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Place cells in the ventral hippocampus of rats

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MANY cells recorded from the dorsal hippocampus of freely moving rats are intensely active only when the rat's head is in a particular part of its environment. For this reason, such units are called 'place cells'. We have investigated whether place cells are also found in the ventral hippocampus. Recordings were made from ventral hippocampal units while rats chased food pellets in a cylindrical arena. The rat's position was simultaneously recorded by tracking a light on the rat's head. Our data show the existence of cells in the ventral hippocampus whose positional firing patterns and electrophysiological properties are very similar to those of dorsal hippocampal place cells.

Key words: Hippocampal formation; Ventral hippocampus; Dorsal hippocampus; Unit recordings; Spatial learning; Memory

Introduction

Lesion and electrophysiological evidence provide converging support for the hypothesis that the dorsal hippocampus plays a critical role in the processing of spatial information.[1] Lesions of the dorsal hippocampus in rats impair performance of a wide variety of spatial tasks.[2] In addition, many cells recorded from the dorsal hippocampus of freely moving rats are intensely active only when the rat's head is in a particular part of its environment.[3,4] It is the location-specific firing of such 'place cells' that most strongly implies a crucial role for the hippocampus in spatial behaviour.[5–8]

In contrast to the well-founded hypothesis that the dorsal hippocampus is an important component of a navigational system, the involvement of the ventral hippocampus in spatial information processing is still questionable. In the first place, the lesion data are somewhat contradictory. In earlier work, dorsal and ventral hippocampal lesions produced comparable deficits in both maze problems and spatial alternation.[9] In agreement, temporary pharmacological inactivations of the ventral hippocampus reliably impair spatial memory.[10] On the other hand, greater deficits in maze learning[11] and water maze navigation[12] have been reported to occur after dorsal than ventral hippocampal lesions.

In addition to the unclear picture so far obtained with methods that degrade hippocampal activity, it is not known whether pyramidal cells in the ventral hippocampus act as place cells. Certainly, it is of interest to ask whether the dorsal and ventral regions of the hippocampus are homologous in this regard. If place cells are in fact found in the ventral hippocampus, it is also of interest to compare their properties with those of dorsal hippocampal place cells. The main results of this paper are that there are place cells in the ventral hippocampus, and that their properties are remarkably similar to those in the dorsal hippocampus.

Materials and Methods

The methods used here were substantially the same as those used for dorsal hippocampal place cells.[4] The recording chamber was a 76 cm diameter, 50 cm high grey cylinder, with a single white cardboard sheet that covered 100° of wall arc. The cylinder was visually isolated from the rest of the laboratory by a cylindrical curtain 250 cm in diameter. The floor of the cylinder was a grey piece of paper that was replaced between sessions.

The subjects were Long–Evans male rats (300–350 g). To permit estimation of positional firing rates everywhere in the cylinder, the rats were food-deprived and then trained in a 'pellet-chasing' task for 10 days. In this task, the rat had to retrieve 20 mg food pellets scattered into the cylinder. Since the food pellets landed in unpredictable places, the rat learned to run almost constantly over the whole floor surface. After training was complete, the rat visited the entire floor area in just a few minutes, and so covered the accessible area several times during a 16 min recording session.

After training, rats were anaesthetized with pentobarbital (40 mg kg^{-1}). A movable array of 10 25 μm electrode wires[13] was stereotaxically implanted in the ventral hippocampus (4.8 P, 4.0 L to bregma[14]) of six rats. The tip of the array was initially positioned at a depth of 6.6 mm from dura, so that when lowered, it passed through CA3 and then CA1. The movement was medial to lateral at an angle of 12° from vertical. Four other rats were implanted with an electrode array aimed at the dorsal hippocampus (3.8 P, 2.7 L to bregma, 2.5 from dura[14]). When lowered, the array passed through CA1 and then CA3. Securing screws were placed over the right olfactory bulb, the left frontal cortex, and the left cerebellar hemisphere. Sterile petroleum jelly was applied to the exposed brain surface and the guide tubing to seal the skull opening. Dental cement was applied over the jelly and around

the guide tubing. Finally, the exposed skull was covered with dental cement, and the bottoms of the three drive screws assemblies were cemented to the skull.

Recordings were made with a system made of the electrode wires, a headstage with a field effect transistor amplifier for each wire and a cable to lead the amplified signals to a commutator. The fixed side of the commutator was connected to a distribution panel. From the panel, the desired signals were amplified 10 000-fold with low-noise differential amplifiers and band-pass filtered from 0.3 to 10 kHz. The signals were then sent to two time-and-amplitude window discriminators (Model DIS-1, Bak Electronics) arranged in series. Accepted spikes were counted for 20 ms intervals. At the end of each such interval (the end of a TV frame—see below), the spike count was sent as a 4-bit binary number to a computer.

In addition to spike data, the head position and head direction of the rat were tracked by locating two coloured light emitting diodes (LEDs). A red LED was positioned on the midline about 1 cm above the head and somewhat forward of the rat's eyes. A green LED, also on the midline was set about 5 cm behind the red LED. Head position was taken as the position of the red LED; head direction was taken from the relative coordinates of the red and green LEDs.[4,15] The two LEDs were independently tracked with a TV-based digital spot follower that received the red and green RGB signals from a CCD colour camera. Each LED was detected in a grid of 256 × 256 square regions (pixels) 6.25 mm on a side, permitting a resolution of about 6° for head direction. For head position tracking, the resolution was reduced by 2 bits in each dimension, yielding a 64 × 64 grid of pixels 25 mm on a side. The X and Y coordinates at the end of each frame were stored in parallel with the number of spikes counted during the 20 ms frame. At 50 Hz, a total of 48 000 sequential samples of position and associated spike count were accumulated in a 16 min recording session.

Beginning 5 days after surgery, the activity from each wire was sampled daily while the rat chased pellets in the cylinder. The electrodes were lowered over a period of several weeks while searching for unitary waveforms of sufficient amplitude to be isolated. Once a unit was isolated, it was recorded during a 16 min session of pellet chasing. For many cells, additional sessions with the cue card rotated or removed were also done.

Data were analysed off-line. To obtain a positional firing rate distribution, the total time the red light was detected in each pixel and the total number of spikes in each pixel was accumulated for the session duration. The rate in each pixel was the number of spikes divided by the dwell time. Colour-coded firing rate maps were used to visualize positional firing rate distributions. In addition, the spatial firing data of individual neurones were numerically analysed (see Table 1).

Table 1. Main parameters of ventral and dorsal hippocampal place cells

	Dorsal place cells (n = 16)	Ventral place cells (n = 18)
Spatial coherence	0.65 ± 0.03	0.56 ± 0.04
Information content[a] (bit per spike)	2.11 ± 0.16	1.85 ± 0.14
Mean size of place fields (in pixels)[b]	98 ± 22	113 ± 15
Number of fields per cell (range)	1.25 (1–3)	1.06 (1–2)
Overall firing rate (AP s^{-1})	1.73 ± 0.28	0.71 ± 0.06**
Mean rate in place field (AP s^{-1})	6.34 ± 0.87	2.16 ± 0.23**
Peak rate in place field (AP s^{-1})	24.06 ± 3.87	6.29 ± 0.99**
Mean spike amplitude (μV)	215 ± 20	157 ± 16 *

Values given as means ± s.e. Comparisons based on two-tailed Student's t-tests. *$p < 0.05$; **$p < 0.001$ compared with dorsal cells.
[a] For comparison, spatial coherence and spike information content for a typical theta cell yield values < 0.40 and 0.2 bit per spike, respectively.
[b] The total size of the cylinder was approximately 700 pixels.

Results

Recordings were made from 57 ventral hippocampal units. Based on electrophysiological properties, ventral hippocampal cells were easily classified in the same two categories found in the dorsal hippocampus.[16] Thirty-six cells were called 'theta cells' by the same criteria used in the dorsal hippocampus. Such units generated only single spikes with short duration negative phases (<0.3 ms) and never fired complex spikes.[17] They fired rapidly at all times [usually faster than 10 action potentials s^{-1} (AP s^{-1})], and their firing was clearly faster during locomotion than during quiet alertness. The other 21 units were considered to be complex-spike (CS) cells because they were seen to fire decrementing bursts of 3–5 action potentials at brief intervals (4–6 ms apart). The negative phase of the much more common single action potentials was longer (always >0.4 ms) than for theta cells. The overall firing rate of CS cells never exceeded 2 AP s^{-1} and was usually about 1 AP s^{-1}.

As for dorsal theta cells, direct observation and formal recordings revealed a much weaker positional signal for ventral theta cells than for most CS cells.[18] We therefore focused on CS cells. Of the 21 CS cells, three were virtually silent everywhere in the cylinder. Seventeen of the other cells had one place field in the cylinder; each was active only when the rat's head was in a specific part (the 'field') of the cylinder and was virtually silent elsewhere. The last cell had two fields. Thus, 18 of the 21 ventral CS cells clearly acted as place cells. Based on previous experience with dorsal CS cells, it is plausible that the three silent units would have place fields in a different apparatus.[6] Figure 1 shows colour-coded firing rate maps for three ventral hippocampal CS cells. As can be seen, the shape of the place field of a given cell could be either crescentic (at the edge of the apparatus) or circular; the field shapes were the same as those seen in the dorsal hippocampus.[4] By inspection of autoscaled firing rate maps, the positional firing properties of ventral place cells were very similar to those of 16 dorsal place cells

FIG. 1. Firing rate maps of three representative ventral hippocampal place cells. **Left**. Unit v3u7 (spatial coherence: 0.68; informational content: 1.88 bit per AP). Median firing rates for colours: yellow, 0.0; orange, 0.71; red, 1.39; green, 2.38; light blue, 3.37; dark blue, 5.52 AP s^{-1}. **Middle**. Unit v4u4 (spatial coherence: 0.83; informational content: 2.4 bit per AP). Note a smaller crescent-like place field at 5 o'clock. Median firing rates (order as above): 0.0; 0.99; 2.23; 3.57; 5.88; 10.0 AP s^{-1}. **Right**. Unit v3u13 (spatial coherence: 0.59; informational content: 0.81 bit/AP). Median firing rates (order as above): 0.0; 0.31; 0.57; 0.89; 1.26; 2.05 AP s^{-1}.

recorded in identical conditions. That is, if firing rate was ignored (as it is in autoscaling), ventral and dorsal place cells were indistinguishable according to several measures that characterize the shape and other structural properties of the positional firing distributions (Table 1). The measures include 'spatial coherence',[18] 'spike information content',[19] place field size,[4] and the number of fields per cell. Spatial coherence is a nearest-neighbour two-dimensional autocorrelation and so estimates the local smoothness of place fields. Spike information content estimates the extent to which uncertainty about the rat's position is reduced by each spike fired by a cell. The size of the place field (minimum set at 9 pixels at least) is calculated by counting the number of adjacent pixels with a firing rate exceeding 0.5 AP s^{-1}. The similarity of these four measures confirmed the similarity of positional firing patterns for ventral and dorsal cells seen by eye.

In contrast to the similarity of positional firing patterns, the firing rate of ventral cells was considerably lower, according to three estimates, including the overall firing rate, the mean rate in the place field and the peak rate in the place field. One explanation of this difference in activity depends on the additional fact that the mean spike amplitude for ventral units was generally lower by about 27% than for dorsal units (Table 1). The lower amplitude of unitary waveforms makes it necessary to be more selective about which waveforms are accepted, thereby lowering the acceptance rate.

In addition to the similar positional discharge patterns of ventral and dorsal place cells in constant conditions, the positional firing patterns of all place cells were affected in the same way by certain manipulations of the environment. The effects of rotating the white cue card were tested for eight cells.[6] The angular position of the field was first determined with the card in 'standard' position in the laboratory frame. The rat was removed from the cylinder and the card was rotated by 90° in its absence. For seven of eight ventral place cells, the place field in the presence of the rotated card also rotated by 90° in the same direction. When the card was rotated back to the standard position with the rat out of the cylinder, the field for all seven cells was back in its original angular location. Thus the white card exerted precisely the same form of stimulus control over ventral place fields as over dorsal fields.[6] An example of the field locations seen with standard-rotated-standard sequence of card positions is shown in Figure 2.

There was also evidence that uncontrolled cues fixed relative to the environment also control the angular location of place fields. First, the place field of one cell did not rotate after cue rotation. Second, deleting the card for an entire session did not affect the parameters of place fields (shape, size, and angular position within the cylinder) of three cells, although it dramatically reduced the firing activity of a fourth cell.

By direct observation during recordings of ventral place cells, there was little or no indication that the

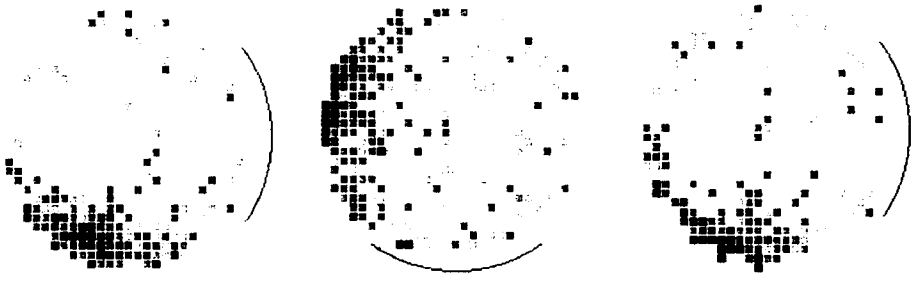

FIG. 2. The effects of cue rotation on the spatial firing pattern of a ventral place cell (unit v5u2). The 90° clockwise rotation of the cue-card (indicated by an arc outside the cylinder) produced equal rotation of the place field. Median firing rates (order as in Fig. 1): 0.0; 0.75; 1.72; 3.2; 6.67; 8.52 AP s^{-1}.

direction in which the head pointed modulated discharge, in agreement with observations on dorsal place cells.[20] For five ventral cells, the total recording time was sufficient (≥ 32 min) to allow us to use the method of Muller *et al*[21] to test the hypothesis that directional firing is accurately predicted from the direction-independent positional firing distribution and the fact that different portions of place fields tend to be visited at different head directions.[21] The agreement between observation and prediction was almost as close as for dorsal cells. This suggests that location is by far the strongest correlate of ventral place cell discharge as it is for dorsal place cells, and that head direction alone or in combination with position is not an important predictor.

Discussion

Our major conclusion is that place cells exist in the ventral hippocampus. Their positional firing patterns are characterized by place fields, just as is true of dorsal place cells. In addition, ventral place cells were classified as complex-spike cells on electrophysiological grounds, as is true of dorsal place cells.

The existence of ventral hippocampal place cells suggests that the hippocampus acts as a unit in processing spatial information. This conclusion is seemingly at odds with the different input patterns to ventral and dorsal hippocampal regions. The dorsal part of the hippocampus receives fibres mainly from the lateral parts of both the lateral and medial subdivisions of the entorhinal cortex (EC). In contrast, the ventral hippocampus receives inputs from more medial parts of the EC.[22] In turn, lateral parts of EC receive major inputs from adjacent perirhinal cortex, whereas medial parts receive important inputs from limbic cortex. Thus, the ventral and dorsal hippocampus receive different (or at least differently processed) sensory information. It is therefore of considerable interest that a simple visual stimulus (the cue card) controls ventral and dorsal place cells in the same way. The apparent homogeneity of place cells could arise from the great effective divergence of output from EC, whose projections spread along at least 25% of the dorso-ventral length of the hippocampal formation.[23] It is also possible that longitudinal connections within the hippocampus are crucial.

The major difference between dorsal and ventral hippocampal place cells was in the lower apparent discharge of ventral cells. As suggested earlier, one explanation of the difference is the lower amplitude of action potentials fired by ventral cells, since a lower amplitude requires narrower windowing during recording sessions, which probably results in missed detections. On the other hand, if the difference is real, the possibility exists that 2-deoxyglucose studies would reveal gradients in the time-averaged activity along the dorso–ventral axis of the hippocampus.

Conclusion

Our data demonstrate that the cell populations in the dorsal and ventral parts of the hippocampus are remarkably similar in both electrophysiological and positional firing patterns. The existence of functionally similar cells everywhere in the hippocampus suggests that it is a functional unit, despite different input patterns. The fact that the functionally similar units are place cells suggests that the entire hippocampus participates in the generation of a map-like representation of the environment.[1] Support for this conclusion is further provided by our recent observation of a consistent disruption of flexible spatial processing following either bilateral[10] or unilateral[24] inactivations of the ventral hippocampus.

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