Exp Brain Res (1997) 117:131–142 © Springer-Verlag 1997

RESEARCH ARTICLE

Kathryn J. Jeffery · James G. Donnett · Neil Burgess
John M. O'Keefe

Directional control of hippocampal place fields

Received: 10 February 1997 / Accepted: 16 May 1997

Abstract Pyramidal cells in the rat hippocampus fire whenever the animal is in a particular place, suggesting that the hippocampus maintains a representation of the environment. Receptive fields of place cells (*place fields*) are largely determined by the distance of the rat from environmental walls. Because these walls are sometimes distinguishable only by their orientation with respect to the outside room, it has been hypothesised that a polarising directional input enables the cells to locate their fields off–centre in an otherwise symmetrical environment. We tested this hypothesis by gaining control of the rat's internal directional sense, independently of other cues, to see whether manipulating this sense could, by itself, produce a corresponding alteration in place field orientation. Place cells were recorded while rats foraged in a rectangular box, in the absence or presence of external room cues. With room cues masked, slow rotation of the rat and the box together caused the fields to rotate accordingly. Rotating the recording box alone by 180° rarely caused corresponding field rotation, while rotating the rat alone 180° outside the environment and then replacing it in the recording box almost always resulted in a corresponding rotation of the fields. This shows that place field orientation can be controlled by controlling the internal direction-sense of the rat, and it opens the door to psychophysical exploration of the sensory basis of the direction sense. When room cues were present, distal visual cues predominated over internal cues in establishing place field orientation.

Key words Hippocampus · Place cells · Idiothetic cues · Interoceptive and exteroceptive cues · Path integration

K.J. Jeffery (✉) · J.G. Donnett · N. Burgess · J.M. O'Keefe
Department of Anatomy and Developmental Biology,
University College London, Gower Street, London WC1E 6BT, UK
Fax: +44-171-391-1306, e-mail: K.Jeffery@ucl.ac.uk

Introduction

Place cells are hippocampal pyramidal cells whose firing is highly correlated with the location of the animal. Observation of these spatially localised receptive fields (*place fields*) led O'Keefe and Nadel (1978) to propose that the hippocampus is where the spatial layout of the environment is represented. Understanding how place cells "know" when to fire may shed light on many aspects of spatial behaviour.

Growing evidence indicates that each place cell responds to a subset of environmental features when these are located at an appropriate distance from the rat (Gothard et al. 1996; O'Keefe and Burgess 1996). Thus, each cell appears to represent a fragment of the environment and the ensemble as a whole to code for its shape (see also Wilson and McNaughton 1993. However, in symmetrical environments, place cells must receive more than just size and shape information in order to establish their fields: some method of differentiating the walls is also required. One way would be to discriminate them on the basis of their orientation with respect to the outside world, provided the rat knew how it was oriented. The purpose of the present experiment was to investigate whether place cells can use the rat's internal direction sense alone to disambiguate two geometrically identical locations within a bilaterally symmetrical environment.

Considerable behavioural and physiological evidence now suggests that rats possess an internal "compass", which can be maintained even in the absence of external sensory cues by means of interoceptive cues such as vestibular and proprioceptive input and motor efference copy (McNaughton et al. 1991; Blair and Sharp 1996; Etienne et al. 1996). We made use of this capability to reset the rat's internal "north" independently of the recording environment, to determine whether the new internal north or the previously experienced local sensory cues would subsequently govern place field location. Place cells were recorded while rats foraged in a rectangular box situated within a larger room (Fig. 1A). In the *dark* condition, the outside room cues were masked, and rotations of the

box alone, the rat alone or both were made so as to explore the role of the local asymmetric box cues (such as odours) compared with the rat's interoceptive orientation in determining place field location. In the *light* condition, rotations of the box alone or of the box and rat together were made with the room cues visible. Our results show that, in the absence of polarising visual cues, the rat's internal direction sense takes precedence in orienting place fields within the recording environment; whereas, in the presence of distal polarising visual cues, these cues predominate. The method of rotating the rat independently of the recording environment provides a means by which the internal direction-sense can be controlled in a relatively pure manner: that is, free of interaction from other cues that could act as ancillary landmarks. It provides a starting point for experiments investigating the mechanisms by which interoceptive and exteroceptive inputs are integrated by place cells.

Materials and methods

Subjects

Five male Lister hooded rats (330–400 g) were housed singly in Perspex cages and maintained on a 12-h light/12-h dark schedule, with lights off at 3 p.m. Each rat was given sufficient food to maintain 90% of its free-feeding weight and allowed unlimited access to water.

Electrodes and microdrives

Single-unit data were obtained with two tetrodes as previously described (O'Keefe and Recce 1993). Each tetrode consisted of four twisted strands of 17-μm-diameter Teflon- or HM-L-coated platinum-iridium (90%–10%) wire cut straight across. The two tetrodes were separated vertically by approximately 0.5 mm to allow one set of four wires to detect unit activity while the other acted as a reference. The tetrodes were mounted in a cannula and advanced through the brain in 25- to 100-μm steps by means of a lightweight microdrive.

During surgery the tetrodes were positioned in the cortex just above the CA1 hippocampal subfield (bregma –3.8 mm AP, 2.2 mm ML and 1.5 mm DV). The remaining length of wire between the brain surface and the bottom of the cannula was protected by means of a sleeve made of 19-gauge tubing, the top of which overlapped the cannula by 1.0 mm and the bottom of which was positioned just below the dura. In this way, when the cannula was lowered during the course of the experiment to its maximum depth, it moved down inside the sleeve and came to rest just above the surface of the brain. The microdrive and tetrodes together weighed approximately 1.20 g.

Surgery

Each rat was chronically implanted with a microdrive as follows. The rat was anaesthetised with a mixture of isoflurane (0.5–2.0%), nitrous oxide (3.0 l/min) and oxygen (1.5 l/min) and mounted in a stereotaxic frame. Electrocardiograph and body temperature were monitored throughout the operation and the isoflurane dose adjusted to maintain surgical anaesthesia. The skull was exposed and cleaned and a 2.0-mm-diameter hole drilled with a trephine bit over the right hippocampus. Seven smaller holes were drilled in the frontal, parietal and occipital bones to allow placement of small jewellers' screws to anchor the assembly. One of the frontal screws was soldered to a gold pin (Amphenol) to provide an electrical ground.

The microdrive and tetrodes were lowered until 1.5 mm of the deeper tetrode were embedded in the brain. The sleeve was then pulled down over the remaining exposed wire and the whole assembly cemented to the skull. The wound was dusted with neomycin/bacitracin antibiotic powder (Cicatrin), and the rat was given an intramuscular injection of buprenorphine (Temgesic, 45 μg) for postoperative analgesia. One week was allowed for recovery before electrophysiological recording began.

Unit recording

Beginning at least 1 week after surgery, each rat was connected to the recording equipment via lightweight hearing-aid wires and a socket that fitted onto the microdrive plug. The potentials recorded on each of the eight electrodes were passed through RC-coupled, unity-gain operational amplifiers, mounted close to the rat's head, and led to recording equipment (Gignomai, UK), where the signal was amplified, filtered and stored on disk. Each of the four wires of one tetrode was recorded differentially with respect to one of the wires of the other, the signal tetrode being that on which complex spike units were appearing. As the microdrive was advanced, this enabled recording from a given cell layer by each tetrode in turn. For unit recording, the signal was amplified 30 000 times and bandpass-filtered (500 Hz to 9 kHz).

The outputs of the four amplifiers were fed into a storage oscilloscope to allow visual inspection of unit activity. One of these signals was also led into an audio amplifier. If no unit activity was evident by visual or auditory inspection, the tetrode array was advanced 50 μm and the rat allowed to sit quietly for at least 20 min. If no units had been found after 150 μm movement, the rat was returned to its home cage and checked again the next day. Once cells had been isolated, their activity was recorded while the rat chased rice grains in a small recording box. Unit activity was determined by monitoring each channel at 20-μs intervals and sampling 50 points/channel whenever the signal on any of the four channels exceeded an empirically derived threshold (a presumptive spike). Each spike event was stamped with the time since the start of the recording and the location of the animal. The data were stored on a hard disk and later transferred to a Sun 4 workstation for analysis.

The experimental setup is shown in Fig. 1A. The top of the figure represents an arbitrarily designated north. Recording was carried out in 2-min-long sessions (with an inter-trial interval of at least 10 min.) in a rectangular box with a base of dimensions 40 cm×60 cm, and walls 25 cm high. The box was not cleaned throughout the experiment, so that it was rich in local (e.g. olfactory) cues. The box was positioned on a small motorized turntable in the centre of an area 2 m in diameter, which was separable from the outside room by a set of heavy black curtains. All screening for units took place while the rat sat quietly in the recording box, groomed or walked about. During screening and during some of the recording sessions, the front panel of curtains was drawn back so that the rat could see the outside room.

Rats were screened for the presence of place units with the recording box aligned in the baseline position and with the curtains pulled back to reveal the room. They thus experienced this condition more frequently than any of the others. When place cells had been isolated, recording took place under the various conditions described below while the rat foraged for grains of cooked, sweetened rice tossed into the box by the experimenter, who moved around to avoid becoming a static landmark. The ongoing position of the rat was monitored by a video camera mounted directly above the platform and converted into *x*-*y* co-ordinates by a TV tracking system (Gignomai, UK), which detected a small d.c. light mounted on the recording cable near the rat's head. Every 20 ms the position of the rat was collected and stored with the unit data so that the spatial location of each instance of cell firing could be determined.

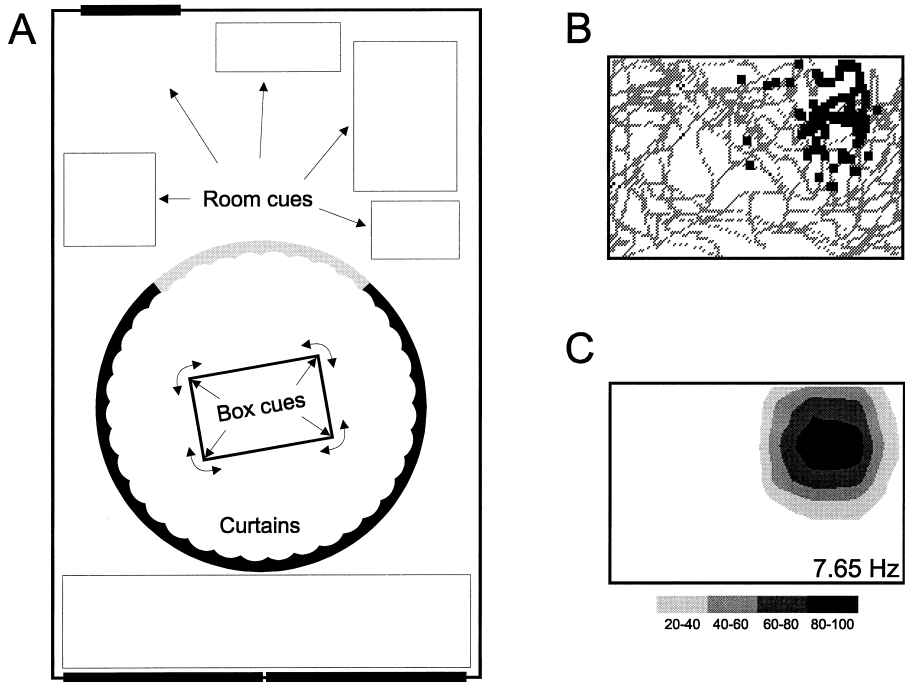

Fig. 1 **A** The experimental set-up. The wall at the *top* is the arbitrary north wall of the room. Within the laboratory, a recording box with a base of 60×40 cm and walls 25 cm high was situated inside a curtained arena 2 m in diameter. The front panel of curtains (*grey area*) could be withdrawn to reveal the outside room, and the box could be rotated slowly (0.15 rpm) either with or without the curtains closed. **B** Example of raw data recorded from a single trial. The *stippled area* represents the path of a rat as it foraged for 2 min in the recording box, while complex spike cells were recorded from its hippocampus. Each *small black square* represents an instance of a place cell firing, superimposed on the location of the rat at the time. The cell shown here fired most strongly whenever the rat was in the north-east corner of the box. **C** Contour plot of the firing rate of the cell in **B**, after averaging. Each contour plot is autoscaled to the peak firing rate on that trial (shown in the *bottom right corner of the box*). The percentage range of the peak rate represented by each shade of grey is shown in the *key*. All subsequent firing-rate contour plots are shown autoscaled in this way

Place cell recording

When well-isolated place cells with stable fields were found, they were subjected to either or both of the investigations outlined below. All rotations that involved the rat were made slowly (0.15 rpm), with the intention of making the rotation undetectable by the rat's vestibular apparatus. To simplify description, the static distant cues in this experiment will be referred to as the "room cues" and the rotating local cues will be called the "box" cues. The end of the room depicted at the top of Fig. 1A was arbitrarily designated as north.

Dark protocol

The steps of this procedure are shown on the left-hand side of Fig. 2. In this condition, the distant room cues were masked as much as possible so that the relative influences on place fields of the box cues and the rat's direction sense could be assessed. To accomplish this, after an initial baseline trial to determine the location of the place field, the curtains were drawn around the box and the room lights switched off, so that the only illumination came from the rat's headlamp and a slight reflected glow from the video tracker. Thus, the rat could see its immediately surrounding environment (the box) but probably little more than that.

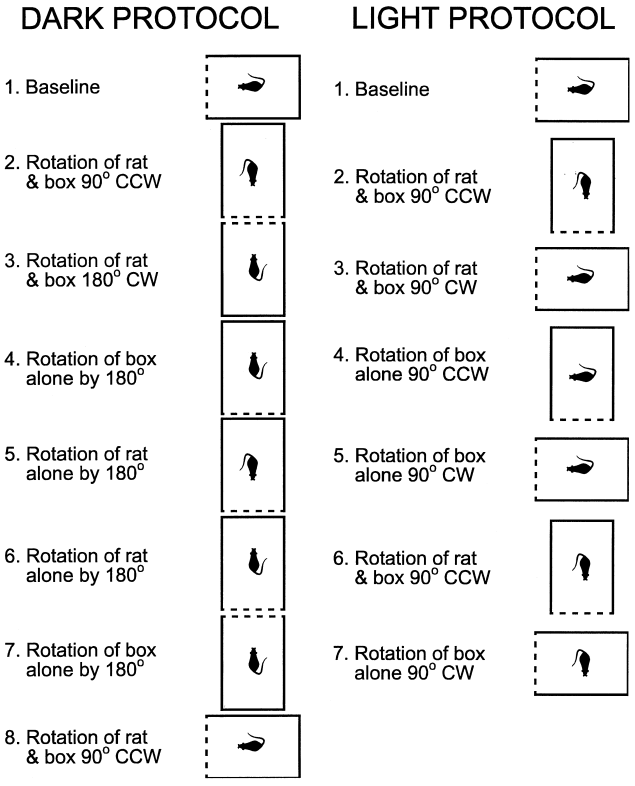

Fig. 2 Descriptions of the sequences in the dark and light protocols are detailed in Materials and methods. The wall of the recording box that was originally west with respect to the room is shown by the *dotted line*. The rat icon in each diagram is pointing towards the rat'shypothetical "internal" west. Note that in the dark protocol the rat's west and the box west are unaligned in steps 4 and 6, and both are unaligned with the room from steps 2–7. In the light protocol, the rat's interoceptive direction sense is aligned with the box (but not the room) in steps 2 and 6, the room (but not the box) in step 4 and neither the room nor the box in step 7 (*CCW* counter-clockwise)

Each cell was then subjected to a sequence of environmental manipulations to assess whether the orientation of its place field inside the recording box in the dark condition was mainly determined by the box cues or by the interoceptive directional sense of the rat. Note that in this protocol all rotations other than the first and last were 180°, so only non-geometric aspects of the box could be used to distinguish one end from the other. After each manipulation, cells were recorded while the rat foraged in the box for 2 min.

Step 1. A second baseline trial was recorded, this time in the dark and with the curtains closed.

Step 2. The box containing the rat was then slowly rotated 90° counterclockwise (CCW) so that its long axis was aligned north-south rather than east-west, to determine whether the room cues outside the curtain were influencing the place field.

Step 3. The box and the rat were rotated together by 180° clockwise (CW), to ensure that the room cues still did not have control over the place field. All subsequent rotations were of 180° and they took place with the box in this alignment (north-south with respect to the outside room). This was done to ensure that the distant room cues were always oriented 90° from the original orientation of the box and/or the rat, so that any influence they might have on place fields was no more biased towards one orientation than the other.

Step 4. The rat was lifted gently (so as not to disorient it), the box rotated 180° underneath it and the rat replaced in the box. This was to determine whether the contribution of the box cues to the place field localisation was due to geometric or non-geometric cues. If it was the geometric cues, then rotation of these by 180° should leave the place fields unaltered; whereas, if it was the non-geometric cues, then the place fields should rotate accordingly.

Step 5. The rat was lifted out of the recording box and placed in a second, square box with a base of dimensions 40×40 cm and walls 40 cm high, which was then placed on the motorised turntable. This was accomplished by translating the rat and the boxes sideways but taking care not to rotate either. This box was slowly rotated 180° in either direction (randomly determined) and the rat then replaced in the recording box for 2 min of recording. The rat was always lifted out from and replaced into the recording box over the west wall of the box (with respect to the room), so that this wall did not behave as a static landmark (with respect to the orientation of the rat).

Step 6. The process described in step 5 was then repeated in reverse to confirm its effects. The direction of rotation was sometimes the same and sometimes different from that of the previous trial.

Step 7. The box was then rotated without the rat once more, so restoring the alignment of the rat's interoceptive directional sense with the original orientation of the box.

Step 8. The box and rat were rotated slowly 90° CCW, restoring the box to its original orientation with respect to the outside room, and a final baseline trial was recorded (still in the dark). To summarise, the types of manipulation in the dark condition were as follows:

1. Rotation of the box and rat together
2. Rotation of the box alone
3. Rotation of the rat alone

Light protocol

The steps of this procedure are shown on the right-hand side of Fig. 2. These trials were undertaken with the curtains drawn back and the room lights on, to compare the relative influences of the distant room cues, the local box cues and the rat's interoceptive sense of direction. The dissociation between room and box cues was assessed in two ways, either with the rat's interoceptive direction sense aligned with the room cues (that is, the box rotated alone) or aligned with the box cues (the box and rat rotated together). Finally, the room and box cues were aligned with each other, but misaligned with the rat's interoceptive direction sense.

Step 1. A baseline recording was made in the light, with the curtains open.

Step 2. The box containing the rat was slowly rotated 90° CCW to determine whether the place field rotated along with the box and the rat or whether it appeared to be influenced by the (now visible) room cues.

Step 3. The box containing the rat was slowly rotated 90° CW back to its baseline orientation.

Step 4. The rat was lifted gently, the box rotated 90° CCW underneath it and the rat replaced in the box. This was to determine whether the place field would be influenced more by the local box cues or by the combination of the room cues and the rat's interoceptive direction sense, both of which should agree that the box was now in a rotated position with respect to themselves.

Step 5. The rat was lifted and the box rotated 90° CW, back to its original orientation.

Step 6. The box containing the rat was slowly rotated 90° CCW (as in step 2).

Step 7. The rat was lifted and the box rotated alone 90° CW. This was to determine whether the rat's direction sense influenced the place field when both the box cues and the room cues were in alignment. The types of manipulation in the light condition are summarised as follows:

1. Rotation of the box and rat together: (a) so as to dissociate their orientation from that of the room; and (b) so as to restore their orientation with that of the room
2. Rotation of the box alone: (a) so as to dissociate its orientation from those of the rat and the room; (b) so as to restore its orientation with those of the rat and the room; and (c) back to baseline, so as to restore its orientation with that of the room but dissociate it from that of the rat

Some cells were subjected to the dark protocol, some to the light protocol and some to both (in variable order, to avoid fatigue effects). Alterations were made to the order of the steps in some of the earliest cells recorded, so not all cells were observed through all of the above steps.

Data analysis

This was performed on a Sun 4 workstation using tetrode analysis software (Gignomai, UK). The waveforms were separated by clustering them on the basis of the height at the negative peak, the positive peak or the peak-to-peak amplitude.

At the start and at or near the end of a recording session, baseline recordings were made. During these trials, the box was oriented in its initial position, with its long axis lying east-west, and the rat's interoceptive direction sense was aligned with the box (that is, the rat had not been rotated independently of the box, or vice versa).

Only cells that still had clear place fields on the last baseline recording were analysed. A place field was defined as location-specific firing (not more than two clear peaks) whose peak rate after smoothing was greater than 0.5 Hz. The following analyses were undertaken to assess whether a cell's firing had changed in response to manipulation of the box and/or the rat.

Characterisation of place fields

To determine the location and peak firing rate of each place field, a 64×64 grid was placed on the camera viewing area (about

130×130 cm) and overlapping square bins of size 20×20 cm were placed around each grid point. For each bin, the number of spikes fired by each cell and the time spent there by the rat was determined. The firing rate at each grid point was mapped as a grey-scale plot (see Fig. 1B, **C**) with linear interpolation between grid points. Contour plots were autoscaled so that each grey gradation represented 20% of the peak firing rate. The point at the centre of the bin containing the highest firing rate was used as a measure of the location of the peak of a place field. The standard deviation (SD) of the locations of the spikes about the location of the peak rate was used as a measure of the size of the field.

The following analysis was undertaken in order to determine whether a cell's field had rotated along with the box and/or the rat, whether the field had shifted to some other location within the box or whether its firing had altered completely. First, an assessment was made of the intrinsic variability of place fields under baseline conditions (where the rat's interoceptive direction sense was aligned with both the box and the outside room). For every place cell, the location of the peak firing rate for each baseline trial was determined, and the distances between all pairs of peaks were averaged to give an estimate of variability for that cell. These values were then compared across the whole population of cells to give a general mean and SD of the variability of peak location. Assuming the variability to be normally distributed, the mean distance ±2 SD was used to provide an estimate of how far a field should be found from its original location with 95% confidence, given that its underlying location was the same. Peaks located further than this from the expected position were assumed to reflect a significant shift in the field's location.

Dark protocol

Analysis of the dark protocol trials was aimed at answering the following question: following a rotation, did a place field follow the rat, the box, both (when these were rotated together) or neither? Following each rotation, two expected locations were therefore calculated for each trial: the location of the field if it had maintained the same position with respect to the rat's interoceptive direction sense, and its location if it had maintained the same position relative to the box (Fig. 3A, Table 1). Because not all trials were run for every cell, the location of the field in the immediately preceding trial was used to generate the predicted locations for a given trial. If a field had moved to an unpredicted location, the following trial was discarded.

The actual (measured) position of the field following a rotation was then compared with the two predicted values and the field flagged as having followed the box, the rat, both (when the box and the rat were rotated together) or neither. Occasionally, a field's measured location fell within the range of both predicted locations even when these were incongruent. This might happen, for example, with fields lying close to the centre of the box. In these cases, the trials were discarded.

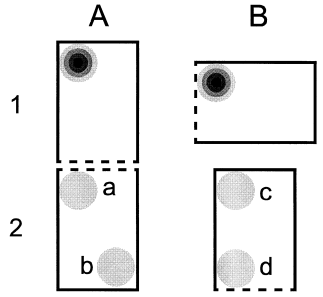

Fig. 3A, B Predicted locations of the fields following rotation. **A** Box rotated alone: *a*, predicted new field location if the field orientation was mainly determined by the orientation of the rat; *b*, predicted new location if it was mainly determined by local cues belonging to the box. **B** Box and rat rotated together in the light: *c*, predicted location if the field had mainly stayed with the room and was principally determined by the two closest walls; *d*, predicted location if the field had rotated along with the box and the rat

Light protocol

For the light protocol, the question of whether a field had followed the rat or the box after a particular manipulation was less easy to assess, because fields often "broke down" (e.g. became diffuse, or dropped below the 0.5-Hz peak rate threshold) following rotations in the light and so could not be used to provide a reference location for the following trial. Therefore, the question asked was: Was the observed location of a field consistent with the rat's current orientation, the box, both or neither, irrespective of where it had been on the immediately preceding trial? That is, the predicted locations were based on the baseline location plus the known intervening manipulations.

In the light condition, an additional predicted location was generated: the position of the field if it had maintained the same orientation in the box with respect to the outside room (Fig. 3B). For this predicted location, it was assumed that a place field was probably determined by the distances to the two closest walls of the box (see O'Keefe and Burgess 1996). If the relevant walls were determined on the basis of their orientation with respect to the room (rather than with respect to the ongoing interoceptive direction sense of the rat), then, following a rotation, the field should be found at the corresponding distance from the two walls that now possessed this orientation. For any given trial, two of the three possible determinants (rat, box and room) were always in alignment, so there were only ever two different predicted locations. As for the dark trials, if the measured location of a field happened to fall within the 95% confidence area of both predicted locations, the trials were discarded.

As well as ascertaining rotations for individual fields, behaviour of the population of fields following each manipulation was compared statistically by comparing distances between each observed field and its two predicted locations using two-tailed paired *t*-tests. The first rotation between the dark and light trials was compared using a χ^2-square test, in order to assess the effect of visible room cues on the rotation of the fields.

Histology and cell localisation

After completion of recording, each rat was killed with an overdose of pentobarbitone sodium (Lethobarb, 10 mg) and perfused transcardially with saline followed by paraformaldehyde. The brain was extracted and stored in formalin, and was later sliced parasagittally in frozen sections 40 μm thick, mounted and Nissl-stained to allow visualisation of the electrode track. The location of each cell was estimated from the depth of the electrode at implantation plus the distance through which the microdrive had been advanced. This distance was superimposed on the electrode track obtained histologically.

Results

Only cells that still had well-localised place fields on the final baseline trial were analysed in detail (n=34). Of these, 7 were subjected to some or all of the dark protocol, 13 to some or all of the light protocol and 14 to some or all of both. The cells recorded in the dark condition included 7 single cells and 7 pairs of simultaneously recorded cells. The cells recorded in the light condition included 5 single cells, 6 pairs, two sets of 3 and one set of 4. Histological analysis showed the cells to be localised within the CA1 hippocampal subfield.

The mean and SD of the peak location variability for the population of cells was determined as described in the Materials and methods, giving values of 9.0±5.4 cm. Modelling the distribution of variability as normal, it would be expected that repeated recordings of the same place field would therefore show peaks falling within 19.8 cm (i.e. mean+2 SD) of the original location 95% of the time. Fields lying outside of this range were hence assumed with 95% confidence to have a significantly different location.

Dark protocol

One trial from one cell and the entire set of trials from another cell were discarded because the observed place fields were found within the 95% confidence range of both predicted locations, even though these were incongruent. The behaviour of the remaining 20 fields, including the distances from each observed field to its predicted locations is shown numerically in Table 1. A typical example from a single cell is illustrated in Fig. 4.

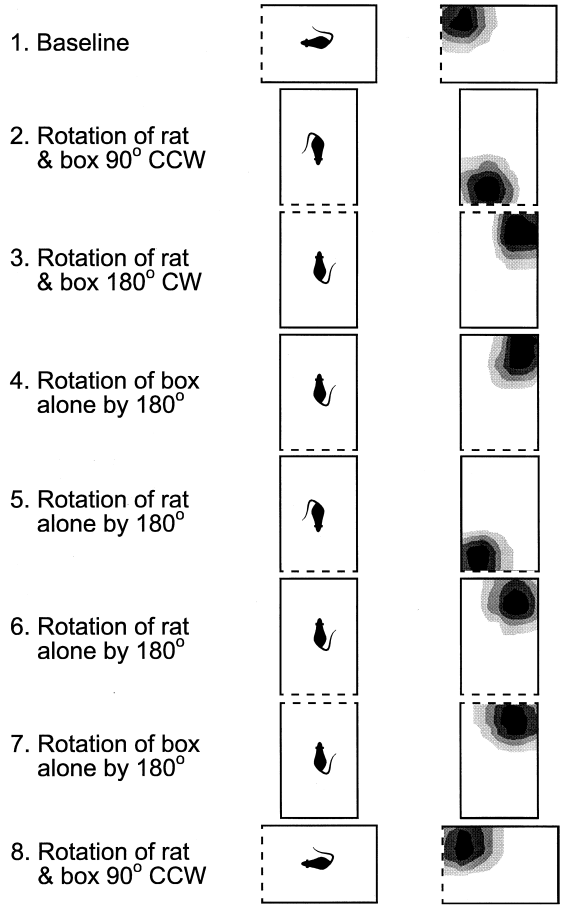

Fig. 4 Behaviour of a typical place field (in this case situated in the north-west corner of the box) following rotations according to the dark protocol. Note that, in each trial, the place field's orientation was aligned with the rat's interoceptive direction sense rather than with the physical, non-geometric cues of the box: that is, it failed to rotate when the box alone was rotated (steps 4 and 7) but rotated 180° when the rat was so rotated. The peak firing rates (hertz) for the 8 steps were, respectively: 10.7, 5.5, 5.4, 7.9, 7.1, 7.1, 3.5, 6.0, 12.3

The overall behaviour observed at each step was as follows:

1. Step 0. Initial baseline trials were recorded with the curtains open and the room lights on.
2. Step 1. Baseline trials were recorded with the curtains closed and the room lights off. These changes to the environment resulted in no change in mean peak firing rate (5.30 Hz in both cases) nor in the size of the fields [$t(17)=0.12$, $P=0.91$].
3. Step 2. When the box and rat were rotated together 90° CCW, all of the fields tested ($n=20$) were found to have rotated with the rat and the box.
4. Step 3. When the box and rat were rotated together slowly in the opposite direction by 180°, 16 of 18 fields (89%) rotated their position along with the rat and the box.
5. Step 4. The rat was held by the experimenter while the box was rotated 180° alone. When the rat was replaced in the box, the mean distance of the observed fields from the predicted position had they rotated with the box did not differ significantly from the distance to the predicted position had they remained oriented with the rat [$t(14)=0.63$, $P=0.54$]. When examined individually, 6 of 15 fields (40%) had followed the box and 8 of 15 (54%) had remained with the rat, while one field (7%) took up a position consistent with neither location. An example of two (simultaneously recorded) cells that followed the box when it was rotated alone, and also followed the rat when it was rotated alone, is shown in Fig. 5.
6. Step 5. When the rat was removed from the recording box, rotated slowly by 180° and replaced in the recording box, the fields were now significantly closer to the location predicted by the rat's orientation than that predicted by the box [$t(14)=5.21$, $P<0.0005$], suggesting that the rat's (rotated) interoceptive direction sense was influencing the location of the fields. This was confirmed when the fields were examined individually: 13 of 15 (87%) had rotated with the rat and only one field (7%) had remained with the box. One field (7%) was found close to neither predicted position. One field was tested after the rat had been placed in the rotating box but not actually rotated. This field also failed to rotate, confirming that merely placing a rat in a different box was unlikely to cause fields to rotate their positions in this way.
7. Step 6. After the rat-alone rotation was repeated, the fields again were found significantly closer to the location predicted by the rat's new orientation than that predicted by the box [$t(14)=8.09$, $P<0.0001$]. When examined individually, 14 of 15 fields (93%) had rotated with the rat and no fields remained with the box. One field (7%) was close to neither predicted position.
8. Step 7. After rotation of the box alone, the fields were again closer to the location predicted by the rat's orienta-

Table 1 The behaviour of place fields subjected to the dark protocol. The number of fields varies from trial to trial because not all fields were subjected to all steps, and because some trials were discarded (see Materials and methods). The numbers in the *three rightmost columns* show the number of fields that were found to be located within the 95% confidence interval of the predicted location indicated by the column heading

	Fields (*n*)	Mean peak rate (Hz)	Mean field SD (cm)	Mean (SE) distance from (cm)		Fields that stayed with (*n*)		
				Location by rat predicted	Location predicted by box	Box	Rat	Neither
Step 0	20	5.3	12.0					
Step 1	18	5.3	11.7	5.3 (0.7)	5.3 (0.7)	18	18	
Step 2	20	4.8	12.7	5.9 (1.0)	5.9 (1.0)	20	20	
Step 3	18	5.5	13.3	10.2 (2.9)	10.2 (2.9)	16	16	2
Step 4	15	5.6	13.2	24.6 (3.9)	19.4 (4.6)	6[a]	8	1
Step 5	15	4.4	11.8	35.1 (2.6)	9.6 (2.9)	1	13[a]	1
Step 6	15	3.5	12.3	33.9 (2.4)	8.5 (1.2)1		14[a]	1
Step 7	6	4.1	13.6	29.3 (2.6)	13.0 (3.5)	[a]	5	1
Step 8	15	3.8	15.1	7.2 (1.0)	7.2 (1.0)	15	15	

[a] Indicating where either the box or the rat was rotated independently of the other following the previous trial

tion than that predicted by the box [$t(5)=3.89$, $P<0.05$]. Rotation of the box was not accompanied by rotation of the place fields in any case ($n=6$); in one case, the field's location was consistent with neither location.

9. Step 8. Rotation of the rat and the box together by 90° CCW (back to baseline): all fields tested ($n=15$) rotated with the rat and the box. The mean distance from the predicted location was 7.2±1.0 cm.

A summary of the dark trials is as follows:

(1) rotation of box and rat together (steps 2, 3 and 8); the fields rotated with the rat and the box in 51 of 53 cases (96%);
(2) rotation of box alone (steps 4 and 7); the fields rotated with the box 6 of 21 times (29%), remained with the rat 13 of 21 times (62%) and shifted altogether once (5%);
(3) rotation of rat alone (steps 5 and 6); the fields rotated with the rat 27 of 30 times (90%); one field (3%) stayed with the box and one field (3%) shifted altogether.

Light protocol

Preliminary findings suggested that rotation of more than 90° in the light tended to be associated with erratic behaviour of the place fields, so only 90° rotations were made in this condition. This meant that the predicted locations of fields were sometimes relatively close. For 18 trials, therefore, the observed position of a field fell within the 95% confidence range of both predicted locations, and so these trials were discarded. Omission of these trials did not affect the pattern of results. Because the rotations were only of 90° in this protocol, the effect of the non-geometric box cues alone was not examined (that is, the box was not rotated 180°).

By contrast with the dark protocol, rotation with the room cues present produced much more variable results, suggesting that the visible room cues were able to influence the place cells. For this reason, the predicted positions were generated on the basis of the baseline position,

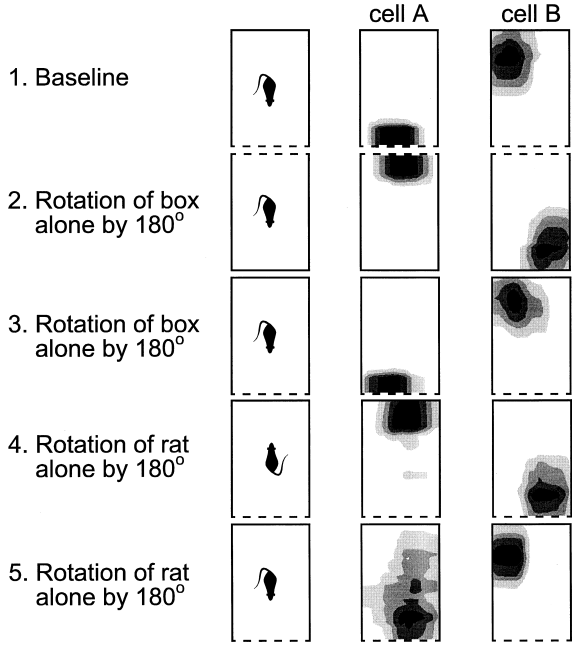

Fig. 5 An illustration of place fields, from two simultaneously recorded cells, that rotated on both occasions when the box was rotated alone (steps 2 and 3) and also when the rat was rotated alone (steps 4 and 5). Note that the place field of cell A became progressively more dispersed following the rat-alone rotations. The peak firing rates (hertz) for cell A were 3.2, 4.3, 4.9, 2.7, 3.0, and for cell B were 8.1, 6.3, 10.9, 4.5, 3.5

Table 2 The behaviour of place fields subjected to the light protocol

	Fields (*n*)	Peak rate (Hz)	Field SD (cm)	Mean (SE) distance from (cm)			Fields stayed with (*n*)			
				Predicted by box	Predicted by rat	Predicted by room	Box	Rat	Room	None
Step 1	27	5.3	134				27	27	27	–
Step 2	20	2.5	170	17.8 (2.7)	17.8 (2.7)	27.1 (2.5)	8	8	3[a]	9
Step 3	26	4.7	141	9.4 (1.8)	9.4 (1.8)	9.4 (1.8)	24	24	24	2
Step 4	19	2.1	190	19.6 (3.1)	29.1 (3.2)	29.1 (3.2)	8[a]	2	2	9
Step 5	23	5.3	149	8.9 (2.0)	8.9 (2.0)	8.9 (2.0)	20	20	20	3
Step 6	13	2.6	159	20.9 (1.9)	20.9 (2.8)	23.7 (4.0)	5	5	5[a]	3
Step 7	10	5.3	125	7.9 (1.9)	26.0 (2.8)	7.9 (1.9)	9	1[a]	9	—

[a] Indicating where one of the box, rat or room was misaligned with respect to both of the other two on the trial

rather than the immediately preceding trial: (cf. the dark protocol). The behaviour of the fields is shown numerically in Table 2, and Fig. 6 shows the behaviour of two cells from two different rats.

The overall behaviour observed at each step was as follows:

1. Step 1. Baseline trials were recorded with the curtains open and the room lights on.
2. Step 2. When the box and rat were rotated together 90° CCW, the fields were closer to the location predicted by the orientation of the box and rat than to that predicted by the room [$t(17)=-2.61$, $P<0.05$]. When the fields were examined individually, 8 of 20 fields (40%) had rotated with the box and the rat, 3 of 20 fields (15%) remained in a constant location with respect to the room (e.g. see Fig. 9, cell B) and 9 of 20 (45%) showed firing that altered completely. In 3 of these 9 cases, the field shifted to an unpredicted location, and in 6 cases it ceased (i.e. peak rate fell below 0.5 Hz) or became spatially non-specific. This finding contrasts with the equivalent manipulation in the dark condition, in which all of the fields rotated with the rat and the box.
3. Step 3. When the box and the rat were restored to their baseline orientations by a rotation of 90° CW, all of the predicted locations were congruent and the mean distance of the fields from this location was 9.4±1.8 cm. When examined individually, 24 of 26 fields (92%) now had locations close to their baseline location. Of the remaining two fields, one maintained its new location with respect to the box (that is, it rotated 90° CW with the box and the rat, even though it had failed to rotate on the previous trial), and the other failed to regain any field at all (peak rate <0.5 Hz).
4. Step 4. When the rat was lifted up and the box rotated 90° CCW underneath it, the fields were significantly closer to the location predicted by the box than that predicted by the combined orientation of that rat and the room [$t(18)=-3.09$, $P<0.01$]. Of the individual fields, 8 of 19 fields (42%) were found to have rotated with the box and 2 of 19 fields (11%) to have remained

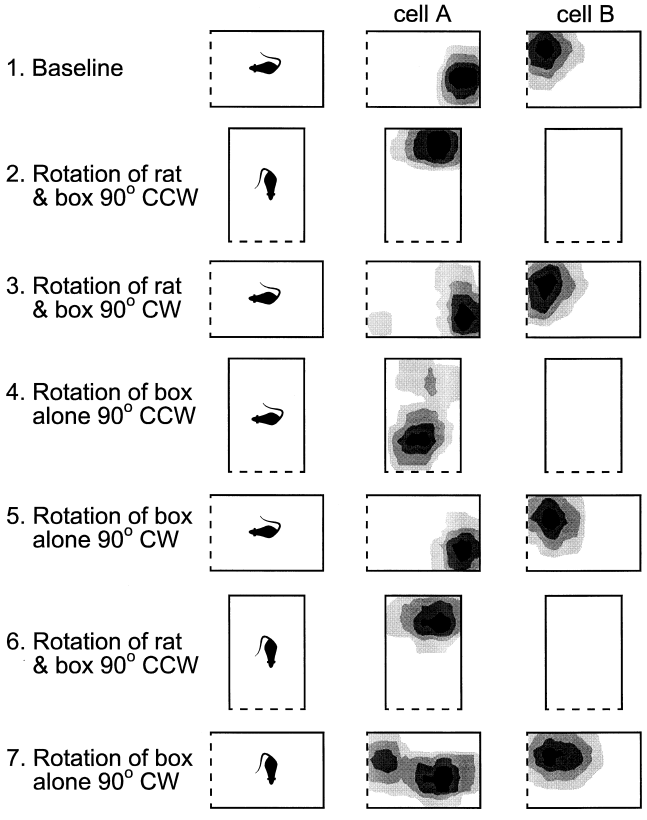

Fig. 6 Two examples of the behaviour of place fields (from different rats) following rotations in the light condition. The place field of cell A rotated concordantly with the rat and the box when these were rotated together (steps 2, 3 and 6). Note, however, that on occasions when the rat's interoceptive direction sense was in conflict with the box (steps 4 and 7), the field became more dispersed and developed two lobes, one apparently corresponding to each geometrically equivalent location with respect to the box. The place field of cell B disappeared (i.e. fell below 0.5-Hz peak rate) on every occasion when the box was misaligned with the room, regardless of the rat's interoceptive direction sense. The peak firing rates (hertz) for cell A were 3.5, 4.3, 6.1, 1.7, 5.1, 3.4, 3.0, and for cell B were 2.3, 0.5, 2.2, 0.1, 3.1, 0.2, 1.7

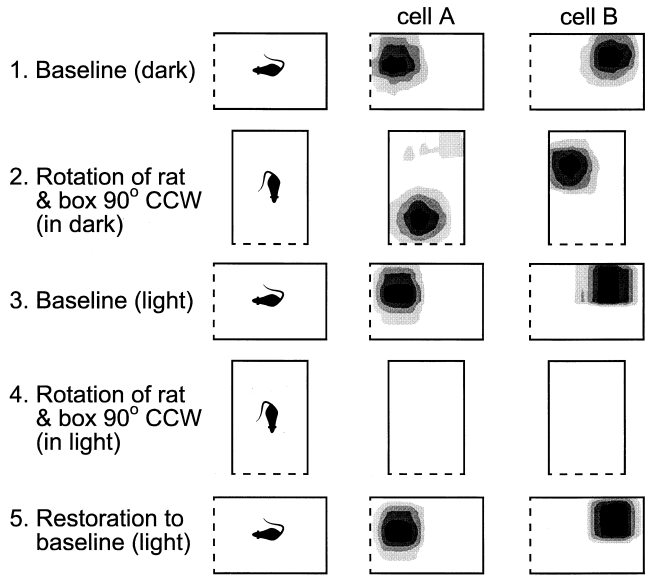

Fig. 7 Comparison of rotations in the dark and light conditions, for two simultaneously recorded cells. When the box and rat were rotated together in the dark (step 2) the fields rotated accordingly. However, when the procedure was repeated during the light protocol, with the room cues visible (step 4), the fields broke down (peak rate <0.5 Hz). The peak firing rates (hertz) for cell A were 4.6, 3.2, 2.8, 0.4, 3.5, and for cell B were 5.4, 4.4, 1.3, 0.1, 0.9

with the room. Of the remaining 9 of 19 fields (47%), 1 shifted its location and 8 ceased their firing or became spatially non-specific. Two examples (from different rats) of fields rotating with the box, rather than remaining oriented with the rat and the room, are shown in Fig. 8.

5. Step 5. When the rat was lifted up and the box restored to its original orientation underneath it, the mean distance from the location predicted by the box, rat and room was now 8.9±2.0 cm. Of the individual fields, 20 of 23 (87%) returned to their baseline locations within the box. The remaining 3 fields had developed stronger second fields in a different location within the box (though the original fields were still present; see Fig. 9).
6. Step 6. When the box and rat were rotated together by 90° CCW, the fields were no closer to the location predicted by the rat and the box than that predicted by the room [$t(11)$=–0.45, P=0.66]. Of the individual fields, 5 of 13 (38%) rotated with the box and rat and 5 (38%) remained with the room. Of the remaining 3 cells, 2 had fields consistent with neither location and 1 had no field.
7. Step 7. When rat was lifted up and the box restored to its baseline orientation without the rat, the fields were significantly closer to the location predicted by the combined orientations of the box and the room than to that predicted by the rat [$t(9)$=5.01, P<0.001]. Of the individual fields, nine of ten (90%) were found to be consistent with the orientation of the box and the room. Only one field was consistent with the orientation of the rat.

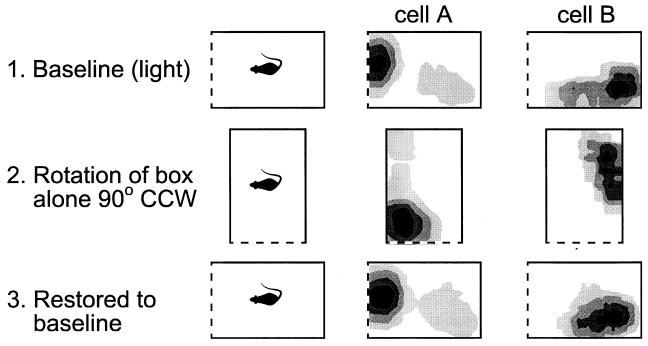

Fig. 8 Two place fields, recorded from different rats, that rotated with the box when it was rotated alone. The peak firing rates (hertz) for cell A were 10.6, 8.4, 4.8, and for cell B were 4.5, 1.1, 6.6

A summary of the results of the light trials is as follows:

1. Rotation of box and rat together: (a) so as to dissociate their orientation from the room (steps 2 and 6). The fields rotated with the rat and the box 13 of 33 times (39%), stayed with the room 8 of 33 times (24%) and either shifted or broke down 12 of 33 times (36%); (b) so as to restore their orientation with that of the room (step 3). The original position was re-established by 24 of 26 fields (92%), while 2 of 26 fields (8%) shifted or broke down.
2. Rotation of box alone: (a) so as to dissociate its orientation from the rat and the room (step 4). Fields rotated with the box 8 of 19 times (42%), remained with the rat and the room twice (11%) and shifted or broke down 9 of 19 times (47%); (b) so as to restore its orientation with those of the rat and the room (step 5). The original position was re-established by 20 of 23

Table 3 Behaviour of place fields when two sets of cues were aligned in opposition to the third. *Cues aligned* indicates the isolation of the various influences on place cell firing (*Box alone* means the box was rotated independently of the rat and the room; *Box & rat* means the box and rat were rotated together, independently of the room, etc.)

Cues aligned	Trials[a] (n)	0%[b]	50%[b]	100%[b]
Box alone	1	11 (58%)		8 (42%)
Rat alone	1	9 (90%)		1 (10%)
Room alone	2	13 (62%)	5 (24%)	3 (14%)
Box & rat	2	10 (48%)	6 (29%)	5 (24%)
Box & room	1	1 (10%)		9 (90%)
Rat & room	1	17 (89%)		2 (11%)

[a] Number of trials in the rotation sequence in which each condition occurred

[b] Percentage of times place fields followed the factor(s) depicted in the *leftmost column*. For example, for trials in which the box was rotated independently of the rat, 11 fields (58% of those tested) never followed the box (i.e. followed it 0% of the time) and 8 fields (42% of those tested) always followed the box (i.e. followed it 100% of the time). The strongest effect was seen when the box was aligned with the room: in this case, only one field (10% of those tested) failed to align itself with these cues

fields (87%) while 3 of 23 fields (15%) shifted or broke down; (c) back to baseline (step 8). Of the ten fields tested, nine (90%) were aligned with the box and the room and one field (10%) remained rotated with the rat.

Finally, the relative influences of the box, rat, room or pairwise combinations of these were assessed for each individual cell by finding the percentage of trials in which the field was oriented with each factor or pair of factors. The results are shown in Table 3. In general, the influence of the box (including, it should be noted, both geometric and non-geometric cues) showed a slight predominance over the others, and a combination of the box and the room cues together exerted a strong control over the fields, 90% of fields being always aligned with these cues when they were congruent.

Comparison of dark and light protocols

Slow rotation of the box and the rat together over 90° CCW was undertaken in step 2 of both the dark and the light protocols, and so the behaviour of the fields was compared to evaluate the effect of the presence of visible room cues. Fields rotated significantly more often with the box and the rat in the dark condition (20 of 20 times) than in the light condition (8 of 20 times; $\chi^2 = 14.40$, $df=1$, $P<0.001$). Examples of two fields that rotated in the dark but broke down (i.e. peak rate fell below 0.5 Hz) in the light are shown in Fig. 7.

Double fields

Figure 9 shows two examples of fields that took up a new position with respect to the box and then maintained both this new position and the previous position, when the box was returned to its baseline orientation. This observation raises the possibility that the new component of the field had been retained from the previous trial. One of the cells was recorded the following day and still showed the additional field.

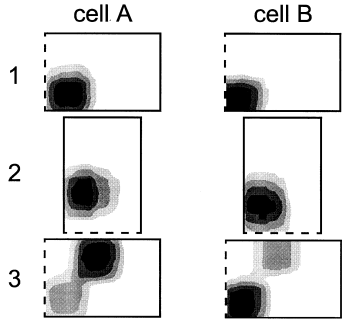

Fig. 9 Formation of double fields. These place fields, recorded from two different rats, failed to rotate with the box when it was rotated in the light (step 2), but adopted a different position within it (perhaps determined by the room cues). When the orientation of the box was restored (step 3), the new component of the field was retained, possibly supported by a new association with the box cues. Cell A was recorded the following day and still showed this additional component to its field. The peak firing rates (hertz) for cell A were 5.7, 3.5, 6.6, and for cell B were 5.5, 8.8, 3.8

Discussion

The main finding of this study is that the rat's internal direction sense could be manipulated independently of exteroceptive sensory cues and thereby control place field location in a recording environment possessing twofold rotational symmetry. When the environment was made asymmetric by the addition of distal visual polarising cues, the interoceptive direction sense in most cases no longer controlled place field location, even when supported by the local geometry of the recording box.

The finding that rotations of the rat were accompanied by rotations of the place fields was remarkably robust, even though the rat was transferred to and from the recording environment by hand. Since each rat was lifted out and in again over the same wall, the position of entry into the recording box could not be used by the rat to orient the environment, since it was "north" (with respect to the rat) before rotation and "south" after the rotation (c.f. Sharp et al. 1990). Since there were no other cues that had rotated along with the rat that could be used to establish heading within the recording box, the rat must have brought its orientation with it; that is, its own internal direction sense must have been used to break the symmetry of the box.

These results extend previous findings suggesting that the rat's interoceptive direction sense influences place cell firing (Sharp et al. 1995; Wiener et al. 1995). In those studies, rats were rotated along with part or all of the recording environment, and place fields were found to rotate correspondingly as long as the rotations were made slowly, suggesting a vestibular influence on place field orientation. Fast rotations were unaccompanied by field rotation, suggesting that the added vestibular input conveyed information to the place cells that the environment had rotated. However, because the recording environment was rotated along with the rat in these studies, there are two possible interpretations of the findings. It may be that the failure of fields to shift following fast rotations was because the direction sense signalled to place fields that the (rotated) intramaze cues were unstable indicators of orientation, forcing them to rely on the extramaze (room) cues instead. In this case the interoceptive directional cues might simply act as a switch, telling the fields to rely either on intramaze or extramaze cues for their orientation, rather than signalling orientation per se. Alternatively, the vestibular input might have provided a quantitative signal that told the place fields how *much* the environment had rotated, allowing them to compensate for the rotation independently of any help from the extramaze cues.

Our experiments go some way towards disambiguating these two alternatives. Because in most of the dark rota-

tions the recording environment remained unrotated with respect to the outside room, rotation of the fields following rotation of the rat in these circumstances could not have been due to influence from either intramaze or extramaze polarising cues. This shows that the interoceptive direction sense of the rat is able to orient place fields without exteroceptive help and reveals an important property of the direction sense, because this provides a mechanism by which the directional orientation of the representation of a new environment could be established so as to make it congruent with that of an adjoining familiar environment, a property that may be useful in learning to navigate to new goals (McNaughton et al. 1991; Knierim et al. 1995; Taube and Burton 1995; McNaughton et al. 1996).

The role of the direction sense in guiding spatial behaviour is currently attracting interest because of the discovery of head direction (HD) cells in the anterior thalamic nucleus (ATN; Taube 1995), lateral dorsal thalamic nucleus (LDN; Mizumori and Williams 1993), postsubiculum (PS; Taube et al. 1990a, b) and other cortical areas (Chen at al. 1994a, b). HD cells fire only when the rat's head is facing in a particular direction, irrespective of the location of the rat, and are postulated to be the neural substrate of the internal compass. Goodridge and Taube (1995) have shown that the direction preference of HD cell firing can be maintained even when the sole orienting visual cue is removed, suggesting that interoceptive inputs to the cell may sustain firing. This information could be supplied by vestibular inputs (Blair and Sharp 1996), proprioceptive inputs and/or motor efference copy. In addition, information from the sense organs about the speed of movement, for example, optic flow (Blair and Sharp 1996) or air speed across the vibrissae, may also contribute. Taube and Burton (1995) found that the preferred firing direction of HD cells was maintained as a rat traversed from a familiar environment into a novel, differently shaped one. This may be either because a coherent influence from extramaze cues matched preferred firing directions across the two environments, or because the interoceptive direction sense enabled the preferred firing direction to "bridge" the two environments. Our findings with place cells support the latter explanation.

Although the place fields recorded here often rotated with rotations of the box (with or without the rat), in no case was a rotation seen of one field with respect to another, simultaneously recorded field, although in several instances one cell shifted its field entirely or stayed locked to the room while another stopped firing. This is in agreement with the findings of Sharp et al. (1995) and suggests either that place fields are constrained (possibly by virtue of their interconnectivity) to maintain a topologically invariant representation, or else that the room cues contributed a coherent signal. Our hypothesis is that the signal is being mediated by the directional system, which is under the influence of both interoceptive and exteroceptive information (Goodridge and Taube 1995).

The influence of directional information from an interoceptively supported internal compass probably also explains several previous findings regarding place field determination. Muller and Kubie (1987) and O'Keefe and Speakman (1987) found that place fields were still present after polarising cues were removed from a symmetrical environment, suggesting that information about them was being retained during the absent-cue phase of the task. Possibly, the cells were using an ongoing internal representation of heading to retain the orientation of the environment (though not always robustly; see Muller and Kubie 1987). Sharp et al. (1990) found that, in a bilaterally symmetrical environment, a place field's location could be determined by the entry location of the rat into the environment. Since the entry location possessed no sensory qualities in itself, its subsequent effect on place fields may have been mediated by an ongoing representation of the orientation of the environment, established at the time the rat was placed into the environment.

Two sets of findings in the present experiment indicate that exteroceptive information was also able to influence the place cells. First, following rotations of the box alone in the dark, several cases were seen of fields that rotated with the box rather than remaining with the rat. Examples of two such fields are shown in Fig. 5. In this case, the box-alone rotation was repeated immediately afterwards, to confirm its effects. Since the box had twofold rotational symmetry and the rotations were of 180°, only non-geometric aspects of the box could have influenced these place fields in this way. Interestingly, these fields also subsequently rotated with the rat, as did three of the other four box-rotating fields observed, suggesting that both types of information impinge on individual cells.

Second, the results of the light protocol indicate that interoceptive information could not always support place fields when it conflicted with information about distant landmarks. Figure 8 shows two such examples. During the masked condition, slow rotation of the rat resulted in an equivalent rotation of the fields. However, when the box and the rat were rotated together in the presence of the room cues, the cells failed to fire. Clearly, the distal cues were often able to override both the box cues and the rat's interoceptive direction sense.

The box cues alone were sometimes able to override the other two influences (Fig. 7, Table 3). Note that in the light, the physical non-geometric box cues were not examined independently of the shape of the box, so it is not possible to dissociate their relative effects. Nevertheless, the finding that the box (shape and/or local cues) was sometimes able to override the combined effects of the rat's interoceptive cues and the room cues was somewhat surprising, given that most studies have shown that place fields do not depend on local non-geometric cues O'Keefe and Burgess 1996). Because the rats in the present experiment had had much experience with the rotating box, often in the dark, it may be that stronger associations had been formed with the box cues than with the room cues in this experiment than in others. The finding that interoceptive information can be overridden by visual informa-

tion is in agreement with those of several previous studies in rodents, both behavioural (Etienne et al. 1996) and physiological (Goodridge and Taube 1995; Taube and Burton 1995), which show that familiar visual cues take precedence over interoceptive movement-based cues in establishing an animal's heading within its environment (though not invariably; see Chen et al. 1994a, b; Wiener et al. 1995).

The technique of rotating the rat independently of its recording environment opens the door to parametric studies investigating how interoceptive and exteroceptive information are integrated by the place cells; for example, to determine how robust is the interoceptive signal and what happens when it is placed in conflict with exteroceptive cues (including box geometry). In addition, this method of functionally dissociating inputs to the place cell system may also be useful in investigating plastic changes in the place representation (Jeffery 1996).

Double fields

Occasionally, a rotation of the box or the rat caused a splitting of the field into two subcomponents, one that accorded with each set of cues (Fig. 9). This is a phenomenon that was reported by Sharp et al. (1990) and also by O'Keefe and Burgess (1996), and it provides direct evidence that place cells receive more than one source of input and that these are dissociable. That double fields were observed only rarely suggests that the influence of the subsidiary inputs was usually overridden by the strongest input, perhaps by a competitive winner-take-all mechanism. After a few tens of minutes, double fields usually resolved themselves in favour of one or other component, though they occasionally persisted. The finding of double fields is interesting, because it suggests either that the internal direction sense is in conflict or that it is not the only input used to polarise the environment and there is conflict between directional and local (geometric) influences on place cells. Again, this question could be resolved by observing HD cells directly during this paradigm.

To summarise, the present results show that when the interoceptive direction sense is manipulated by slow rotations of the rat, place cells can use this sense to polarise a visually symmetrical environment, independently of other (non-visual) polarising cues. The technique of rotating the rat independently of the recording environment appears to be a reliable way of resetting its internal compass, at least under the conditions used here, and may be useful in investigating the relative contributions of interoceptive and exteroceptive information in forming spatial representations.

Acknowledgements The authors are grateful to Dave Edwards, Clive Parker and Steve Burton for technical assistance. Supported by a Medical Research Council programme grant and a Human Frontier Science Program grant, and a Royal Society fellowship to N.B.

References

Blair HT, Sharp PE (1996) Visual and vestibular influences on head-direction cells in the anterior thalamus of the rat. Behav Neurosci 110:643–660

Chen LL, Lin L-H, Green EJ, Barnes CA, McNaughton BL (1994a) Head-direction cells in the rat posterior cortex. I. Anatomical distribution and behavioural modulation. Exp Brain Res 101:8–23

Chen LL, Lin L-H, Barnes CA (1994b) Head-direction cell sin the rat posterior cortex. II. Contributions of visual and idiothetic information to directional firing. Exp Brain Res 101:24–34

Etienne AS, Maurer R, Séguinot V (1996) Path integration in mammals and its interaction with visual landmarks. J Exp Biol 199:210–209

Goodridge JP, Taube JS (1995) Preferential use of the landmark navigational system by head direction cells in rats. Behav Neurosci 109:49–61

Gothard KM, Skaggs WE, Moore KM, McNaughton BL (1996) Binding of hippocampal CA1 neural activity to multiple reference frames in a landmark-based navigation task. J Neurosci 16:823–35

Jeffery KJ (1997) LTP and spatial learning – where to next? Hippocampus 7:95–110

Knierim JJ, Kudrimoti HS, McNaughton BL (1995) Place cells, head direction cells and the learning of landmark stability. J Neurosci 15:1648–1659

McNaughton BL, Chen, LL, Markus, EJ (1991) "Dead reckoning", landmark learning, and the sense of direction: a neurophysiological and computational hypothesis. J Cogn Neurosci 3:190–202

McNaughton BL, Barnes CA, Gerrard JL, Gothard K, Jung MW, Knierim JJ, Kudrimoti H, Qin Y, Skaggs WE, Suster M, Weaver KL (1996) Deciphering the hippocampal polyglot: the hippocampus as a path integration system. J Exp Biol 199:173–85

Mizumori SJY, Williams JD (1993) Directionally sensitive mnemonic properties of neurons in the lateral dorsal nucleus of the thalamus of rats. J Neurosci 13:4015–4028

Muller RU, Kubie JL (1987) The effects of changes in the environment on the spatial firing of hippocampal complex-spike cells. J Neurosci 7:1951–1968

O'Keefe J, Burgess N (1996) Geometric determinants of the place fields of hippocampal neurons. Nature 381:425–428

O'Keefe J, Nadel L (1978) The hippocampus as a cognitive map. Oxford University Press, London

O'Keefe J, Recce ML (1993) Phase relationship between hippocampal place units and the EEG theta rhythm. Hippocampus 3:317–330

O'Keefe J, Speakman A (1987) Single unit activity in the rat hippocampus during a spatial memory task. Exp Brain Res 68:1–27

Sharp PE, Kubie JL, Muller R (1990) Firing properties of hippocampal neurons in a visually symmetrical environment: contributions of multiple sensory cues and mnemonic processes. J Neurosci 10:3093–3105

Taube JS (1995) Head direction cells recorded in the anterior thalamic nuclei of freely moving rats. J Neurosci 15:70–86

Sharp PE, Blair HT, Etkin D, Tzanetos DB (1995) Influences of vestibular and visual motion information on the spatial firing pattern of hippocampal place cells. J Neurosci 15:173–189

Taube JS, Burton HL (1995) Head direction cell activity monitored in a novel environment and during a cue conflict situation. J Neurophysiol 74:1953–1971

Taube JS, Muller RU, Ranck JB (1990a) Head-direction cells recorded from postsubiculum in freely moving rats. I. Description and quantitative analysis. J Neurosci 10:420–435

Taube JS, Muller RU, Ranck JB (1990b) Head-direction cells recorded from postsubiculum in freely moving rats. II. Effects of environmental manipulations. J Neurosci 10:436–447

Wiener SI, Korshunov VA, Garcia R, Berthoz A (1995) Inertial, substratal and landmark cue control of hippocampal CA1 place cell activity. Eur J Neurosci 7:2206–19

Wilson MA, McNaughton BL (1993) Dynamics of the hippocampal ensemble code for space. Science 261:993–994