Context-independent directional cue learning by hippocampal place cells

Subhojit Chakraborty, Michael I. Anderson, Amir M. Chaudhry, Julie C. Mumford and Kathryn J. Jeffery
Department of Psychology, University College London, 26 Bedford Way, London WC1H OAP, UK

Abstract

In a symmetrical environment possessing no other polarizing visual cues, the spatially localized firing of hippocampal place cells can be primarily orientated by a reliable distal visual stimulus, such as a white cue card. However, if such a directional cue is made unreliable by being frequently moved in full view of the rat, the rat's internal sense of direction comes, over the course of a few days, to control the orientation of place fields instead. We investigated whether this simple form of 'cue-instability' learning would transfer to a new context, in which the firing patterns of the place cells become reorganized and in which a new spatial representation is thus active. We found that after cue-instability learning, the 'remapped' place field representation in the new environment was also orientated by the internal sense of direction of the rat rather than by the cue card, showing that the cue learning generalized from one context (and hence spatial representation) to another. This contrasts with another kind of place cell learning, in which the cells can acquire the ability to discriminate two spatial locations in one context but do not transfer this discrimination to a new context. We discuss the different effects of context changes on learned place cell activity in terms of the possible architecture of the inputs to place cells.

Introduction

Pyramidal cells in the hippocampus of rats exhibit spatially localized firing and have been termed 'place cells'. Their regions of neuronal activity (termed 'place fields') are analogous to the receptive fields of sensory cortical cells (O'Keefe & Dostrovsky, 1971) except that they are allocentric (world-centred) rather than egocentric (body-centred). Place cell ensembles are thought to form a spatial representation of the environment akin to a map that can be used for spatial navigation (O'Keefe & Nadel, 1978). Understanding how this map is formed and the rules by which it is modified is of great interest. The present study explores whether a particular kind of modification of the place cell representation, acquisition of new information about a directional cue, generalizes to a new context.

Place cell activity in rats is influenced by a variety of factors that include, among others, the geometry of the environment (O'Keefe & Burgess, 1996; Lever et al., 2002), objects located both within and outside the immediate environment (Muller & Kubie, 1987), and also less tangible aspects of the environment like colour and odour (Bostock et al., 1991; Anderson & Jeffery, 2003; Hayman et al., 2003; Jeffery et al., 2003), and the internal state of the subject (Markus et al., 1995; Wood et al., 2000; Ferbinteanu & Shapiro, 2003). These stimuli fall into the broad category of 'spatial context' (Nadel & Willner, 1980; Mizumori et al., 1999; Jeffery et al., 2004). Following a change in the environment, place cells reorganize their discharge pattern by: (a) having field(s) at a different location; or (b) switching off/on if previously active/silent, leading to a phenomenon known as 'remapping' (Muller & Kubie, 1987). Remapping to a large change in the

environment is usually 'complete', affecting all observed cells, though this is not invariably the case (see Knierim, 2003 for a review).

In addition to being localized by the geometric cues provided by the boundaries of the environment, place cells require directional information to orientate their firing. In a rotationally symmetrical environment lacking polarizing visual stimuli, the cells can be orientated by the rat's internal direction sense, provided by movement-related ('idiothetic') cues (Jeffery et al., 1997). Idiothetic cues comprise a number of different signals, such as vestibular, optic flow, proprioceptive and motor efference, and are integral to path integration (Taube et al., 1995; Blair & Sharp, 1996; see Etienne & Jeffery, 2004 for a review). When polarizing visual stimuli are present, however, the cells use these in preference, showing that stable visual cues provide directional information as well (Muller & Kubie, 1987; Muller et al., 1987; Jeffery & O'Keefe, 1999). However, if a visual landmark is mobile and hence rendered unreliable as a directional cue, place cells then come to rely on idiothetic cues and disregard the unreliable visual landmark (Knierim et al., 1995; Jeffery & O'Keefe, 1999). We consider this phenomenon to be, in effect, an example of 'learning' by the place cells, insofar as the cells come (as a result of experience) to change their patterns of activity in response to the same set of inputs as previously. It should be pointed out that learning by place cells does not necessarily equate to learning by the rat as a whole, but we will henceforth use the term 'learning', for simplicity, to refer to acquired changes in place cell behaviour. The experience-dependent change in responsiveness to a cue card, which we term 'cue-instability learning', is the focus of the present study.

Our interest was in how reorganization of the place cell representation, caused by changes to the environmental context, would affect this cue-instability learning. Recently we demonstrated that another form of place cell learning, in which the cells acquired a discrimination between two adjacent locations, was dependent on the spatial

context of the environment (Hayman *et al.*, 2003). New information acquired by the cells in a familiar context (e.g. a black box) through repeated exposure did not appear to be available to them in a novel environment (e.g. a white box). In other words, place cells that learned to discriminate (evident as remapping) two adjacent but identical recording environments based on extra-maze cues in one context failed to do so in another, novel context. The current study was undertaken to investigate whether cue-instability learning would also depend on the spatial context of the environment.

We recorded place cells from rats in a square recording box, surrounded by curtains in front of which was hung a single polarizing visual cue card. The relative influence on the place cells of this cue card vs. the rat's internal sense of direction was assessed by placing the cue card and the rat's internal sense of direction in conflict, to see which dominated in controlling the orientation of the place fields. This was achieved by covering the rat and rotating it slowly by 90 or 180°, meanwhile moving the cue card, usually by a different amount (also 90 or 180°) and then recording to see how the place fields were now orientated. Initially the place fields were predominantly orientated by the cue card, as expected. Rats were then allowed, over the course of several days, to see that the salient visual landmark was not stationary; rather it was mobile and hence unreliable as a directional reference. Subsequently, when tested under the same conflict conditions as before, place fields now followed the rat's internal direction sense rather than the cue card. This transfer of control from the cue card to the internal direction sense has previously been shown to be dependent on the rats having seen the card move (Jeffery & O'Keefe, 1999).

After control had transferred from the cue card to the internal directional cues, the spatial context of the environment (colour) was altered in order to induce remapping of place fields, as in previous studies (Bostock *et al.*, 1991; Anderson & Jeffery, 2003; Hayman *et al.*, 2003; Jeffery *et al.*, 2003). The discharge characteristics of place cells in the novel context were then compared with the activity in the familiar context to determine whether their place fields would be controlled by the cue or the rat. Our interest was in whether the directional information acquired by place cells in one context (that a salient visual cue was unreliable for orienting) would still be available to place cells in a novel context.

Materials and methods

Subjects

Four adult male Lister Hooded rats (300–450 g) were used for this experiment. The rats were housed individually in Perspex cages and maintained on a light/dark schedule with lights at half strength to create simulated dusk (19:00–20:00 h) and dawn (07:00–08:00 h), and 11 h of full light (08:00–19:00 h) and full darkness (20:00–07:00 h). Each rat was maintained at 90% of its free-feeding weight with *ad libitum* access to water. The animals were handled individually for at least 1 week prior to surgery.

All procedures in this study were licensed by the UK Home Office and adhered to the restrictions and provisions contained in the Animals (Scientific Procedures) Act 1986.

Electrodes and microdrives

For each rat, four tetrodes (Recce & O'Keefe, 1989) were constructed from four interwound 25-µm-diameter platinum-iridium wires (California Fine Wire, USA) and were inserted into a microdrive assembly (Axona Ltd, St. Albans, UK). The microdrive allowed the tetrodes to be advanced together, with one full turn of the screw being approximately equivalent to 200 µm of movement dorso-ventrally. Three of the tetrodes were cut level with each other, the fourth one staggered back by up to 1 mm.

Surgery

Rats were surgically implanted with the moveable microelectrodes (attached to the microdrive assembly) placed in the neocortex overlying the dorsal hippocampus as follows. Anaesthesia was induced with 0.2 mL midazolam and fentanyl/fluanisone (2.7 mL/kg i.p.) and maintained with isoflurane and oxygen (3.0 L/min). Once a surgical level of anaesthesia was attained, the top of the rat's head was shaved and the rat was placed in a stereotactic frame. The body of the animal was covered with bubble-wrap to minimize heat loss. The eyes were covered with petroleum jelly (Vaseline) to protect the cornea from drying and damage. During the entire period of surgery, the rats were monitored for an adequate level of anaesthesia by frequent inspection of the reflexes and respiration. The head of the rat was then cleaned and disinfected with iodine. The scalp was incised along the midline and retracted to expose the skull surface. Bregma and lambda, the two skull landmarks, were then adjusted so as to lie in the horizontal plane.

A 2-mm-diameter burr hole was made overlying the right dorsal hippocampus, and the tetrodes were implanted stereotactically just above the CA1 hippocampal region (bregma: −3.8 mm AP, 2.5 mm ML, 1.5 mm DV). One of the rats, as part of a pilot study, had ibotenic acid (0.15 µL) injected bilaterally aimed at the anterior dorso-lateral thalamic nucleus (bregma: −1.5 mm AP, 1.5 ML, 4.5 mm DV), although subsequent histology showed the attempted lesion to be unsuccessful. The electrode wires were slowly lowered into the neocortex by retracting the dura. A metallic sleeve was pulled down to protect the exposed wires. The whole assembly was then secured to the skull using jeweller's screws and dental acrylic. One of the screws was soldered to a ground wire from the microdrive assembly to enable the rat to be electrically grounded.

Buprenorphine (45 µg im) was given as a postoperative analgesic, enrofloxacin (2.5 mg s.c.) as a prophylactic systemic antibiotic and neomycin powder over the skull as a local antibiotic. Following surgery, rats were placed in a cage and monitored periodically till they were fully awake and moving about. The rats had free access to food for 1 week following surgery, and were mildly food-restricted again thereafter.

Place cell recording

Recording commenced 1 week after surgery. Recording was done using multichannel recording equipment (Axona Ltd). The rats were connected to the recording device via lightweight hearing-aid wires and a socket attached to the microdrive plug. The potentials recorded on each of the 16 electrodes of the four tetrodes were passed through AC-coupled, unity gain operational amplifiers mounted on the rat's head and fed to the recording system. The signal was amplified (20 000–40 000 times) and bandpass filtered (500 Hz−7 kHz). Each of the four wires of one tetrode was recorded differentially with respect to one of the wires of another tetrode. One of the recording channels was dedicated to acquiring the EEG signal.

Screening for hippocampal cells took place in a room separate from the actual experimental room, to minimize the learning of extraneous cues in the recording environment by the rats. Tetrodes were advanced 200 µm daily in steps of 50–100 µm until hippocampal ripples appeared. From this point onward tetrodes were advanced in steps of 25 µm and not more than 50 µm a day until complex spikes appeared.

Once place cells were isolated in the screening room, the rat was transported to the experimental room in an opaque box. From then on, every day, the rat was directly taken to the experimental room in an opaque box.

After the rat was connected to the recording equipment, continuous tracking of its position was achieved via a small infrared LED on the head-stage assembly, which was monitored by a monochrome video camera in the ceiling, mounted directly above the mid-position of the recording area. The video image was passed to a tracking system (Axona Ltd) which detected, every 20 ms, the position of the infrared LED and converted into x–y coordinates, to provide the location of the rat for off-line comparison with unit activity. While recording unit activity from neurons, each channel was monitored every 20 μs, and 50 points per channel were sampled whenever the signal on any of the four channels exceeded a given threshold (a presumptive spike). Also, each spike event was stamped with the time elapsed since the beginning of the recording and stored along with the concurrent location of the animal. All data were collected and stored on hard disk for offline analysis at a later time.

Experimental set-up

The experimental room had, in its centre, a circular area 2.5 m in diameter that was surrounded by heavy black curtains, with a small area to one side of the room for the recording devices and computers. In the centre of the curtained arena was a square foam-board box made with either black or grey inner walls that was 70 cm long and 34 cm high, with a floor that was made of the same material. The box rested on a rotating circular platform at a height of 46 cm. A motorized turntable could drive this platform either clockwise or counterclockwise at 0.08 r.p.m. (intended to be below the detectable range for the rats). The environment had a fourfold rotational symmetry, as the curtains did not provide any visual cues to indicate the orientation of the square box. This symmetry was interrupted by suspending a large white cue card (74 × 102 cm) in front of the curtains and behind one of the four walls of the box (Fig. 1). Four spotlights were attached to the curtain behind the four walls of the box, allowing the cue card to be lit brightly when it was in any of its four cardinal positions (south, north, east, west). As the main room lights were turned off for the entire time that the rat was in the room, the spotlit card was the only salient polarizing landmark. The position of the card could be varied from trial to trial; the rotation of the box could also be changed either 90 or 180° clockwise or counterclockwise. Three of the rats were exposed initially to the black box followed by the grey box (providing the change in context to the environment) and the fourth to the grey box followed by the black box.

Experimental protocol

Once place cells with stable place fields were isolated, recording started in the experimental room. Within the darkened central curtained-off area, the rat was lifted from its opaque box, connected to the recording apparatus and placed in the square experimental box. The rat was always introduced to the environment with the cue card positioned in the south location, and the experimenter always entered and exited the environment at different locations along the curtain so as not to provide any confounding stable directional cues to the rat.

Each session began with a baseline trial during which the rat foraged the box for 6 min while place cells were recorded. Following the baseline trial, rats were confined within the square box by means of another small cardboard wrap-around box (35 × 27 × 23 cm) with just
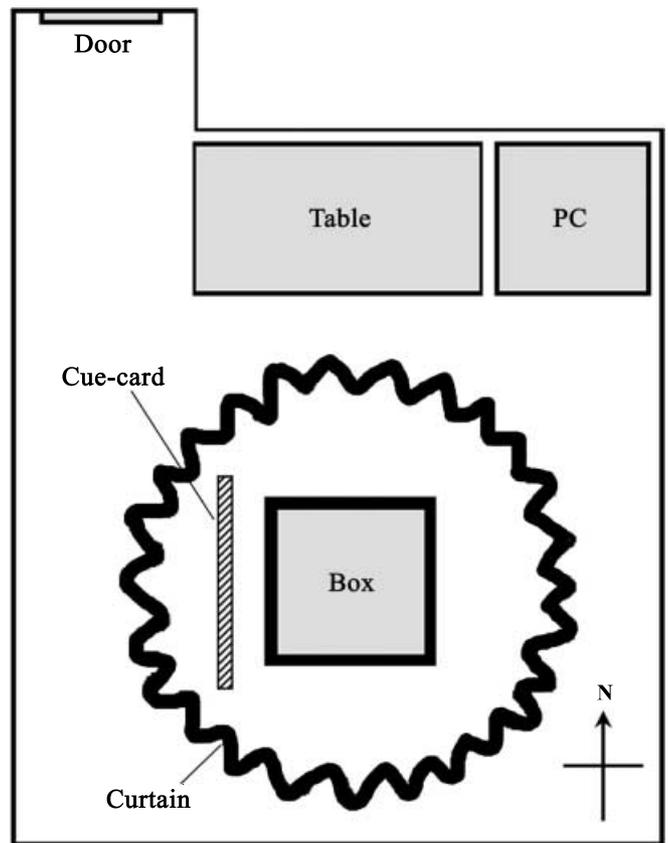

FIG. 1. Diagram of the experimental room layout. The rats were transported in a covered box into the curtained arena, and placed in the square box (labelled in the figure). The room lights were switched off whenever the rat was present and the only source of light within the arena was provided by a spotlight above the cue card. The box, situated on a motorized turntable, could be slowly rotated clockwise or counter-clockwise. Rotation of the box was very slow so as to be below the vestibular detection level of the rat. The cue card was hung from the curtain and could be positioned in any of the four cardinal locations (north, south, east or west). Four spotlights, that could be switched on or off, were also present in the four cardinal positions close to the ceiling. The compass rose indicates an arbitrary "north".

a small opening at the top for the passage of recording cable wires. The spotlight was then turned off and the box was rotated, clockwise or counter-clockwise either 90° or 180°, in complete darkness. At the same time the cue card was manually removed and silently placed at another location. Sometimes the rat and the card were rotated by the same amount, to check that stable uncontrolled cues in the room outside the curtains did not exert any effect on the orientation of place fields. However, our interest was in the behaviour of place fields in a discordant situation (with a conflict between the box rotation and card rotation) and so the majority of our recordings were following such disjunctive rotational sessions. A 90° rotation took approximately 3 min; a 180° rotation took 6 min. A further delay of 3 min was added to the 90° turn in order to provide temporal equivalence with a 180° rotation. The spotlight above the newly relocated cue card was then illuminated and the rat was released from the confines of the wraparound box into the main box again. A couple of minutes were given for the rat to reorient itself, and a further 6-min recording session was then conducted. During recording sessions, the rat foraged within the environment and was rewarded randomly with small grains of cooked rice. A session consisted of a block of at least four cue card + box rotations, whereby all four of the cardinal positions of the cue card were tested at least once. Each session usually terminated with the card in the south, to enable

comparisons under conditions of equivalent environmental input (although, of course, the rat's internal state may have differed due to the rotations it experienced during the session).

After ascertaining that there was robust following of the cue card by the place cells − defined as the fields rotating with the cue card in at least three of four consecutive trials (generally achieved after a couple of days of recording) − rats were subjected to a learning period. During this session rats were free to roam around the square box and were meanwhile exposed to pseudo-random visible movement of the cue card by either 90° or 180°. This was achieved by turning on the spotlight at the new location followed by unhooking of the card from the curtain, carrying it to one of the three other cardinal positions, hanging it up again in full view of the rat and finally turning off the spotlight at the previous location. Thus, the card could be seen by the rat to be unstable and hence an unreliable cue for providing directional information. This manipulation was carried out 10 times daily with an interval of 10 min between each card rotation. From about the fifth day of this learning phase, another recording session (identical to that previously described) was again carried out to determine whether the place fields now rotated with the card or with the internal directional sense of the rat (i.e. whether the cells had come to ignore the unreliable visual card as a cue for orientation and instead follow the more stable idiothetic cues). The duration of the learning period varied depending on individual rats and ranged from 5 to 15 days of the continuous learning schedule. Once place fields reliably followed the rat in at least three out of the four disjunctive card + rat rotations ($P \geq 0.75$), the learning phase was considered to be complete. At this stage, the square box (black or grey) was changed to another box with identical dimensions but differing inner wall colours (grey or black, respectively), constituting a change in context. During this change-over, the rat was put in the opaque box and placed in another room. After the changeover, further recording sessions were conducted using similar rotation protocols (disjunctive card + rat rotation in the dark).

To summarize, the entire experiment in a rat consisted of the following three recording sessions: (a) prelearning; (b) postlearning in the familiar context; and (c) postlearning in the novel context, henceforth referred to as Pre, Familiar and Novel, respectively.

Place field measures

Analysis of data was done offline using Tint analysis software (Axona Ltd). The trajectory of the rat was smoothed using a boxcar algorithm with a boxcar width of 400 ms. The collected waveforms were separated as clusters, usually by plotting the peak-to-peak amplitude of each spike on one electrode against that on each of the other three as a series of scatterplots. Occasionally, the voltage at time *t* was added as an extra parameter to help differentiate closely related waveforms. The clusters were distinguished by hand on the first trial and then by an automatic clustering algorithm based on the parameters obtained from the initial manual separation. These parameters consisted of the centroid of the cluster in multidimensional space and a cluster boundary defined by an ellipse, the long axis of which passed through the origin, and the length and width of which were 3 SDs from the centroid. Cells were included in the subsequent analysis if they met the following visually discriminated criteria: (a) waveforms were typical of hippocampal pyramidal cells (e.g. slow afterhyperpolarizations, large spike-widths); (b) during the cluster cutting process, clusters were clearly separable; and (c) the firing rate maps showed evidence of spatial firing patterns. These criteria led to the exclusion of putative theta cells and other non-spatial cells. Cells that met these criteria also had to fire ≥ 20 spikes

and show peak rates of ≥ 1 Hz in a trial to be subjected to further analysis.

To determine the location of a cell's place field in the recording environment, the camera viewing area was divided into square pixels of side ≈ 2.25 cm. The firing rate for a given cell in each pixel was evaluated by dividing the number of spikes in that pixel by the amount of time spent by the rat there. An algorithm that replaced the value in each pixel with the average of the value in that plus the surrounding eight pixels then smoothed the firing rate map. Place fields were plotted as contour maps normalized to the peak-firing rate with five levels, each level representing a 20% proportion of the peak-firing rate for that map.

Further analysis was undertaken using custom-written programs in MATLAB (The MathWorks, Natick, MA, USA). Cells with a peak frequency (derived from the pixel with the highest rate) of less than 1.0 Hz or with total number of spikes below 20 in any trial were excluded from additional analysis and were deemed to have stopped firing. Each pixel in its firing rate map for such a trial was set to zero for the remapping algorithm described below. Sometimes the first few trials were discarded, as the place fields were messy and poorly defined. Occasionally, the environment boundaries, which were estimated by the tracking software, differed slightly between trials. For a given session, therefore, because square maps of the same size were required for the correlation analysis, the firing rate maps were matched in size by, if necessary, 'stretching' them uniformly using interpolation to form square maps of the size of the largest map. This stretching was never by more than 2–3 pixels and did not appreciably change the place field size or shape.

Analysis protocol

Analyses were then performed on the place fields to determine how the firing in a given trial compared with the firing of other trials in that session. Two kinds of transformation were tested for: rotation (to see whether a field rotated but otherwise remained in the same 'place') and, for trials where the context was changed, complex remapping (Muller & Kubie, 1987; to see whether a field had altered its firing pattern completely). As described elsewhere (Anderson & Jeffery, 2003; Hayman *et al.*, 2003), firing rate data from pairs of trials were assessed for similarity using pixel-to-pixel Pearson's correlations and ignoring zero rate – zero rate pixels which could spuriously inflate the correlation values.

Rotations were tested for as follows. For each pair of consecutive trials, which we shall call trial A and trial B, firing rate data from trial A were correlated with each of the four rotated versions of data from trial B in turn (where the amount of rotation was 0, 90, 180 or 270°). Thus, four correlation coefficient values were obtained. The highest correlation value so generated indicated which rotated version of trial B was most similar to (the unrotated) trial A. In order to assess the response of the recorded cell population, this correlation algorithm was run using pooled data from all cells in both trials (i.e. the population data were arranged in two columns, one column per trial, before computing each correlation value). The method of pooling data from all cells in both trials was preferred to averaging the individual cell correlations because the latter may have allowed cells contributing only a few spikes to unfairly bias the mean. In fact, as shown in Table 1, this ensemble analysis did not produce results that differed materially from analysis of single-cell data. The algorithm had the following provisos: (a) if a cell stopped firing in either or both trials, it did not contribute to the correlation, except for cells that contextually remapped in response to the change in the colour of the recording box

TABLE 1. Comparison of the mean correlations (± SEM) obtained for each trial type

	Rotation type	Ensemble	Individual
Pre trials	Rat	−0.03 (0.05)	−0.01 (0.1)
	Card	0.50 (0.06)*	0.53 (0.06)*
	Room	−0.04 (0.04)	0.02 (0.06)
	Other	−0.09 (0.04)	−0.06 (0.06)
Familiar trials	Rat	0.28 (0.05)*	0.27 (0.07)*
	Card	−0.07 (0.03)	−0.04 (0.03)
	Room	−0.01 (0.05)	0.01 (0.03)
	Other	−0.05 (0.02)	−0.03 (0.02)
Novel trials	Rat	0.46 (0.04)*	0.51 (0.06)*
	Card	−0.16 (0.05)	−0.03 (0.08)
	Room	−0.11 (0.02)	−0.08 (0.01)
	Other	−0.13 (0.06)	−0.11 (0.00)

The correlations were obtained by comparing a given field with the preceding field after it had been subjected to each of the putative rotations (with the rat, with the cue card, etc.). The highest correlation is taken to reflect the rotation the field actually made. The correlations were obtained using the ensemble analysis vs. individual cells for the three trial types, and then averaged across animals. The two analyses yielded equivalent values, and showed a transfer of control (*) from the cue card (Pre trials) to the rat (Familiar trials) which persisted, and indeed strengthened, following the context change (Novel trials).

(vide infra); (b) while comparing between the last Familiar trial and the first Novel trial, if a cell contextually remapped by switching on or off in the new environment, then the cell's firing rate map in its active trial was compared with an empty map.

Following a discordant rotation of box/rat vs. cue card, the place fields could orientate with the card (now at its new location), with the internal sense of direction of the rat (for simplicity termed 'with the rat', although local box cues may have made a contribution), with the room (i.e. the field did not rotate, remaining fixed to the room coordinates) or with the fourth possibility which we have termed 'other'. The rotation that produced the highest correlation was considered to be the rotation actually made by the place fields.

The correlations produced from each trial pair were statistically compared within a session, to determine which was the principal influence on place cell rotation (card, rat, room or 'other'). Prior to all parametric statistical analysis, correlation coefficients were adjusted using Fisher's r-to-Z transformation. Differences between the correlation coefficients obtained in these four conditions ('card', 'rat', 'room' and 'other') were tested with a series of repeated measures ANOVAs for each of the Pre, Familiar and Novel sessions. Where necessary, Geisser–Greenhouse adjustments to the degrees of freedom were made. If the ANOVA showed a significant main effect of condition, a repeated measures t-test for individual comparisons with post-hoc Bonferroni corrections was undertaken.

A series of repeated measures ANOVAs was also performed to compare the effect of various rotations (card, rat, room, 'other') across the three different trial types (Pre, Familiar, Novel). When the ANOVA showed a significant main effect, individual comparisons by repeated measures t-tests with post-hoc Bonferroni corrections were then made across sessions to determine whether the principal influences on the place fields differed across different sessions (either because of learning, as in the Pre, Familiar comparison; or because of remapping, as in the Familiar, Novel comparison).

Histology

With the conclusion of the experiment, each animal was anaesthetized with isoflurane gas followed by an injection of sodium pentobarbital

(i.p.) and then transcardially perfused with saline followed by paraformaldehyde (4%). The brains were removed and stored in paraformaldehyde (4%) for at least 1 week before sectioning commenced. The brains were sliced at 40 μm on a freezing microtome. The sections were mounted, stained with Cresyl violet and inspected to verify electrode placement.

Results

Three rats contributed cells in all the three sets of trial conditions (Pre, Familiar and Novel). The fourth rat contributed cells to the first two conditions but none to the Novel trials, possibly consequent to the electrodes having moved during the changeover. Our interest here was in ensemble behaviour (assumed to reflect operation of the directional system) and previously we have shown that place cells rotate as ensembles in the conditions like those used here (Jeffery, 1998; Jeffery & O'Keefe, 1999). In other words, if one field orientated to the cue then all the others did so too. For that reason, in our previous study we used the 'best' field in a given set of trials, and compared the locations of the field peaks. In the current study we made use of the fact that sometimes more than one cell was present, potentially yielding better information about the ensemble behaviour, and so we calculated ensemble correlation coefficients using all the cells present on a given trial. Between one and seven cells contributed to each ensemble. Occasionally a cell or two would appear randomly in individual trials and these were included in the correlation analysis for that specific rotation. As previously, we never observed simultaneously recorded cells to show differential orienting patterns. As mentioned earlier, we also ran the correlational analysis with individual cells to check that the ensemble analysis did not obscure any differential behaviours.

Pre trials

Recordings from place cells were made while rats foraged in the initial experimental environment (black box for three rats, and grey for one rat) under conditions where the rotation of the box and the rat were at variance, to evaluate the orientation pattern of the place fields in each of these mismatched rotations. We were interested to see which of the four attributes − the visual cue card, the internal sense of direction of the rat, the room or the 'other' − was used by the place fields as a reference for orientation. As previous studies have also found (Muller & Kubie, 1987; Jeffery, 1998; Jeffery & O'Keefe, 1999), the ensemble activity pattern of all the cells analysed revealed a very strong tendency for place fields to orientate to the visual cue card, even in disjunctive rotations of the card vs. the rat/recording box. An example is shown in Fig. 2, where it can be seen that the place field faithfully followed the visual cue regardless of which way the rat was rotated. Figure 7 is a bar graph plotting correlation coefficient values of place fields for the three recording sessions. The mean Pearson's correlation coefficient for the fields rotating with the visual cue card from all the rats recorded was 0.50 (± 0.05 SEM), whereas for the other conditions (rat, room or 'other') it was only −0.03 (± 0.06 SEM), −0.04 (± 0.04 SEM) and −0.09 (± 0.04 SEM), respectively (Table 1). A repeated measures ANOVA comparing the correlation coefficients for the different conditions revealed a significant main effect of condition ($F_{1.985, 43.673} = 38.713$, $P < 0.001$). The differences among individual conditions were further analysed with repeated measures t-tests, which revealed that the orientation with the cue card yielded significantly greater correlation coefficients than the other three conditions (Table 2).
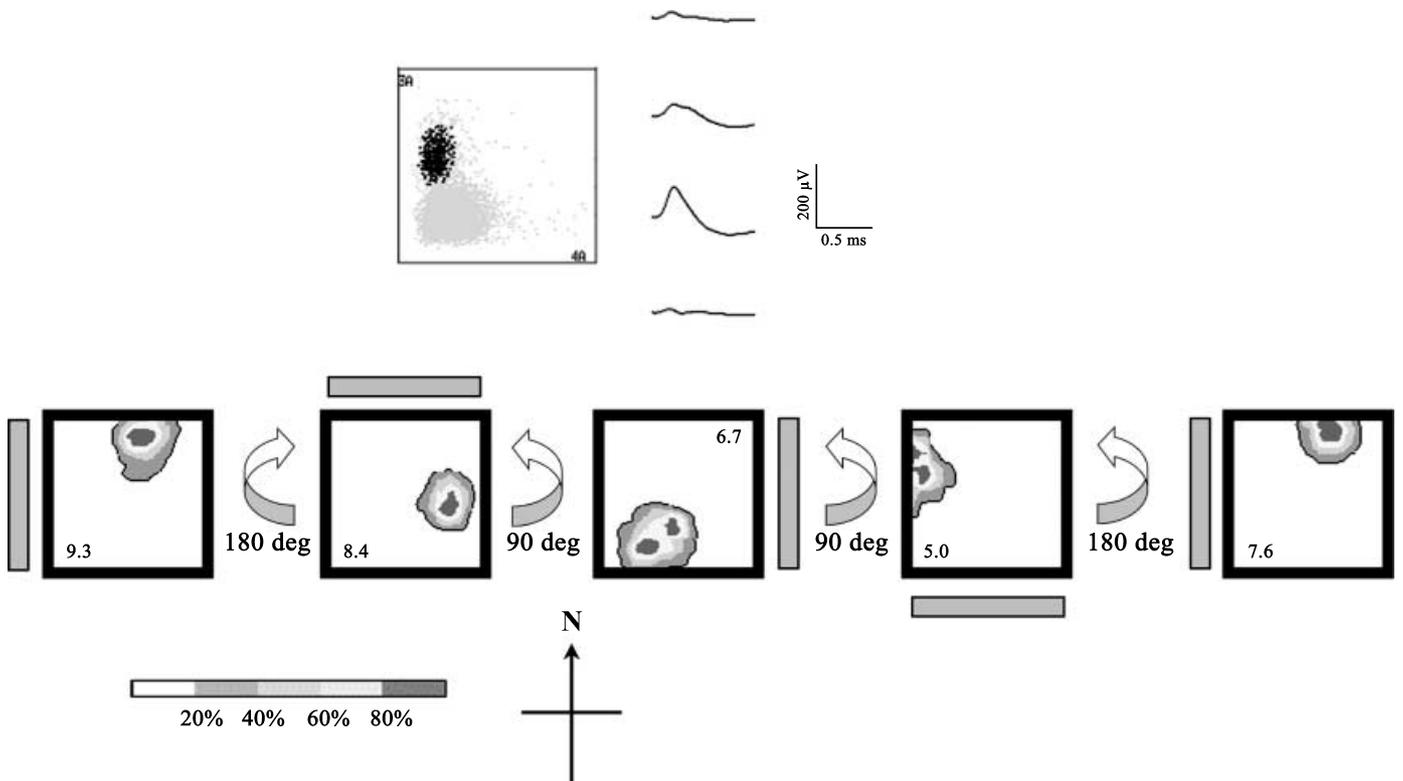
FIG. 2. A place cell from a rat in the black box recorded before the learning schedule began (Pre trials). The top traces show the cell's cluster (as it appeared when amplitudes on two of the electrodes were compared), together with the associated waveform. The bottom panels show how the field behaved across the five trials within the session. The position of the cue card is shown by the hatched rectangle. The rotations of the rat and the box are shown as curved arrows between trials, going from left to right in the row in succession, with the magnitude of the rotation denoted below each arrow. The place fields are shown as contour maps with five levels and each level representing 20% of the peak-firing rate. The mean firing rate in Hz is shown for individual trials. The place field depicted here is orientated by the cue card, as shown by the fact that it maintains the same relationship with respect to the cue card in all successive trials shown, regardless of the rotation of the rat/box. Pre, prelearning session.

TABLE 2. Repeated measures *t*-statistics for determining the influence of orientation of place fields with the card and the rat in the three trial sessions (Pre, Familiar, Novel) and their rotational manipulations

Trial types	Rotation comparisons	Correlation coefficients	*t*-statistics	*P*-level
Pre	Card vs. Rat	0.5/−0.03	$t_{22} = 6.408$	< 0.001
Pre	Card vs. Room	0.5/−0.04	$t_{22} = 6.805$	< 0.001
Pre	Card vs. Other	0.5/−0.09	$t_{22} = 9.554$	< 0.001
Familiar	Rat vs. Card	0.28/−0.07	$t_{17} = -5.679$	< 0.001
Familiar	Rat vs. Room	0.28/−0.01	$t_{17} = 3.056$	= 0.007
Familiar	Rat vs. Other	0.28/−0.06	$t_{17} = 6.371$	< 0.001
Novel	Rat vs. Card	0.46/−0.06	$t_{17} = -7.883$	< 0.001
Novel	Rat vs. Room	0.46/−0.11	$t_{17} = 10.903$	< 0.001
Novel	Rat vs. Other	0.46/−0.13	$t_{17} = 12.278$	< 0.001

The α-level was calculated using a Bonferroni correction (0.05/3 = 0.017).

Familiar trials

Once it was established that place cells consistently followed the salient cue card in disjunctive rotations of the card vs. the rat/box, individual rats were then subjected to a learning protocol. During the days of learning, the rat was able to observe the cue card as it changed position. The cue card began in any of the four cardinal positions, remained there for 10 min, then the spotlight was switched on in another position and the cue card moved across before the spotlight at the earlier position was finally switched off. Ten such trials were performed in a pseudorandom manner daily; the box was not rotated and the rat was uncovered throughout. This procedure was designed to allow the rat to observe that the cue card was not a reliable directional reference. A minimum of 5 days was allocated for learning, with further days only if required depending on the reliability of shifting patterns of the place fields (see Materials and methods). The learning period, over which the visually unstable landmark lost the ability to control place fields, varied with individual rats even though the daily schedule of rotating the card in full view of the rat was kept rigid and constant. The time period ranged from 5 to 15 days (5, 9, 15 and 7 days for the four rats). A behaviour observed in common to all the rats, beginning from the middle of the time epoch just mentioned (depending on individual rats) was that they often would spring to the top of the box-wall in an attempt to jump out of the environment. This behaviour was absent closer to the completion of the learning phase.

Modification of place cell responsiveness to the cue card was ascertained by recordings showing locking of place fields to the internal direction sense of the rats rather than to the card, occurring in a majority of the discordant box/card rotations (in at least three of four consecutive rotations). After training, the ensemble activity of all the cells in most of the discordant trials showed that the place fields relied on idiothetic cues as their directional reference. Figure 3 shows an example of a place cell with a field that followed the rat's internal direction sense rather than being fixed with respect to the cue card. One of the rats in the latter stages of the learning phase occasionally showed, albeit in only one of many trials within a given session, place
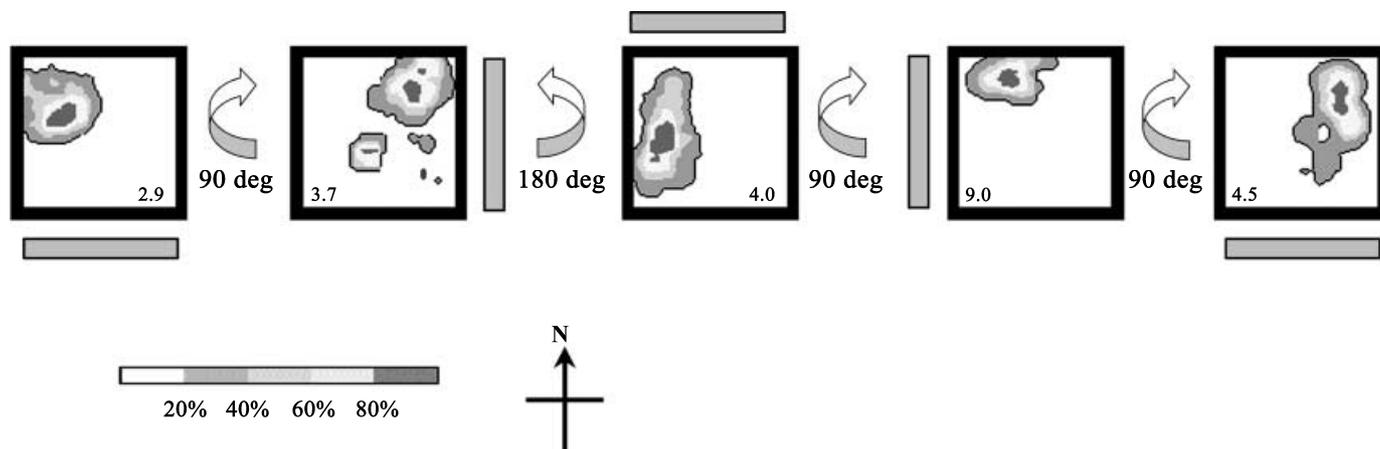
FIG. 3. Place field from a cell in one rat in the black box following completion of the learning protocol, i.e. from Familiar trials, showing that the field rotates by the same amount as the rotation of the rat, or in other words the place field follows the internal (idiothetic) cues faithfully after the rat has experienced the cue card as an unreliable indicator of direction. All other legends are same as in Fig. 2. Familiar, postlearning familiar context. The slight changes in field shape seen in this and the next figure were not consistent findings, and were probably due to variability resulting from the short recording times.

fields that remained fixed to room coordinates (for which we were unable to determine any systematic reason). This was seen over several days of recording following the daily learning schedule and was not related to any particular rotation or location; rather, it appeared randomly. We considered the learning phase to be complete at this stage for this particular rat as in all of the other rotational trials the place fields rotated with the rat (i.e. the rat-following was above chance level). Figure 4 shows an example of a place cell from this rat whose place fields in one of the discordant trials did not change in spatial location relative to the previous trial. In the other trials, the place fields robustly followed the idiothetic cues, as is evident from the bar graph in Fig. 7.

The average Pearson's correlation coefficient for rotations corresponding to the internal sense of direction of the rat was 0.28 (± 0.05 SEM), whereas for the other conditions (card, room or 'other') it was only −0.07 (± 0.03 SEM), −0.01 (± 0.05 SEM) and −0.05 (± 0.02 SEM), respectively (Table 1). A repeated measures ANOVA revealed a significant main effect of condition ($F_{1.754, 29.812} = 13.542$, $P < 0.001$). The differences among individual conditions were further analysed by a repeated measures t-test showing that the correlation coefficients for rotation with the internal sense of direction of the rat

were significantly greater than the other three conditions, in marked contrast to the *Pre* trials that revealed strong cue card following (see Table 2).

Remapping

After place cell learning was at criterion levels, the rat was removed from the box and placed into an opaque container. During this time, the box was changed from black to grey (3 rats) or vice versa (1 rat). The rat was then replaced into the new box and a full set of recording trials performed, to assess: (a) remapping; and (b) whether the remapped cells followed the card or the rat. A total of 18 cells from three rats contributed to the analysis of contextual remapping ($n = 7$, $n = 8$, $n = 3$) − the fourth rat did not show place cell activity in the new box, perhaps because of electrode drift in the changeover period. Of the active cells, four were new cells that switched on with the appearance of new place fields (as shown in middle row of Fig. 5) and another four cells responded by switching off their place fields in the Novel session trials. The remainder responded by reorganization of their place fields, as is evident in Fig. 5. The first two rows in Fig. 5
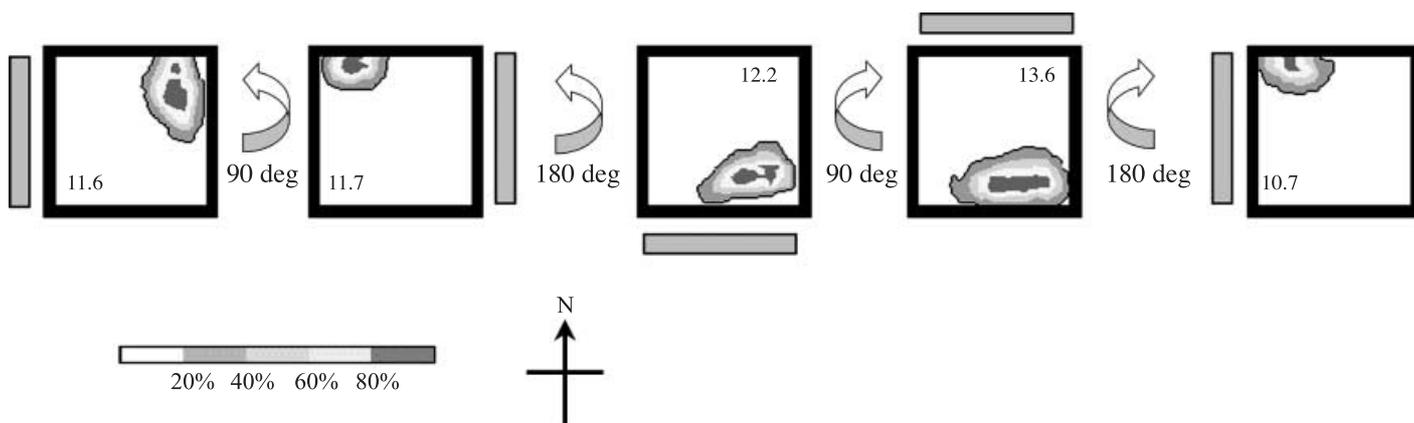

FIG. 4. Place field of a cell in another rat from Familiar trials showing that the orientation of the field did not alter between trial 3 and trial 4 (remained fixed to the room coordinates), even though in all other trials recorded it followed the idiothetic cues consistently. All other legends are same as in Fig. 2. Familiar, postlearning familiar context.

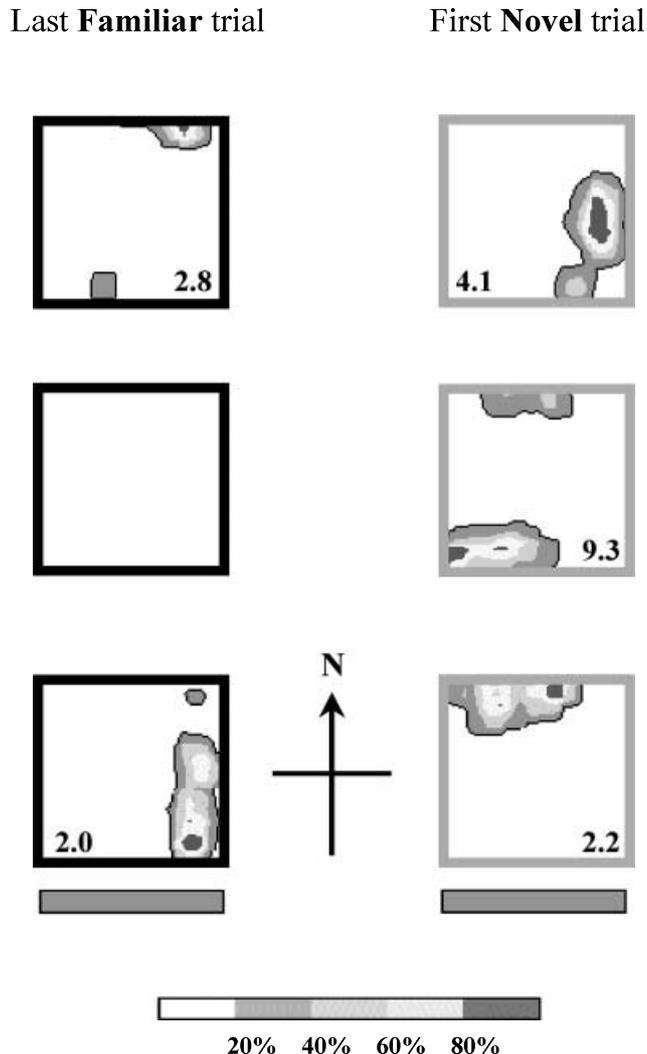## Last **Familiar** trial   First **Novel** trial

FIG. 5. Three place cells with fields from the last recorded trial in the Familiar session (black box) shown in the left and the same cell recorded in the first trial of the Novel session (grey box) to show remapping to a change in spatial context. The cue card is in the south location for both the conditions. The first two rows are examples of place fields from simultaneously recorded place cells from one rat. The first row shows a place field located close to the north-east wall in the black box to have been relocated close to the middle of the east wall. The second row shows a cell that was inactive in the black box to be active in the grey box. The last row shows place-correlated firing of a cell from another rat. Here the field has shifted from being close to the south-east corner to being at the middle of the north wall. All other legends are same as in Fig. 2. Familiar, postlearning familiar context; Novel, postlearning novel context.

show two simultaneously recorded place cells from one rat. The cell in the top row shifted its field from a corner to the middle of a wall, and the cell in the middle row changed from being silent to being active in the first Novel trial. The third row in Fig. 5 is another example of remapping from a different rat, wherein the fields shifted from being close to a corner in the last Familiar trial to a position along the middle of the wall in the first Novel trial. Remapping to the change in spatial context was quantified by comparing the activity of the recorded cell population in the last Familiar trial and the first Novel trial in the three rats individually (refer to Materials and methods).

Following learning and prior to the change in spatial context induced by change in the colour of the box, place fields continued to be orientated by the rat's internal sense of direction. During the

changeover period the rat was placed in an opaque box and then introduced to the new environment. It was not known how the idiothetic cues would update a field's location during the intervening transfer phase. Moreover, in enclosed experimental setups like ours, place cells often have place fields along the walls and in corners of the boxes that add to the problem of distinguishing true remapping from a simple rotation. To overcome these problems, rather than examining individual cells, ensemble activity was compared between the last Familiar trial with all the rotated versions of the ensemble activity of place cells in the first Novel trial. Thus, even if it was hard to distinguish whether the field from a given cell had remapped or rotated, the data from several cells would provide a clearer picture, due to the heterogeneity of true remapping.

The comparisons revealed that the mean correlation coefficient of the population activity of place cells was close to zero (0.02 ± 0.11 SEM, -0.04 ± 0.05 SEM, -0.13 ± 0.02 SEM for the three rats), suggesting that a new representation was now active in these rats in the contextually altered environment. These results are similar to previous studies on contextual remapping from this and other labs (Bostock *et al.*, 1991; Anderson & Jeffery, 2003; Hayman *et al.*, 2003; Jeffery *et al.*, 2003).

Novel trials

With a change in the spatial context, a new spatial representation was now active for the place cells in these rats. To test whether information about cue card instability from the previous environment was still available to the place cells that fired in the new spatial context, further disjunctive trials were carried out.

Results show that the newly remapped fields still preferentially followed the rats' internal sense of direction rather than the cue card, as clearly seen in Figs 6 and 7. The average Pearson's correlation coefficient for the fields rotating with the internal sense of direction of the rat was 0.46 (± 0.04 SEM), whereas for the other conditions (card, room or 'other') it was only -0.06 (± 0.05 SEM), -0.11 (± 0.02 SEM) and -0.13 (± 0.06 SEM), respectively (Table 1). A repeated measures ANOVA revealed a significant main effect of condition ($F_{2.008, 34.130} = 66.504$, $P < 0.001$). The differences among individual conditions on further analysis by a repeated measures *t*-test showed that the Pearson's correlations for rotation with the internal sense of direction of the rat were significantly greater than the other three conditions, i.e. similar to that observed in the Familiar trials (see Table 2). Thus, despite the fact that new place field representations had formed, our results demonstrate that for these rats, the acquired information about the cue's instability transferred to the new environmental context.

Comparison across testing phases

Having analysed the different trial types separately, we then compared the results across testing phases to determine whether there was, as expected, a statistical change in the responsiveness of fields to the cue card as the experiment progressed. This was done both using the ensemble analysis and analysis of individual cells. Because these procedures yielded closely similar results (see Table 1), for clarity only the ensemble data are reported here.

The correlation coefficients were analysed with a 3×4 repeated measures ANOVA with 'Condition' (Pre, Familiar and Novel) and 'Rotation' (card, rat, room and 'other') as factors. The analysis revealed a significant main effect of 'Condition' ($F_{2,34} = 4.787$, $P = 0.015$) and 'Rotation' ($F_{2.201, 37.416} = 39.101$, $P < 0.001$), and
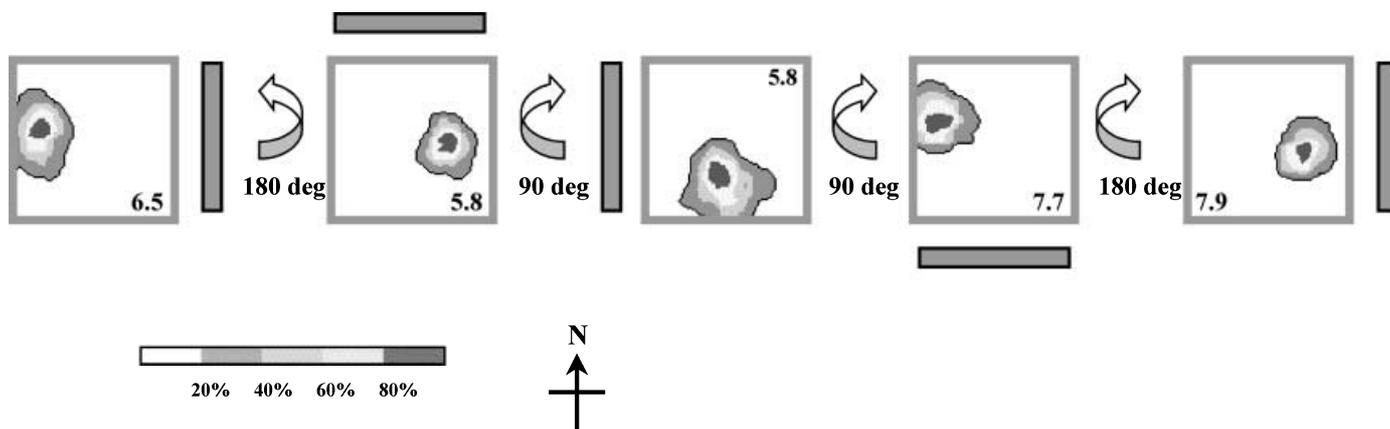
FIG. 6. Place field of a cell from a rat following change of spatial context (by a change in colour of the box: here from black to grey), i.e. from Novel trials. The response of the place field to disjunctive rotations of cue card/box is similar to that observed in Familiar trials, in other words, they still reliably follow the rat's internal sense of direction. All other legends are same as in Fig. 2. Familiar, postlearning familiar context; Novel, postlearning novel context.
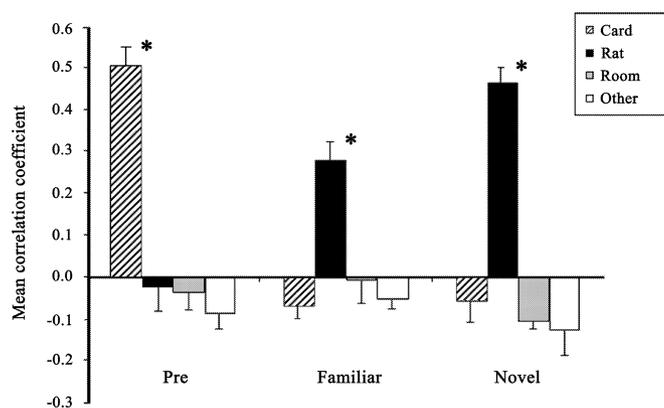

FIG. 7. Bar graph plotting mean Pearson's correlation coefficient against the different trial sessions (Pre, Familiar, Novel) for rotation of the place fields with 'card', 'rat', 'room' and 'other' (± SEM). Prior to the learning phase (Pre trials), place fields use the cue card as a stronger reference than the other three conditions. Following learning, the control of place field orientation is passed to the rat's internal sense of direction (Familiar trials). The learning appears to transfer to the new environment (Novel trials) consequent to change in the spatial context, as suggested by the place field continuing to follow the idiothetic cues of the rat. Asterisk indicates significance at $P < 0.001$. Familiar, postlearning familiar context; Novel, postlearning novel context; Pre, prelearning.

also a significant interaction ($F_{3.774, 64.166} = 24.863$, $P < 0.001$). A series of repeated measures ANOVAs exploring the effect of 'Condition' at each level of 'Rotation' revealed that this interaction was largely due to differences between Pre, Familiar and Novel for 'card' ($F_{2,34} = 51.964$, $P < 0.001$) and 'rat' ($F_{2,34} = 18.892$, $P < 0.001$). No effect of 'Condition' was found for 'room' or 'other' (for both $P > 0.05$).

The differences in the conditions were then subjected to repeated measures t-tests. When Pre trials were compared with Familiar, cue card following was significantly greater for the Pre trials ($t_{17} = 8.618$, $P < 0.001$) and rat following was, conversely, significantly greater for the Familiar trials ($t_{17} = -3.583$, $P = 0.002$), revealing the effect of cue-instability learning. When Pre trials were compared with Novel trials, cue card following was also significantly higher for the Pre trials ($t_{17} = 7.460$, $P < 0.001$) and rat-following was significantly higher for the Novel trials ($t_{17} = -5.405$, $P < 0.001$). This shows that the

remapped place fields did not behave like fields did when the rats were naive, but more like how they behaved after learning, reflecting a transfer of the acquired information into the remapped representation. Interestingly, when Familiar trials were compared with Novel trials a significant difference was also found: in this case, rat following was even greater in the Novel condition ($t_{17} = -3.051$, $P = 0.007$), although cue card following did not differ between the groups. This difference may reflect an attentional effect due to the context change. These statistical results suggest a strong influence of experience on place-correlated firing, in the first instance, and remapping on place field orientation in the second instance.

Histology

The histology revealed that the electrodes in all rats were placed in region CA1 of the hippocampus. The rat that had ibotenic acid injected near the anterior dorso-lateral thalamic nuclei showed no lesion effect whatsoever, suggesting that the agent had probably been introduced into the third ventricle and washed away. This rat otherwise showed behaviour and physiology that was indistinguishable from the other rats in the study, and so its results were retained.

Discussion

The present study demonstrates the following: (a) that a prominent visual cue serves as a strong directional reference for place fields to orientate in disjunctive cue card/rat rotations (as seen in Pre trials). (b) that following repeated exposure of the rat to the movement of the cue card, place cells 'learn' about the instability of the landmark, so that their field locations come to be consistently orientated by the internal sense of direction of the rat (as in Familiar trials). (c) that learning about landmark instability in one familiar context is transferred to a novel context, wherein although the place cells remap, their (remapped) place fields continue to follow internal directional cues rather than the landmark (as evident from Novel trials). In other words, this type of directional cue learning is independent of spatial context. This finding contrasts with another kind of place cell learning, location discrimination, which was found to be context-specific (Hayman *et al.*, 2003). Possible reasons for this difference are discussed below.

The results from the Pre and Familiar trials replicate earlier studies (Jeffery, 1998; Jeffery & O'Keefe, 1999), which showed that when a

visual cue card and the rat's internal sense of direction were placed in conflict, place fields initially used the cue card as a directional reference, before learning that that the cue card was no longer stable, following which they tended to orientate by the internal ('idiothetic') directional cues instead. Such findings suggest that place cells receive multiple, sometimes competing sources of directional information. This is supported by findings from an earlier study by Knierim *et al.* (1998), who recorded place cell activity while rats foraged randomly in a cylindrical environment in the centre of a curtained arena with a prominent visual landmark. With abrupt rotation of the cylinder by 45°, visual stimulus controlled the place field location, whereas a 180° rotation showed a variable pattern where in some circumstances place field locations were influenced by the visual cue and in others a complete remapping was observed wherein existing place fields disappeared and new fields appeared. Our results never did show complete remapping of place fields even when the mismatch between the information provided by the distal visual stimulus and the idiothetic cues was large, as in 180° card/box rotations. Other studies have also demonstrated an interaction between idiothetic and external cues. For example, Rotenberg & Muller (1997) found that small changes of a cue card caused place fields to rotate accordingly, confirming an input from this visual stimulus, but large changes of the cue card did not, suggesting that with a large conflict, place cells are more influenced by the rat's internal sense of direction. Such studies suggest that there is a constant competition going on among the different types of information (external or internal) providing sensory inputs to the place cells, with their relative importance being revealed by their dissociations in such experiments. Interestingly, in our study, one of the rats tested in the Familiar trials showed place fields that occasionally did not rotate, suggesting an input not only from the visual landmark and the internal direction sense, but also from the room (Fig. 3). However, this oddity was noticed in usually only one of many discordant rotations on any given day. This is a good example of the ongoing competition for the control of place fields among the various sensory stimuli under such situations. This anomalous behaviour could be accounted for by considering that auditory stimuli, perhaps emanating from the computer and the recording system from a fixed location outside the curtained area, might act as a directional reference.

Following exposure to the sight of the mobile cue card, place fields eventually stopped being controlled by the visual landmark and began to rotate by the same amount as the rat and the box instead. In previous studies we showed that rotation of the rat independently of the recording box is sufficient to cause place fields to rotate (Jeffery *et al.*, 1997; Jeffery & O'Keefe, 1999), and thus we assume that control of the fields passed from the visual cue to the rat's internal directional (idiothetic) cues, though local box cues may have contributed (as the box and the rat were rotated together in the present study). The learning period varied considerably among the rats tested.

A behavioural feature observed in all the four rats during the learning period was that many times the rat tried to escape from the test box. This seemed to be particularly pronounced at around the middle of the time over which control of the place fields was being transferred from the cue card to the internal cues, although we did not quantify this. Recordings from place cells during this period revealed sudden appearances and disappearances of place fields in various rotational trials, and place field locations randomly followed either the visual stimulus or the idiothetic cues or remained stationary (although always behaving coherently within a particular ensemble). The competitive interplay of the different sensory inputs was thus evidently in action until the idiothetic cues finally 'won'. This conflict may have had a bearing on the behaviour of the rats, insofar as to

prompt them to escape from the environment all together. This escape type of behaviour disappeared as idiothetic cues began to control place field orientation. By the end of the 'learning' period, place fields were rotating reliably with the rat/box rather than with the visual cue as they had done initially. We refer to this alteration as 'directional-cue-instability learning'.

Directional-cue-instability learning reflects the capacity of the system not only to weigh up different sources of directional information (visual, idiothetic, etc), but also to modify the weighting depending upon experience. This altered weighting suggests an interplay of visual and movement-related (idiothetic) cues, an interplay that enables subjects to path integrate (see Etienne & Jeffery, 2004 for a review). Under normal circumstances, when an animal navigates in an environment these two systems are in close agreement, and generally directional representation is subjected to continuous updating by visual cues (Goodridge & Taube, 1995). While visual cues dominate when the conflict is relatively small, thus 'resetting' the path integrator, if there is a large mismatch then the idiothetic cues take control (Rotenberg & Muller, 1997). Cue-instability learning shows that this interaction is plastic, so that even highly salient landmarks can be disconnected if they turn out not to be reliable indicators of direction.

The question of interest in the present experiment is whether this cue-instability learning transfers from one spatial context to a different one. A change in context brought about by a non-spatial sensory alteration in the environment after completion of the learning phase causes place cell remapping, as shown by a number of earlier studies (Bostock *et al.*, 1991; Anderson & Jeffery, 2003; Hayman *et al.*, 2003; Jeffery *et al.*, 2003). This indicates that a new place representation is active in the new context. In a previous study of another kind of place cell learning (Hayman *et al.*, 2003), we found that the learning, which we termed 'location discrimination', did not transfer to a new context, i.e. following the remapping induced by the context change, place cells did not discriminate the locations in a novel context even though the same cells did so in the familiar context (the one in which the discrimination was acquired). In the present study we therefore changed the context to see whether directional-cue-instability learning does or does not generalize across contexts. We found that, in contrast to location discrimination, directional-cue-instability learning in fact seems to be context independent.

The persistence of directional-cue-instability learning across contexts, despite place cell remapping, suggests two things: (a) the directional signals to place cells are unaffected by remapping; and (b) this directional information is integrated with the other inputs to place cells upstream of the place cells themselves. Arguments in support of these hypotheses are as follows. First, following the learning phase, when the control of place fields was transferred from the card to the idiothetic cues, almost all simultaneously recorded cells showed a similar pattern of shifts of their place field locations (with occasional exceptions due to 'messy' fields). This coherent behaviour is in marked contrast with that observed in a recent study (Anderson & Jeffery, 2003) where place cells exhibited heterogeneous behaviour in their place field location following changes in spatial context. If synapses directly onto place cells were involved in bringing about these changes, one would expect differential behaviour of the cells during the learning phase, as it is unlikely that all cells would learn (i.e. undergo modification of their inputs) at the same rate. Thus, it seems that the signal controlling the orientation of place fields is homogeneous, and therefore likely that the resolution of the competition among various directional inputs is resolved upstream of the hippocampal place cells. Countering this, one could argue that the local network dynamics of the place cell representation might still implement the changes seen after learning, inducing homogeneous

behaviour despite heterogeneous inputs. This could be resolved by temporarily inactivating the hippocampus during the learning phase. If directional-cue learning happens outside of the hippocampus, then hippocampal inactivation should not interfere with the learning. On the other hand, if it happens within the hippocampal network itself, then the cells should fail to 'learn', and the fields should orientate to the visual stimulus instead.

If it is accepted that cue-instability learning is probably happening upstream of the place cells, the question arises as to where in the brain these experience-dependent changes occur. The CA1 place cells receive many inputs from a variety of sources, but the location of the changes elicited by experience of the mobile cue card may well occur in structures that process both visual and idiothetic directional information and pass this information to the hippocampus. Place cells probably receive their directional inputs from a network of head direction cells, which are located in different regions of the brain, predominantly in the postsubiculum (Taube *et al.*, 1995), anterior thalamic nuclei (Blair & Sharp, 1995; Taube, 1995) and posterior cortex (Chen *et al.*, 1994). Head direction cells have been shown to receive both idiothetic and visual information (Knierim *et al.*, 1995; Taube & Burton, 1995; Blair & Sharp, 1996). Firing of anterior thalamic nuclei head direction cells precedes that of postsubicular head direction cells by 25 ms (Blair *et al.*, 1997), and lesion of the former leads to abolition of head directional cell activity in the postsubiculum. Thus, in this network, the postsubiculum, receiving both visual information (Goodridge & Taube, 1997) and movement-related information transferred from the anterior thalamus, appears to be a good candidate structure to be involved in processing the learning phenomenon described here. However, arguably such learning could take place anywhere along the visual processing pathway, and further experiments are needed to determine the site of such plasticity.

Why is it that some kinds of place cell learning are context-dependent (Hayman *et al.*, 2003) while others, as we show here, are not? The likely reason is to do with the adaptive significance of the various stimuli, and the function they perform in driving place cells. Directional stimuli are often distant landmarks, and in the real world are unlikely to change their behavioural significance as the context changes. By contrast, in the location-discrimination study of Hayman *et al.* we argued that the acquired stimuli became, themselves, part of the 'context', and thus became bound to the representation at the level of contextual modulation, hence their failure to transfer to a new context in which a different set of context inputs was active. Thus, the place representation draws a distinction between stimuli that are context-specific, and those (like directional stimuli) for which transfer across contexts is adaptive.

The distinction between context-dependent and context-independent place cell learning adds to the growing body of evidence suggesting that the stimuli that drive place cells are functionally differentiated, with different kinds performing different roles. Thus, we find that acquired inputs relating to the location of place fields behave differently in response to context changes from acquired inputs relating to orientation. This functional differentiation is adaptive, and is also in keeping with the idea that the hippocampus is a specialized structure for performing specific computational functions on particular kinds of stimuli, rather than a general all-purpose associative device.

Acknowledgements

Abbreviations

Familiar, postlearning trials in the familiar context; Novel, postlearning trials in the novel context; Pre, prelearning trials.

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