [Computer software]. Seattle: University of Washington, Department of Psychology.
- Leutgeb, S., & Mizumori, S. J. Y. (2002). Context-specific spatial representations by lateral septal cells. *Neuroscience*, *112*, 655–663.
- Leutgeb, S., Ragozzino, K. E., & Mizumori, S. J. Y. (2000). Convergence of head direction and place information in the CA1 region of hippocampus. *Neuroscience*, *100*, 11–19.
- McDonald, R. J., & White, N. M. (1993). A triple dissociation of memory systems: Hippocampus, amygdala and dorsal striatum. *Behavioral Neuroscience*, *107*, 3–22.
- McDonald, R. J., & White, N. M. (1994). Parallel information processing in the water maze: Evidence for independent memory systems involving dorsal striatum and hippocampus. *Behavioral and Neural Biology*, *61*, 260–270.
- McGeorge, A. J., & Faull, R. L. M. (1989). The organization of the projection from the cerebral cortex to the striatum in the rat. *Neuroscience*, *29*, 503–537.
- McIntyre, C. K., Pal, S. N., Marriott, L. K., & Gold, P. E. (2002). Competition between memory systems: Acetylcholine release in the hippocampus correlates negatively with good performance on an amygdala-dependent task. *Journal of Neuroscience*, *22*, 1171–1176.
- McNaughton, B. L., Barnes, C. A., Meltzer, J., & Sutherland, R. J. (1989). Hippocampal granule cells are necessary for normal spatial learning but not for spatially-selective pyramidal cell discharge. *Experimental Brain Research*, *78*, 485–496.
- McNaughton, B. L., Barnes, C. A., & O'Keefe, J. (1983). The contribution of position, direction, and velocity to single unit activity in the hippocampus of freely-moving rats. *Experimental Brain Research*, *52*, 41–49.
- McNaughton, B. L., O'Keefe, J., & Barnes, C. A. (1983). The stereotrode: A new technique for simultaneous isolation of several single units in the central nervous system from multiple unit records. *Journal of Neuroscience Methods*, *8*, 391–397.
- Mizumori, S. J. Y., Cooper, B. G., Leutgeb, S., & Pratt, W. E. (2001). A neural systems analysis of adaptive navigation. *Molecular Neurobiology*, *21*, 57–82.
- Mizumori, S. J. Y., & Leutgeb, S. (2001). Directing place representation in the hippocampus. *Reviews in the Neurosciences*, *12*, 347–363.
- Mizumori, S. J. Y., Miya, D. Y., & Ward, K. E. (1994). Reversible inactivation of the lateral dorsal thalamus disrupts hippocampal place representations and impairs spatial learning. *Brain Research*, *644*, 168–174.
- Mizumori, S. J. Y., Pratt, W. E., Cooper, B. G., & Guazzelli, A. (2002). The behavioral implementation of hippocampal processing. In P. E. Sharp (Ed.), *The neural basis of navigation: Evidence from single cell recording* (pp. 197–216). Boston: Kluwer.
- Mizumori, S. J. Y., Pratt, W. E., & Ragozzino, K. E. (1999). Functions of the nucleus accumbens within the context of the larger striatal system. *Psychobiology*, *27*, 214–224.
- Mizumori, S. J. Y., Ragozzino, K. E., & Cooper, B. G. (2000). Location and head direction representation in the dorsal striatum of rats. *Psychobiology*, *28*, 441–462.
- Mizumori, S. J. Y., Ragozzino, K. E., Cooper, B. G., & Leutgeb, S. (1999). Hippocampal representational organization and spatial context. *Hippocampus*, *9*, 444–451.
- Mizumori, S. J. Y., & Williams, J. D. (1993). Directionally-selective mnemonic properties of neurons in the lateral dorsal nucleus of the thalamus of rats. *Journal of Neuroscience*, *13*, 4015–4028.
- Moita, M. A. P., Rosis, S., Zhou, Y., LeDoux, J. E., & Blair, H. T. (2003). Hippocampal place cells acquire location-specific responses to the conditioned stimulus during auditory fear conditioning. *Neuron*, *37*, 485–497.
- Morris, R. G. M., Garrud, P., Rawlins, J. N. P., & O'Keefe, J. (1982, June 24). Place navigation impaired in rats with hippocampal lesions. *Nature*, *297*, 681–683.
- Muir, G. M., & Bilkey, D. K. (2003). Theta- and movement velocity-

- related firing of hippocampal neurons is disrupted by lesions centered on the perirhinal cortex. *Hippocampus*, *13*, 93–108.
- Muller, R. U., & Kubie, J. L. (1987). The effects of changes in the environment on the spatial firing of hippocampal complex-spike cells. *Journal of Neuroscience*, *7*, 1951–1968.
- Muller, R. U., Poucet, B., Fenton, A., & Cressant, A. (1999). Is the rat hippocampus part of a specialized navigation system? *Hippocampus*, *9*, 413–422.
- Nadel, L., & Payne, J. D. (2002). The hippocampus, wayfinding and episodic memory. In P. E. Sharp (Ed.), *The neural basis of navigation: Evidence from single cell recording* (pp. 235–248). Boston: Kluwer.
- Nadel, L., & Wilner, J. (1980). Context and conditioning: A place for space. *Physiological Psychology*, *8*, 218–228.
- O'Keefe, J., & Conway, D. H. (1978). Hippocampal place units in the freely moving rat: Why they fire where they fire. *Experimental Brain Research*, *31*, 573–590.
- O'Keefe, J., & Dostrovsky, J. (1971). The hippocampus as a spatial map. Preliminary evidence from unit activity in the freely moving rat. *Brain Research*, *34*, 171–175.
- O'Keefe, J., & Nadel, L. (1978). *The hippocampus as a cognitive map*. Oxford, England: Clarendon.
- O'Keefe, J., & Recce, M. L. (1993). Phase relationship between hippocampal place units and the EEG theta rhythm. *Hippocampus*, *3*, 317–330.
- O'Keefe, J., & Speakman, A. (1987). Single unit activity in the rat hippocampus during a spatial memory task. *Experimental Brain Research*, *68*, 1–27.
- Oliveira, M. G., Bueno, O. F. A., Pomarico, A. C., & Gugliano, E. B. (1997). Strategy used by hippocampal- and caudate-putamen-lesioned rats in a learning task. *Neurobiology of Learning and Memory*, *68*, 32–41.
- O'Reilly, R. C., & Rudy, J. W. (2001). Conjunctive representations in learning and memory: Principles of cortical and hippocampal function. *Psychological Review*, *108*, 311–345.
- Packard, M. G., Hirsh, R., & White, N. M. (1989). Differential effects of fornix and caudate nucleus lesions on two radial maze tasks: Evidence for multiple memory systems. *Journal of Neuroscience*, *9*, 1465–1472.
- Packard, M. G., & Knowlton, B. J. (2002). Learning and memory functions of the basal ganglia. *Annual Review of Neuroscience*, *25*, 563–593.
- Packard, M. G., & McGaugh, J. L. (1996). Inactivation of the hippocampus or caudate nucleus with lidocaine differentially affects expression of place and response learning. *Neurobiology of Learning and Memory*, *65*, 65–72.
- Packard, M. G., & Teather, L. A. (1999). Dissociation of multiple memory systems by posttraining intracerebral injections of glutamate. *Psychobiology*, *27*, 40–50.
- Pearce, J. M., Roberts, A. D., & Good, M. (1998, November 5). Hippocampal lesions disrupt navigation based on cognitive maps but not heading vectors. *Nature*, *396*, 75–77.
- Quirk, G. J., Muller, R. U., & Kubie, J. L. (1990). The firing of hippocampal place cells in the dark depends on the rat's recent experience. *Journal of Neuroscience*, *10*, 2008–2017.
- Ragozzino, K. E., Leutgeb, S., & Mizumori, S. J. Y. (2001). Conditional coupling of dorsal striatal head direction and hippocampal place representations during spatial navigation. *Experimental Brain Research*, *139*, 372–376.
- Ranck, J. B., Jr. (1973). Studies on single neurons in dorsal hippocampus formation and septum in unrestrained rats: I. Behavioral correlates and firing repertoires. *Experimental Neurology*, *41*, 461–531.
- Reep, R. L., Cheatwood, J. L., & Corwin, J. V. (2003). The associative striatum: Organization of cortical projections to the dorsocentral striatum in rats. *Journal of Comparative Neurology*, *467*, 271–292.
- Rolls, E. T. (1994). Neurophysiology and cognitive functions of the striatum. *Reviews in Neurology*, *150*, 648–660.
- Rolls, E. T., Thorpe, S. J., & Maddison, S. P. (1983). Responses of striatal neurons in the behaving monkey. 1. Head of the caudate nucleus. *Behavioural Brain Research*, *7*, 179–210.
- Rose, G. (1983). Physiological and behavioral characteristics of dentate granule cells. In W. Seifert (Ed.), *Neurobiology of the hippocampus* (pp. 449–472). New York: Academic Press.
- Schultz, W. (2000). Multiple reward signals in the brain. *Nature Reviews: Neuroscience*, *1*, 199–207.
- Schultz, W., Apicella, P., Romo, R., & Scarnati, E. (1995). Context-dependent activity in the primate striatum reflecting past and future behavioral events. In J. C. Houk, J. L. Davis, & D. G. Beiser (Eds.), *Models of information processing in the basal ganglia* (pp. 11–27). Cambridge, MA: MIT Press.
- Schultz, W., Tremblay, L., & Hollerman, J. R. (2003). Changes in behavior-related neuronal activity in the striatum during learning. *Trends in Neuroscience*, *26*, 321–328.
- Shapiro, M. L., Tanila, H., & Eichenbaum, H. (1997). Cues that hippocampal place cells encode: Dynamic and hierarchical representation of local and distal stimuli. *Hippocampus*, *7*, 624–642.
- Tanila, H., Shapiro, M. L., & Eichenbaum, H. E. (1997). Discordance of spatial representation in ensembles of hippocampal place cells. *Hippocampus*, *7*, 613–623.
- Tremblay, L., Hollerman, J. R., & Schultz, W. (1998). Modifications of reward expectation-related neuronal activity during learning in primate striatum. *Journal of Neurophysiology*, *80*, 964–977.
- Vanderwolf, C. H. (1969). Hippocampal electrical activity and voluntary movement in the rat. *Electroencephalography and Clinical Neurophysiology*, *26*, 407–418.
- Vertes, R. P., & Kocsis, B. (1997). Brainstem-diencephalo-septohippocampal systems controlling the theta rhythm of the hippocampus. *Neuroscience*, *81*, 893–926.
- Whishaw, I. Q., & Vanderwolf, C. H. (1973). Hippocampal EEG and behavior: Changes in amplitude and frequency of RSA (theta rhythm) associated with spontaneous and learned movement patterns in rats and cats. *Behavioural Biology*, *8*, 461–484.
- White, N. M., & McDonald, R. J. (2002). Multiple parallel memory systems in the brain of the rat. *Neurobiology of Learning and Memory*, *77*, 125–184.
- Wiener, S. I., & Korshunov, V. A. (1995). Place-independent behavioural correlates of hippocampal neurons in rats. *NeuroReport*, *7*, 183–188.
- Wiener, S. I., Paul, C. A., & Eichenbaum, H. (1989). Spatial and behavioral correlates of hippocampal neuronal activity. *Journal of Neuroscience*, *9*, 2737–2763.
- Wilson, C. J. (1995). The contribution of cortical neurons to the firing pattern of striatal spiny neurons. In J. C. Houk, J. L. Davis, & D. G. Beiser (Eds.), *Models of information processing in the basal ganglia* (pp. 29–50). Cambridge, MA: MIT Press.
- Wise, S. P., Murray, E. A., & Gerfen, C. R. (1996). The frontal cortex-basal ganglia system in primates. *Critical Reviews in Neurobiology*, *10*, 317–356.
- Wood, E. R., Dudchenko, P. A., & Eichenbaum, H. (1999, February 18). The global record of memory in hippocampal neuronal activity. *Nature*, *397*, 613–616.
- Young, B. J., Fox, G. D., & Eichenbaum, H. (1994). Correlates of hippocampal complex-spike cell activity in rats performing a nonspatial radial maze task. *Journal of Neuroscience*, *14*, 6553–6563.
- Zinyuk, L., Kubik, S., Kaminsky, Y., Fenton, A. A., & Bures, J. (2000). Understanding hippocampal activity by using purposeful behavior: Place navigation induces place cell discharge in both task-relevant and task-irrelevant spatial reference frames. *Proceedings of the National Academy of Sciences, USA*, *97*, 3771–3776.

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