

Relationships between Place Cell Firing Fields and Navigational Decisions by Rats

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This study examined the performance of spatial problems by rats when purely behavioral manipulations disturb the relationship between the place cell representation and the cues used to solve the problems. Place cells were recorded while rats performed a task in which they had to locate a goal in a gray cylinder. In the “far” task, the unmarked goal was displaced by a large fixed distance from a white card on the cylinder wall. In the “near” task, the unmarked goal was directly in front of the card. Finally, in the “cue” task the goal was marked by a black disk on the cylinder floor. Relationships between visible stimuli and place cell activity were manipulated by conducting either “hidden” (with the rat in its home cage) or “visible” (with the rat in the recording apparatus) rotations of the wall card and, when present, independent rotations of the black disk. Hidden card rotations generally caused equal firing field rotations, whereas

visible card rotations often did not cause fields to move. In the far task, visible card rotations were associated with a strong decrease of correct responses in the card-referred goal area. Most rats tended to search the goal in the field-referred area. In the near task, visible card rotations were associated with a moderate decrease of performance, with rats searching the goal at the wall card. Finally, field placements had no effect on performance in the cue task. Thus, visible rotations tended to disrupt the relationship between firing fields and cues in all tasks but impaired performance only in the task that required map-based navigation. These results provide strong new evidence in favor of the spatial mapping theory of hippocampal function.

Key words: hippocampus; unit recordings; place cells; spatial navigation; rat; spatial memory

For at least the last two decades, the notion that several distinct behavioral strategies can be used to efficiently reach specific goals has become widely acknowledged. For example, a rat swimming in a water tank to reach a hidden platform can do so using distal cues (Morris, 1981). This ability seems to require the use of a spatial representation, or cognitive map, of the environment. If the escape platform is visible, however, the rat has simply to swim to it directly, a behavior that requires no cognitive map. These two strategies are usually referred to as place navigation and beacon navigation (or guidance), respectively (O’Keefe and Nadel, 1978).

The spatial mapping theory of hippocampal function proposes that the rodent hippocampus is a specialized neural machine that must be intact for rats and mice to solve spatial problems on the basis of place navigation but not to solve guidance-type tasks (O’Keefe and Nadel, 1978). In support of this hypothesis, the ability of rats to go to unmarked goals (such as a hidden platform in a water tank) using cues far from the goal is severely compromised by hippocampal lesions (Morris et al., 1982; Rasmussen et al., 1989; Moser et al., 1993; for review, see Poucet and Ben-

hamou, 1997). In contrast, the ability to go directly to a goal marked by local cues is preserved after hippocampal damage (Jarrard et al., 1984; Morris et al., 1986b; Rasmussen et al., 1989).

The main foundation of the spatial mapping theory is the “place cell” phenomenon (O’Keefe and Dostrovsky, 1971). Place cells are hippocampal pyramidal cells that discharge intensely only when a rat’s head is inside a stable, cell-specific region called the “firing field.” This location-specific activity suggests that place cells are the essential units of the putative environmental map, and it has a direct corollary: manipulations that produce abnormal location-specific firing must also impair performance in place navigation tasks. This prediction is confirmed by recent studies on mice genetically modified to have impaired long-term potentiation (LTP). In each case, LTP defects produce abnormal place cells and reduce performance in place navigation tasks (McHugh et al., 1996; Rotenberg et al., 1996, 2000; Cho et al., 1998). Similarly, senescent rats, epileptic rats, or rats with a treatment-induced impaired LTP have defective place cells and perform poorly in place navigation tasks (Morris et al., 1986a; Barnes et al., 1997; Tanila et al., 1997b; Kentros et al., 1998; Liu et al., 2001). In short, although special training can ameliorate the behavioral consequences of even gross hippocampal lesions (Eichenbaum et al., 1990; Whishaw et al., 1995), treatments that generate place cell abnormalities seem to reliably induce abnormalities of navigational behavior.

This finding supports the mapping theory, and additional favorable evidence exists (O’Keefe and Speakman, 1987; Lenck-Santini et al., 2001). Nevertheless, the weaknesses associated with even sophisticated lesion-type methods (Jarrard et al., 1984;

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McNaughton et al., 1986; Steele and Morris, 1999) imply that a more direct, rigorous approach is required that attempts to relate purposeful behavior to place cell discharge. As an illustration of this approach, Zinyuk et al. (2000) recently recorded place cell activity in rats that either had simply to forage in a circular arena or were trained to solve a place navigation task in the same arena. They found that rotation of the arena disrupted place cell discharge in a vast majority of foraging rats. In contrast, most place cell firing patterns recorded from navigating rats were preserved during the rotation. This result shows that simply changing the behavioral requirements to force the rat to pay attention to its location affects place cell activity (Bures et al., 1997). It fails, however, to relate the nature of place cell signal to the rat's actual navigation behavior.

To move in this direction, we have looked at performance by normal animals in beacon and place navigation tasks after purely behavioral manipulations that disturb the relationship between the place cell representation and the cues used to solve the problems. The theory predicts that such disturbances will disrupt performance of place navigation but not of beacon navigation. To test this prediction, rats were trained in several tasks that required either map-based place navigation or simply heading toward a strong marker stimulus. To modify relationships between visible stimuli and place cell activity, we made "hidden" or "visible" rotations of the card on the cylinder wall and, when present, independent rotations of the disk on the cylinder floor. Hidden rotations were made with the rat away from the cylinder and generally caused equal firing field rotations (Muller and Kubie, 1987). Visible rotations were made while the rat was inside the cylinder and often did not cause fields to move (Rotenberg and Muller, 1997). Our basic finding is that visible rotations tended to disrupt the relationship between firing fields and cues in all tasks but impaired performance only in the spatial problem that required map-based navigation. Our results therefore provide strong new evidence in favor of the spatial mapping theory of hippocampal function (O'Keefe and Nadel, 1978).

MATERIALS AND METHODS

Subjects

Seventeen Long–Evans black-hooded male rats (R. Janvier, St. Berthevin, France) weighing 300–350 gm were used. They were housed one per cage on a natural light/dark cycle in a temperature-controlled room ($20 \pm 2^\circ$) with *ad libitum* access to water. On arrival, they were handled daily for 2 weeks. Next, the rats were food deprived to 85% of *ad libitum* body weight and trained in the place preference task (see below) for 4 weeks before electrode implantation.

Apparatus

The apparatus was a gray cylinder 76 cm in diameter and 50 cm in height. The floor was made of a circular piece of plastic-impregnated wood. The cylinder was surrounded by a 2.5-m-high opaque circular curtain 2.5 m in diameter. Lighting was provided by four 25 W bulbs fixed to the ceiling at symmetrical positions above the cylinder. A white card attached to the wall of the cylinder covered 100° of internal arc; the card was bisected by a 1.5-cm-wide black vertical stripe. During training, the wall card was centered at 45° in the overhead view from a camera fixed to the ceiling directly above the apparatus. When activated, a food dispenser above the cylinder dropped food pellets at random locations on the apparatus floor. A radio that was tuned to an FM station was fixed to the ceiling above the cylinder center and provided background noise >70 dB to mask uncontrolled directional sounds. The experimenter stood in an adjacent room that contained the unit recording system, the computer, a TV monitor that displayed the overhead view from the camera, and a panel that controlled the food dispenser.

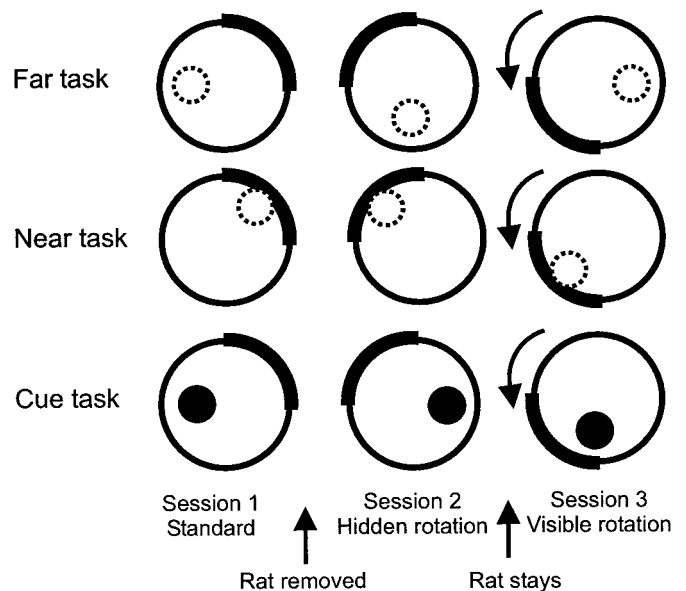


Figure 1. Schematic representation of the protocol. Three recording sessions were conducted in all tasks. After the standard session, the wall card was rotated 90° CCW after the rat had been returned to its home cage (hidden card rotation). Then, the wall card was rotated 90° CCW while the rat stayed in the cylinder (visible card rotation). In the far task, the unmarked release zone (dotted circle) was away from the wall card. The angle between the goal zone center and the wall card was constant, regardless of the angular position of the card. In the near task, the unmarked release zone (dotted circle) was positioned directly in front of the black bisector of the wall card. In the cue task, the goal location was indicated directly by a black metal disc (shown as a solid black circle) put on the cylinder floor. The disk was moved in a pseudorandom fashion between each pair of sessions so that it neither stayed in its previous position nor stayed in register with the wall card.

Behavioral procedures

General behavioral training. Behavioral training was done before electrode implantation. At first, rats were trained to retrieve 20 mg of food pellets scattered on the apparatus floor. Three 15 min such sessions were done daily for 3 d. Next, rats were trained in the place preference task (Rossier et al., 2000). Common to all three experimental conditions (far, near, and cue tasks), the rat had to enter a circumscribed goal zone and stay there for at least 2 sec. When this condition was met, the overhead dispenser released a single 20 mg pellet. Because the released pellet could land anywhere in the cylinder, the rat usually had to leave the goal area to find the pellet. To receive another reward, the rat had to spend at least 3 sec outside the goal zone, even if the pellet happened to land in the goal zone.

Far task. In the far task, the goal zone was an unmarked 10-cm-radius circle the center of which was 19 cm away from the cylinder center along the radius that made a 135° angle with the black bisector of the wall card (Fig. 1). The angle between the goal zone center and the wall card was constant, regardless of the angular position of the card. The only known sources of orientation information were the wall card, the goal zone as indicated by operation of the pellet feeder, and self-motion cues.

In this task and the near task, training was done in four steps, each of which was conducted in 30 min sessions. In step 1, which lasted 3 d, the feeder was activated each time the rat entered an 18-cm-radius circle. In step 2, which also lasted 3 d, the rat had to stay inside the goal zone for 2 sec before a pellet was released. In step 3, which lasted 8 d, the radius of the goal zone was reduced by 1 cm per day to a final radius of 10 cm. In step 4, which lasted 8 d, the rat was familiarized with a partial extinction procedure in which the pellet feeder was turned off at the beginning of each session. At first, the duration of the unreinforced period was 30 sec. This duration was doubled every 2 d so that at the end the duration of the unreinforced period reached a maximum of 4 min. The extinction period was introduced so that rats could indicate their choice of the goal zone location without any potentially corrective information from the pellet feeder.

Near task. Training in the near task was identical to that in the far task except for the location of the goal zone, which was an unmarked circle positioned directly in front of the black bisector of the white card (Fig. 1).

Cue task. In the cue task, the goal zone was directly indicated by a 20 cm black metal disc that was put on the cylinder floor. The goal zone was set one-half out along one of the cardinal radii (N, E, S, W) of the cylinder as viewed from overhead and moved to another cardinal radius in a pseudorandom fashion between each pair of sessions (Fig. 1). During all phases of training, the release zone was coextensive with the metal disk, so that across sessions no information about the drop zone location was provided by either the stimulus card or any uncontrolled cues fixed in the environment. In step 1 of training, the feeder was activated each time the rat visited the goal disk. In step 2, the rat was trained to stay in the disk for at least 2 sec to release a pellet. Finally, in step 3, the same partial extinction procedure was introduced with the unreinforced interval reaching a maximum of 4 min.

In all three tasks, training was considered complete when the rat reached a criterion of two rewards per minute in a session.

Surgery

At the end of training, surgery to implant an array of 10 microwire electrodes was done under sterile conditions and general anesthesia. The electrodes were made of 25 μm nichrome wire and formed a bundle threaded through a piece of stainless steel tubing (Kubie, 1984). Each wire was attached to a pin on the outside of a circular connector. The tubing was attached to the center pin of the connector and served as the animal ground as well as a guide for the microwires. The connector, tubing, and wires could be moved down in the brain by turning screws attached to the connector into nylon cuffs that were attached to the rat's skull.

The tips of the electrode bundle were implanted above the dorsal CA1 pyramidal cell layer. The rat was anesthetized with pentobarbital (40 mg/kg, i.p.), injected with atropine sulfate (0.25 mg/kg, i.p.) to prevent respiratory distress, and put in a Kopf stereotaxic apparatus. The skull surface was exposed and holes for the electrodes and to anchor the electrode carrier were drilled at appropriate locations. Three miniature screws and a T-shaped screw were placed in the skull to anchor the recording-electrode array. The tips of the recording electrodes were implanted at stereotaxic coordinates: 3.8 mm posterior and 3.0 mm lateral to bregma and 1.5 mm below the dura (Paxinos and Watson, 1986). Once the electrodes were in place, sterile petroleum jelly was applied to the exposed brain surface and around the guide tube for the electrodes. Next, dental acrylic was put over the jelly and around the tube to cover the skull hole. Finally, the bottoms of the three drive-screw assemblies were attached to the anchor screws. As a postoperative treatment, the rats received an intramuscular injection of antibiotic (terramycin, 60 mg/kg). The animals were given 1 week to recover from surgery before recordings were made.

At the completion of the experiment, each rat was killed with a lethal dose of pentobarbital and perfused intracardially with 0.9% saline followed by 4% formalin. Just before death, positive current (15 μA for 30 sec) was passed through one of the microwires to deposit iron that could be visualized after reaction with potassium ferrocyanide (Prussian blue). The brain was removed and stored for 1 d in 3% ferrocyanide. Later, 40 μm coronal sections were made. Every fifth section was stained with cresyl violet for verification of electrode placements.

Recording methods

Beginning 1 week after surgery, the activity from each microwire was screened daily while the rat underwent additional place preference task sessions. The electrodes were lowered over a period of several weeks while we searched for unit waveforms of sufficient amplitude to be isolated. Because several days were necessary before the first recordable cells were reached in the hippocampus, enough time passed for postoperative performance to recover to preoperative levels. Once a unit was isolated, it was usually recorded for four successive sessions (see below).

Screening and recording were done with a cable attached at one end to a commutator that allowed the rat to turn freely. The other end of the cable was connected to a light-emitting diode (LED) for tracking the rat's head position, a headstage with a field effect transistor amplifier (FET) for each wire, and finally a connector that mated with the electrode connector cemented to the rat's skull. The FETs were used to amplify signals before they were led to the commutator via the cable. The fixed side of the commutator was connected to a distribution panel. From the panel, the desired signals were amplified 10,000-fold with low-noise

differential amplifiers, bandpass filtered from 0.3 to 10 kHz, and sent to a 250 kHz analog-to-digital board in a Pentium computer. The data acquisition system (DataWave, Longmont, CO) recorded a 1 msec burst of 32 samples at 32 kHz each time the voltage exceeded an experimenter-defined threshold. Before the initial recording session, spike discharges of single units were separated using on-line clustering software (DataWave Discovery) to simplify later off-line separation. Briefly, scatterplots of the most characteristic waveform parameters (e.g., peak voltage and waveform duration) were generated from the signals emanating from putative units recorded on each channel.

The rat's head position was tracked by locating the LED set on the midline 1 cm above the head and 1 cm behind the headstage. Tracking was done with a TV-based digital spot follower that received red-green-blue signals from a CCD color camera fixed to the ceiling of the experimental room above the apparatus. The LED was detected at 50 HZ in a grid of 256 \times 256 square regions (pixels) that was reduced at analysis stage to a 64 \times 64 grid of pixels 26 mm on a side.

Testing protocol

Each electrode in a rat was checked two to three times a day during performance of the place preference task, ensuring that asymptotic performance was maintained even if no recording was made for several days. If no recordable cell could be isolated, the electrode bundle was advanced 25–50 μm . Cells selected for recording were well discriminated complex-spike cells that showed clear location-specific firing. Only waveforms of sufficient amplitude ($>100 \mu\text{V}$ with a background noise level $<30 \mu\text{V}$) were recorded. The waveforms and firing patterns were inspected before each session to check for constancy.

The aim of the protocol in all three tasks was to obtain some sessions in which firing fields followed card rotation and other sessions in which fields did not follow card rotation (see below). To this end, two kinds of 90° card rotations were made: those done in the absence of the rat (hidden rotations) and those done in the presence of the rat (visible rotations). Rotenberg and Muller (1997) showed that firing fields usually remain stable in the laboratory frame after visible 180° rotations. In contrast, 180° hidden rotations are usually followed by equal rotation of firing fields. In the present study, our initial guess was that fields would follow 90° hidden rotations but stay fixed in the laboratory frame after 90° visible rotations. This expectation was mainly borne out in the near and far tasks but often violated in the cue task.

The session sequence was similar in the far and near tasks (Fig. 1). Once at least one cell was isolated, three consecutive sessions were run. In the first (standard) session, the wall card and goal zone were in the same locations as during training. After this session, the rat was disconnected and returned to its home cage. The arena was cleaned and the card rotated 90° counterclockwise (CCW). Because the goal zone location was always tied to the card location in the near and far tasks, the goal location also rotated 90° CCW. The rat was brought back into the arena and reconnected, and session 2 ("hidden rotation") was done. At the end of session 2, the experimenter entered the recording room and rotated the wall card 90° CCW while the rat was in the arena; once again the goal zone rotated equally. Session 3 ("visible rotation") was then done.

The session sequence in the cue task started with a standard session in which the wall card was in the position used during training and the goal disk was randomly placed at one of its four possible locations. The rat was then disconnected and put in its home cage. In the rat's absence, the card was rotated 90° CCW, and the goal disk was rotated away from its previous location to one of the other two possible positions. Session 2 (hidden rotation) was then done. At the end of session 2 the experimenter rotated the card 90° CCW and rotated the goal disk by either 180° or 270° so that it neither stayed in its previous position nor stayed in register with the card. Session 3 (visible rotation) was then done.

As indicated above, each session for all tasks began with a 4 min extinction period during which the pellet feeder was off so that rats had to perform without feedback provided by food delivery. The feeder was then switched on for the remaining 12 min of each session.

The complete three-session protocol was repeated for each rat whenever a new cell or set of cells was isolated. The repetition allowed for the possibility that some aspects of the behavior, the cell activity, or both would vary in a sequence-dependent fashion. As described in Results, some outcomes indeed varied with the sequence number. It is important to note, however, that in almost all cases the effects on behavior and place cells covaried, so that knowing how a stimulus manipulation affected place cells in general predicted how behavior would be altered.

Thus, the overall pattern of results is simple despite the existence of time-order effects.

Data presentation and analysis

Unit analysis. The first step in off-line analyses was to refine boundaries for waveform clusters that were defined before recording. Candidate waveforms were discriminated on the basis of at most eight characteristic features including maximum and minimum spike voltage, spike amplitude (from peak to trough), time of occurrence of maximum and minimum spike voltages, spike duration, and voltage at two experimenter-defined points of the waveforms. The settings established for a given session were generally used for subsequent sessions. Once single units were well separated, positional firing rate distributions were calculated. The total time the light was detected in each pixel (dwell time) and the total number of spikes in each pixel were accumulated for the session duration (16 min). The rate in each pixel was the number of spikes divided by the dwell time. For each session, a firing rate map was constructed using the method described by Muller et al. (1987) to visualize the positional firing rate distribution. In such maps, pixels in which no spikes occurred during the whole session are displayed as white. The highest firing rate is coded as purple, and intermediate rates are shown as orange, red, green, and blue pixels from low to high. The values used as boundaries between categories were determined for the map of the first session recorded for a given cell. To permit comparisons among positional firing distributions across several sessions for a cell, the rate categories used for subsequent sessions were the same as for the first session.

Firing field analyses. A firing field was defined as a set of at least nine contiguous pixels that shared at least one edge and with firing rate above the grand mean rate. Visual assessments of field positions were complemented by numerical estimates of field rotation between sessions. Pixel-by-pixel cross-correlations between firing rate maps of consecutive sessions were calculated as the corresponding positional firing patterns were rotated against each other in 1° steps. The rotation associated with the highest correlation (R_{Max}) was taken as the rotation of the field between the two sessions. A field was considered to rotate with the card if the angle associated with R_{Max} was $90 \pm 10^\circ$ (90° being the amount of card rotation).

Because visible card rotations were expected to cause firing fields to go out of register with the wall card, it was possible to analyze the relationship between place cell firing patterns and behavior. To do so, sessions were put into one of two categories. The first, “consistent” category contained sessions in which field positions remained in register with the card location after 90° card rotations. The second, inconsistent category contained sessions in which fields did not follow card rotation so that their fields went out of register with the card. In turn, we saw three general kinds of inconsistent sessions. In the first, fields remained at the same angular position after card rotation as before and so were stationary in the laboratory frame. In the second kind of inconsistent sessions, fields adopted unpredictable angular locations after card rotation. In the third, fields of two or more simultaneously recorded cells rotated to different extents; this outcome is similar to the “discordant ensembles” reported by Tanila et al. (1997a). For the most part, inconsistent sessions for hidden rotations occurred only in the cue task. For visible rotations the outcomes were more complex and are described in Results.

Behavioral analyses. For each recording session, the number of “adequate entries” into predefined true or virtual 20-cm-diameter goal zones were recorded. An adequate entry into a given goal occurred when the rat spent at least 2 sec inside that zone; two successive entries into a goal were scored only if they were separated by at least 3 sec spent elsewhere in the apparatus. In this way, we could determine how many rewards the rat would have obtained during the 4 min extinction period in the experimenter-defined goal zone relative to the card or (in the case of the cue task) the metal disk. We could also ask how many rewards would have been obtained for other, virtual goal locations during the extinction period. For instance, we could ask how many rewards would have been obtained if the goal zone were defined relative to the laboratory frame or to firing fields. We could also determine the number of rewards that were actually obtained during the final 12 min of each session during which the pellet feeder was switched on. In this way, we could ask whether feedback from the feeder could help to correct mismatches between the rat’s current notion of the goal zone and the experimenter-defined goal zone.

RESULTS

Selection of cell sample

Useful cell recordings and behavioral activity were obtained from 15 rats, 5 in the far task, 4 in the near task, and 6 in the cue task. All accepted pyramidal cells had to satisfy four criteria. (1) The extracellular waveforms had to be $>100 \mu\text{V}$ in amplitude; this is three times baseline noise. (2) The candidate waveform had to show complex spikes that are bursts of decremting amplitude spikes with intervals <10 msec (Fox and Ranck, 1981). (3) The cell had to exhibit a clear firing field during screening and the first standard recording session. (4) To permit assessment of the effects of rotating stimuli on the cylinder wall, the field had to be well away from the cylinder center.

In a few instances, session sequences were stopped because the waveform could no longer be seen or because its shape or amplitude changed so much that we could not be confident it was the same unit. In general, this occurred when the rat was unplugged and put in its home cage before the next session. In the event of difficulties with waveform recognition, the entire session sequence was discarded.

A final, behavioral criterion for including a session sequence in the data set was good performance during the initial standard session. In practice, this meant a rat had to make on average at least two correct responses per minute for us to be confident that it had learned the task. This rate of correct responses makes it possible to assess stimulus-induced changes in performance.

Far task

Hidden rotations of the wall card were made in 33 sessions in which 48 place cells were recorded. On the basis of visual inspection of firing rate maps, further confirmed by angular cross-correlation analyses (see section on firing field analysis), fields were observed to rotate with the card in 31 of 33 sessions (Table 1). In the remaining two sessions, fields did not follow the card. Instead, they were stable relative to the laboratory.

Visible card rotations were made in 31 sessions (46 cells). In contrast to hidden card rotations, visible card rotations resulted in corresponding field rotation in only seven sessions (12 cells). In the remaining 24 sessions, fields were usually stable relative to the laboratory (14 sessions; 17 cells), although a small number rotated through an angle different from 90° (6 sessions; 8 cells). In the remaining four sessions (nine cells), simultaneously recorded fields were seen to be affected differently by visible card rotations (e.g., with one field rotating 90° , whereas other fields were stable or rotated at an angle different from 90°). Interestingly, fields that followed the card were mostly found during the rat’s initial exposure to the visible card rotation. Thus, the first visible card rotation caused field rotation in four of five rats, whereas by the fifth repetition visible rotation never induced field rotation. Each row in Figure 2 shows firing fields for the same six place cells arranged as columns; the top row is for the initial standard session, the middle row is after the hidden rotation, and the bottom row is after the visible rotation (all cells were recorded separately). In line with the overall pattern of results, the fields for all of the example cells followed the hidden rotation. In contrast, only the fields of the cells in the two leftmost columns followed the visible rotation; the fields of the next two cells stayed fixed in the environment, whereas the fields of the last two cells rotated by an amount outside the range $90 \pm 10^\circ$. The effects of visible rotations on fields were considered consistent for the leftmost two cells and inconsistent for the others. The recognizable appearance of fields after inconsistent sessions indicates that

Table 1. Summary table of main results

	Number of instances with 90° field rotation		Performance change index		Goal searched by rats during inconsistent rotations
	Hidden rotations	Visible rotations	Hidden rotations	Visible rotations	
Far task ($n = 5$ rats)					
Sessions	31/33	7/31			Field-referred: 4/5
Fields	46/48	12/46	+0.01 ± 0.05	-0.43 ± 0.07	Card-referred: 1/5
Near task ($n = 4$ rats)					
Sessions	27/28	11/27			Field-referred: 0/4
Fields	49/52	15/49	-0.03 ± 0.03	-0.09 ± 0.05	Card-referred: 4/4
Cue task ($n = 6$ rats)					
Sessions	8/18	5/14			Field-referred: 0/6
Fields	14/35	8/26	-0.04 ± 0.04	-0.07 ± 0.03	Card-referred: 0/6 Cue-referred: 6/6

although the strength of card control is much weaker for visible rotations, we saw no indication of the major changes in positional firing patterns (new fields or silence) characteristic of remapping for place cells (Muller et al., 1991).

Performance during the extinction period and its relationship to firing field locations

Behavioral performance during the extinction period was compared for the standard/hidden rotation session pair and the hidden/visible rotation pair. To measure the effects of card rotations, we computed a “performance change index” (PCI) as $(A -$

$B)/(A + B)$, where A and B are the number of adequate entries into the correct release zone after and before card rotation, respectively. This index varies from -1.0 to $+1.0$ and is negative for decreases in performance and positive for increases in performance after card rotation. The PCI would be 0.0 if rotation did not affect performance.

A PCI histogram for the standard/hidden rotation session pair is shown in Figure 3A; the mean PCI is 0.01 ± 0.05 SEM. A t test indicates that this value is not distinguishable from 0.0 ($t_{32} = 0.24$; $p = 0.81$). A second histogram is shown for the hidden/

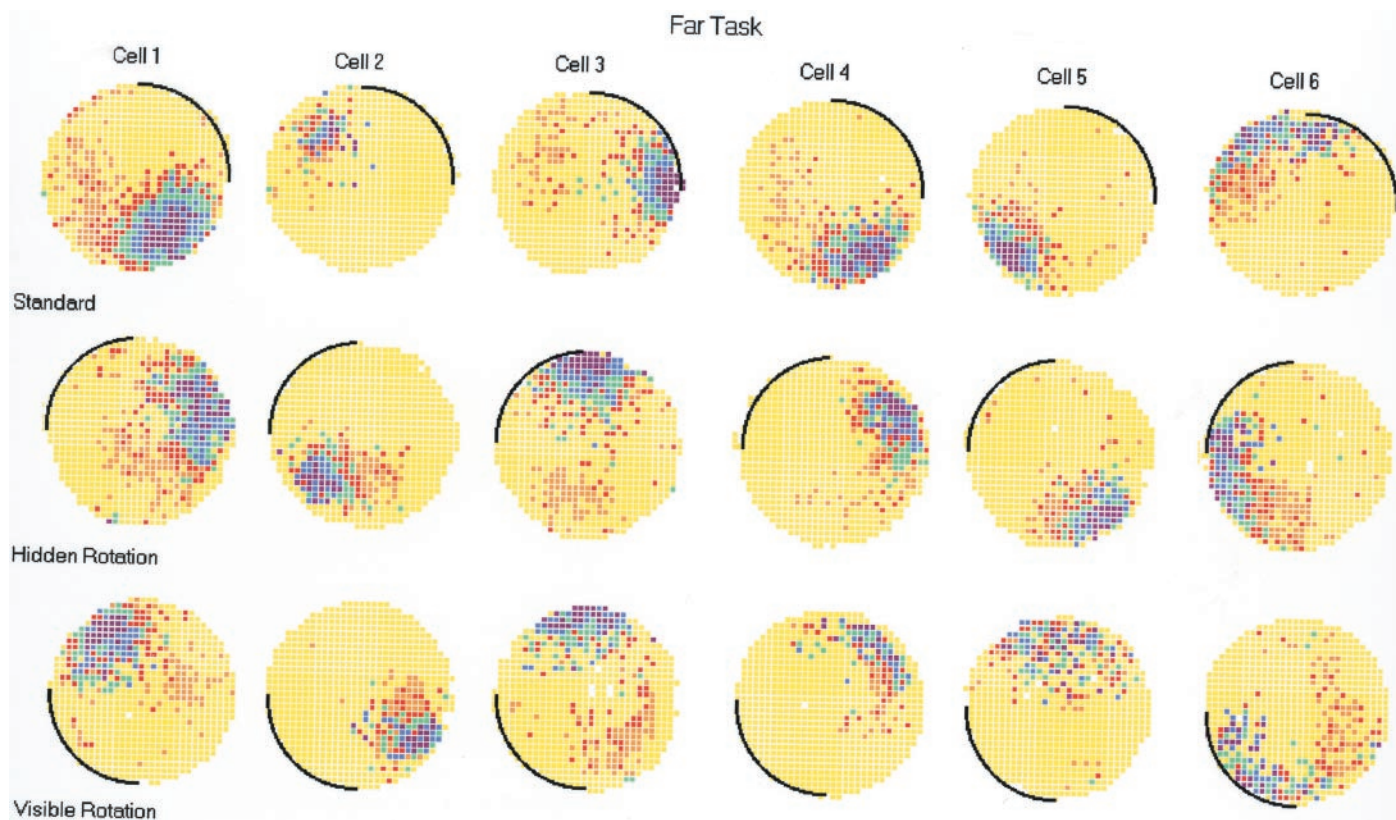


Figure 2. Firing rate maps of six cells in the far task. The fields of all cells followed the hidden card rotation. The fields of cells 1 and 2 (leftmost columns) also followed the visible card rotations, whereas the fields of cells 3 and 4 (middle columns) were stable after the visible rotation. The fields of cells 5 and 6 (rightmost columns) rotated by an amount outside the range $90 \pm 10^\circ$.

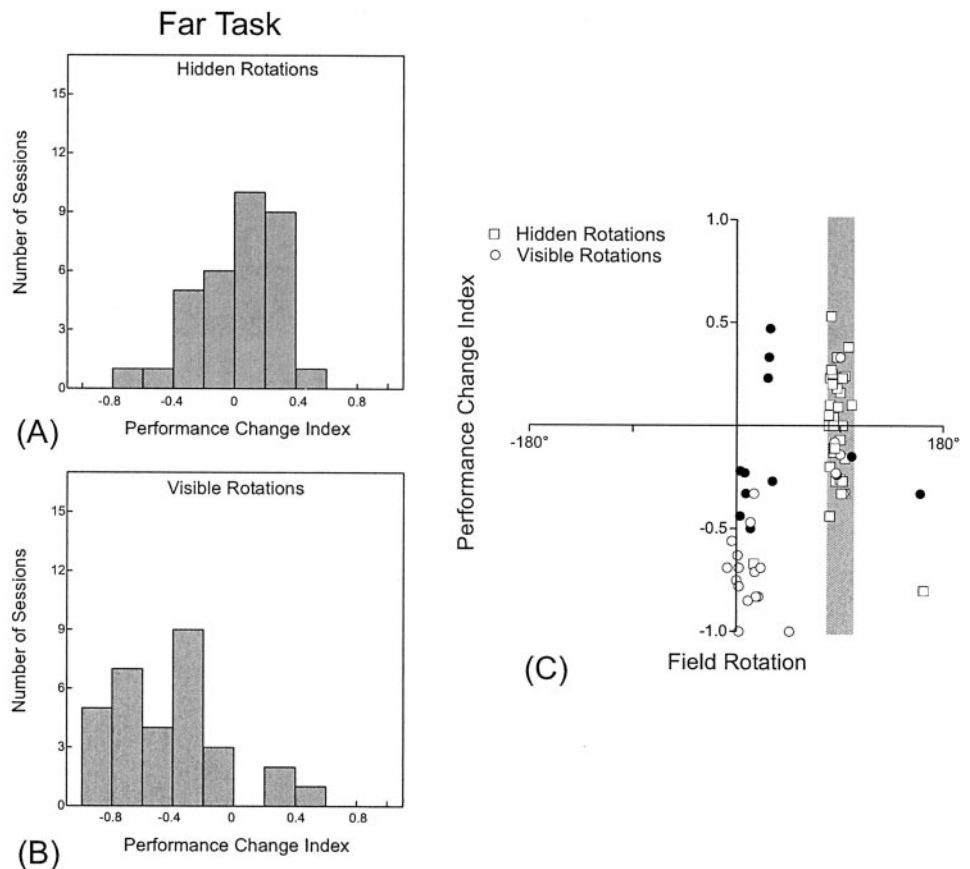


Figure 3. Performance change index in the far task. The PCI was computed for the extinction period as $(A - B)/(A + B)$, where A and B are the number of adequate entries into the correct release zone after and before card rotation, respectively. *A*, PCI histogram for the standard/hidden rotation session pair. *B*, PCI histogram for the hidden/visible rotation session pair. PCIs were much lower after the visible than after the hidden rotation ($p < 0.0001$). *C*, Plots of individual PCIs after hidden (\square) and visible rotations (\circ) against field rotation. The vertical gray stripe represents $90 \pm 10^\circ$. Consistent field locations (within the gray stripe) in general predicted preserved performance, whereas inconsistent field rotations (points outside the gray stripe) in general predicted performance decrements. Solid circles show PCIs after visible rotations for rat 4 (see Results).

visible rotation session pair in Figure 3*B*; the mean PCI is -0.43 ± 0.07 SEM, a value significantly lower than zero ($t_{30} = 6.49$; $p < 0.001$). A t test confirms that the performance change index is much lower after a visible rotation of the wall card than after a hidden rotation of the wall card ($t_{62} = 5.50$; $p < 0.0001$). Thus, hidden rotations that in general produced consistent field rotations left performance during the extinction period unchanged. In marked contrast, the visible rotations that most often produced inconsistent field rotations also caused a strong decrease in performance.

The relationship between induced field rotation and the performance change index is made explicit in Figure 3*C*, where the effects of individual hidden rotations are plotted as *open squares* and the effects of individual visible rotations are shown as *open circles*. In this plot, it is evident that the PCI–field rotation points fall into two clusters, showing that inconsistent field rotations in general predict performance decrements whereas consistent field locations in general predict preserved performance. Performance decrements after visible rotations were seen after inconsistent sessions regardless of whether the ensemble of firing fields remained in register (were concordant) or rotated differently (were discordant). Detectable exceptions to the clustering pattern are early visible rotations that induced equal field rotations and caused no decrement of PCI; these cases are seen as *open circles* in the cluster near 90° . Thus, in this navigational task, the ability to reliably return to the card-referred release zone suffers if the place cell representation goes out of register with the card.

A second type of exception to the overall clustering pattern in Figure 3*C* is revealed by the set of *solid circles* near 0° that are for

visible sessions for one rat, identified as rat 4. This animal was able to locate the card-referred release zone even though its place cell representation did not rotate after visible rotations. This interesting dissociation of behavior and firing fields is considered again below.

Goal search patterns during the extinction period after inconsistent rotations

Each session started with a 4 min period during which no rewards were given, regardless of adequate entries into the card-referred release zone. We could therefore investigate the rat's expectation of the correct location. This analysis is of special interest for inconsistent sessions because it allows us to determine whether the rat tended to go to the card-referred or field-referred release zones; these locations are defined in Figure 4*A*. Because most inconsistent fields were stable relative to the laboratory environment, the field-referred area was usually stable relative to the laboratory. To estimate zone preference, we calculated the number of rewards that would have been obtained in the card-referred and field-referred release zones if the feeder had been on. We define zone preference as $(C - F)/(C + F)$, where C is the number of rewards that would have been in the card-referred zone and F is the number that would have been in the field-referred zone. This value is plotted against field rotation for inconsistent sessions in Figure 4*B* for the exceptional rat 4 (*solid circles*) and all other rats (*open circles*). From Figure 4*B*, it is evident that for the majority of rats (four of five), performance would have been judged good if the correct release zone were field- and not card-referred.

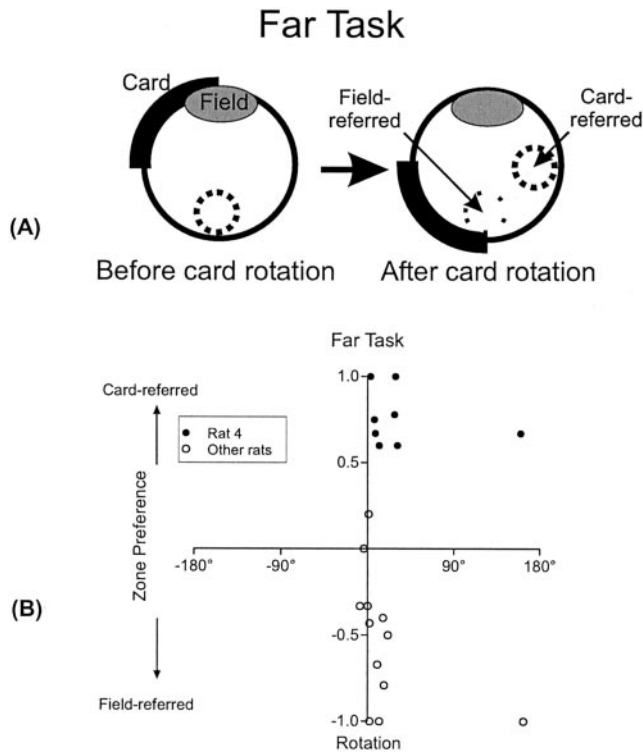


Figure 4. Plots of zone preference against field rotation in the far task (inconsistent sessions). *A*, When a field (shown in gray) does not follow the card rotation, the rat may focus its search in the card-referred or field-referred location. The figure shows the two locations for a field that was stable after the card rotation. *B*, Zone preference during the extinction period was defined as $(C - F)/(C + F)$, where C is the number of rewards that would have been in the card-referred location and F is the number that would have been in the field-referred location. *Solid circles* represent rat 4; *open circles* represent all other rats. Although rat 4 searched in the card-referred location, the other rats searched in the field-referred location.

Within-session changes in performance

Once the feeder was switched on immediately after the extinction period, in principle it could provide feedback to the rat about the card-referred release zone location. We therefore asked whether performance improved during inconsistent sessions by measuring for each 4 min block of the session the number of correct responses. We saw a tendency for improvement across the session (Fig. 5) that was significant according to an ANOVA ($F_{(3-75)} = 3.83$; $p < 0.02$). Thus, the average within-session performance improved gradually, although there was no tendency for field positions to shift. It should be noted, however, that even by the last 4 min period of inconsistent sessions, the number of rewards per minute of 1.28 was much lower than the reward rate of 2.39 per minute in consistent sessions ($t_{25} = 4.73$; $p < 0.001$).

Near task

Hidden rotations of the wall card were made in 28 sessions in which 52 place cells were recorded (Table 1). Fields were observed to rotate with the card in 27 of 28 sessions (49 cells). The remaining hidden rotation session was classified as inconsistent because several simultaneously recorded cells rotated to different extents.

Visible card rotations were made in 27 sessions (49 cells) and resulted in corresponding field rotation in only 11 of 27 sessions (15 cells). Fields remained at the same angular location in the

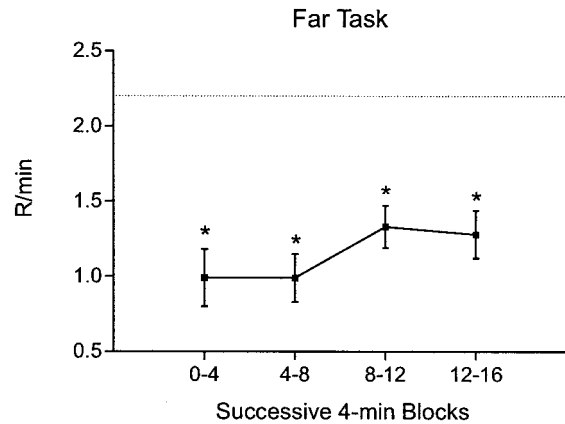


Figure 5. Within-session time course of performance in the far task (inconsistent sessions). This figure shows the mean (\pm SEM) number of correct responses in the card-referred location across successive 4 min blocks. The *dashed line* represents the average performance level during pre-rotation sessions. * $p < 0.01$ relative to baseline performance.

environment in six sessions (14 cells) or rotated by an angle other than $90 \pm 10^\circ$ in seven sessions (8 cells). In the remaining three sessions (12 cells), the fields of simultaneously recorded cells rotated by different amounts (discordant ensembles). In agreement with the sequence effect seen in the far task, fields that followed visible card rotations were found only during early exposures of individual rats to visible rotations. Thus, the first visible card rotation caused equal field rotation in four of four rats, whereas no fields rotated in response to the fourth visible rotation. Figure 6 is organized in the same way as Figure 2 and summarizes in columns how the firing fields of six separately recorded cells appeared in the initial standard session (*top row*), after the hidden rotation (*middle row*), and after visible rotation (*bottom row*). As in the far task, the hidden rotation caused a consistent rotation of the fields of six of six cells, whereas the visible rotation caused a consistent field rotation for only two of six (leftmost) cells. Also as in the far task, we saw no evidence of remapping in inconsistent sessions.

Performance during the extinction period and its relationship to firing field locations

Performance change index histograms for the near task are shown in Figure 7. Figure 7*A* is for standard/hidden rotation session pairs, whereas Figure 7*B* is for hidden/visible rotation pairs. Both histograms are centered near zero and have similar dispersions. A t test indicates that the PCI distributions are not reliably different from each other ($t_{53} = 1.28$; $p = 0.205$). We also find that the mean PCI for standard/hidden rotation session pairs of -0.03 ± 0.03 SEM is indistinguishable from zero ($t_{27} = 1.28$; $p = 0.213$). On the other hand, the mean PCI for hidden/visible rotation pairs of -0.09 ± 0.04 SEM is reliably lower than zero ($t_{27} = 2.31$; $p < 0.05$). This suggests that average performance is degraded after visible card rotations, but the effect is very small.

The relationship between PCI and firing field location for the near task is shown in Figure 7*C*. As in the far task, two main clusters of points are visible, one at $90 \pm 10^\circ$ and the second near 0° , although this second cluster is not very tight. What is clear, however, is that inconsistent field rotations produced by visible card rotations are not associated with much degradation of performance. Indeed, performance during the single inconsistent field rotation caused by a hidden card rotation did not reduce

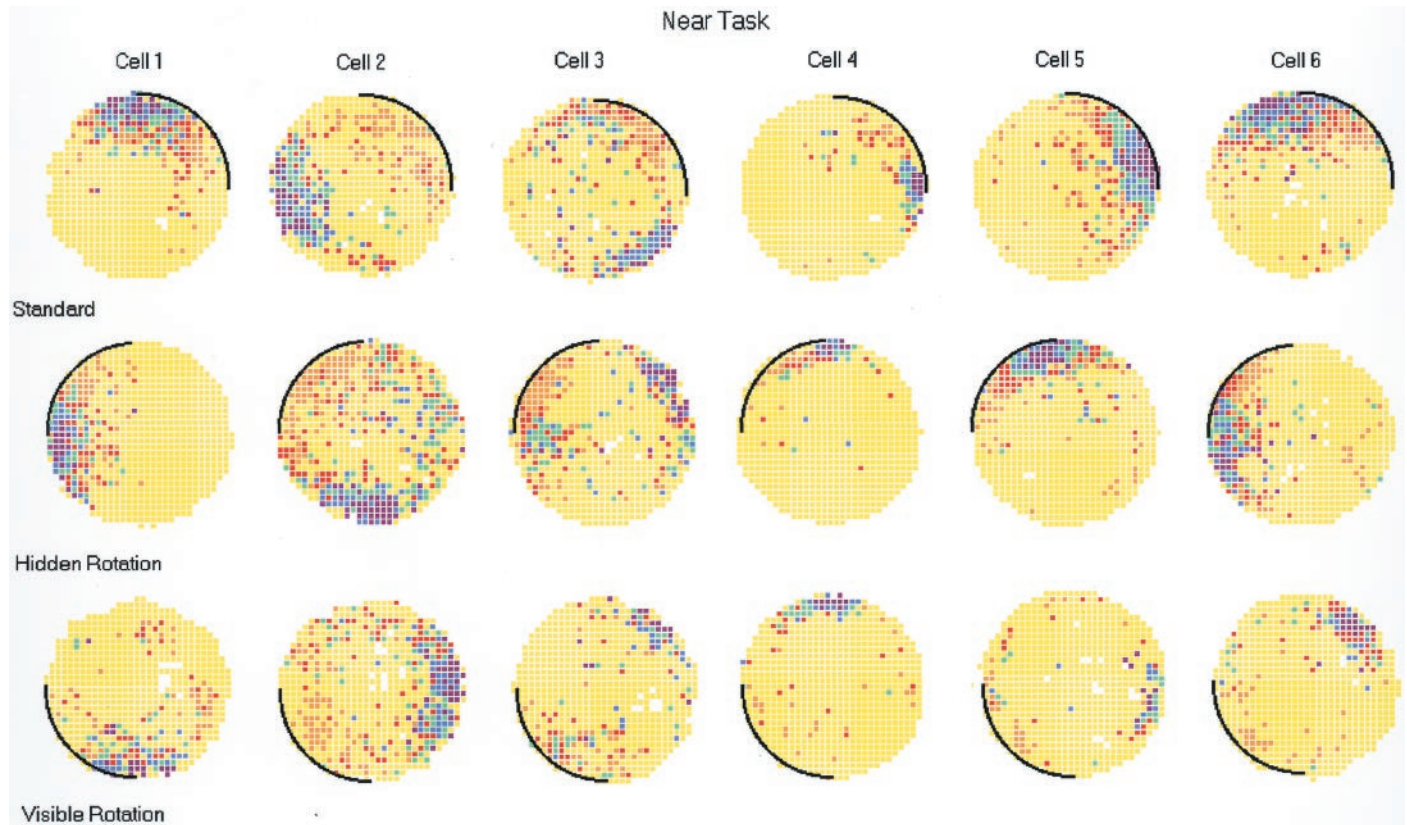


Figure 6. Firing rate maps of six cells in the near task. The fields of all cells followed the hidden card rotation. The fields of cells 1 and 2 (*leftmost columns*) also followed the visible card rotations, whereas the fields of cells 3 and 4 (*middle columns*) were stable after the visible rotation. The fields of cells 5 and 6 (*rightmost columns*) rotated by an amount outside the range $90 \pm 10^\circ$.

performance. Thus, if the release zone location is marked by a beacon (the card), rats are able to get to the correct place even if their place cell representation is out of register with the behavioral requirements.

Goal search patterns during the extinction period after inconsistent rotations

To investigate the rat's expectation of the correct location for inconsistent sessions, we defined the card-referred and field-referred release zones as shown in Figure 8*A*. A plot of zone preference against field rotation is shown for inconsistent sessions in the near task in Figure 8*B* from which it is clear that the four rats go to the card-referred release zone regardless of whether the fields follow or do not follow the wall card. There is, however, an indication that the rats do not simply ignore the field-referred location. Thus, the rats make more adequate entries into the field-referred location than into a neutral circular area of equal size ($t_{12} = 2.70$; $p < 0.05$). It is interesting that the search patterns can be influenced by both the card-referred and field-referred coordinate systems (Fenton et al., 1998).

Within-session changes in performance

As in the far task, the number of correct responses during inconsistent sessions were separated into successive 4 min blocks. An ANOVA showed no significant effect of blocks ($F_{(3-48)} = 0.96$; NS), suggesting that no improvement took place with time. There were reliable decreases in performance, however, in inconsistent sessions for the first (extinction) and last 4 min blocks as shown in Figure 9.

Cue task

Hidden 90° card rotations were done in 18 sessions in which 35 place cells were recorded (Table 1). Firing fields rotated by $90 \pm 10^\circ$ in eight sessions (13 cells), rotated by 0° in three sessions (7 cells), and rotated by other angles in the remaining seven sessions (15 cells). The proportion of hidden rotation sessions in which field was controlled by the wall card (8 of 18) is lower than expected from previous work (Muller and Kubie, 1987) and significantly lower than the proportion controlled by the card in the far task (31 of 33; $z = 3.20$; $p < 0.001$) and the near task (27 of 28; $z = 3.28$; $p < 0.001$). Presumably, this decrease in control by the card is caused by interference from the independently moved metal disk.

Visible card rotations were done in 14 sessions (26 cells). Firing fields rotated by $90 \pm 10^\circ$ in five sessions (8 cells), rotated by 0° in four sessions (8 cells), and rotated by other angles in the remaining five sessions (10 cells). In contrast to the far and near tasks, we saw no trend in visible sessions for control by the wall card to decrease with repeated exposures, and in fact no time trend was discernable. Overall, control by the wall card was erratic for both hidden and visible rotations in the cue task despite the clear clustering near 90° visible in Figure 11*C*; however, cue control was not transferred to the disk. This was shown by examining the correlation between pairs of consecutive firing rate maps with the second map in the pair rotated by an angle equivalent to the disk rotation. This analysis was conducted for inconsistent field rotations and failed to yield significant correlations for either hidden ($r = -0.05 \pm 0.04$; 22 cells) or visible rotations ($r = -0.02 \pm 0.03$;

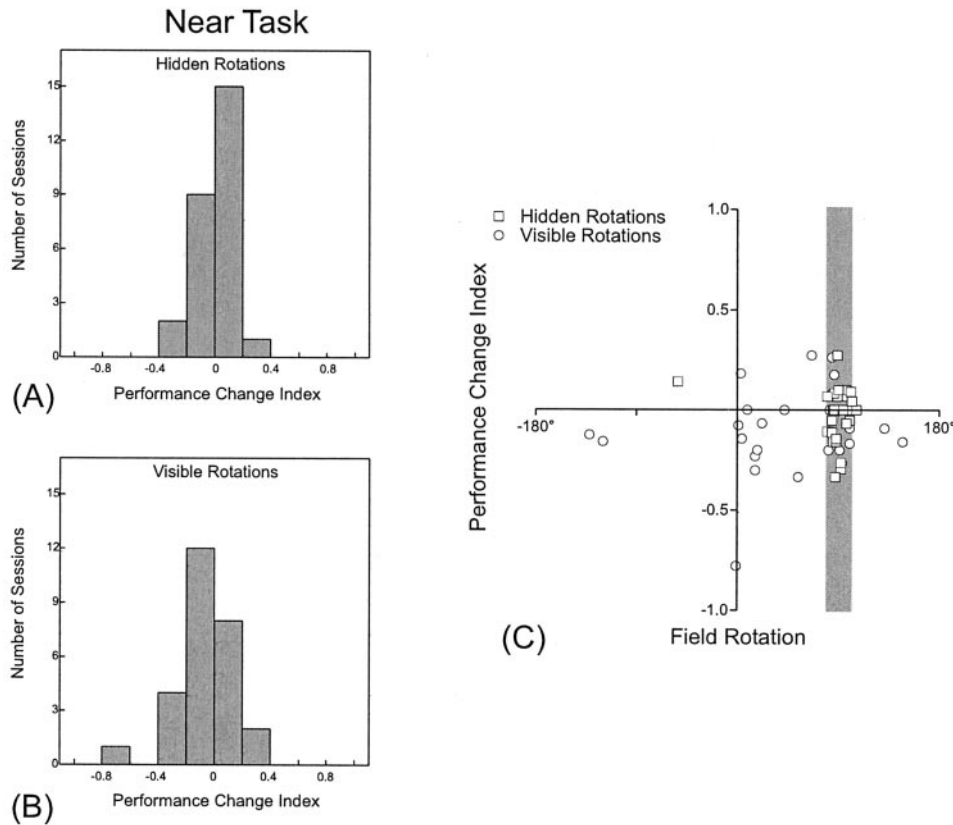


Figure 7. Performance change index in the near task. *A*, PCI histogram for the standard/hidden rotation session pair. *B*, PCI histogram for the hidden/visible rotation session pair. The two distributions were not reliably different from each other. *C*, Plots of individual PCIs after hidden (\square) and visible rotations (\circ) against field rotation. The vertical gray stripe represents $90 \pm 10^\circ$. Preserved performance was seen after both consistent (within the gray stripe) and inconsistent field rotations (points outside the gray stripe).

18 cells). Figure 10 shows as columns firing fields from four separately recorded cells in standard sessions (*top row*), hidden card (*middle row*), and visible card (*bottom row*) sessions. Note that the rather simple relationship between the type of card rotation and ensuing field rotation seen for the far and near tasks does not hold for the cue task. The fields of the first three cells followed the hidden card rotation, but only the field of cell 1 followed the visible rotation. The field of the rightmost cell did not follow either the hidden or visible card rotation.

Histograms of the performance change index are given for hidden card rotations in Figure 11*A* and for visible card rotations in Figure 11*B*; these indicate that neither rotation type strongly affected performance. The mean PCI of -0.04 ± 0.04 SEM after hidden rotations is not reliably different from 0.0 ($t_{17} = 1.08$; $p = 0.3$). In contrast, the mean PCI of -0.07 ± 0.03 SEM after visible rotation was significantly lower than 0.0 ($t_{13} = 2.50$; $p < 0.05$). Thus, there is a trend for visible rotation to cause marginally decreased performance. The notion that this trend is minimal is corroborated by the lack of a reliable difference between the mean PCIs for the two rotation types ($t_{30} = 0.637$; $p = 0.53$).

Figure 11*C* shows the relationship between PCI and field rotation for the cue task. There is a clear cluster of points in the $90 \pm 10^\circ$ range and a broad dispersion of points elsewhere along the rotation axis. There is, however, no trend for the PCI to be higher or lower regardless of field rotation for either hidden or visible card rotations. All six rats searched for the goal at the black disk on the floor. Thus, performance in a second beacon task is unaffected by disruptions of the relationship between the visual appearance of the environment and the place cell representation. This uncoupling of performance is still more striking than in the near task because control of field rotation was disturbed even for hidden rotations in the cue task.

DISCUSSION

The aim of this study was to test in a new way predictions of the spatial theory of hippocampal function (O'Keefe and Nadel, 1978). To this end, place cells were recorded as individual rats performed one of three variants of the place preference task (Rossier et al., 2000) in which food reinforcement was provided only if the rat went to a release zone inside a cylindrical chamber. The three variants could be classified according to the nature of the problem and according to the nature of the stimulus provided to solve the problem. In the first classification, the far task was a place navigation task in that the release zone was distant from a single informational stimulus, whereas the near and cue tasks were beacon navigation tasks in that the release zone was close to the informational stimulus. In the second classification, the informational stimulus for the far and near tasks was a card on the cylinder wall, whereas in the cue task the card was irrelevant and the informational stimulus was instead a disk that was coextensive with the release zone.

To test the theory, we sought a method of disrupting the relationship between the informational stimulus and the place cell representation. We expected that such a disruption would impair performance of the place navigation task (i.e., the far task) but would leave unaffected performance of the beacon navigation tasks (i.e., the near and cue tasks). Our expectations were based on the notion that the far task requires map-based navigation using cues that establish a stable allocentric framework, whereas the near and cue tasks require only that the rat heads toward a strong marker stimulus at the secondary goal (the release zone).

Three recording sessions were made for each place cell or set of simultaneously recorded place cells: a standard session, a hidden card rotation session, and a visible card rotation session.

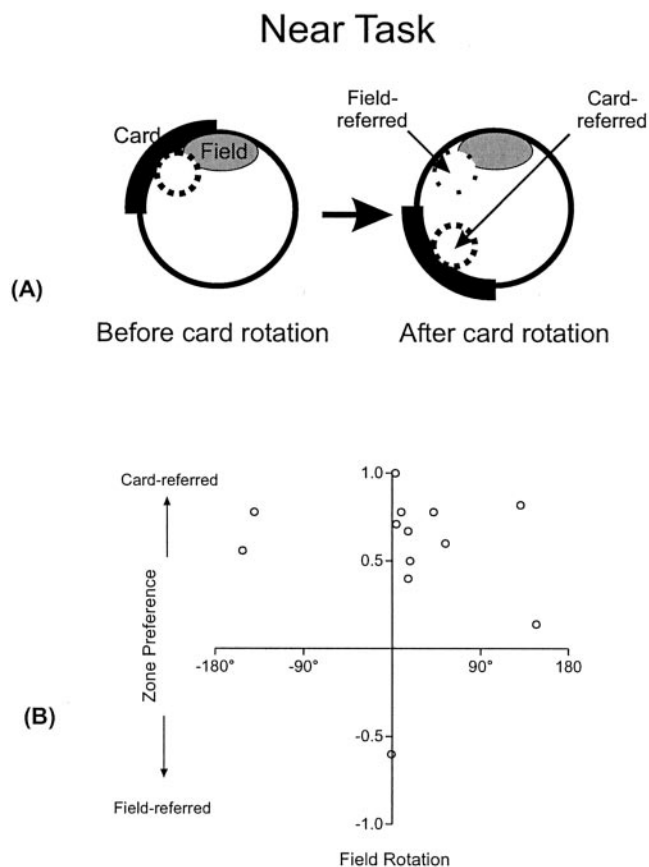


Figure 8. Plots of zone preference against field rotation in the near task (inconsistent sessions). *A*, When a field (shown in gray) does not follow the card rotation, the rat may focus its search in the card-referred or field-referred location. This figure shows the two locations for a field that was stable after the card rotation. *B*, Zone preference during the extinction period. Rats generally searched in the card-referred location.

In the cue task, the marker disk was also rotated, independent of the card, between each session pair. The standard/hidden session pair tested the salience of the white card, whereas the hidden/visible pair was intended to disrupt the relationship between firing fields and the card. We found that firing fields almost always followed hidden rotations in the far and near tasks but less often in the cue task. The variable coupling between the firing fields and the card after hidden rotations in the cue task did not reduce the reward rate whether or not the fields followed the card or the goal disk, a first indication that a consistent relationship between the place cell representation and informational stimuli is not essential in a guidance or beacon task. It is interesting that the requirement to go directly to the disk weakened the relationship between place cells and the card without any significant degree of control transfer to the disk. It is also interesting that neither the hidden nor especially the visible rotation induced remapping; the place cell representation was apparently unchanged except for its orientation relative to the laboratory frame.

In agreement with the effects of 180° visible rotations (Rotenberg and Muller, 1997), the most common outcome was for firing fields to remain fixed in the environment after the 90° visible rotations used here. The tendency of fields to not move in response to visible rotations was seen regardless of the task, but 90° field rotations were seen in some cases and rotations different from 0° or 90° were seen in others. Importantly, the probability of

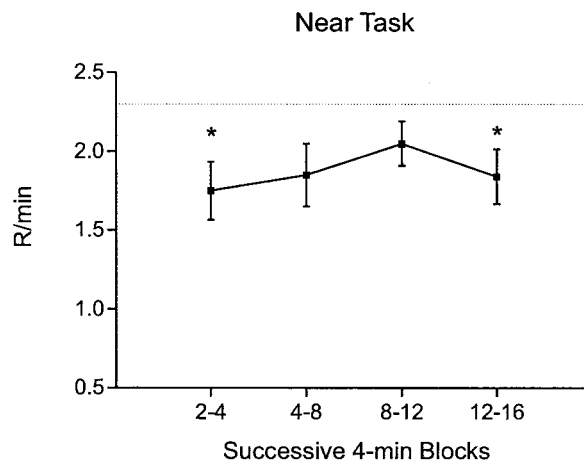


Figure 9. Within-session time course of performance in the near task (inconsistent sessions). This figure shows the mean (\pm SEM) number of correct responses in the goal (card-referred) location across successive 4 min blocks. The dotted line represents the average performance level during pre-rotation sessions. * $p < 0.01$ relative to baseline performance.

a 90° field rotation after a visible card rotation decreased to zero with successive exposures of individual rats to this manipulation; this issue is addressed again below.

The central result of this study is that disruptions of the relationship between firing fields and the card induced by visible rotations worsened performance in the far task but had no effect on performance in the near or cue tasks. Thus, our results strongly support the direct predictions of the spatial mapping theory that (1) the place cell representation must not only be intact but must bear the correct relationship to the environment for efficient behavior in map-based spatial tasks. We take this as the general outcome and treat the exceptional case below. (2) The place cell representation is irrelevant for efficient behavior in simpler spatial tasks that require only a guidance strategy. These findings parallel lesion evidence that hippocampal integrity is more critical for place navigation than for nonspatial navigation (O'Keefe and Conway, 1980; Morris et al., 1986b; Packard and McGaugh, 1996).

Several other issues arise in a more detailed analysis of the far task. First, one of five rats in this task found a strategy for maintaining performance even though firing fields did not move after visible card rotations. There are two rather different ways in which this could happen. First, the rat might have learned a heading-vector strategy despite our intention of inducing a spatial or true navigational strategy, an outcome seen in previous work by Poucet (1985). In this view, the rat calculated the correct vector that points from the card to the release zone, a method that can be performed in the absence of a functional hippocampus (Pearce et al., 1998). Second, the rat may have been able to re-represent the location of the card (and therefore the release zone) using the stable place cell representation. Temporary inactivations of the hippocampus could be used to dissociate these two possibilities because they would leave performance unchanged in the first case but impair performance in the other. Regardless of the correct explanation, the number of spatial solution strategies open to rats appears to be quite great, and the precise nature of the task does not necessarily constrain an individual animal to use or abandon hippocampally based methods.

A related issue concerns our finding that the decrement of

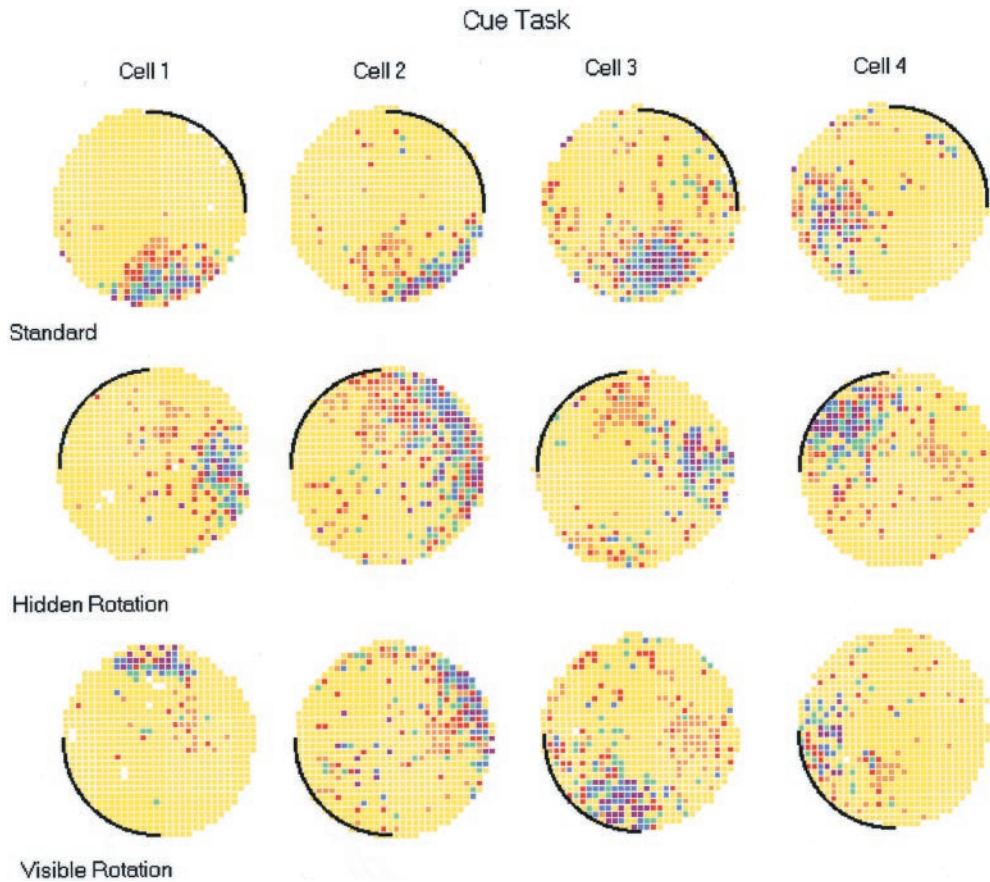


Figure 10. Firing rate maps of four cells in the cue task. The fields of cells 1–3 followed the hidden card rotation, but only the field of cell 1 also followed the visible card rotation. The field of cell 2 was stable after the visible rotation, whereas the field of cell 3 rotated by an amount outside the range $90 \pm 10^\circ$. Cell 4 had a field that did not follow either hidden or visible card rotations.

performance in the far task was not immediate but instead occurred after one or more session sequences in which firing fields followed visible card rotations. This is fascinating because it shows that the other individual rats were able to get to the release zone by continuing to use the card as an informational stimulus. Nevertheless, in later visible rotations, they chose to ignore the card (leaving field positions unchanged) at the expense of a reduced number of reinforcements. In a similar vein, activating the pellet feeder after the extinction period during later visible rotations produced little performance improvement despite the availability of accurate feedback. These decrements of performance were not caused by a lack of motivation because the running behavior did not suffer in either case and because the actual behavior was not random but would have yielded a large number of reinforcements if the release zone had not rotated after the visible card rotation. How can this unexpected and seemingly unnecessary drop in performance be explained? Here again there are two possibilities that are not necessarily mutually exclusive. First, it may be that the decrease in the amount of food earned by failing to maintain performance was not very great. On the basis of the number of pellets obtained and the food given in the home cage, we estimate that the performance decrement caused a 3% change in the total food per day. Alternatively, the reduced performance may be an extension of the well known propensity of rats to use spatial strategies for solving problems; the loss of efficiency may indicate that rats greatly prefer consistent spatial representations. In the present context, we note that the amount of training it took rats to reach the criterion of two pellets per minute was much greater for the cue than for the far or near tasks. To further study the relationship between perfor-

mance, reinforcement, and representational organization, it would be very interesting to repeat some of our experiments in a water maze where the motivational level is much greater than it was here.

The near task was designed to induce rats to use a guidance strategy. Visible rotations generally did not produce field rotations, so that the relationship between the informational stimulus and the place cells was disrupted. We observed a small performance decrement during the extinction period, but all rats searched for the goal mainly at the card-referred rather than field-referred location. In our view, the main pattern of results confirms the notion that the place cell representation is not essential for performance in a guidance task.

In the cue task, successful performance required a nonspatial beacon strategy and as expected was totally unaffected by inconsistent field placements. Searches during the extinction period focused on the goal disk regardless of field location. As noted above, control of fields by the card after hidden rotations was weaker than in the far and near tasks. We speculate that the goal disk acted as a cue that interfered with the control exerted by the wall card. Although intra-maze objects may fail to act as valid spatial landmarks (Cressant et al., 1997), they need not be ignored. For example, Rivard et al. (2000) demonstrated that a transparent barrier in the recording cylinder could control fields in its vicinity, although distant fields were unaffected by barrier manipulations. Although the goal disk is certainly not comparable to a three-dimensional barrier, its behavioral significance may have increased its salience as a landmark.

Overall, our results are in line with previous studies in which place cell activity was monitored during performance of a spatial

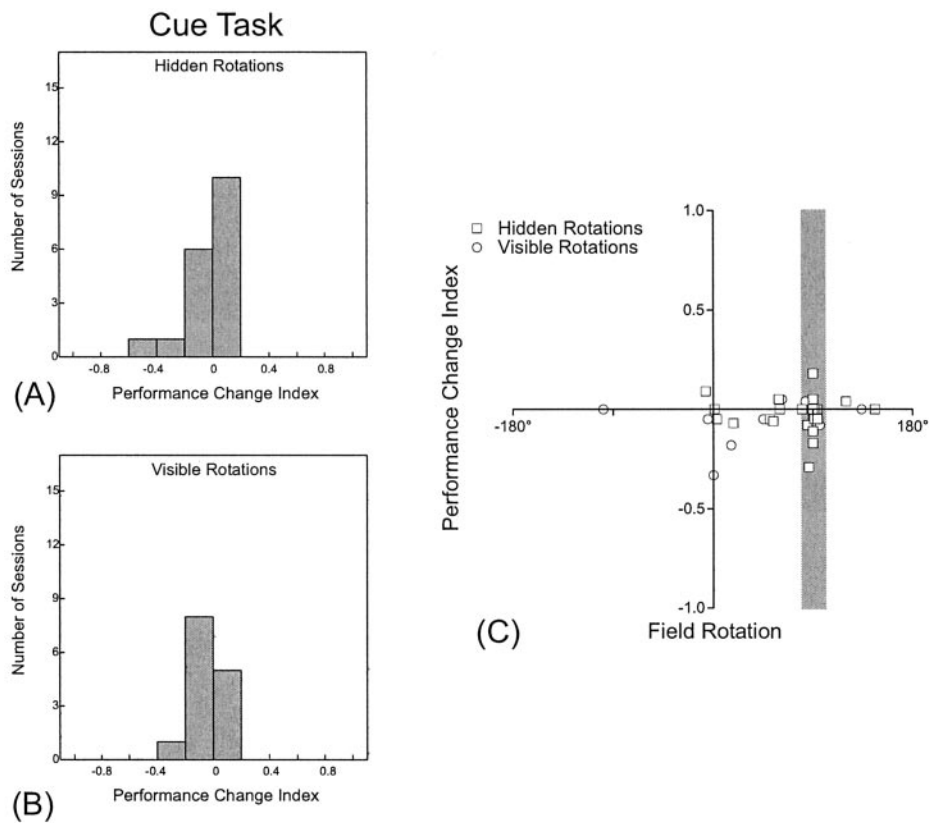


Figure 11. Performance change index in the cue task. *A*, PCI histogram for the standard/hidden rotation session pair. *B*, PCI histogram for the hidden/visible rotation session pair. The two distributions are not reliably different from each other. *C*, Plots of individual PCIs after hidden (\square) and visible rotations (\circ) against field rotation. The vertical gray stripe represents $90 \pm 10^\circ$. Preserved performance was seen after both consistent (within the gray stripe) and inconsistent field rotations (points outside the gray stripe).

task (O'Keefe and Speakman, 1987; Lenck-Santini et al., 2001). The results are also consistent with the Dudchenko and Taube (1997) study on head direction cells which showed that their discharge can predict spatial choices on a radial maze. They are, however, in conflict with the more recent work of Golob et al. (2001) that showed a weak relationship between head direction cell firing and spatial behavior. A possible resolution of the discrepancy lies in a lack of certainty of the strategy used by rats in the Golob et al. (2001) experiments; this possibility arises from our finding that spatial problems can be solved by rats in different ways, despite the intention of the investigators to force a certain strategy.

In summary, we find that consistency of firing fields with informational stimuli is usually essential for efficient performance in a navigational task but not in guidance or beacon navigation tasks. Noticeably, reliable place cell location-specific signals were observed in all tasks, i.e., whether or not the rat had a spatial navigation task to accomplish [see also Trullier et al. (1999)]. Therefore, although place cells continuously provide background information as to the rat's location, this information appears critical only for true spatial navigation. We therefore conclude, as proposed by the spatial theory of hippocampal function, that the rodent hippocampus participates in solutions of place navigation tasks but not of simpler guidance tasks.

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