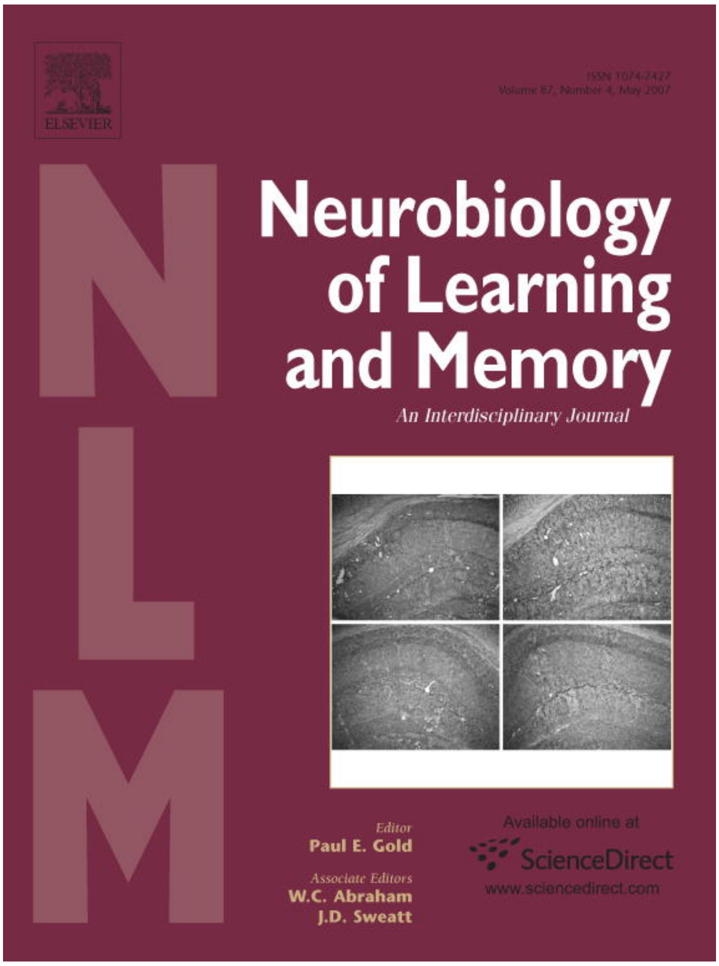
ISSN 1074-7427
Volume 87, Number 4, May 2007
ELSEVIER
NLM
Neurobiology of Learning and Memory
An Interdisciplinary Journal
Editor
Paul E. Gold
Associate Editors
W.C. Abraham
J.D. Sweatt
Available online at
ScienceDirect
www.sciencedirect.com

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ScienceDirect
ELSEVIER
Neurobiology of Learning and Memory 87 (2007) 495–509
Neurobiology of Learning and Memory
www.elsevier.com/locate/ynlme

Memory influences on hippocampal and striatal neural codes: Effects of a shift between task rules

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Received 27 July 2006; revised 20 September 2006; accepted 21 September 2006
Available online 19 January 2007

Abstract

Interactions with neocortical memory systems may facilitate flexible information processing by hippocampus. We sought direct evidence for such memory influences by recording hippocampal neural responses to a change in cognitive strategy. Well-trained rats switched (within a single recording session) between the use of place and response strategies to solve a plus maze task. Maze and extra-maze environments were constant throughout testing. Place fields demonstrated (in-field) firing rate and location-based reorganization [Leutgeb, S., Leutgeb, J. K., Barnes, C. A., Moser, E. I., McNaughton, B. L., & Moser, M. B. (2005). Independent codes for spatial and episodic memory in hippocampal neuronal ensembles. *Science, 309*, 619–623] after a task switch, suggesting that hippocampus encoded each phase of testing as a different context, or episode. The task switch also resulted in qualitative and quantitative changes to discharge that were correlated with an animal's velocity or acceleration of movement. Thus, the effects of a strategy switch extended beyond the spatial domain, and the movement correlates were not passive reflections of the current behavioral state. To determine whether hippocampal neural responses were unique, striatal place and movement-correlated neurons were simultaneously recorded with hippocampal neurons. Striatal place and movement cells exhibited a response profile that was similar, but not identical, to that observed for hippocampus after a strategy switch. Thus, retrieval of a different memory led both neural systems to represent a different context. However, hippocampus may play a special (though not exclusive) role in flexible spatial processing since correlated firing amongst cell pairs was highest when rats successfully switched between two spatial tasks. Correlated firing by striatal cell pairs increased following any strategy switch, supporting the view that striatum codes change in reinforcement contingencies.

Keywords: Place cells; Spatial memory; Response memory; Striatum; Hippocampus; Movement representation

1. Introduction

Hippocampus (HPC) may contribute to episodic learning and memory by processing contextual information (Fanselow & Poulos, 2005; Kim & Fanselow, 1992; Maguire et al., 1998; Mizumori, Ragozzino, Cooper, & Leutgeb, 1999b; Nadel & Wilner, 1980; Smith & Mizumori, 2006; Suzuki & Eichenbaum, 2000). HPC pyramidal neurons exhibit a robust spatial–temporal context code (Buzsaki, 2005; Jeffery & Hayman, 2004; Mizumori, Cooper, Leutgeb, & Pratt, 2000a; Mizumori et al., 1999b; Nadel & Payne, 2002; Nadel & Wilner, 1980; Wills, Lever, Cacucci, Burgess, & O'Keefe, 2005) that is often expressed in terms of location-specific firing (or place fields; O'Keefe & Dostrovsky, 1971; Ranck, 1973). Context sensitivity is demonstrated by subtle to dramatic changes in place fields following alterations of the external sensory environment (Leutgeb et al., 2005; Muller & Kubie, 1987), or internal sensory states (Knierim, Kudrimoti, & McNaughton, 1998). The importance of the temporal context is reflected in the dynamic relationship between cell firing and the ongoing theta rhythm (O'Keefe & Recce, 1993), spike-timing-dependent plasticity (Mehta, Barnes, & McNaughton, 1997; Mehta, Quirk, & Wilson, 2000), prospective or

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doi:10.1016/j.nlm.2006.09.008

retrospective coding of behavioral trajectory (Ferbinteanu & Shapiro, 2003; Frank, Brown, & Wilson, 2000; Wood, Dudchenko, & Eichenbaum, 1999), and the initially rapid, then gradual modification of place fields in response to novel environments (Frank, Stanley, & Brown, 2004; Leutgeb, Leutgeb, Treves, Moser, & Moser, 2004; Mehta et al., 2000; Wilson & McNaughton, 1993).

If HPC is important for context processing relevant to episodic memory, it should be possible to demonstrate that memory processes influence hippocampal neural population codes. It has been surprisingly difficult to verify a direct link between hippocampal spatial context codes and memory processes (e.g. Cooper & Mizumori, 2001; Jeffery, Gilbert, Burton, & Strudwick, 2003; Lenck-Santini, Muller, Save, & Poucet, 2002; Lenck-Santini, Save, & Poucet, 2001). A test of this relationship requires that (internal and external) sensory information, behaviors (i.e. specific actions and movement trajectories), and motivation are 'clamped' while memory demands vary. Moreover, animals should be tested in hippocampal-dependent memory tasks. The experimental design of this study met both of these conditions as we tested the hypothesis that retrieval of a different, previously established memory should signal HPC to represent a different context. Rats were trained to switch (within the *same* recording session) between two cognitive strategies to solve a plus maze task. Neural recordings took place during asymptotic performance, a time when long-term memory influences should be strong. Leutgeb et al. (2005) suggested that location-based place field remapping reflects the representation of a different context, while remapping defined by changes in the within-field firing rate signals changes in the detailed processing of the same context. If switching between cognitive strategies involves retrieval of different memories, HPC place fields should show evidence of rate and location remapping.

To evaluate the selectivity of HPC responses, we also tested whether striatal (STR) place cells (Eschenko, Guazzelli, & Mizumori, 2004; Mizumori, Ragozzino, & Cooper, 2000b) differed from HPC in terms of their response to strategy shifts. Furthermore, to determine if memory retrieval influences are restricted to spatial representations, we examined whether cognitive shifting impacts egocentric movement correlates of either HPC or STR neurons (Jog, Kubota, Connolly, Hillegaart, & Graybiel, 1999; McNaughton, Barnes, & O'Keefe, 1983b; Mizumori et al., 2000b; Ranck, 1973).

2. Materials and methods

2.1. Animals

Male rats were housed in an environmentally controlled room, and tested during the light period (12:12 L/D cycle). All methods were in compliance with the UW IACUC and NIH guidelines for the care and use of animals in research. Rats were maintained at approximately 80% of ad libitum weights via restricted food intake throughout testing.

2.2. Apparatus

The rats were tested on an elevated plus maze configured by using four arms of an eight-arm radial maze (described in more detail in Eschenko et al., 2004 and Smith & Mizumori, 2006). Essentially, four black Plexiglas runways extended from a center platform. The remaining four runways were made inaccessible throughout testing; one maze arm served as an intertrial platform. Distinct visual cues were fixed onto black curtains that surrounded the maze.

2.3. Behavioral training and surgical procedures

Rats were adapted to drink chocolate milk on the maze, and then trained according to either place or response versions of the plus maze task (Eschenko et al., 2004). Both versions included the same possible start locations at distal ends of opposite arms (e.g. north and south). Three maze arms (one start, one correct, and one incorrect goal arm) were available during any given trial. At the beginning of a trial, the rat was placed on a start location facing the curtains. It was then allowed to visit all available maze arms until it obtained reward. If a rat did not reach the reward within 3 min, it was placed on the intertrial platform. After reward consumption, the experimenter placed the rat on the intertrial platform for 10–20 s while the goal arm was re-baited. 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 (Fig. 1A, left panel). For the response task, the start and goal 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 (Fig. 1A, right panel). Ten trials (five from each start location in a pseudo-random order) were presented each day until choice accuracy was 90% or above. Then, recording electrodes were implanted.

Rats were anesthetized with sodium pentobarbital (40 mg/kg initial dose; 0.05 cm^3 supplements as needed). Atropine sulfate (0.2 mg/kg) was administered to minimize respiratory distress. Four stereotrodes were implanted per hemisphere: two above medial dorsal STR (A-P: 0.2–1.2 mm, L: 1.5 mm, D-V: 1.7 mm) and two above dorsal HPC (A-P: 3.5–4.5 mm, L: 2.5 mm, D-V: 1.7 mm). A reference electrode was inserted into corpus callosum. Rats were injected perioperatively with an antibiotic (Baytril, 5 mg/kg, s.c.) and an analgesic (ketoprofen, 5 mg/kg, s.c.).

Following postsurgical recovery, rats were re-trained on the maze. During the first 10 trials (Phase 1) each rat ran the task on which it had been originally trained (place or response). Then the rat was placed on the intertrial platform for 1 min during which time the room lights were turned off. This period of darkness was meant to induce retrieval of the memory that is appropriate for Phase 2. During the next 10 trials (lights on) the reward contingency was changed according to one of three conditions (Fig. 1): Condition 1. *Between-Strategy Place–Response* (Fig. 1A): animals that performed the place task in the first phase of the session performed according to the response task rules during Phase 2. Condition 2. *Between-Strategy Response–Place* (Fig. 1B): animals that performed the response task in Phase 1 performed according to the place task rules during Phase 2. In this way, neural activity could be recorded simultaneously from HPC and STR as rats performed a plus maze task according to one strategy during Phase 1 (either place or response) and another strategy during Phase 2 (either response or place) of a single recording session (Fig. 1). The same maze and environment were used for the different test situations, thereby insuring common sensory, behavioral, and motivational experiences. This control enabled comparisons of neural responses when behavior is guided by different cognitive strategies.

To test whether neural responses reflected the engagement (or disengagement) of spatially guided behavior rather than a cognitive strategy switch per se, we also included a group of rats that was trained to switch between two place strategies (Condition 3, the *Within-Strategy Condition*; Fig. 1C). Rats performed the place task in Phase 1, the reward location was changed to the opposite maze arm in Phase 2. The task-switch sequence remained the same across days for individual rats.

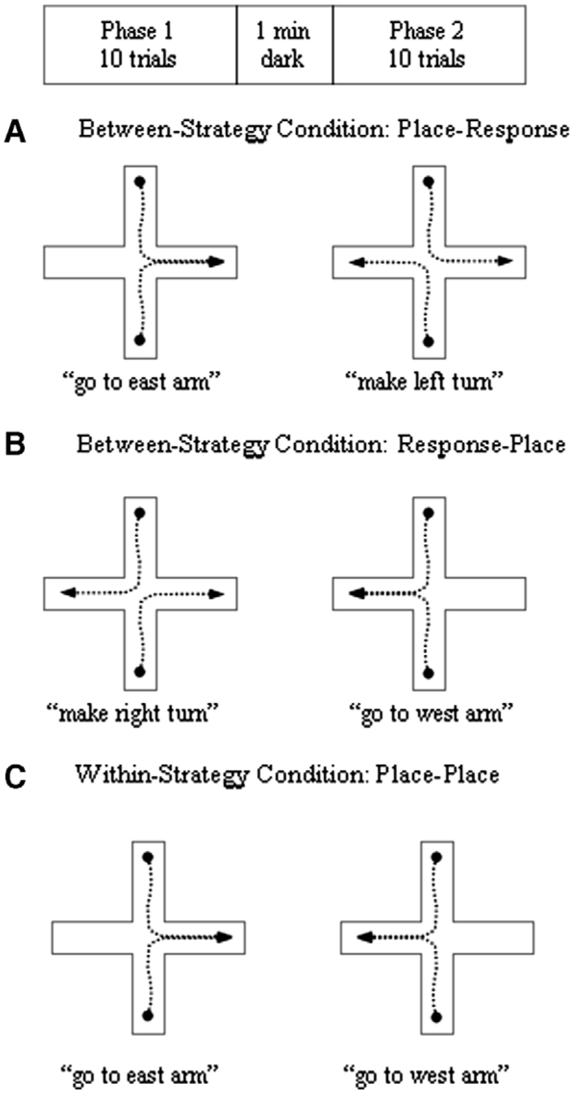

Fig. 1. Schematic illustrations of the three behavioral test conditions. Bars across the top of each column show the sequence of events. For each condition, top-down views of the plus maze contain arrows indicating the correct path taken by rats. The 1-min period of darkness was meant to facilitate retrieval of the memory appropriate for Phase 2.

2.4. Electrophysiological and behavioral recording

The stereotrode and microdrive assemblies have been described (McNaughton, Barnes, Meltzer, & Sutherland, 1989; McNaughton, O'Keefe, & Barnes, 1983a; Eschenko et al., 2004). The tips of paired lacquer-coated tungsten wires (20 μm diameter each) were gold plated to 50–100 kΩ (tested at 1 kHz). Electrodes were checked daily for spontaneous cellular activity via a pre-amplification headstage (NB labs, Denison, TX; sampling frequency of 26–32 kHz). Electrodes were lowered in 22 μm increments (up to 250 μm/day) until 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. Recording sessions began when single unit activity was well isolated on HPC and/or STR recording electrodes. Each recording session consisted of 20 trials. If the unit signal(s) remained the next day the electrodes were lowered further in order to sample new neurons.

Electrophysiological data were acquired on a DataWave Neuroscience Workstation (DataWave Technologies). Incoming signals were amplified 4000–10,000 times and filtered (600 Hz–6 kHz). Impulses that exceeded a user-defined threshold initiated a 1-ms sampling period. Units were isolated using an interactive cluster-cutting routine that processed waveforms on the basis of numerous spike parameters. A rat's position (Dragon Tracker; Boulder, CO) was estimated according to the position of an anterior diode array located 5 cm above the rat's head. A second, smaller diode array was located 5 cm above the back of the rat. The orientation of the rat's head by considering together with the locations of both diode arrays (sampling frequency = 20 Hz; resolution = 1.5–2.0 cm).

2.5. Data analysis

Various analysis routines (DataWave Technologies, and software by S. Leutgeb, A. Guazzelli, and C. Higginson) were used to analyze unit characteristics and behavioral data. Standard waveform properties of isolated units were verified to be the same during the entire recording session (Eschenko et al., 2004). Event Flags marked the beginning and end of each phase within a given session. Data from intertrial intervals and the 1-min period of darkness were excluded from the analysis to insure that the data analyzed corresponded only to times when rats were actively engaged in the task.

2.5.1. Classification and analysis of location-specific neurons

As might be expected for neurons that are thought to contribute to complex mnemonic functions, place cell responses are typically identified and characterized according to a number of criteria. These measures reveal different aspects of the clarity of a place cell's signal relative to a single location in space. As shown in many laboratories, place fields are complex neural representations that can vary in terms of size, firing rate within the field (in-field firing rate), and the signal clarity (ratio of the in-field firing rate relative to the firing rate when the rat is outside of the field location). Consistent with Leutgeb et al. (2005), changes in these measures can be considered a form of 'rate remapping' that reflects alterations in the extent to which details of a specific context are evaluated. The locations of place fields are also observed to change as a function of experimental manipulations, and this may reflect the use of alternate neural networks that represent a different context. In both cases of representational reorganization, it is worth noting that the reliability with which the signal is generated with each successive pass through the field location can also vary. Thus, a measure of the reliability of firing is useful for it provides an index of changes in the place field signal over time. Therefore, to capture the often multidimensional response patterns of place fields, we first defined place fields according to these different parameters, and then used these same measures to characterize changes in place fields across testing phases.

For each cell, separate spatial plots were generated for Phase 1 and Phase 2 of each session. These plots illustrated the firing rate distribution as a function of the rat's location. If the average firing rate for a pixel (2.8 × 2.8 cm) exceeded a preset threshold (20% of the maximum firing rate), it was highlighted on the plot. A cell was considered to exhibit location-selective firing if it satisfied the following criteria that have been used in previous studies (e.g. Eschenko et al., 2004). The particular values selected for each criterion reflect the statistical reliability needed for adequate sampling. (1) The above threshold firing occupied at least four adjacent highlighted pixels (minimum *place field size* of 31.4 cm^2). (2) The place field *firing rate specificity* ratio (within-field firing rate/out-of-field rate) was 3.0 or higher. (3) The place field *location specificity* measure (field size/total number of highlighted pixels) exceeded 0.3. (4) The probability that a given place cell fired as the rat traversed the place field location exceeded 0.33 (*place field reliability*). All HPC and STR neurons that satisfied the above criteria were subjected to further analysis.

A spatial (Pearson's) correlation analysis was used to quantify the changes in the locations of place fields across the two phases of the session. The maze area was divided into squares (12.9 × 12.9 cm). The average firing rate within each square during Phase 1 was correlated with the firing rate of the same cell recorded for the identical location during Phase 2. Only squares visited by the rat in both blocks of trials were analyzed.

As is often observed in studies of place fields, responses to experimental manipulation are frequently bimodal. Therefore, in addition to analysis of the absolute values for the measures described above, field reorganization was evaluated by calculating a normalized "difference index" (DI) that reflected the magnitude of change across phases:

$$DI = (b_2 - b_1)/(b_2 + b_1),$$

where b_1 and b_2 are values of corresponding parameters during the Phase 1 and Phase 2, respectively. This index varied from −1.0 to +1.0 and was negative when the parameter's average was reduced during Phase 2. A DI of zero indicates no change.

2.5.2. *Classification and analysis of movement-specific neurons*

Firing rates were correlated with movement velocity and acceleration for neurons that showed average firing rates greater than 1 Hz, and neurons that displayed firing characteristics that conformed to the classic definition of HPC theta/noncomplex spike cells (e.g. Ranck, 1973). Significant (linear) relationships between neural firing rates and velocity (range: 4.5–58.5 cm/s; bin size: 9.0 cm/s) or acceleration (range: 4.5–94.5 cm/s^2; bin size: 10.0 cm/s^2) were identified using a 95% confidence interval ($\alpha = 0.05$; Eschenko et al., 2004). Correlation coefficients were calculated separately for Phases 1 and 2. Neurons that demonstrated significant linear relationships between firing rate and velocity or acceleration during at least one phase were selected for comparisons between phases.

2.5.3. *Analysis of correlated firing*

A Pearson's correlation analysis (50-ms bin width) was used to evaluate temporally correlated firing amongst simultaneously recorded pairs of HPC neurons and pairs of STR neurons. Only neurons that fired during both test phases were included. Pairs of neurons were considered to show correlated firing if the obtained correlation coefficient was at least two standard deviations away from the correlation value expected by chance alone. Chance correlation was the average correlation for 100 noncorrelated cell pairs in which each cell in a pair was recorded from a different animal. Care was taken to make sure that all rats contributed data to this determination of random correlation. Changes in correlated firing were estimated by comparing correlation values obtained before and after a task switch.

2.6. *Histology*

At the end of each experiment, rats were deeply anesthetized with sodium pentobarbital. Brains were fixed via intracardial infusion of phosphate-buffered saline, followed by 0.9% formalin. Electrodes were slowly withdrawn from the brain, which were then extracted and allowed to soak in 30% sucrose formalin solution for at least 48 h before being sectioned on a cryostat. Standard Cresyl violet histological methods were used to identify nuclei. Recording sites were verified by comparing depth measurements at the time of recording with electrode track reconstructions derived from examinations of the histological sections.

3. Results

3.1. *Behavioral acquisition of place and response tasks*

3.1.1. *Pre-surgical training*

All rats were first trained to use either a place or response strategy until they reached asymptotic performance. The average learning curves from 18 rats (seven place learners and 11 response learners) are presented in Fig. 2. Striking differences in the rate of task acquisition were found between the place and response learners. Overall, response learners required more than twice the number of trials (227.3 ± 21.8, mean ± SE) to achieve the criterion performance of 90% correct choices compared to place learners (94.3 ± 11.3 trials). A repeated measures ANOVA (sessions 1–7 × strategy) revealed both a significant sessions effect ($F_{1,13} = 9.94$, $p < .001$) and a strategy effect ($F_{1,13} = 20.97$, $p < .001$). There was no session by strategy interaction ($F_{1,13} = 2.47$, ns). Thus, although rats learned both versions of the plus maze task, the place task was acquired more quickly than the response task.

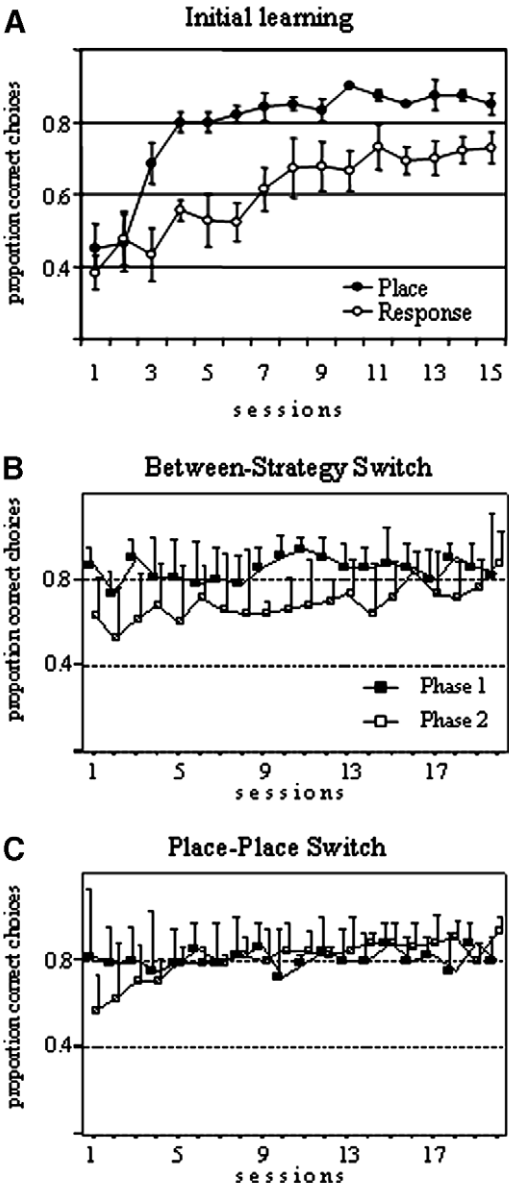

Fig. 2. (A) Rats were first trained to perform 10 trials on a plus maze according to either a place or response strategy. Choice accuracy rapidly improved for place-trained rats (filled circles). Although rats eventually learned to perform according to a response strategy (open circles), the learning was much slower. (B and C) Choice accuracy during Phase 1 (filled circles) remained high during both place and response training. Phase 2 performance (open circles) also remained high across test days for the Between-Strategy and the Within-Strategy conditions.

3.1.2. *Asymptotic performance*

There were no significant effects of task order on the behavior or unit activity of animals trained to first use a place (Phase 1), then response (Phase 2) strategy (place–response group; $n = 3$ rats), and animals trained to first use a response, then place strategy (response–place group; $n = 3$ rats). Therefore, behavioral and neural data from these groups were combined to form a *Between-Strategy* condition. For rats that performed according to different place strategies, the reward was first located on the east maze arm (Phase 1), then the west maze arm (Phase 2), or vice versa. There were no differences in behavioral or neural responses when the reward location switched from east to west ($n = 4$ rats), or west to east maze arms ($n = 2$ rats). Therefore, data were combined to form the within-strategy, *Within-Strategy* condition.

Fig. 2 shows the mean proportion of correct trials per session for Phases 1 and 2. The average proportion correct for all of the Phase 1 sessions was not different: 0.81 ± 0.04 (*Between-Strategy* condition), and 0.80 ± 0.08 (*Within-Strategy* condition). The performance level during Phase 1 remained stable in all groups, indicating that learning a second task rule did not affect performance according to the first task rule (repeated measures ANOVA; all p's $> .05$). Gradual improvement in Phase 2 performance was observed for both conditions ($F_{16,135} = 3.95$, $p < .01$).

3.2. Histological results

Examination of the recording tracks confirmed that HPC units were recorded both in CA1 and dentate gyrus/hilar regions of dorsal HPC. Data were combined across areas since we did not detect regional specificity of the responses reported above. STR units were confined to dorsal medial STR. As reported previously (Eschenko et al., 2004; Mizumori et al., 2000b), the anatomical localization of the place and movement-correlated neurons did not appear to be topographically organized. The fact that many more striatal neurons were recorded in STR than HPC is likely due to the failure of a few electrodes on HPC drives, and does not reflect a meaningful difference in information representation.

3.3. General characteristics of HPC and STR neural representations

Neural measures from Phases 1 and 2 were combined to estimate average values. Across all conditions, 89 HPC neurons ($n = 11$ rats) and 290 STR neurons ($n = 11$ rats) satisfied the criteria for classification as place cells (see Section 2). The basic properties of STR and HPC neuronal signals generally resembled those reported previously (e.g. Table 1; Eschenko et al., 2004). This conclusion was based on measures that defined cells as place cells (described in Section 2).

The average absolute value of the correlation between firing rates and the acceleration of the animals as they traversed the maze was also comparable between structures ($r = .80 \pm .01$ and $.81 \pm .01$ for STR ($n = 190$ cells) and HPC ($n = 80$ cells), respectively, $F_{1,269} = 0.46$, ns). However, of the acceleration-correlated HPC cells, a greater proportion showed positive rather than negative correlations when compared to STR cells ($X^2 = 24.18$, $p < .0001$; HPC—73.8%, STR—54.2% positively correlated). The average correlation between cell firing rates and movement velocity was also nearly identical between structures (STR: $r = .88 \pm .01$, $n = 125$ cells; HPC: $r = .88 \pm .01$, $n = 55$ cells). The proportion of cells showing positive and negative correlations, however, differed ($X^2 = 8.62$, $p < .001$). A greater proportion of correlated HPC neurons (70.9%) showed positive correlations than STR neurons (49.6%). It appears, then, that movement state significantly regulates cell firing in both HPC and STR. However, the HPC network may be more tightly coupled to movements of high velocity and acceleration. This is generally consistent with the fact that movement has a significant influence on the HPC theta rhythm.

Table 1
General characteristics of hippocampal and striatal place fields

Parameter	Hippocampus	Striatum
Spike width (μs)	323.1 ± 7.6	344.3 ± 3.8
Mean rate (Hz)	0.82 ± 0.08	0.75 ± 0.04
Within-field rate (Hz)	3.66 ± 0.19	4.26 ± 0.15
Field reliability	0.64 ± 0.02	0.61 ± 0.01
Firing rate specificity	11.69 ± 1.35	12.65 ± 0.66
Field size (cm^2)	255.3 ± 22.6	193.0 ± 6.1
Location specificity	0.48 ± 0.02	0.45 ± 0.07

3.4. Reorganization of HPC spatial codes after changes in task demand

3.4.1. Between-Strategy (Place–Response or Response–Place) conditions

Twenty-nine cells (1–14 cells per each of five rats) contributed to the following analysis. Data were combined for these two conditions since there were no significant differences in neural firing properties before or after the task switch. A large proportion of neurons revealed dramatically altered place fields during Phase 2. A Difference Index (DI; reflecting the magnitude of change) showed that many neurons responded to the strategy switch by either increasing or decreasing place field reliability, in-field firing rate specificity, and/or location specificity (Fig. 3). Other place fields remained stable after a strategy switch (near zero values). Given that the direction of changes in the place field measures was bidirectional, it is not surprising that the average place field within-field firing rate, field reliability, location and rate specificity did not change after the task switch (all p's $> .05$). A spatial correlation analysis that compared the spatial distribution of cell firing across commonly visited locations in the two test phases revealed scores ranging from –0.09 up to 0.96 (mean = 0.34 ± 0.06; Table 2). Thus, some fields changed locations while others did not. Individual cell examples of changes in field locations are shown in Fig. 4. Interestingly, for a small group of cells, we observed trajectory-selective firing (also

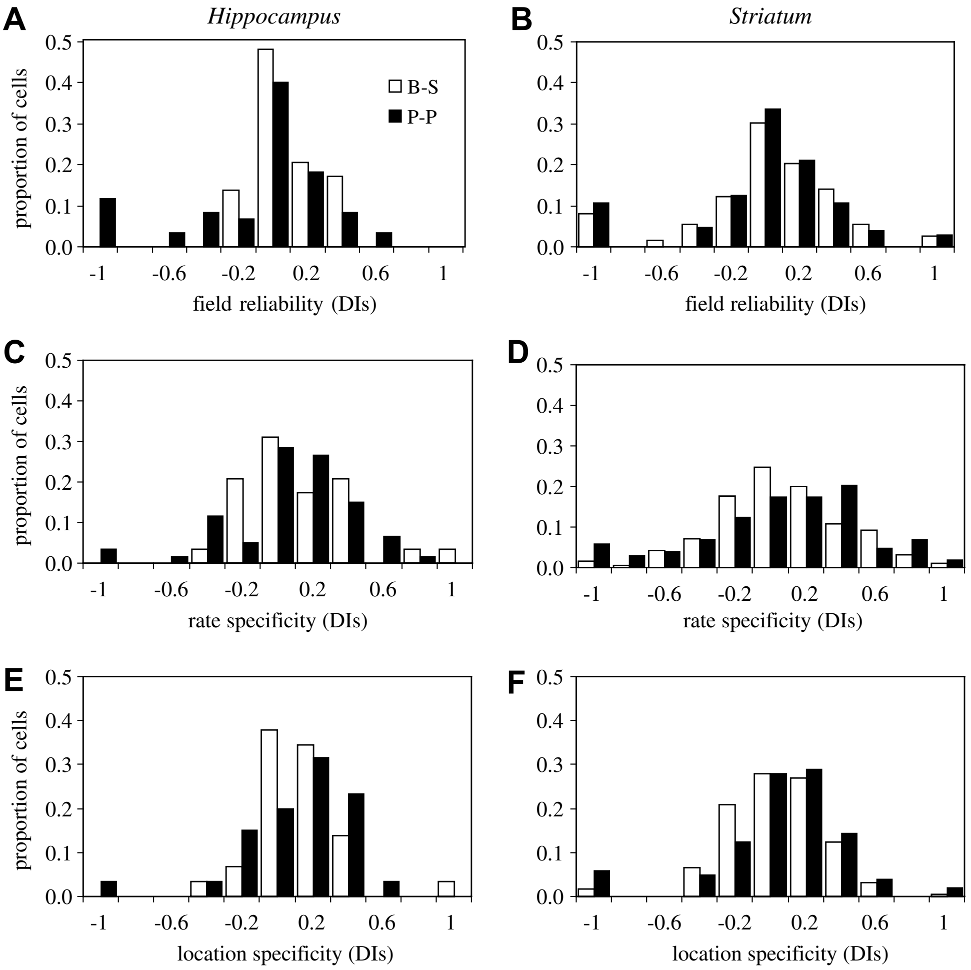

Fig. 3. The distribution of difference indices (DI) for field reliability (A and B), within-field firing rate specificity (C and D), and location specificity (E and F) for HPC and STR neurons. DIs quantify the magnitude of change after a strategy switch. The behavioral conditions are denoted as follows: open bars, Between-Strategy (B-S) conditions; hatched bars, Within-Strategy: Place–Place (P–P) condition. It can be seen that many (but not all) neurons responded to the cognitive shift while other neurons did not. Also note that neural responses were bidirectional in that increased and decreased values were observed for different cells.

Fig. 4) as reported by others (e.g. Wood et al., 1999). Apparently, such conditional discharge depends on the current cognitive strategy since it was observed to differ in Phases 1 and 2. Place field reliability during performance of the first task (regardless of whether it was place or response) was positively correlated with spatial correlation score ($r = .46$, $p < .05$). Thus, fields with more reliable within-field firing tended not to reorganize after a strategy switch.

In sum, the observed pattern of change indicates that both rate and location remapping resulted from the strategy switch. This supports the view that a large proportion of HPC place cells encoded a different context following retrieval of a different memory. The reorganization was not complete since 30–50% of the fields did not respond to the task switch according to the above measures. The fact that partial, and not complete, remapping was observed suggests that features that were common across the two test phases (e.g. room cues and the maze) could have been encoded by the same neural activity pattern.

3.4.2. *Within-Strategy (Place–Place) condition*

The responses of 60 HPC place neurons ($n = 6$ rats; 3–19 cells per rat) were evaluated. Fig. 4 illustrates that the firing characteristics of 20–40% of cells decreased or increased reliability, rate specificity, and location specificity after the reward shift. Since the direction of change was bidirectional, the group means for within-field firing rate, location and rate specificity remained unchanged (all p's $> .05$). In contrast, the average place field reliability significantly decreased after the reward location was switched (paired t-test: $t_{59} = 2.78$, $p < .01$). Spatial correlation analyses similarly revealed a wide range of responses (–0.22 to 0.96), averaging 0.28 ± 0.04 (Table 2). Therefore, similar to the pattern observed for cells recorded when animals switched between place and response strategies, we observed partial reorganization in terms of rate and location remapping. Spatial correlation scores did not distinguish the *Within-Strategy* condition from the *Between-Strategy* condition ($F_{1,88} = 0.75$, ns). However, a significant and selective effect of strategy was observed on place field reliability

Table 2
Summary of hippocampal and striatal place field responses to strategy shifts

Parameter	Hippocampus		Striatum	
	Between Strategy	Within-Strategy (Place–Place)	Between Strategy	Within-Strategy (Place–Place)
Spatial correlation	0.34 + 0.06	0.28 + 0.04	0.30 + 0.02	0.36 + 0.03
Change in reliability	0.14 + 0.02	0.29 + 0.04*	0.29 + 0.02	0.29 + 0.03
Change in rate	0.23 + 0.04	0.26 + 0.03	0.29 + 0.02	0.35 + 0.03
Between-phases comparisons				
Reliability	=	⇓	=	⇓
Location Spec.	=	=	⇓	=
Cell-pair corr.	=	⇑	⇑	⇑
Relationship to spatial correlation scores				
Accuracy ⟺ Spatial correlation	—		⇑0.14	
Reliability ⟺ Spatial Correlation	0.46	—	0.34	0.21
Location Spec ⟺ Spatial Correlation	—	0.41	0.20	0.44
Number	29	60	186	104

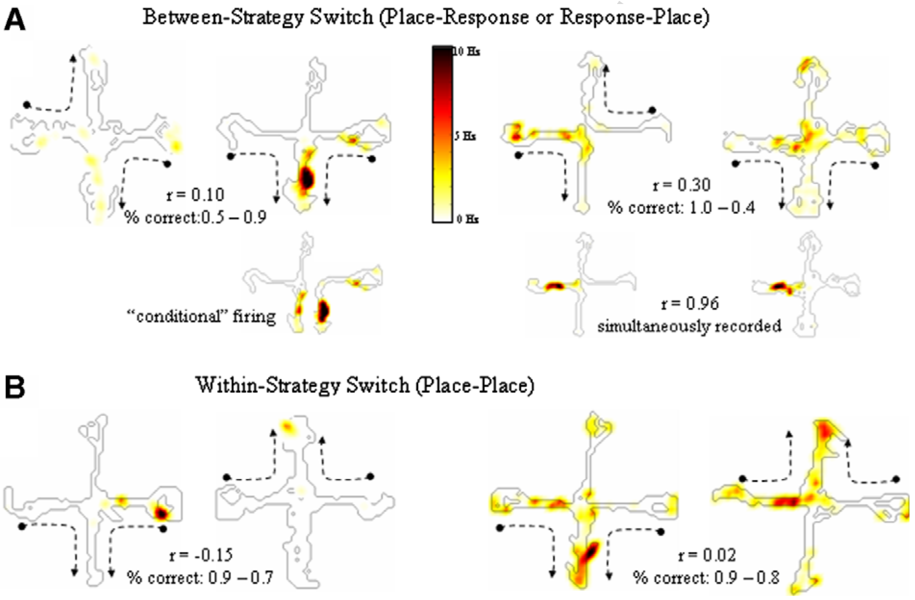

Fig. 4. Individual color density figures show changes in location-specific firing by HPC place cells after a strategy switch. (A-left half) The leftmost plot shows that during Phase 1, very little firing was observed. The rightmost plot shows that a place field appeared on the south maze arm, but that this field was "conditional" in that it was observed only when the rat arrived on the south arm from the east, but not west, arm (shown immediately below). Spatial correlation scores are indicated between the summary plots for each Phase of test. '% correct' refers to the percent of trials in which a correct response was observed per phase. (A-right half) Place field responses of two simultaneously recorded place cells during Phases 1 and 2 (leftmost and rightmost) of test. The first cell (top row) showed redistributed firing patterns after the task rule switched, while the second cell (bottom row) showed a persistent place field on the west arm. (B) Two examples of the dramatic effects of cognitive shift on place field locations during the Within-Strategy: Place–Place condition. [Calibration bar applies to all examples.]

($F_{1,88} = 4.23$, $p < .05$). Field location specificity during Phase 1 performance was positively correlated with spatial correlation score ($r = .41$, $p < .01$). Thus, neurons with more specific place fields during Phase 1 tended to not change firing patterns after the reward location was changed in Phase 2. As was the case during the *Between-Strategy* condition, we observed a few instances in which place fields reorganized even though the location visited and behavioral trajectory were identical in Phases 1 and 2.

3.4.3. HPC unit summary

A large proportion of individual HPC neurons responded to a switch in the cognitive demands of a well-learned task by changing place field reliability, specificity and/or location *regardless of the nature of the cognitive switch* (Fig. 3). This comprises direct evidence that altering memory functions (in this case, memory retrieval) can induce significant rate and location remapping (Leutgeb et al., 2005) of HPC place fields. That is, when a different memory is retrieved, HPC codes appear to reflect a different context. When considering the entire population of responses, however, different patterns of change were observed for the different switch conditions. Neural recordings during the *Between-Strategy* condition showed that the population averages of the various place field measures did not change with a shift in task demand. In contrast, cells recorded during the *Within-Strategy* condition showed significantly reduced place field reliability after a task switch.

It was also observed that different combinations of place field characteristics (e.g. specificity and field location) became highly correlated under certain test conditions, and not others. Thus, changes in strategy affected not only the absolute value of each variable, but also the relationships between variables. As an example, for the *Between-Strategy* condition, reliability and spatial correlation scores were related since the reliability of place cells recorded during Phase 1 predicted the degree of location reorganization during Phase 2. During the *Within-Strategy* condition, on the other hand, location specificity (and not reliability) correlated with spatial correlation scores. In other words, the specificity of the spatial location signal predicted whether fields changed locations after the task switch. Task related differences in the relative importance of different place field measures could account for the inconsistency with which a single place field parameter has been related to behavioral performance.

To test whether the effects of a task switch are unique to HPC processing, comparable analyses were performed on simultaneously recorded STR place cell responses.

3.5. Reorganization of STR spatial codes after changes in task demand

3.5.1. Between-Strategy (Place–Response or Response–Place) conditions

A total of 186 STR cells ($n = 5$ rats; 4–119 cells per rat) were analyzed for their responses to task switches. According to most measures, there were no clear differences in neural responses between Place–Response and Response–Place groups (all p's $> .05$). Therefore, neuronal data from both groups were combined to comprise the *Between-Strategy Condition*. Fig. 3 shows the broad distribution of DIs when comparisons were made between Phases 1and 2 in terms of place field reliability, within-field firing rates, and place field specificity. While many STR place fields remained stable after the task switch, other neurons showed dramatic changes (either decreased or increased) in each of these parameters. Despite the substantial change displayed by individual neurons, the population average field reliability remained unchanged after the strategy switch. In contrast, the average field location specificity was significantly reduced in Phase 2 ($t_{185} = 2.67$, $p < .01$). Examples of individual cell responses are shown in Fig. 5.

The broad range of spatial correlation coefficients (−0.23 to 0.93; mean 0.30 ± 0.02) indicates that a subpopulation of neurons responded to the strategy switch by a change in the spatial firing pattern (even for trajectory paths that were in common between Phases 1and 2), while the location selectivity of other fields remained stable. Regression analyses revealed that the field reliability and location specificity in the Phase 1 were positively related to spatial correlation scores ($r = .34$, $p < .01$ and $r = .20$, $p < .01$, respectively; Table 2), indicating that fields with more reliable and location-selective firing showed less pronounced reorganization after a strategy switch.

3.5.2. Within-Strategy (Place–Place) condition

One hundred four STR neurons ($n = 6$ rats; 1–48 cells recorded per rat) with location-selective firing properties were recorded during 61 sessions. Most STR neurons responded to the change in reward location with reduced reliability of firing within the place field ($t_{103} = 2.20$, $p < .05$). The group means of the remaining place field parameters did not change after reversal of reward

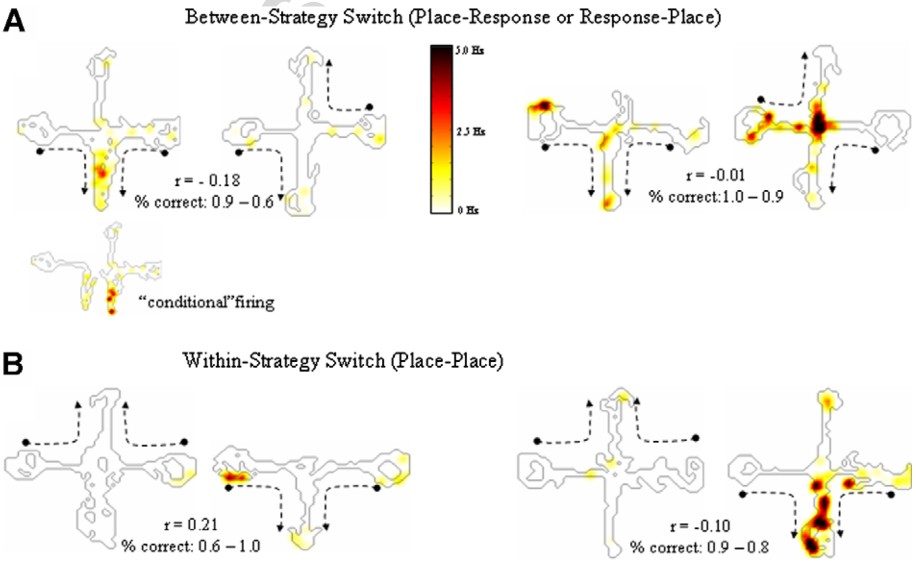

Fig. 5. Illustration of STR place cell responses to the different switches in task rule. Often dramatic reorganization was observed for either Between-Strategy (A) or Within-Strategy (B) Switch Conditions. Note that similar to HPC place fields, 'conditional' firing was observed for STR place fields (A, left half). The place field for the top left cell recorded in the Between-Strategy condition was observed primarily when the rat entered the south arm from the east, but not west, start location.

location. Despite similar group mean values, the distribution of DIs showed a range of individual neuronal responses in terms of changes in field reliability, within-field firing rate, and location specificity (Fig. 3). While the firing properties of some neuron responses remained stable, those of other cells showed decreased or increased values after the strategy shift.

The spatial correlation analysis revealed a similar pattern of results. The correlation coefficient scores ranged from –0.34 up to 0.95, averaging 0.36 ± 0.03 (Table 2). Substantial spatial reorganization was observed in some neurons while stable location-specific firing was observed for other neurons. Field reliability and specificity measures were positively correlated with spatial correlation scores (reliability: $r = .21$, $p < .05$; rate specificity: $r = .47$, $p < .01$; and location specificity: $r = .44$, $p < .01$). Thus, the more reliable and specific place fields showed greater stability after a shift in strategy condition.

3.5.3. STR unit summary

Evidence for rate and location remapping was demonstrated for individual STR place fields after either *Between-Strategy* or *Within-Strategy* task switch. Thus, like HPC place cells, STR place cells code situations with different task demands as a different context. The neural responses were bidirectional in that both enhanced and reduced place field specificity and reliability were observed, resulting in no change in the population averages. Place field specificity, however, was significantly lower for the *Between-Strategy Condition* relative to the *Within-Strategy Condition* (Table 2). Place field reliability was significantly lower for the *Within-Strategy Condition* relative to the *Between-Strategy Condition* (Table 2).

3.6. Comparison between STR and HPC place cell responses to changes in task demand

A two-way ANOVA (brain structure × type of switch) did not reveal brain structure effects in terms of the spatial correlation score, field reliability, field location, and rate specificity (all *p*'s > .05). This was the case for both common and different field locations between Phases 1 and 2, as well as common behavioral trajectories. There was a significant brain structure effect in terms of the *magnitude* of change for two place field measures: within-field firing reliability ($F_{1,378} = 4.44$, $p < .05$) and field rate specificity ($F_{1,378} = 6.27$, $p < .05$). Both reliability and specificity became more pronounced during Phase 2 for STR, but not HPC, neurons. Spatial correlation scores were correlated with the accuracy of behavioral performance for STR, but not HPC neurons ($r = .14$, $p < .05$ and $r = -.15$, ns, respectively; Table 2), indicating that more accurate performance after a task switch was associated with STR place fields that remained in the same location after the switch. Thus, STR processing seemed generally more predictive of accurate performance in Phase 2, a finding that is perhaps due to the greater specificity and reliability of the spatial code. Finally, similar to HPC, STR place cells exhibited task-related differences in the relative importance of different place field measures. These differences could reflect different neurocomputations that are required to solve the different tasks.

3.7. Temporally correlated discharge within HPC and STR

It was of interest to determine whether temporally correlated firing amongst HPC or STR neurons was sensitive to changes in cognitive strategy. The average correlation score for random cell pairs was 0.0039 ($SD = 0.0124$). Correlation scores for simultaneously recorded cell pairs (regardless of the type of behavioral correlates shown by each cell) were considered statistically significant if the absolute value of the correlation score was at least two standard deviations above the average based on random pairings (i.e. at least 0.0172). A total of 1625 cell pairs were analyzed from 12 rats over 247 sessions.

3.7.1. HPC–HPC cell pairs

Many simultaneously recorded unique pairs of HPC neurons ($n = 346$ pairs) showed significant correlation scores. During Phase 1, the absolute value of the correlation scores did not differ across the two experimental conditions (Fig. 6), nor did they differ as a function of cognitive strategy per se (i.e. place or response; $p > .05$). A two-factor ANOVA (phase × experimental group) revealed a significant difference across phases ($F_{1,344} = 17.82$, $p < .001$) and a significant interaction between group and phase of training ($F_{1,344} = 4.52$, $p < .05$). Therefore, cells were differentially correlated as a function of the type of task switch. Specifically, significant differences were found between Phases 1and 2 for only the *Within-Strategy* condition ($t_{247} = -5.54$, $p < .001$; Fig. 6; Table 2). This indicates that HPC neural firing became more correlated when rats switched between two spatial tasks as opposed to between spatial and nonspatial tasks.

3.7.2. STR–STR cell pairs

STR cell pairs (1279 pairs) showed significantly correlated discharge that varied according to strategy-switch conditions ($F_{2,1277} = 114.51$, $p < .001$). These variations were not due to the type of strategy used during Phase 1 (response or place; $p > .05$; Fig. 6). Rather, the two switch conditions differed in terms of the magnitude of change in correlation after a task switch, as revealed by a significant Phase by condition interaction effect ($F_{1,1277} = 43.67$, $p < .001$). Subsequent comparisons revealed that although the cell-pair comparison became significantly stronger in both experimental conditions ($t_{829} = -4.70$, $p < .001$ and $t_{448} = -7.90$, $p < .001$ for *Between- and Within-Strategy* groups, respectively; Fig. 6; Table 2), the phase effect was greater for the *Within-Strategy* condition. That is, STR firing became more correlated when rats switched strategies regardless of the particular task rule. However, the increase was greatest for the *Within-Strategy* condition.

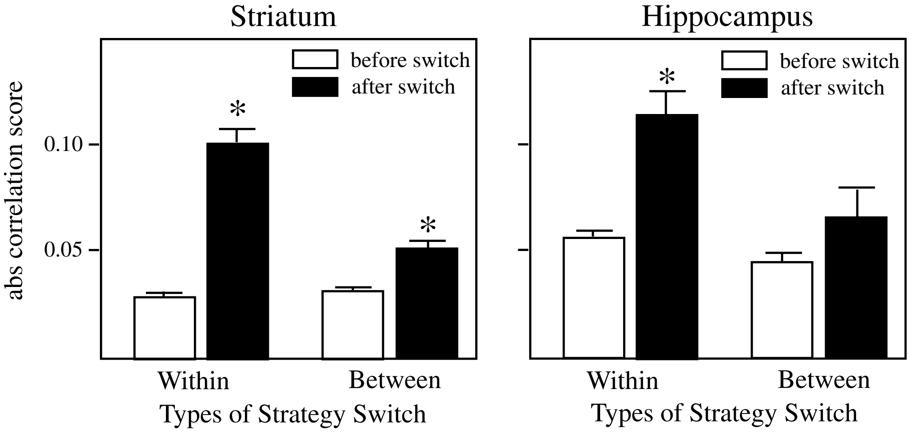

Fig. 6. Summary of the correlation analysis for pairs of cells recorded in hippocampus or striatum. The absolute (abs) value of the correlation coefficients shows that HPC pairs increased correlative discharge only during the Within-Strategy condition, suggesting that output signal strength may be stronger when flexible spatial processing is required. In contrast, STR correlative discharge increased after both Between-Strategy and Within-Strategy conditions.

3.8. Response of movement-correlated firing following changes in task demand

Three types of responses were observed for movement-related neural activity after a strategy switch: (1) different, yet significant correlations with acceleration or velocity across both test phases, (2) a loss of correlated firing during Phase 2, and (3) the appearance of movement-related firing in Phase 2. We first report the proportion of cells that changed velocity or acceleration coding after Phase 1 regardless of the type of response. Then, we present changes in the magnitude of response by comparing significant r-values only for cells that showed significant correlations during both test phases.

3.8.1. Acceleration-tuned HPC and STR neurons

A total of 190 STR and 80 HPC cells showed significant correlations between firing rate and movement acceleration (all p's $> .05$). The firing rates of 55.3% of STR neurons and 53.7% of HPC neurons either lost or acquired correlated firing after a task switch. A comparable proportion of HPC and STR neurons changed acceleration-correlated discharge after the task switch in the *Within-Strategy* condition (58.2% of HPC cells and 66.2% of STR, respectively) when compared to cells recorded during the *Between-Strategy* condition (44.0% of HPC cells and 48.3% of STR, respectively; Table 3). Moreover Table 3 shows that while the average magnitude of change in correlation strength was the same for HPC cells regardless of the nature of the strategy switch (about 50% change), STR neurons showed a larger magnitude response during the *Within-Strategy* condition when compared to the *Between-Strategy* condition ($F_{1,84} = 6.57$, $p < .05$; see Figs. 7 and 8 for examples). Thus, STR underwent different forms of reorganization of egocentric movement information depending upon the specific cognitive demands of the task. This was not the case for HPC acceleration-tuned cells.

3.8.2. Velocity-tuned HPC and STR neurons

HPC ($n = 55$ cells) and STR ($n = 125$ cells) neurons exhibited significant correlations with movement velocity. A large proportion of neurons (about 80%) of both groups responded to a strategy switch by either decreasing or

Table 3
Responses by movement-related striatal and hippocampal neurons

	Hippocampus			Striatum		
	n (cells)	Proportion acquired or lost corr.	Magnitude of change %	*n* (cells)	Proportion acquired or lost corr.	Magnitude of change %
Acceleration-tuned neurons						
Between-strategy	25	44.0	50.1 ± 25.8	116	48.3	28.0 ± 2.4
Within-strategy	55	58.2	51.3 ± 9.5	74	66.2	43.0 ± 7.0[*]
Velocity-tuned neurons						
Between-strategy	15	80.0	18.3 ± 9.5	75	77.3	98.8 ± 40.8
Within-strategy	40	82.5	31.2 ± 10.8	50	78.0	22.5 ± 7.1

[*] Significant difference across test conditions.

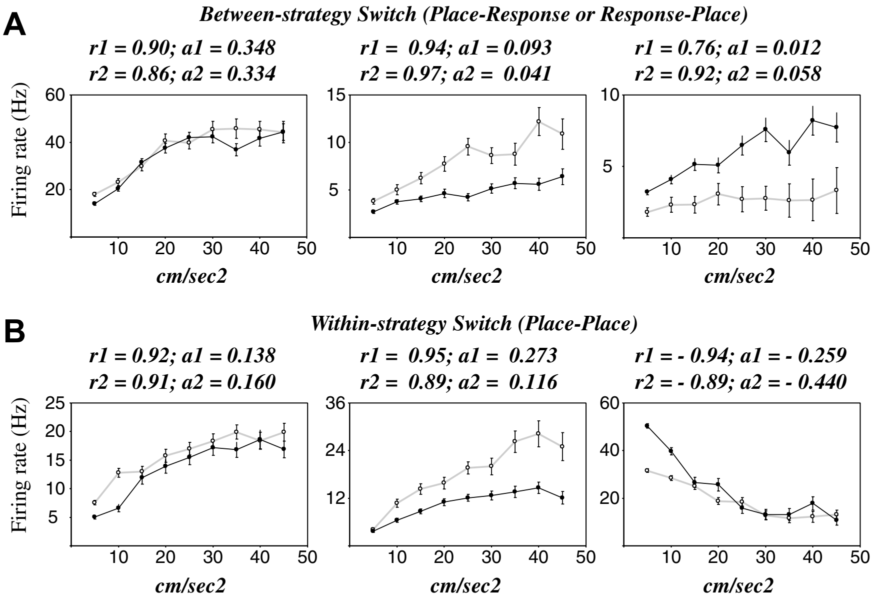

Fig. 7. Individual cell examples of changes in acceleration-correlated firing by HPC neurons. Three examples are provided per Between-Strategy (A) and Within-Strategy (B) condition. For each example, the firing rate per unit of acceleration is shown for Phase 1 trials (open circles) and Phase 2 trials (closed circles). It can be seen that some cells developed or lost the behavioral correlate, or did not change. (r and a-values are shown for Phase 1 (r_1, a_1) and Phase 2 (r_2, a_2).)

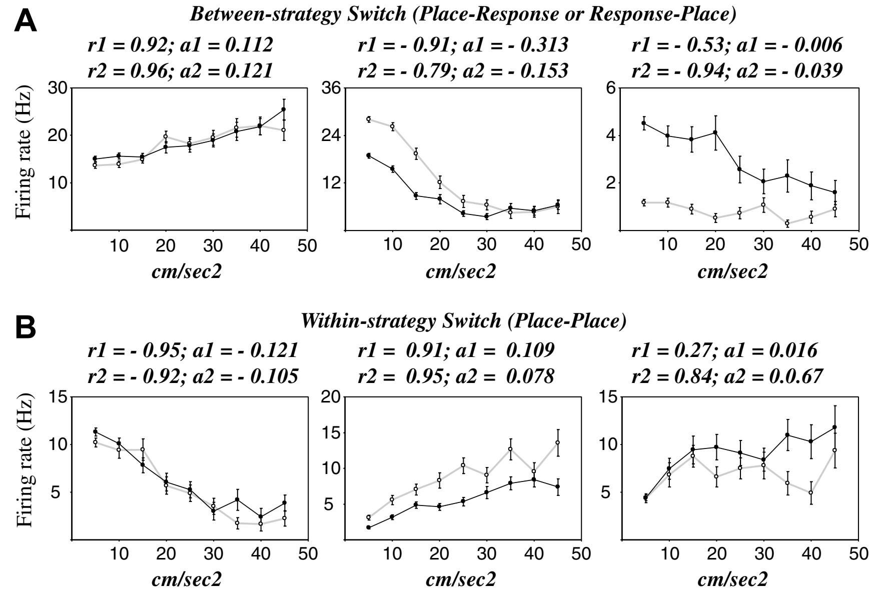

Fig. 8. Individual cell examples of changes in acceleration-correlated firing by STR neurons. As in Fig. 7, a variety of responses were observed for Between-Strategy (A) and Within-Strategy (B) test conditions.

increasing velocity-correlated firing (Table 3). This was the case regardless of the type of strategy switch.

In summary, the correlation between HPC and STR firing rates and acceleration and velocity was dramatically affected by changes in cognitive strategy. About half or more of the cells responded to the strategy switch by losing correlated firing altogether, or by establishing correlated firing that was not present during Phase 1. Of cells that showed correlated firing during both test phases, up to about half changed the strength of the correlation after a strategy switch. Interestingly, acceleration-tuned STR but not HPC neurons responded differently depending upon the type of strategy switch. An important implication of the finding of the strategy-dependent expression of egocentric movement codes within HPC and STR is that movement correlates are not a passive reflection of the current movement state of the animal. This is consistent with an earlier finding that the same HPC and STR egocentric movement codes vary according to the specific environmental context, and not just the ongoing behavior (Eschenko et al., 2004).

4. Discussion

The assumption that established memories guide HPC processing was evaluated by testing whether HPC neural representations change when rats switch between learned task strategies. HPC place cells showed clear evidence of rate and location remapping after rats switched between well-learned cognitive strategies, suggesting that HPC encoded each strategy condition as a different context. Egocentric movement correlates of HPC neurons also showed evidence of qualitative and quantitative changes after the task switch, indicating that the impact of strategy shifting extends beyond spatial information processing. The additional finding that similar types of neural representations in dorsal STR were affected by the task switch shows that retrieving a different memory has broad, simultaneous effects on the neural activity landscape across diverse neural systems. These data support the view that existing memories help to define, or organize, HPC neural representations of the spatial context (e.g. Jeffery & Hayman, 2004; Mizumori et al., 1999b, 2000a; Nadel & Payne, 2002; Nadel & Wilner, 1980).

4.1. HPC neural responses

HPC neurons responded to any shift in cognitive strategy with dramatic changes in place field reliability, in-field firing rates, and the locations of place fields. Thus, the kind of HPC representational reorganization observed reflected both rate and location remapping (Leutgeb et al., 2005). Such a shift in activity of individual neurons did not always correspond to a significant population response: for example, the population reliability score was observed to change only for the *Within-Strategy* condition even though individual cells showed dramatic responses to all strategy shift conditions. Interestingly, this same test condition was associated with the only significant increase in correlated firing amongst HPC neurons (Fig. 6). Therefore, although individual HPC neurons were sensitive to multiple types of strategy shifts, the greatest overall change in HPC firing at the population level occurred when rats switched spatial strategies. This may indicate that HPC plays a special (although not exclusive) role in flexible spatial processing.

Our data also demonstrate that the output strength of HPC may vary both qualitatively (e.g. in terms of signal reliability, signal specificity, and temporally correlated firing) and quantitatively (e.g. increasing or decreasing magnitude of correlated discharge) depending upon task demands (Mizumori, Eschenko, Gill, & Davis, 2004). There was no relationship between the type of response and spike width, suggesting that particular kinds of responses were not selective to particular kinds of neuron. Also for a given place field, a change in reliability, location specificity, or rate specificity did not predict the type or magnitude of change among the remaining two variables. Thus, there did not appear to be discrete subpopulations of neurons that showed similar patterns of change. This was the case for both HPC and STR neurons. Consequently, it appears that the population code within these structures reflects a complex, context-specific array of single cell activity that can vary individually in terms of place field reliability, location specificity and rate specificity. A change in context may result in the activation of a different (but overlapping) set of neurons; each neuron may show distinct reliability, location specificity and rate specificity relative to the previous context. Such a complex and dynamic form of context representation underscores the ability of HPC to select from a large number of combinatorial patterns as it continuously evaluates context information during diverse learning situations (e.g. Eschenko et al., 2004; Mizumori et al., 2004).

In all cases, we observed partial (not complete) representational reorganization. That is, some cells showed impressive changes following a task switch while other cells did not. Cells showing stable field reliability and specificity in the face of strategy changes may receive direct entorhinal cortex projections, connections that presumably convey information from cortical memory systems (e.g. Hafting, Fyhn, Molden, Moser, & Moser, 2005; Leutgeb et al., 2005; Mizumori et al., 1999b). This conclusion appears challenged by the finding that the most specific place fields showed the least change in location after the strategy shift in the *Within-Strategy* condition. That is, an explicit memory manipulation did not destabilize many of the place fields. This result suggests an additional possibility that the *persistence* of a place fields recorded during asymptotic performance can be at least in part determined by local intraHPC circuitry (e.g. recurrent neural circuits). A potential scenario, then, is that rats trained to flexibly use spatial information may recall information during Phase 1 in such a way that the most spatially selective HPC place fields code information about the constant features of similar (but not identical) events. Context (or Phase)-specific features, on the other hand, may be derived from cells that exhibit more broad place fields. The fact that a relationship between place field specificity and the persistence of field locations was observed only during the *Within-Strategy* condition indicates that this relationship was not a result of factors such as the quality of unit isolation or the passage of time. Rather, an implication is that the relationship between specific place field properties may vary depending upon task conditions. Indeed, for the *Between-Strategy* condition, place field reliability (and not specificity) predicted the stability of fields after a task switch. In contrast, place field specificity (and not reliability) was correlated with field stability after a strategy switch for the *Within-Strategy (Place–Place)* condition. Such unique relationships may reflect task-specific learned associations.

A common and reasonable assumption regarding the movement-sensitive neural correlates of HPC neurons has been that these cells relay information about an animal's current behavioral state. Our findings show that the extent to which this is true depends on nonmovement variables such as the current cognitive strategy. It is possible that movement-related cell discharge inform HPC computations about context-specific learned behaviors that in turn may help to define multidimensional spatial context codes (Eschenko et al., 2004; Mizumori et al., 2004).

4.2. HPC neural representation and episodic memory

Efforts to relate HPC neural representation (primarily place fields) to learning and memory have reported changes in place fields relative to exploration of new environments (e.g. Leutgeb et al., 2005; Wilson & McNaughton, 1993), attention to spatial context (Kentros, Aghihotri, Streater, Hawkins, & Kandel, 2004), or altered behavioral performance of well-learned tasks (e.g. Ferbinteanu & Shapiro, 2003; Frank et al., 2000; Jeffery & Hayman, 2004; Wood et al., 1999). These changes in rate codes are context-dependent (Smith & Mizumori, 2006; Eschenko et al., 2004), a finding that is generally consistent with the hypothesis that HPC is important for contextual learning (e.g. Anagnostaras, Gale, & Fanselow, 2001; Maren, 2001; Myers & Gluck, 1994; Smith, Wakeman, Patel, & Gabriel, 2004). To the extent that changing cognitive strategies reflects the retrieval of different memories, the present findings demonstrate a significant influence of memory operations on the highly integrated HPC neural codes that distinguish contexts. HPC may contribute to episodic learning and memory (Tulving & Markowitsch, 1998) by distinguishing significant events according to whether familiar situations, or contexts, have changed (Hasselmo & Wyble, 1997; Lisman, 1999; Lisman & Grace, 2005; Mizumori et al., 1999b, 2000a; Vinogradova, 2001). The partial reorganization of representations may reflect a match–mismatch comparison between the current context and contextual features that are expected based on past experience. The expectation component of this comparison (represented by stable representations across similar contexts) should be based on past experiences, or memories. While established memories may direct current HPC processing, this influence can in turn be used to ensure subsequent and/or continued HPC retrieval of appropriate memories. Thus, the dynamic interactions between HPC and long-term memory networks may contribute to the continual updating of memory representations.

4.3. STR neural responses

Similar types of HPC and STR representations were compared in terms of their responses to a strategy shift. Although some differences were found, the striking result was that large numbers of both HPC and STR neurons responded to the strategy shifts in similar ways. STR neurons also showed both increased and decreased place field specificity and reliability scores, and enhanced or diminished velocity and acceleration correlates. Like HPC, the exhibition of many STR place fields depended solely on the cognitive strategy and not behavioral trajectory, sensory conditions, or motivation (e.g. Fig. 5). Both rate and location-based remapping were observed, suggesting that, like HPC, STR encoded the different task conditions as different contexts. That both HPC and STR responded to the strategy shift indicates that a single change in memory function can have broad influence over diverse neural systems.

STR neurons may be particularly relevant for coding changes in expected reinforcement variables (e.g. Schultz & Dickinson, 2000) and behaviors (e.g. Lauwereyns, Watanabe, Coe, & Hikosaka, 2002). More generally, STR may operate continuously (regardless of the type of task) to enable comparisons between the expected reinforcement consequences of learned, context-relevant behaviors, and the actual reinforcement received. The results of such a comparison may be used to update future (previously learned) expectations of the reinforcing effects of behavioral responses (Mizumori, Pratt, & Ragozzino, 1999a). Such a function is essential to accurately and rapidly switch cognitive strategies. This interpretation of the functional significance of striatal processing is consistent with our finding that correlated firing by STR increased after a strategy switch (regardless of the type). Furthermore, a growing literature shows that an intact striatum is necessary to correctly change cognitive strategy (e.g. Monchi, Petrides, Strafella, Worsley, & Doyon, 2006; Pisa & Cyr, 1990; Ragozzino, 2002; Ragozzino, Ragozzino, Mizumori, & Kesner, 2002; Thompson, Guilford, & Hicks, 1980; Whishaw, Mittleman, Bunch, & Dunnett, 1987). The cholinergic system may play a particularly important role in this regard (e.g. Ragozzino & Choi, 2004; Ragozzino, Jih, & Tzavos, 2002). During accurate navigation, then, animals likely utilize both HPC and STR modes of processing to allow for rapid and adaptive responding to changing situational contexts.

Although recent place cell studies support the view that HPC mediates new learning, the relationship between place fields and long-term memory remains elusive. This study provides the first direct evidence that explicit manipulation of memory retrieval results in the generation of a different context code in HPC. Such an influence extends to coding of nonspatial information within HPC, and to neural processing in nonHPC systems (e.g. STR). While both HPC and STR were sensitive to the strategy-switch manipulation, details of their responses differed. The differential responses were consistent with the postulated difference between HPC and STR contributions to learning and memory (e.g. Kesner, Bolland, & Dakis, 1993; Packard & McGaugh, 1996).

Acknowledgments

This work was supported by NIMH Grant MH58755. We thank Chris Higginson for developing the data analysis software, Eric Samuelson for help with behavioral testing, and Denise Davis, Katy Gill, Min Jung Kim, Adria Martig, Corey Puryear, Susan Sara, and David Smith for comments on an early draft.

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