Distal Landmarks and Hippocampal Place Cells: Effects of Relative Translation Versus Rotation

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ABSTRACT: Hippocampal neurons are selectively active when a rat occupies restricted locations in an environment. These place cells derive their specificity from a multitude of sources, including idiothetic cues and sensory input derived from both distal and local landmarks. Most experiments have attempted to dissociate the relative strengths and roles played by these sources by rotating one set against the other. Few studies have addressed the effects of relative translation of the local cue set versus salient distal landmarks. To address this question, ensembles of place cells were recorded as a rectangular or circular track was moved to different locations in a room with controlled visual landmarks. Place cells primarily maintained their firing fields relative to the track (i.e., occupying new locations relative to the distal landmarks), even though the track could occupy completely nonoverlapping regions of the room. When the distal landmarks were rotated around the circular track, however, the place fields rotated with the landmarks, demonstrating that the cues were perceptible to the rat. These results suggest that, under these conditions, the spatial tuning of place cells may derive from an interaction between local and idiothetic cues, which define the precise firing locations of the cells and the relationships between them, and distal landmarks, which set the orientation of the ensemble representation relative to the external environment. *Hippocampus 2003;13:604–617.* © 2003 Wiley-Liss, Inc.

KEY WORDS: spatial orientation; single units; navigation; spatial learning; cognitive maps

INTRODUCTION

Principal neurons of the CA1, CA3, and dentate gyrus (DG) subfields of the rat hippocampus fire selectively when the animal occupies certain locations in an environment (O'Keefe and Dostrovsky, 1971; O'Keefe, 1976; Muller et al., 1987; Jung and McNaughton, 1993). Early research showed that rotation of distal landmarks caused the preferred firing locations ("place fields") to follow the landmarks and ignore local surface cues (O'Keefe and Conway, 1978; Muller and Kubie, 1987), although the local cues were shown to have an influence in blindfolded and deafened rats (Hill and Best, 1981). The surface cues in these experiments were perhaps not salient compared with the distal landmarks, however, and recent studies have demonstrated that more salient local apparatus cues (Young et al., 1994; Gothard et al., 1996a; Shapiro et al., 1997; Save et al., 2000; Knierim and McNaughton, 2001; Knierim, 2002b) and self-motion information (Sharp et al., 1995; McNaughton et al., 1996; Knierim et al., 1998; Zinyuk et al., 2000; Knierim, 2002a; Stackman et al., 2002) can have powerful influences over place cell firing locations, even in the presence of salient distal cues. The precise ways in which these various sources of information interact to produce the spatial tuning of place cells are still largely unknown, however.

Most studies that have addressed the relative influence of local, apparatus-based cues and distal landmarks have rotated one set of cues versus the other set. Only a few studies have tested the influence of translating local landmarks in an environment, and they have found that many place cells near these objects move with the objects (Gothard et al., 1996a,b). Few detailed studies have addressed the effects of relative translations of an entire behavioral apparatus relative to the distal landmarks in an environment. O'Keefe (1979) provided an anecdotal description of an experiment in which a platform was translated across a room; he reported that some cells maintained their fields relative to the distal landmarks, whereas other cells maintained their fields on the platform itself. These early results were not described quantitatively or studied thoroughly, however. O'Keefe and Burgess (1996) reported that only 3 of 28 place fields were tied clearly to the laboratory framework when a square- or rectangle-shaped apparatus was moved in the laboratory. Few details about this result were reported, however, and it is unclear whether there were salient distal

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landmarks that were visible to the rat as it foraged for food in the high-walled enclosure (see also Lever et al., 2002).

The major finding reported by O'Keefe and Burgess (1996) was the demonstration that the walls of a rectangular enclosure control the firing locations of place cells when the walls are shifted to alter the shape of the enclosure. In these types of enclosures, the walls and the cues on them can be described as both local apparatus cues and distal landmarks. They have local-cue qualities in that they are part of the recording chamber and thus the rat has direct tactile access to them, but they also have distal-cue qualities in that they are at the perimeter of the rat's field of view (Cressant et al., 1997). Thus, it remains ambiguous whether distal landmarks that are further removed from the recording apparatus will have a strong control over place fields when the apparatus is translated relative to the cues. This issue is important, for many behavioral tests are run in situations in which the animal performs on a restricted track or enclosure (e.g., 8-arm maze, T-maze, water maze), with distal cues on the walls or ceiling that are clearly removed from the within-track cues. It is often assumed that the distal visual cues provide the primary information used to define locations in these tasks (Zipser, 1985; Cohen and Eichenbaum, 1993; Pearce et al., 1998; Brunel and Trullier, 1998; Best et al., 2001), but the recent emphasis on local-cue and self-motion influence on place cells and spatial behavior (Mittelstaedt and Mittelstaedt, 1980; Etienne, 1992; Weisend et al., 1995; McNaughton et al., 1996; Whishaw et al., 1997; Zinyuk et al., 2000; Save et al., 2000; Stackman et al., 2002) makes it essential to understand the precise role that these distal landmarks play relative to the local apparatus cues in controlling the behavior of place cells under these common experimental conditions.

To investigate these interactions, ensembles of place cells were recorded as rats ran around a track that was moved to different locations of the room in three dimensions. In other sessions, the track was left in the center of the room and the distal landmarks were rotated around the track. If, under these conditions, the distal cues were a strong determinant of place cell firing, then the place fields should be drastically altered when the track was moved about the room. Most place fields remained bound to locations on the track, however, even though these same cells shifted their locations on the track when the distal landmarks were rotated. These results lend support to O'Keefe and Nadel's (1978) original view of the role of distal landmarks as providing predominantly orientation information to the distributed representation of the environment embodied by place cell firing.

MATERIALS AND METHODS

Subjects

Six male rats (three Long-Evans and three Fischer-344), aged 5–9 months, were housed individually on a 12:12 h reversed light/dark cycle. Recordings were performed during the dark portion of the cycle. The rats were maintained at 80–90% of their free-feeding weights. Animal care, surgical procedures, and euthanasia were performed in accordance with National Institutes of Health (NIH) and University of Texas-Houston Health Science Center Institutional Animal Care and Use Committee (IACUC) guidelines.

Recording Techniques

Under surgical anesthesia, a recording device (Neuro-hyperdrive, Kopf Instruments, Tujunga, CA) allowing the independent manipulation of 6–18 tetrodes was implanted over the right hemisphere (3.5–4.5 mm P, 1.4–2.5 mm L from bregma). After 2–7 days of recovery, the tetrodes were slowly advanced over the course of several days and positioned in the CA1 pyramidal cell layer by monitoring the depth profile of hippocampal sharp waves (Buzsaki, 1986) and observing the increase of multi-unit activity. Some tetrodes were further lowered until the presence of strong gamma activity (Bragin et al., 1995a), large dentate spikes (Bragin et al., 1995b), and low rate units (Jung and McNaughton, 1993) suggested that they were in the dentate gyrus. All tetrode advancement sessions were performed as the rat sat quietly or slept in a towel-lined dish next to the recording electronics and computer outside the curtained behavioral area.

Training

Two types of apparatus were used in the experiments: a circular track (56-cm inner diameter [ID], 76 cm outer diameter [OD]) and two rectangular tracks (first track: 10-cm-wide arms, 45 × 50-cm OD; second track: 9-cm-wide arms, 49 × 59 cm OD). The tracks stood on blocks 13 cm above a small rectangular table (61 × 51 cm). The tracks, which contained no salient surface cues, were wiped clean with 70% ethanol before each recording session. Lighting was provided by a single 25-W bulb centered on the ceiling. A circle of black curtains (275-cm diameter) reaching from ceiling to floor surrounded the track. Attached to the curtains or standing on the floor at the perimeter of the room were a number of salient distal landmarks. For three rats, the visual cues consisted of a triangular, dotted piece of cardboard, a string of three plastic saucers, a striped cardboard circle, and a large white paper drape hung on the curtain. A hula-hoop was placed on the floor leaning against the white paper drape. For the remaining rats, the cues consisted of a brown cardboard circle, a white box, an intravenous (IV)-fluid stand with a lab coat and a blue drape, a black-and-white striped card, a roll of brown wrapping paper, and a white card hanging on the curtain or placed on the floor at the perimeter of the curtain. There were no differences in the results from these two sets of landmarks. A white noise generator was located directly beneath the small table on which the tracks stood. For the training sessions, the rat was carried directly into the room on a pedestal, the headstage was connected to the recording cable, and the animal was placed on the track at a random starting point. The task consisted of running clockwise around the track for chocolate sprinkles placed at arbitrary locations on the track (about two rewards per lap), such that no local areas of the track were preferentially associated with food reward. The experimenter moved around the track frequently so as not to become a stable landmark for the rat. Occasional attempts by the rat to move counterclockwise were discouraged by blocking its progress with a piece of cardboard.

TABLE 1.

*Sequence of Session Types for Each Subject**

	Recording day			
Rat	1	2	3	4
18	Circle[a]	Circle (16)		
19	Rectangle (2)	Circle (5)		
20	Abort[b]	Abort[b]	Circle (9)	
22	Circle (18)	Circle	Rectangle (8)	Rectangle 2 (10)[c]
30	Rectangle (10)	Rectangle	Circle (8)	Circle
31	Rectangle (19)	Rectangle	Circle (23)	Circle

*The number of cells analyzed in each data set is shown in parentheses. With the exception of rat 18, the first day of each track type was analyzed in detail. There were no obvious differences between the days that were analyzed in detail and the other days that were not (although the small number of repetitions of each apparatus in this experiment leaves open the possibility of greater differences with increasing repetitions).

[a]This day was not analyzed in detail because the 45-degree rotation sessions were not performed. The results of the translation sessions were similar to the analyzed data from day 2.

[b]These recording sessions were aborted after the first standard session due to poor behavior of the rat. The rat did not experience any translation or rotation sessions on these days.

[c]This experiment was performed on a new rectangular track in a new room (see text).

Before the experiments described in this report, the rats in this study had experience running for food reward on different tracks in another room with different cues. Therefore, training sessions with the particular cue configuration, apparatus, and room used in the present experiment ranged from 1–7 sessions over 1–2 days.

Experimental Protocol

Each day before the behavioral sessions, baseline data were collected from the rat during sleep or awake immobility for 20–30 min next to the computer outside the curtained area. These data were compared with a baseline session at the end of the day to help assess overall recording stability. After the baseline session, the rat was placed in a covered box and, after 30 s, was taken in the box on a brief walk in the computer room and around the track two to three times, in order to disrupt the animal's ability to maintain a strong sense of direction between the curtained behavioral area and the external environment (Knierim et al., 1995; Jeffery and O'Keefe, 1999). The headstage was attached and the rat was placed on the track at a random starting point. Neuronal signals were recorded with the Cheetah data acquisition system (Neuralynx, Tucson, AZ). After 10–15 laps, the rat was again taken on a brief random walk in the box. Standard sessions were performed with the track in the center of the room, with the distal cues positioned as during training. For days in which the rectangular track was used, the recording sequence was as follows: (1) standard 1, (2) vertical translation, (3) standard 2, (4) east translation, (5) west translation, (6) standard 3, (7) north translation, (8) south translation, and (9) standard 4. For days in which the circular track was used, the recording sequence was: (1) standard 1, (2) vertical translation, (3) standard 2, (4) east translation, (5) west translation, (6) standard 3, (7) 45° rotation of distal landmarks, (8) 45° further rotation, (9) standard 4.

Data Analysis

One-dimensional firing rate arrays were generated by dividing the track into equal-sized position bins (~2.5 cm/bin) and, for each bin, dividing the number of spikes fired by the amount of time the rat occupied that bin. The firing rate arrays were smoothed by averaging each bin with its immediate neighbors. Place field similarity across sessions was quantified by calculating the Pearson product-moment correlation between the firing rate arrays corresponding to the two sessions. For translation sessions, correlations were computed if the cell met the following criteria for at least one of the two sessions being correlated: (1) the spatial information score (a measure of spatial tuning based on information theory) (Skaggs et al., 1993, 1996) was $\geq$1 bit; (2) the cell fired $\geq$50 spikes, a minimum number to ensure reliability of the spatial information score (Skaggs et al., 1996); and (3) the statistical significance of the information score was $P < 0.01$. This probability level was calculated by a Monte Carlo type analysis, in which the spike data were time-shifted relative to the rat's position data by some random fraction of the session length, and the information score was calculated for 100 of these random time-shifted firing rate maps. If the information score of the real rate map was greater than all 100 random time-shifted rate maps, then the score was considered to be significant at the 0.01 level (Gothard et al., 1996b). Each rat experienced 2–4 days of recording, on either the circular track or both types of tracks. Data were analyzed separately

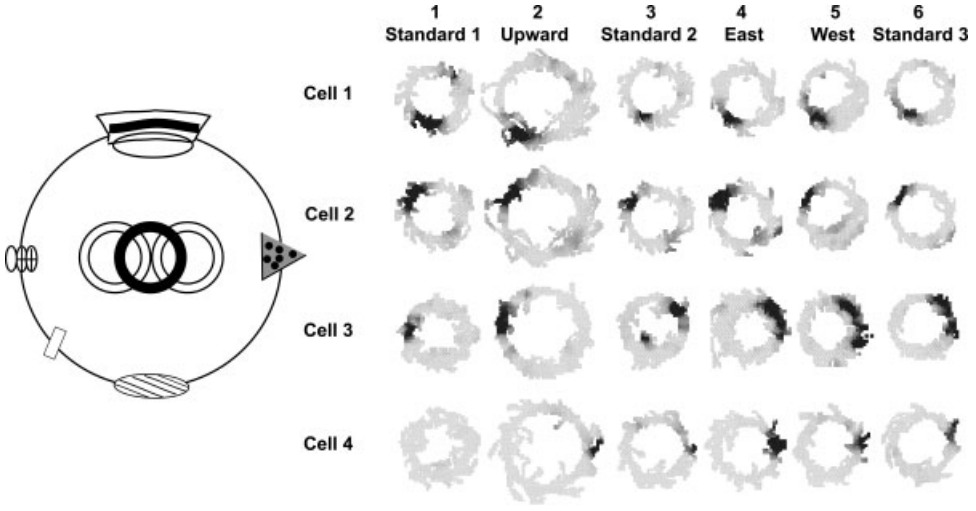

FIGURE 1. Representative examples of effects of circular track translations. At left is a scale drawing of the locations of the track relative to the room. At right are four representative examples. Cells 1 and 2 exemplify the typical response, in that the place cells remained bound to the track. Cells 3 and 4 exemplify the responses of a minority of cells that changed in some sessions but were bound to the track in most sessions. In general, place cells fired in their appropriate locations on the track from the first lap of each session.

for the circular track and for the rectangular track. Because recordings were made at the same electrode locations across days, only the first experience on each track was analyzed for each rat (Table 1). For statistical comparison, the correlation scores (r) were converted to a normal distribution by

$$z = 0.5 * \log[(1 + r)/(1 - r)]$$

and analysis of variance (ANOVA) tests were performed on the transformed z-scores.

Rotation Analysis for the Circular Track

For each cell, the Pearson product-moment correlation between its firing-rate arrays in the prerotation and postrotation sessions was measured, and then the firing rate bins of the postrotation session were shifted by one bin, equal to a 5° rotation. The firing rate array of the prerotation session was correlated with the 5°-shifted array of the postrotation session, and then the postrotation session bins were again shifted by 5°. This was repeated 71 times, and the rotation angle that produced the highest correlation was taken as the amount that the place field had rotated between the two sessions. The same criteria as above were applied to determine which cells to include in each correlation pair.

RESULTS

Multiple single units from CA1, CA3, and/or dentate gyrus (mean 11.6 units with place fields per day) were recorded from six rats. Of the 79 principal cells analyzed in detail for the circular track sessions, 55 were from CA1, 5 were from the dentate gyrus granule cell layer, and 19 were from the region of the hilus in which the CA3 and dentate gyrus cell layers overlap. Because histology was not performed immediately after recordings, the identity of these latter cells remains ambiguous. Of the 39 cells analyzed in detail for the rectangular track sessions, 22 were from CA1, 5 were from the dentate granule layer, and 12 were from the region where CA3 and the dentate granule layer overlap. There were no differences in the responses of the neurons from the different areas, so all neurons were analyzed together.

Translations of the Circular Track

Figure 1 shows the place fields for representative cells as the circular track (an apparatus that does not provide any corners or other geometric cues that might signal location on the track) was moved around the environment. The first session was a standard session, followed by sessions in which the track was raised vertically 48 cm, lowered to the standard location, moved 33 cm to the east, moved 67 cm to the west, and then returned to the standard location. Cells 1 and 2 were completely bound to the track coordinates, regardless of the 3-dimensional location of the track in the room. Cells 3 and 4 represent a minority of cells that changed in one of the early manipulations and then remained tied to the track. Cell 3 was part of an ensemble of 14 cells recorded simultaneously that either rotated their place fields by ~150° (10 cells) or remapped (4 cells) when the track was moved from the vertically raised position (session 2) to the standard position (session 3). Such anomalous rotations of place fields relative to the distal cues have been reported previously (Jung and McNaughton, 1993; Knierim et al., 1995, 1998). When the track was subsequently translated east and west in the horizontal plane, the place cells retained their new locations on the track regardless of the location of the track in the room. Cell 4 originally had no field on the first standard session but gained a new field when the track was raised to the vertical position. It retained this new field on the track in all subsequent sessions.

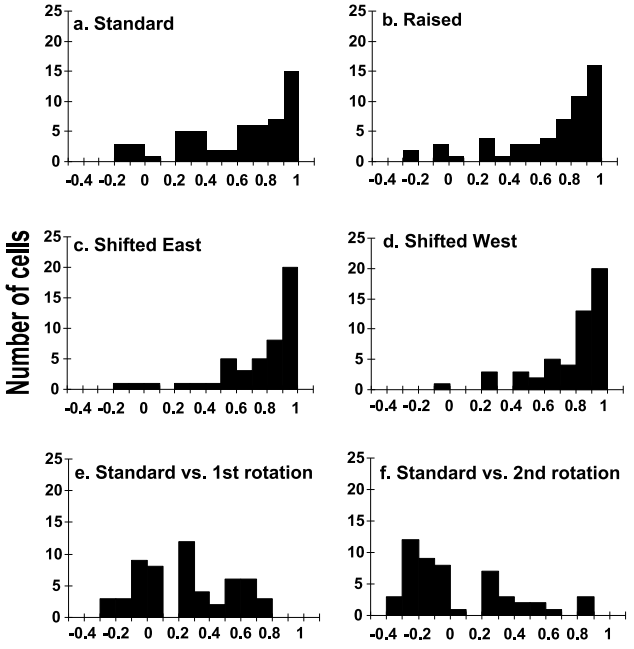

FIGURE 2. Spatial correlation distributions between circular track sessions. A: Median correlation between the two standard sessions before and after the east-west translations was 0.73, indicating that most place fields maintained the same field, although a minority changed between the sessions. B: Median correlation between the first standard session and vertically translated session was 0.78. If place fields had completely changed their firing locations on the track as the result of the manipulation, the median correlation would be close to 0 or negative (Knierim and McNaughton, 2001). C: Median correlation between the eastward translated session and the standard session preceding it was 0.86. D: Median correlation between the eastward translated session and the westward translated session was 0.87. E: Median correlation between the first 45°-rotation session and the standard session preceding it was 0.13. F: Median correlation between the second 45°-rotation session and the standard session (standard 3) was −0.09.

These results were quantified by calculating for each session pair the pixel-by-pixel correlation of firing rates between sessions. Figure 2A shows the distribution of the correlations for the standard sessions that immediately preceded and followed the east-west translations. As expected, most cells had a high correlation between these standard sessions (median = 0.73). Figure 2B–D shows the distribution of correlations between the first standard session and the vertically translated session (Fig. 2B; median = 0.78), between the east-translated session and the standard session preceding it (Fig. 2C; median = 0.86), and between the east-translated and the west-translated sessions (Fig. 2D; median = 0.87). For statistical comparison, the correlations were transformed to a normal distribution, and an ANOVA showed no significant differences among these distributions ($F_{3,204}$ = 2.28, n.s.). For each session pair shown in Figure 2, we also calculated for each cell the difference in mean firing rate, the difference in information score, and the difference in place field size (based on the method of Muller et al., 1987). ANOVAs showed no significant differences among the session pairs for any of these measures.

The correlation analysis described above is an attractive quantitative test, because it does not require occasionally arbitrary judgments about whether a place field is qualitatively similar enough to be called the same field in two different sessions. Nonetheless, this analysis can be insensitive to certain effects, such as changes in place field firing rate. That is, a strong place field in one session may fire only a few spikes in another session but, if the spikes are in the same location, the correlation between the two sessions will be high. Although no significant effects were seen in overall firing rate among the different track locations, it is possible that individual cells showed different effects on different trials. To complement the correlation analysis, cells were categorized, according to the criteria for having a place field (see Methods), into four groups: having a place field in both sessions, having no place field in either session, having a significant place field after the translation only, and having a significant place field before the translation only (Table 2). For the cells that had place fields in both sessions, the median correlation was 0.90, showing that the cells typically fired at the same location on the track. In only six cases was the correlation <0.4; these cases are shown in parentheses in Table 2. It is important to note that this type of classification scheme will unavoidably lead to arbitrary assignments; for example, a cell that has an information score of 0.95 in one session and 1.05 in the other, while only marginally different, will be classified as having a place field in only one of the sessions. Thus, the exact numbers in each category are not of particular interest. Rather, the important point is whether the pattern of numbers changes between the standard sessions and the translation sessions. A χ^2 analysis demonstrated that there was no effect of translation on the categorization scheme (χ^2= 7.29, n.s.). Thus, this analysis supports the correlation analysis.

Rotations of the Distal Landmarks

It is known that local cues and idiothetic cues can exert an influence over place cells, especially when the distal landmarks are unavailable or are perceived as unstable (Hill and Best, 1981; Quirk et al., 1990; O'Keefe and Speakman, 1987; Knierim et al., 1995; Best et al., 2001). It is possible that the distal landmarks in the present experiment were not salient, or that they were somehow perceived as unstable and therefore had no influence over the place fields. To test this possibility, place cells were recorded during two extra sessions on the circular track (immediately after the last

TABLE 2.

*Classification of Response Types for the Circular Track**

	Standard 2–3	Standard 1–Vertical	Standard 2–East	East–West
"Gain"	18	12	11	13
"Lose"	11	9	7	11
Maintain	27 (1)	38 (5)	31 (0)	31 (0)
No field	25	22	32	26

*Numbers in parentheses indicate cells that had correlations of < 0.4.

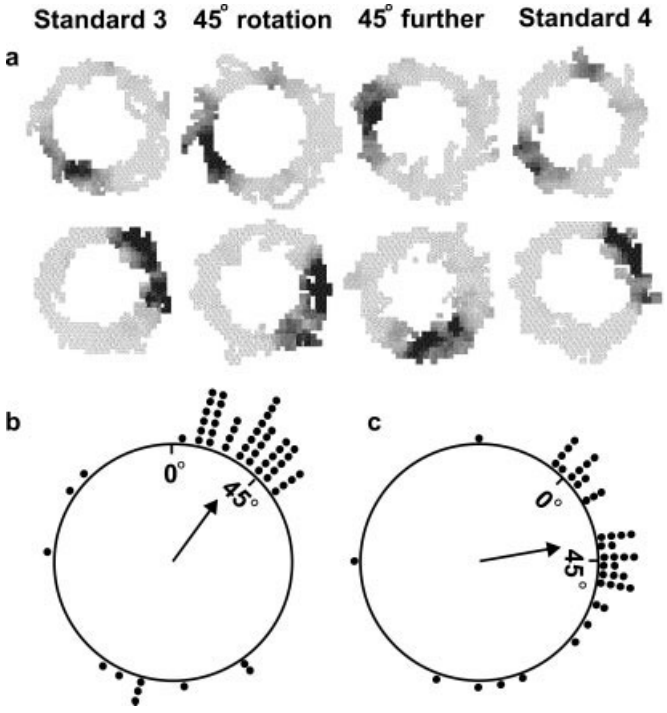

FIGURE 3. Effects of distal cue rotation. A: Representative examples of cells that rotated their place fields along with the 45° rotation of the distal landmarks. B: Amount rotated by each place field between the first rotation session and the standard session preceding it. The mean rotation was 35°. C: Amount rotated by each place field between the first and second rotation sessions, in which the distal landmarks array was rotated by a further 45° (90° total rotation compared with the standard session). The 0° reference is plotted relative to the 45° reference of the previous session, to illustrate how the place fields rotated relative to the laboratory frame of reference. The mean rotation was 38°, demonstrating again that the cells on average rotated their fields in the same direction as the distal landmarks.

translation session of the day) in which the distal landmarks were rotated in 45° increments relative to the track. In contrast to the translation sessions, the rotation sessions caused the place fields to be weakly correlated between sessions (Fig. 2E,F). An ANOVA of the transformed correlations between the standard sessions (Fig. 2A), between the standard and 45°-rotated session (Fig. 2E), and between the standard and 90°-rotated session (Fig. 2F) was highly significant ($F_{2,135} = 42.6$, $P < 0.0001$). The correlations were weak in these sessions because rotation of the distal landmarks usually caused the place fields to rotate along with the landmarks or to otherwise change their firing properties (Fig. 3A). Figure 3B,C shows the amount that each place field rotated after the first and second 45° rotation sessions; the mean rotation angle was ~35° between each session, indicating that the distal cues controlled, albeit imperfectly, the firing of the place cells after the rotation. These results replicate the classic findings that rotation of distal landmarks causes place fields to rotate accordingly, and they show that the predominance of the local and idiothetic cues during the translation sessions was not the result of the rats' inability to perceive, or tendency to disregard, the distal cues. In two animals, the fields did not follow the second rotation (between sessions 7 and 8), staying on average at the 0° mark. The lack of distal cue control in these rats is likely the result of uncontrolled laboratory cues dominating over the controlled distal landmarks (O'Keefe and Speakman, 1987). In some sessions there was a partial remapping after the cue rotations, perhaps as the result of conflicts between the distal landmarks and the rat's internal representation of direction (Knierim et al., 1995, 1998). Regardless of whether the cue rotations produced a corresponding rotation of the place fields or a partial remapping of the fields, these results demonstrated that the cells were affected by rotations of the distal landmarks and controlled by them in ways similar to those reported in the literature.

Translations of the Rectangular Track

Figure 4 shows the place fields for representative cells as the rectangular track was moved around the environment. The first session on the rectangle was a standard session, in which the track was located in the center of the room at the same position occupied during all prior training trials. In subsequent sessions, the track was translated 48 cm vertically, back to the standard location, 60 cm to the east, 120 cm to the west, back to the standard location, 38 cm to the north, 76 cm to the south, and finally back to the standard location. For cells 1 and 2, the place fields fired on the same location on the track regardless of where the track was located in the room. Note that when the track was located at the north, east, south, and west locations, it occupied completely nonoverlapping regions of the room, corresponding to widely different distributions of angles to the distal landmarks, yet the place fields of these cells were completely insensitive to these differences.

Identical results were obtained in an extra set of sessions run on one rat, in which the location of the rectangular track was rapidly shifted with the rat still on the track (Fig. 5). After a full standard session, the rat ran one lap in the standard location and then the track and rat were shifted rapidly to the east. In the next session, after one lap at the standard location, the track and rat were shifted rapidly to the west. In these sessions, in addition to the changes in bearings to distal landmarks, the rat received passive idiothetic information that it was being moved across the room, yet 13 of 15 place fields were still bound to the track after the standard-east shift and 14 of 15 place fields were bound to the track after the standard-west shift.

Figure 4 also shows examples of place fields that changed their firing properties in one or more of the translation sessions. Cell 3 maintained the same field on the track during the first four sessions (although the firing rate began to decrease in session 4). The firing rate was greatly reduced when the track was shifted to the west, although the cell still fired a few spikes in the same track location. Interestingly, when the track was returned to the standard position (session 6), the cell was still fairly quiet, firing only a few spikes. When the track was shifted to the north, the cell regained a strong place field at the same track location, and maintained this field for the remainder of the sessions.

Cell 4 maintained its place field for the first three sessions, then became much quieter when the track was shifted to the east (session 4), firing a few spikes in the same track location. When the track was shifted to the west, the cell regained a strong place field

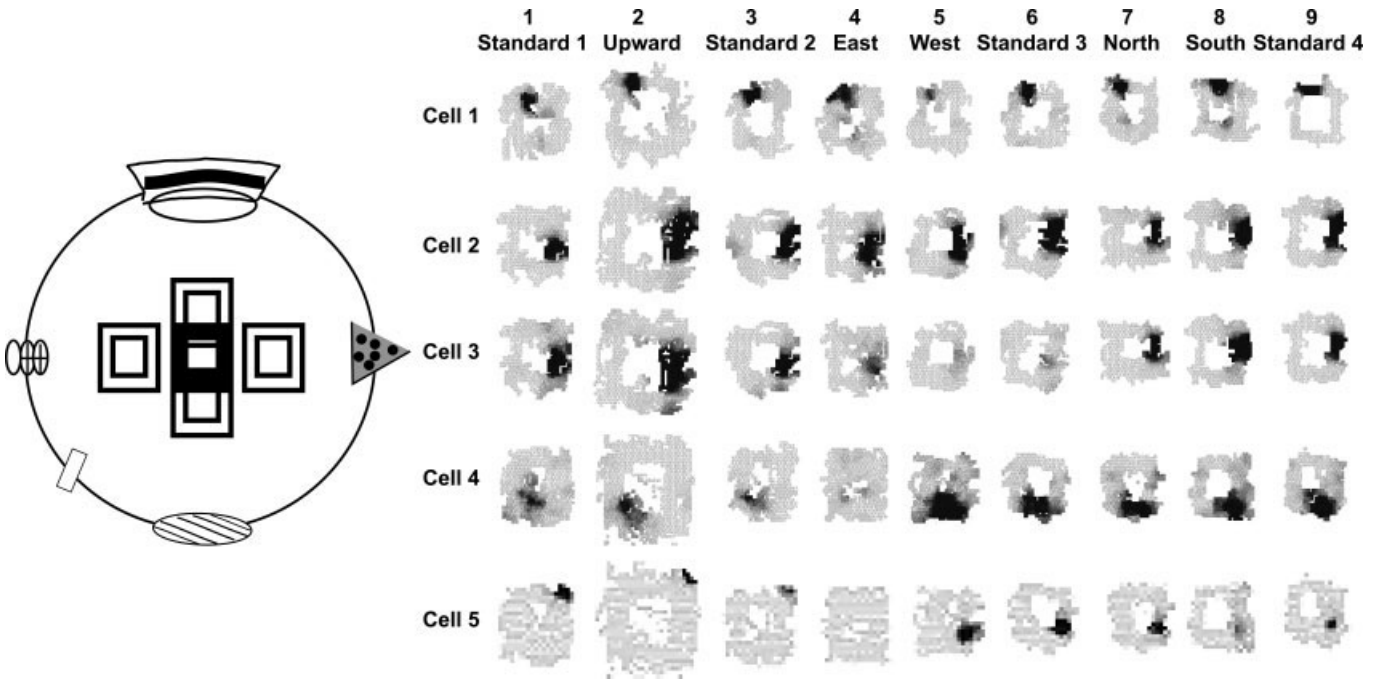

FIGURE 4. Representative examples of effects of rectangular track translations. At left is a scale drawing of the locations of the track relative to the room. At right are five representative examples. Cells 1 and 2 fired at the same location on the track regardless of the location of the track in the room. Cell 3 had a place field on the same location on the track for the first four sessions. When the track was shifted to the west, the cell fired weakly at the same location (about two spikes per lap); it maintained this weak firing when the track was returned to the standard location (standard 3). The cell regained a robust place field when the track was shifted north, and it maintained this field in the remaining sessions. Cell 4 maintained a place field in all sessions except the east session, although the field was stronger and larger in the remaining five sessions. Cell 5 had a place field on the same track location for the first three sessions, then became quiet when the track was shifted east. When the track was shifted west, the cell developed a new field in a new location on the track, and it maintained this field in all subsequent translations of the track.

on the proper arm, but the field became stronger and larger than the original. This larger field was then maintained for all the remaining sessions. Cell 5 was recorded simultaneously with cell 4. When the track was shifted to the east, the cell lost its place field, and then developed a new field when the track was shifted west. It maintained this new field for the rest of the sessions, even when the track was returned to the standard position, firing on the same location on the track when the track was in the west, standard, north, and south positions.

Figure 6 shows the distribution of correlations for the rectangle data in the format shown previously for the circular track data. Figure 6A shows the distributions of correlations for the two standard sessions immediately preceding and following the east and west translations; the median correlation was 0.67. The remaining histograms show the correlations between the first standard and the vertical translation (Fig. 6B; median = 0.77); between the second standard session and the east translation (Fig. 6C; median = 0.49); between the east and the west sessions (Fig. 6D; median = 0.52); between the third standard and the north translation (Fig. 6E; median = 0.59); and between the north and the south sessions (Fig. 6F; median = 0.78). The correlations were transformed into a normal distribution, and an ANOVA demonstrated that there were no significant differences among the distributions ($F_{5,133} = 1.29$, n.s.).

For each session pair shown in Figure 6, we also calculated for each cell the difference in mean firing rate, the difference in information score, and the difference in place field size. There were no significant differences among the session pairs for firing rate or for place field size, but there was a significant difference for the information score ($F_{3,91} = 8.64$, $P < 0.0001$). Post hoc tests showed that there was no change in information from the standard to the vertical session, but that there was a significant average decrease of 0.59 bits of information from the standard to the east translation. When the track was shifted east to west, the information score increased by an average of 0.45 bits.

A similar categorization analysis was performed as was done on the circular track data. This analysis is particularly important for these data, because the overall correlations are lower for the rectangular track compared with the circular track (see below) and because there was a significant effect of the translations on the information score. Table 3 shows the categorization of cells for the rectangular track. For the cells that had a place field that met criteria in both sessions of a pair (Maintain), the median correlation was 0.80, showing that the firing locations were highly correlated on the track; of the 72 samples, only 10 had correlations of <0.40, and these cells were scattered among all six session comparisons. As with the circular track, a χ^2 analysis revealed no significant effect of the translations on the distribution of response types ($\chi^2 = 12.6$, n.s.).

It was of interest to see whether the cells that had significant place fields in both sessions of a pair, but with low correlations, were consistent with the interpretation that the place fields shifted on the track to best align themselves with a particular location in the room. For example, a cell that fired on the east arm during the standard session might fire on the west arm when the track was shifted to the east, as the west arm would be closest to the prior location of the place field relative to the room cues. None of the 10 session pairs with correlations of <0.40 were convincingly consistent with this interpretation, however. Nonetheless, inspection of the other place fields did reveal one cell that may have behaved according to this scenario (Fig. 7). This cell fired at the southeast corner of the track in the second standard session (session 3), as it did on the first standard and vertical sessions (not shown). When the track was shifted to the east, the place field shifted to the southwest corner of the track (session 4). When the track was shifted west (session 5), the cell returned to the southeast corner, and maintained that location back at the standard location (session 6). When the track was shifted north (session 7), the cell lost a strong place field. The place field returned when the track was shifted to the south, but this time the cell fired on the northwest corner of the track (session 8). Interestingly, it maintained this pattern of firing when the track returned to the standard location (session 9). Thus, although complicated, the firing of this cell may be somehow influenced by room location, in that it may shift its firing field on the track to the location that is closest to an absolute location in the room. As this is the only convincing example of such a cell in the data set, however, it is unclear whether this is a real phenomenon or a chance event of arbitrary remapping when the track is shifted. Nonetheless, such cells would be consistent with prior reports from O'Keefe (1976) and O'Keefe and Burgess (1996).

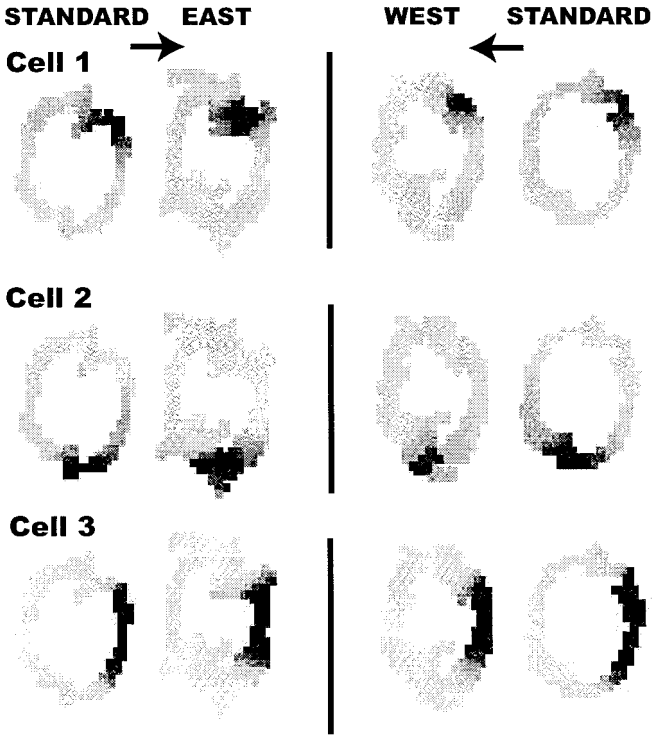

FIGURE 5. Representative examples from one recording session in which the track was rapidly translated with the rat on the track. The rat ran one lap in the standard location, after which the track was moved to the east position. In the next session, the rat ran a lap in the standard location, after which the track was moved to the west position. Cells typically maintained their place fields on the track, even though the rat received passive idiothetic information that the track was being moved to a new location in the room. In the standard-east translation, 13/15 cells maintained their fields on the track. In the standard-west translation, 14/15 cells maintained their fields on the track.

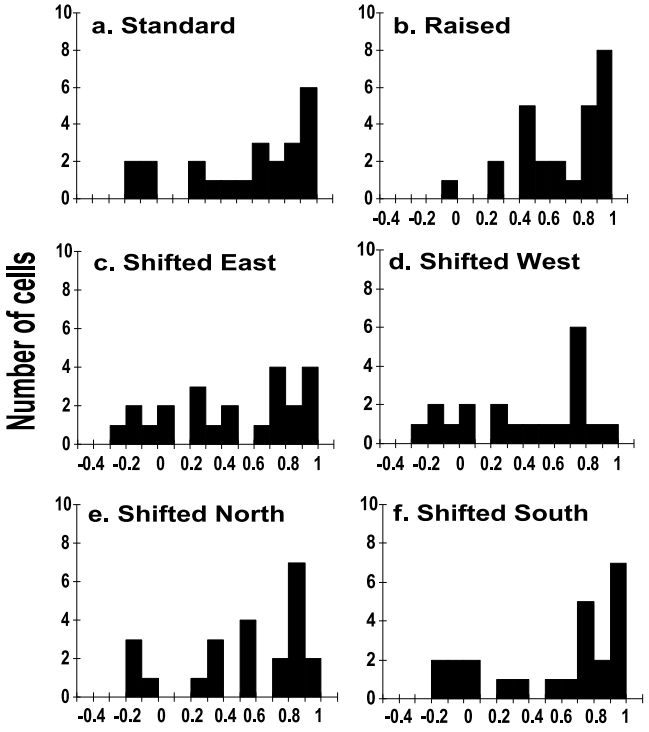

FIGURE 6. Spatial correlation distributions between sessions on the rectangular track. A: Median correlation between the two standard sessions before and after the east-west translations was 0.67, indicating that most place fields maintained the same field, although a minority changed between the sessions. B: Median correlation between the first standard session and the vertically translated session was 0.77. C: Median correlation between the eastward translated session and the standard session preceding it (standard 2) was 0.49. D: Median correlation between the eastward translated session and the westward translated session was 0.52. E: Median correlation between the north session and the standard session preceding it (standard 3) was 0.59. F: Median correlation between the north and the south sessions was 0.78.

Comparison Between Circular and Rectangular Track Data

For both the circular and rectangular tracks, although most cells maintained high correlations when the tracks were translated, some cells had low correlations. The correlations, however, were not statistically different between the standard sessions and between the translated sessions. Nonetheless, inspection of Figures 2

TABLE 3.

*Classification of Response Types for the Rectangular Track**

	Standard 2–3	Standard 1–Vertical	Standard 2–East	East–West	Standard 3–North	North–South
"Gain"	4	4	2	9	7	8
"Lose"	8	8	10	5	7	6
Maintain	14 (2)	16 (0)	12 (4)	9 (2)	10 (1)	11 (1)
No field	14	12	16	17	16	15

*Numbers in parentheses indicate cells that had correlations of <0.4.

and 6 suggests that the place fields were more strongly bound to the circular track than to the rectangular track. To test this, a two-way ANOVA (track type vs session comparison) was performed on the z-transformed data from the four rats for which data from both tracks were collected. (The other two rats, in which only circular track data were collected, were excluded to help prevent a potential bias from intersubject variability.) Because no north and south translations were performed on the circular track, these session types were excluded from the ANOVA. A significant main effect was found for the track type variable ($F_{1,215} = 9.03$, $P < 0.005$), but there was no main effect of the session type ($F_{3,215} = 0.82$, n.s.). The interaction between these two factors was significant ($F_{3,215} = 2.69$, $P < 0.05$). The data from individual rats were inspected for the rectangular track sessions; it was discovered that most of the low correlations came from a single subject (rat 31) that had unstable place fields on the track during the translation sessions. As in the examples of Figure 5C–E, however, the place fields that remapped were not confined to a single room location; rather, they tended to remap between certain sessions and then maintain that field on the track when the track was moved to a new location. For this rat, the median correlation for the center-to-east and the east-to-west translations was 0.10, whereas for the other three rats, the median correlation was 0.78. Interestingly, when the circular track experiment was performed on this rat 4 days later, its place fields were strongly tied to the track (median correlation = 0.90). Thus, there was some degree of both inter-subject and within-subject variability in the degree to which the place fields were bound to the track.

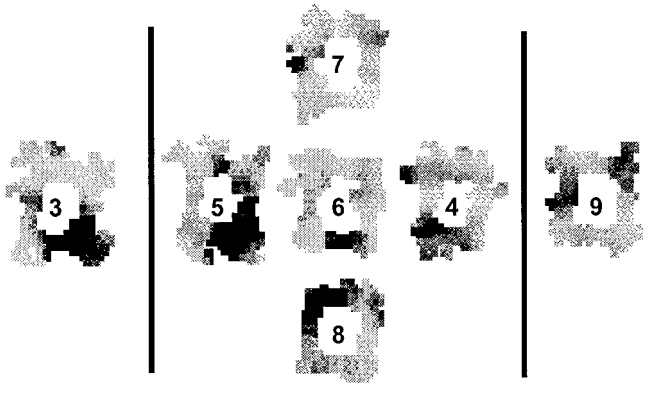

FIGURE 7. One place cell that may have been influenced by an interaction between track and room location. Session numbers are shown in the middle of each place field plot. The first standard and vertical sessions are not shown. This cell fired at the southeast corner of the track in the standard session (session 3), but then the place field shifted to the southwest corner of the track when the track was shifted to the east (session 4), as if the field was firing at the location on the track closest to the original location in the room. When the track was shifted to the west, the cell returned to the southeast corner. When the track was shifted to the north, the cell did not have a strong place field. When the track was shifted south, a strong place field formed on the northwest corner of the track. This firing pattern was then maintained when the track was moved back to the standard location.

One rat that contributed only 2–5 data points to each rectangular track correlation analysis (rat 22) also had a large amount of instability but, like rat 31, the instability did not manifest itself as place fields that were bound to a single room location. Rather, place fields tended to remap between some sessions and remain bound to the track in others. Unlike the other rats, this rat was the only subject that had prior experience of rotational instability of the same distal cues in a prior experiment, which may explain the place field instability here. This rat also contributed most of the low correlations in the circular track data. This rat was subsequently trained on a new rectangular track in another recording room with different visual cues for four sessions over 2 days. When the horizontal track translations were performed in this new, stable environment, most place fields remained bound to the track (median correlation for standard sessions = 0.81; standard to east = 0.87; east to west = 0.84; standard to north = 0.62; north to south = 0.88). Two cells, however, behaved similarly to the cell in Figure 7, in that they appeared to be tied to both the track and the room locations (Fig. 8). Cell 1 was tied to the track for the first four sessions (no vertical session was run on this day). When the track was shifted north, the cell maintained its field on the track but also formed a new field at a similar location in the room frame of reference. This new field was maintained on the track in subsequent sessions. Cell 2 had 2 place fields in the first four sessions that were bound to the track (at the southwest and northeast corners). When the track was shifted to the north, a new field appeared at the southeast corner of the track, in a location in the room similar to the prior location of the northeast corner of the track. Like cell 1, this new field remained bound to the track during subsequent translations of the track. Thus, some cells may have been sensitive to location in room coordinates, but these cells were rare in the

present study (only three examples). In addition, when new subfields formed on the track, these new fields became quickly bound to the track itself.

A further analysis was performed to characterize the pattern of changes that occurred when a place field was altered by the shift of the apparatus. If a place field were tied to a restricted location in the room, the place field should fire only when the track occupied that location. Thus, each place field should be active in only one (or perhaps two) track locations. To test this, the number of track locations (relative to the room) in which the cell fired at the same position on the track was counted for each place field. For example, the circular track occupied four different locations in the room during the experiment (standard, vertical, east, and west). A cell that fired at the same place on the track in all four room locations would thus get a score of 4, whereas a cell that fired at the same place on the track in all room locations would get a score of 6. If a cell had more than one subfield on the track, each subfield was scored separately. For the circular track almost all fields had a score of 4 (Fig. 9A), consistent with the high spatial correlation scores for this track. For the rectangular track, most cells had a score of 4 or 5 (Fig. 9B), consistent with the lower overall spatial correlations. Importantly, however, 93% of the place fields had a score of ≥ 2, showing that they fired at the same place on the track in more than one room location; 80% of the cells fired at the same location on the track at three or more room locations; and 64% of the fields fired at the same location of the track in four or more room locations. Thus, even though translations of the rectangle caused some global perturbation of the place fields, this perturbation could not be explained by the cells' being spatially selective only for restricted locations relative to the room cues.

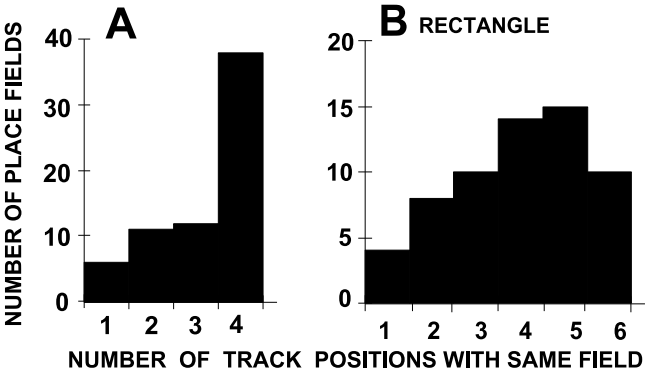

FIGURE 9. Histograms of the number of locations in the room that each place field fired on the same location on the track. A: For the circular track sessions, the track was located in four room positions (standard, vertical, east, west). If a cell fired on the same location on the track in all four room positions, it received a score of 4; if it fired in only one of the four positions, it received a 1. B: For the rectangular track sessions, the track was located in six room positions (standard, vertical, east, west, north, south). Thus, if a cell fired on the same track location in all six room positions, it received a score of 6. For both circular and rectangular track sessions, the overwhelming majority of place fields fired on the same track location in multiple room positions.

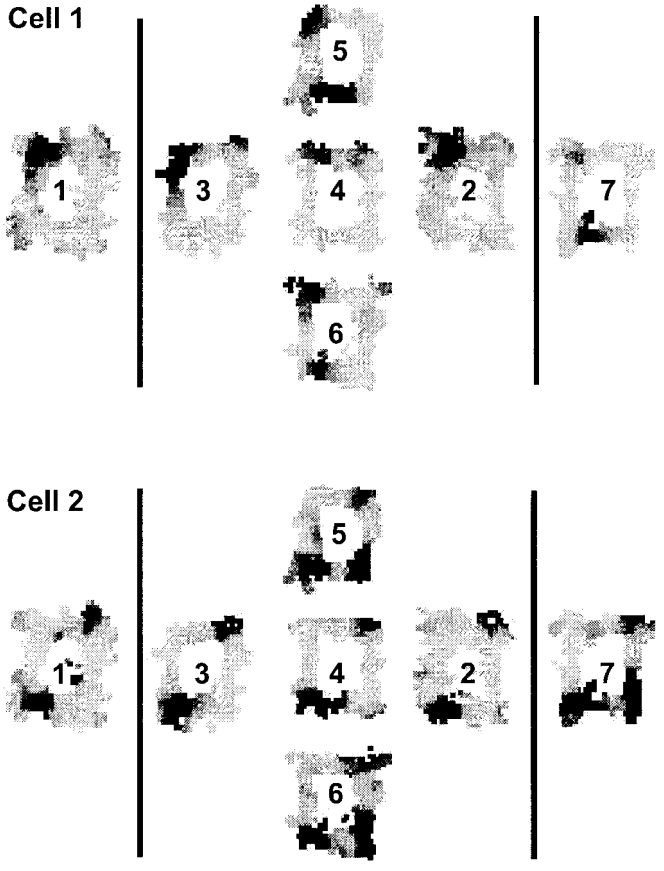

FIGURE 8. Two more place cells that may have been influenced by an interaction between the track and the room location in the extra session ran on rat 22 (Table 1, day 4). In each case, when the track was shifted north, new place fields developed on the south arm of the track in room locations near where the cell fired in the standard sessions. In both cases, these new place fields became immediately bound to the track when it was shifted in subsequent sessions.

DISCUSSION

When an animal moves from one location to another on a behavioral track, place cells are sensitive to differences in location on the order of 10–20 cm. When the track itself was moved to new locations 33–120 cm away in the present study, however, the place cells usually did not discriminate between these different locations, relative to the distal landmarks. These results can be interpreted in light of two different models of hippocampal function: (1) the potentially differing roles of local and distal landmarks in governing place cell activity, and (2) the hypothesized functions of pattern completion and pattern separation.

Local Cues Versus Distal Cues

O'Keefe and Nadel's cognitive map theory argued that distal landmarks were not good candidates for specifying precise locations, because the geometric relationships among distal landmarks do not change much as the animal moves between two adjacent locations (O'Keefe and Nadel, 1978). These investigators argued that local apparatus cues and self-motion information were more suitable to provide the fine-grained information necessary to specify the tight spatial tuning of place cells. Distal landmarks, on the other hand, were highly suitable for setting the overall orientation of the spatial representation relative to the external environment (O'Keefe and Nadel, 1978; Burgess et al., 2000; Hartley et al., 2000). The present study is consistent with this idea, in that the large majority of place cells were more closely bound to the location of the rat on the track than to the location of the rat in the external room. If the cells were using differences in the distances and angles to distal landmarks as the primary input to distinguish two different places on the track, the larger differences in these relationships, when the track was moved across the room, should have caused a significant proportion of cells to change their place fields, become silent, or develop a new field. Instead, compared with local geometry cues and idiothetic cues, the distal cues had a relatively minor influence in determining the firing location of the place fields on the track. When the distal cues were rotated relative to the circular track, however, the place fields tended to rotate to follow the cues.

A number of caveats must be applied to a generalization of this interpretation. There is no clean dichotomy between local and distal cues in most environments. For example, in a high-walled enclosure, such as a cylinder or box, the walls (and cues on them) can be considered local cues, in that they are part of the recording apparatus and the rat can touch, taste, feel, and otherwise interact closely with them. They can also be considered distal cues, in that they are at the perimeter of the apparatus and the rat never moves to the "other side" of the cues. Cressant et al. (1997, 1999) have shown that distinct objects can control the orientation of the place cell map when they are placed at the periphery of a cylinder, but not when they were placed near the center (see also Save and Poucet, 2000; Zugaro et al., 2001). Thus, the same cues have different properties depending on their locations within the recording chamber.

In natural environments, the distinction between local and distal cues can also be vague. Although mountains in the background may always be distal cues, nearer landmarks may act in different ways. When the animal is far from a certain bush, for example, the bush may act as a distal cue, part of the overall panorama of the environment. As the animal approaches the bush, however, it may begin to take on the properties of a local cue. Objects or cues on the walls can have different effects on place fields depending on the distance of the field from the altered cue (Muller and Kubie, 1987; Hetherington and Shapiro, 1997; Fenton et al., 2000a,b), so it is possible that there is a distance-dependent function that determines whether a set of landmarks can control the entire hippocampal map or merely exert an influence over a local subset of place fields next to them.

In certain experimental situations, there is a more clear-cut operational definition of local cues (those on an open platform or track upon which the animal behaves) and distal landmarks (those removed from the track and not directly approachable by the animal). It is under these conditions that the initial studies of place fields were performed (O'Keefe, 1976; O'Keefe and Conway, 1978), and it was determined that the distal cues were stronger than local, track-based cues in controlling the locations of place fields. These are also the conditions under which many behavioral experiments are performed, such as the Morris water maze, the radial-arm maze, the T-maze, and others. The present results suggest that under these conditions, the place cells may construct a representation of position on the behavioral apparatus, rather than a representation of position in the laboratory frame of reference. When the distal cues were rotated relative to the circular track, however, the place fields rotated with the cues, demonstrating that the cues were perceptible to the rat and to the hippocampus. Because there were no strong local cues on the circular track to determine orientation relative to distal cues, it is important to emphasize that these results do not argue for a double dissociation between local cues specifying only location and distal cues specifying only orientation. Indeed, a number of studies have previously demonstrated that local cues can control both the orientation of place field ensembles (Shapiro et al., 1997; Rettenmaier et al., 1999; Zinyuk et al., 2000; Knierim, 2002b) and the locations of individual place fields (Gothard et al., 1996a,b; Muller et al., 2002). The interaction between the orientation of a local apparatus and the orientation of distal landmarks can be complex, however (O'Keefe and Burgess, 1996; Rettenmaier et al., 1999; Knierim and McNaughton, 2001; Cressant et al., 2002). The present results do suggest the possibility, however, of a single dissociation, in that while local cues can specify both location and orientation, distal landmarks may be primarily involved in setting the orientation of the global hippocampal representation of an environment (O'Keefe and Nadel, 1978; Burgess et al., 2000; Hartley et al., 2000; Save and Poucet, 2000), with a weaker influence in defining the precise locations of individual place fields. The distal landmarks are probably also important for the recognition of an environment upon entry, and the activation of the proper hippocampal ensemble that represents that environment (Touretzky and Redish, 1996; Barnes et al., 1997; Kentros et al., 1998).

Prior studies demonstrated that a fraction of place fields next to prominent local landmarks were controlled by them when the landmarks were translated (Gothard et al., 1996a,b; Fenton et al., 2000a). These landmarks might have been the major determinants of the firing location of these place fields. In the present study, however, there were no salient local landmarks that defined precise locations on the track itself. Especially on the circular track, there were no differences on the local surface that distinguished the 12:00 position on the track from the 3:00 position, and the track was wiped clean between recording sessions. Nonetheless, the place fields were tied to the track as an ensemble when it was moved across the room. Thus, some combination of self-motion cues, subtle local cues, and a directional sense must have been used to maintain the cells' firing in the same track locations between sessions, rather than any one salient local landmark.

A number of investigators have suggested that the head direction cell system is the "compass" that sets the orientation of the spatial representation in the hippocampus (e.g., O'Keefe and Burgess, 1996; McNaughton et al., 1996; Muller et al., 1996; Knierim et al., 1998; Burgess et al., 2000). For example, O'Keefe and colleagues have modeled place cells as receiving input from "boundary vector cells"—cells that fire at a gaussian-tuned, allocentric direction and distance from an environment boundary. Place cells gain their specific tuning from combining two or more of the boundary vector cells. In this model, the head direction cells are the source of the allocentric direction information, and they allow the system to distinguish one boundary (e.g., the north wall) from another (e.g., the west wall). Although a few cells recorded by O'Keefe and Burgess (1996) appeared bound to the laboratory frame, they suggested that these cells fired at specific locations relative to the walls (boundaries) of the laboratory, rather than in relation to any set of non-boundary landmarks. The present results can be interpreted in line with these models; that is, the firing locations of the place cells may have been specified by the local geometry of the track and idiothetic information, and the orientation of the map may have been set by the head direction cell system. Those cells that were affected by the translation of the track (especially the rectangular track) may have been tied to the boundaries of the room, rather than to the configurations of the individual landmarks.

Pattern Completion and Pattern Separation

Another way of interpreting these results relies on longstanding hypotheses of the hippocampus as an associative memory system. According to these models, such a system would display two desirable properties: pattern separation and pattern completion (Marr, 1971; McNaughton and Morris, 1987; McClelland and Goddard, 1996; Rolls, 1996). Pattern separation is the transformation of two overlapping input patterns into output patterns that overlap to a smaller degree; storage of these more independent output patterns would help prevent interference and errors of recall. Pattern completion, conversely, is the transformation of a degraded or incomplete version of a previously learned input pattern into the complete, correct output pattern. Hippocampal remapping may reflect a pattern separation process, whereas the relative insensitivity of place fields to removal of individual cues may reflect a pattern completion process.

In this view, the present results can be interpreted as resulting from the pattern completion properties of the hippocampus, rather than as demonstrating a functional dissociation between the roles of local, idiothetic, and distal cues (as argued above). When the rat is placed on the track at the beginning of each session, its view of the environment (encompassing both the track itself and the distal cues) is similar in many ways regardless of the location of the track in the room. It is possible that the hippocampus performs a pattern completion operation on the input, and activates the same representation that was used during training trials in the standard location. In this view, there are no distinctions between local track-based cues and distal landmarks; the place cells fail to change when the track is translated because the differences in the egocentric configurations of cues is not great enough to trigger remapping, and thus the system pattern completes instead.

As with the previous interpretation, a number of caveats can be raised about this explanation. First, although certain properties of place cells have been interpreted in terms of pattern completion and pattern separation, there are no unequivocal studies that demonstrate that the hippocampus actually performs these computational functions. Second, if the hippocampus pattern completes when the animal is introduced onto the track at completely non-overlapping parts of the room, why does it not pattern complete when the animal begins to move along the track? The configuration of cues changes less when the animal moves a few centimeters than when the track is moved to another part of the room. If the hippocampus pattern completes in the latter case, it should pattern complete in the former case as well, and the same cells that were firing at the start of the track should continue to fire as the rat moves along. To break this cycle of endless pattern completion, it is possible that the animal's self-motion information is the primary drive that updates the firing of the place cells, rather than the external sensory input (McNaughton et al., 1996; Whishaw et al., 1997). The one test in which the track was rapidly shifted with the rat on it did not cause the cells to change their firing fields, however, even though the rat was receiving self-motion information (albeit passive motion).

Behavioral Effects

One unanswered question is whether the place fields in the present experiment would have been more strongly bound to the distal landmarks if the rat were performing a behavioral task that caused it to rely on the landmarks. Fenton et al. (1998) demonstrated that rats can keep track of locations relative to both a local and a distal frame of reference simultaneously, although in this experiment the two frames of reference were rotated relative to each other. In a follow-up experiment, place cells were shown to encode each reference frame (Zinyuk et al., 2000). It is unclear, however, whether the same results would apply if the local and distal reference frames were translated relative to each other. There is some behavioral evidence that is relevant to the question. By varying the position of a T-maze in the room and the start location of the rat, Blodgett et al. (1949) trained rats to go to a reward site based on the room cues, on a particular heading direction, on a particular behavioral response, or on combinations of these strategies. The fewest errors were associated with the rats using a directional strategy, and the most errors were associated with the rats using a pure place strategy defined by the extramaze cues. It is possible that, as in the present experiment, the place cells of rats in the experiment carried out by Blodgett et al. (1949) were bound to the local track, causing the animal to perform relative to the local reference frame of the track rather than the reference frame of the room.

A similar, but more complicated, pattern of results was reported by Weisend et al. (1995) in the Morris water maze. After 20 trials of training to find the escape platform in the north quadrant, the water maze was shifted to a new, partially overlapping location in the room. In the next probe trial, rather than swimming to the pool location defined by the room cues, male rats continued to swim to the north quadrant of the pool, which occupied a completely different location

relative to the distal cues than before. This behavioral result is consistent with the hypothesis that the rat's representation of the water maze (and of the goal location) was tied to the boundaries of the pool itself rather than to the external cues (i.e., it was a representation of location in the pool, not of location in the room). Female rats, on the other hand, swam equally to either the north quadrant or the room-defined location. Interestingly, after 80 trials, the males switched to a room-based search location, whereas the females switched to a pool-based strategy. These interesting sex and experience differences make it imperative to understand what the place cells were doing under these conditions and whether their firing properties correlated in a simple fashion with the behavior.

CONCLUSIONS

These results add to the growing evidence that the firing properties of place fields are controlled by a multitude of different cue sources, including local (apparatus-based) cues, distal landmarks, and idiothetic cues. The challenge now resides in discovering the rules that determine how these sources of information interact. Both local and distal cues can have strong influences over place cells when these cues are rotated relative to each other, although differences in the strength of control can result from different experimental conditions. Much less is known about how these sources of information interact when they are translated relative to each other. In this study, the local cues were predominant over the distal landmarks. Along with the behavioral studies, this result is consistent with O'Keefe and Nadel's (1978) proposal that distal landmarks are preferentially involved in setting the orientation of the cognitive map, whereas local cues and idiothetic cues are most useful for specifying precise location information, as well as orientation information. Other interpretations of these results (e.g., pattern completion) are also tenable, however. To disambiguate these potential explanations further, recordings of place cells and head direction cells, in different experimental and behavioral paradigms, will be necessary, as well as a deeper understanding of the properties of the inputs into the hippocampus and the computational principles that underlie hippocampal function.

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