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CONVERGENCE OF HEAD DIRECTION AND PLACE INFORMATION IN THE CA1 REGION OF HIPPOCAMPUS

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Abstract—The hippocampus has long been considered critical for spatial learning and navigation. Recent theoretical models of the rodent and primate hippocampus consider spatial processing a special case of a more general memory function. These non-spatial theories of hippocampus differ from navigational theories with respect to the role of self-motion representations. The present study presents evidence for a new cell type in the CA1 area of the rat hippocampus that codes for directional heading independent of location information (i.e. the angular component of self-motion). These hippocampal head direction cells are controlled by external and idiothetic cues in a similar way as head direction cells in other brain areas and hippocampal place cells.

Convergent head direction information and location information may be an essential component of a neural system that monitors behavioral sequences during navigation. Conflicts between internally generated and external cues have previously been shown to result in new hippocampal place representations, suggesting that head direction information may participate in synaptic interactions when new location codes are formed. Combined hippocampal representations of self-motion and external cues may therefore contribute to path integration as well as spatial memory processing. © 2000 IBRO. Published by Elsevier Science Ltd. All rights reserved.

Key words: hippocampal interneurons, head direction cells, place fields, spatial memory, path integration, navigation.

Theoretical models of spatial navigation suggest the integration of directional information from postsubiculum with location-specific neural codes in hippocampus.[4,26,37,49] In the hippocampal formation, cells that code for head direction (HD) in the horizontal plane are found in postsubiculum.[44] The hippocampus is not required for establishing the preferred direction of postsubicular HD cells in accordance with external cues,[15,16] but postsubicular HD coding is critically dependent on projections from the anterior thalamic nuclei (ATN).[18] Although the hippocampus does not seem to contribute essential information to the directional reference system, the location code in hippocampus remains none the less oriented with HD preferences in ATN and postsubiculum.[10,17,20–22,32,39,45] In addition, reorganization of hippocampal place representations has been documented when sensory inputs remained constant while the perceived orientation of the environment changed (i.e. the internal sense of direction is then different from the orientation of the external sensory cues).[20–22,39] The resulting hippocampal reorganization can simply be seen as correcting for a mismatch between the egocentric and allocentric representation of space or may be more broadly interpreted as a dependence of hippocampal plasticity on the past experience of the animal.

At least two hypotheses regarding the convergence of HD information and hippocampal place representations seem plausible. First, postsubicular HD signals may be conveyed to the superficial layers of entorhinal cortex.[23,42,46] HD signals, however, have not been found in entorhinal areas,[1,28,35] suggesting that such signals, if received, may already be integrated with other afferent information and sent to the hippocampus as a distributed code. Second, HD information may be directly transferred to the hippocampus proper via projections from postsubiculum or retrosplenial cortex.[23,34,42] In accordance with the latter hypothesis, we provide here the first evidence that the HD coding may be received by hippocampal interneurons, which are located in proximity to principal cells that code for location.

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Abbreviations: AC, autocorrelation; ATN, anterior thalamic nuclei; EEG, electroencephalogram; HD, head direction; Hpc, hippocampal; ISI, interstimulus interval.

EXPERIMENTAL PROCEDURES

Subjects and behavioral testing

Six animals were included in the present study based on recordings of a HD signal with hippocampal electrodes. The animals were selected from a total of 33 control animals that were initially used in other studies (see Refs 24 and 29, and unpublished data). All rats were individually housed during the training and testing period and were six to 12 months old at the time of testing. They were trained to retrieve food from the end of the arms of a radial maze (for further description of the behavioral procedures, see Ref. 24). Five of the animals performed a win-shift version of a spatial memory task, and one performed a forced choice task.

Two elevated eight-arm radial mazes with a 19 cm platform and 58 cm × 5.5 cm arms were used for training and recording sessions. The mazes were placed in two different rooms. Each maze was surrounded with black curtains and illuminated by four 25 W light bulbs. Four to five prominent visual cues were displayed inside the curtains. The cues in each recording room remained identical and in fixed positions (i.e. standard condition) unless otherwise noted. One of the mazes was used for training and the majority of the testing sessions. Manipulations were performed in this room as well as in a second room in which the animals had limited experience. Testing included (a) recording sessions that started in standard conditions and were continued in darkness before restoring the initial lighting conditions (light–dark–light), (b) sessions that started with the lights turned off and were continued in standard lighting conditions (dark–light), (c) sessions with trials before and after the visual cues were rotated by 180° followed by additional trials after the cues were returned to their original position (visual cue rotation), and (d) sessions with the set of visual cues inside the curtains replaced or the visual cues altered by raising the curtains (visual cue manipulation). Testing consisted of four to five trials during each phase of the above test conditions. The animals remained in the recording room throughout the session during

Table 1. Characteristic parameters of cingulate and hippocampal head direction units

	Average (Hz)	Baseline (Hz)	Peak (Hz)	Amplitude (μV)	Width (μs)	ISIH mode (ms)	Stability (days)
Cingulate units							
Case 1	19.6	12.9	50.0	59.4	482.6	5	1
	3.0	1.8	8.0	92.5	486.0	17	1
Case 2	23.6	26.7	55.2	114.4	440.6	11	1
	1.9	1.4	10.5	80.8	558.6	8	1
	3.0	0.7	7.1	75.8	751.3	12	1
	16.7	2.0	49.2	81.2	811.8	10	4
Hippocampal units							
Case 3	4.1	4.0	13.2	69.0	178.7	12	2*
	5.9	1.9	41.0	73.3	145.8	10	17
	12.0	8.0	32.6	74.2	153.4	9	31
Case 4	3.0	0.6	17.2	68.9	246.5	15	1
Case 5	15.7	4.8	38.3	153.2	131.8	10	8
Case 6	13.0	11.4	30.7	76.9	167.4	8	1

Average: mean rate during recording session. Baseline: rate during outbound movement on the arm opposite to the preferred direction. Peak: rate during outbound movement in the preferred direction. Spike amplitude and width were measured from the initial negative to the subsequent positive peak. ISIH: interspike interval histogram. Stability: number of days with recordings sessions of the same HD unit. The two units of case 1 were recorded simultaneously. Units for case 2 and 3 are listed beginning with the most dorsal unit.
*Electrode was advanced after two days.

light–dark–light and dark–light testing, but were removed from the room while visual cues were rotated or manipulated. No attempts were made to disorient the animal when it was returned to the recording room. Raising the curtains around the maze revealed a room with a different geometry (rectangular as opposed to quadratic) and with a different set of cues (a table, a lamp, a poster and two doors) that were more distant from the maze than the original cues.

Surgical procedures and unit identification

Surgical procedures were performed according to institutional and NIH guidelines. All efforts were made to minimize animal suffering. Electrodes were manufactured as stereotrodes and initially positioned dorsal to the hippocampal formation as described in Ref. 24. One to three stereotrodes were implanted into each hemisphere. After recovery, the stereotrode assembly was lowered for up to 80 μm daily until single units were identified. The signals were preamplified by unity gain field effect transistors and further amplified up to 10,000 times by a differential amplifier. A digitized signal was recorded when the negative spike amplitude exceeded a predefined threshold. The threshold was selected after examining the waveforms on the oscilloscope and after observing the clusters that were generated on a two-dimensional display of the spike amplitude on each stereotrode wire (Datawave, Longmont, CO, USA). The threshold was set to include all signals of the unit with directional selectivity while listening to the signal using an audio monitor. Unit isolation was re-examined off-line and template matching was used to discriminate waveforms of HD units from spikes of simultaneously recorded units and from the background noise. Template matching permitted the isolation of units with average signal amplitudes that were 1.5–4 times (see Table 1) the background noise level (i.e. about 40 μV) of the recording equipment.

The preferred direction and location independence of the HD signal was monitored throughout each recording session using visual displays of spike generation and the animal's behavior. In addition, inspecting plots of the directional and spatial distribution (at a 2.4 cm × 2.4 cm resolution) of single-unit activity confirmed that the discharge rates were increased in all locations where the animal pointed its head towards the preferred direction. These plots also revealed that the HD correlate was independent of the predominant type of movement (forward motion, turning or immobility) in different locations on the maze.

Single and double diode recordings

Eight units were recorded with a single diode centered above the animal's head and four units were recorded with a double diode setup. The double diode consisted of five to eight diodes centered above the head and a single diode placed about 15 cm behind the head. The tracking system (Dragon Tracker) distinguished the two diode locations based on their apparent size difference. The preferred direction of units that were recorded with the single diode technique was estimated by plotting the rate during the outbound journey on each maze arm against the angular direction of the arm. Units that were recorded with the double diode technique were analysed (a) in the same way as those that were recorded with a single diode and (b) by calculating the vector between the back and the front diodes and generating plots of the preferred direction from these data. A comparison between the two methods of analysis revealed that the preferred direction was correctly estimated from single diode data (with a peak at the nearest 45° bin). The width of the tuning curves was overestimated for single compared with double diode data, whereas peak rates were underestimated for preferred directions that did not approximately correspond to the orientation of maze arms. One HD unit was also tested on a circular platform to examine whether the restricted movement patterns on the eight-arm maze would affect the tuning curves that are generated from the double diode data. The tuning curves that were generated from data on the platform and on the maze were close to identical in peak rate, width and preferred direction.

Unit classification using histological criteria

Electrode tracts were identified in Cresyl Violet-stained material using standard histological procedures. When more than one sterotrode was implanted into a hemisphere, the electrode tracts in individual animals (Fig. 1A) were separated by at least 0.5 mm along the anterior–posterior axis and could be identified in separate sections relative to other electrode tracts. (Case 1) The electrode was lowered after recording HD units. Complex spike cells were first encountered 1050 μm ventral to the HD units. According to the reconstruction of the electrode tract, the recording site was located in the transition zone between the deep cortical layers of retrosplenial cortex and secondary motor areas and the cingulum bundle. In agreement with this presumed electrode location, we found that units in proximity to HD units were not theta modulated and did not have spatial correlates as would be expected from hippocampal neurons. Each of the two HD units was recorded only during a single session and not observed when a recording was attempted on the following day. (Case 2) Four HD units were recorded within 300 μm of each other. The electrode was advanced for 90 μm after the final recording and the tip of the electrode was localized in the corpus callosum, suggesting that the units were recorded in the deep layers of retrosplenial/motor cortex or the cingulum bundle. An electroencephalogram (EEG) signal that was recorded simultaneously with the most ventral HD cell did not show any evidence for theta modulation of the slow-wave signal. Additional interspersed units were not theta modulated and had similar waveforms to HD units. (Case 3) The electrode was left in place after recording the most ventral HD unit and the electrode tip was located in the stratum lacunosum-moleculare (Fig. 1C). The first of three HD units was recorded simultaneously with complex spike cells in the stratum pyramidale while the remaining two units were recorded after the electrode had been

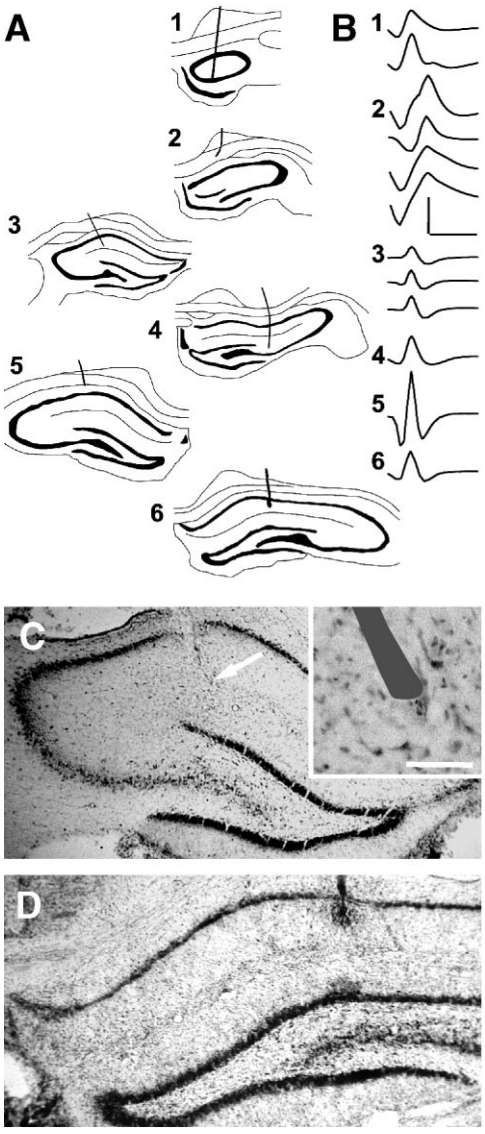

Fig. 1. Histological and physiological criteria for unit identification. (A) The coronal section with the electrode tract is shown for each animal ($n=6$) in the order corresponding to the stereotaxic anterior–posterior coordinate of the recording site [−2.0 mm (from bregma) for case 1, −3.7 mm for case 6]. HD units were recorded at or close to the tip of the electrode tract except in case 1 and 4. In these two cases, the electrode was advanced after recording the HD unit; its location during the recording session was measured by using the final depth as a reference point. (B) One to four HD cells were recorded from each animal. The average extracellular spike is shown for the stereotrode wire with the larger amplitude. Extracellular signals with similar characteristics were also detected on the second stereotrode wire (mean relative amplitude, 36.5%; range, 6.6–57.5%). These signal characteristics provide evidence for spike generation by small neurons rather than axons. Horizontal and vertical scale bars correspond to 100 μV and 500 μs, respectively. Negativity is shown as an upward deflection. (C) Case 3. HD cells were recorded in the stratum pyramidale, 220 μm ventral to the stratum pyramidale, as well as at the final electrode location (indicated by the arrow). The insert shows a high-power photograph of the area around the electrode tip. The area of tissue damage by the electrode tract is marked in gray. Neuronal elements can be observed in the vicinity of the electrode tip. Scale bar = 100 μm. (D) Case 6. A microlesion indicated that the electrode tip was located ventral to the stratum pyramidale. The HD unit was recorded 50 μm dorsal to the final electrode location.

advanced for 220 and 390 μm, respectively. The total distance that the electrode traveled after the recording in the pyramidal cell layer corresponded closely to the distance of the electrode tip from the stratum pyramidale in the histological material. (Case 4) The electrode was advanced after recording a HD unit simultaneously with a complex spike cell. The final electrode position was in the stratum radiatum of CA3. Aligning the depth record with the electrode tract in the histological section indicated that the HD unit was recorded in the stratum pyramidale of CA1. (Case 5) Simultaneous recordings of the HD unit, a theta modulated unit, and a theta modulated slow-wave signal (Fig. 2A) suggest that the electrode tip was located in the alveus/stratum oriens of hippocampus during the recording session. In addition, the signal amplitude and waveform (Fig. 1B) indicated that the extracellular spikes were recorded adjacent to the soma or dendrites of an interneuron.[8] (Case 6) The electrode was advanced 45 μm after recording the HD unit. Complex spike cells were recorded at the final electrode position (Fig. 2B). A microlesion (10 μA for 2 s) identified that the electrode tip was located just below the stratum pyramidale in the histological material (Fig. 1D).

RESULTS

Evidence for location-independent head direction units in hippocampus

Of 33 rats with hippocampal recording electrodes, HD units were observed in six animals. The data from these animals are presented in this report. These cells were recorded from a total of 120 hippocampal stereotrodes each one of which yielded approximately 4.6 complex spike cells and 1.6 interneurons without HD selectivity. The corresponding probability of identifying a unit with HD selectivity was 0.05. The low probability of recording extracellular HD signals and the low signal amplitude (mean ±S.E.M., 85.9±13.5 μV) suggested that the spikes were generated by small neurons or neuronal processes. Since extracellular recordings are strongly biased by cell size,[19] the number of recorded hippocampal HD units per animal is not likely to reflect the relative occurrence of the cell type.

Combined physiological and anatomical data (Figs 1, 2, Table 1) indicated that the recording sites for six units in four animals were located in the hippocampal CA1 region. Two of the CA1 HD units were recorded simultaneously with complex spike cells, two ventral to stratum pyramidale in stratum radiatum and lacunosum moleculare, and two dorsal to stratum pyramidale in alveus/stratum oriens. The HD units ($n=6$) of the two remaining animals (case 1 and 2) were recorded before the electrodes reached the hippocampal formation. Although it cannot be firmly dismissed that the recordings at these dorsal and anterior sites were from thalamocortical fibers enclosed in the cingulum bundle (see Discussion), the spikes are referred to as cingulate units in accordance with the electrode location. The data of extrahippocampal HD recordings are presented for comparison with hippocampal HD units.

The extracellular signals of hippocampal units were predominantly negative, while cingulate signals were initially positive with a later negative deflection (Fig. 1B). The different waveform characteristics resulted in quantitative differences of the apparent negative-to-positive signal duration of hippocampal units (170.6 ± 16.6 μs) and cingulate units (602.1±65.3 μs, $t(5.6)=-6.41$, $P<0.01$). An average baseline rate of 5.1 Hz, a peak rate of 28.8 Hz at the preferred direction, and a peak-to-baseline rate ratio of 11.8 was observed for hippocampal HD units. None of these parameters was significantly different from those of cingulate HD units recorded dorsal to hippocampus (all P-values >0.5). The peak rates of hippocampal HD units corresponded approximately to peak rates of HD cells recorded in ATN, postsubiculum and granular retrosplenial cortex. The peak-to-baseline

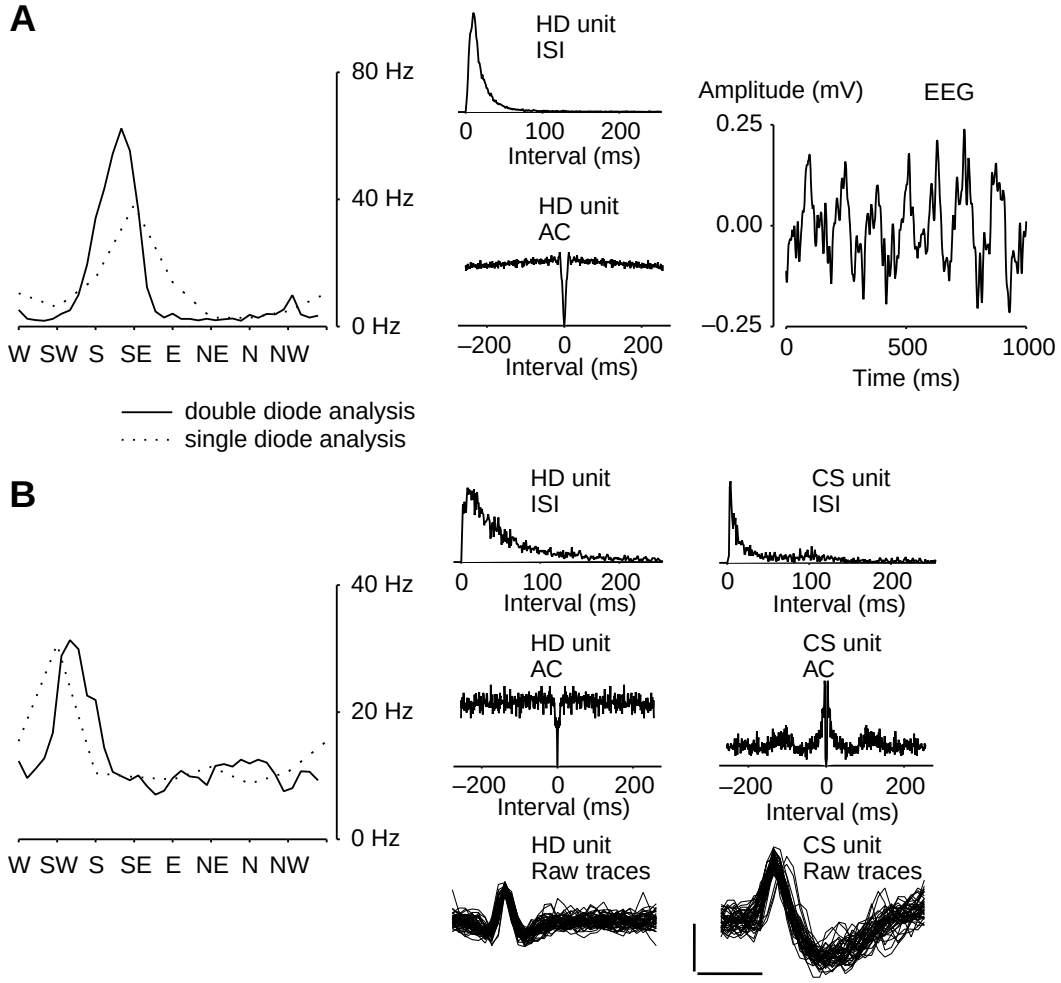

Fig. 2. Tuning curves and oscillatory discharges of hippocampal HD cells. Left: The tuning curves of hippocampal HD cells show a single peak of increased activity when the animal's head was oriented towards the preferred direction. A comparison between single and double diode analysis showed that the preferred direction was correctly estimated from single diode recordings. Middle: Hippocampal HD units were not theta modulated, but the interstimulus interval (ISI) histograms of all units ($n = 12$) showed a peak that corresponded to a spike repetition rate at gamma (60–100 Hz) frequencies. Right: Physiological evidence confirmed that the recording sites for case 5 (A) and 6 (B) were located in hippocampus. (A) A slow-wave (EEG) signal was recorded from the same recording electrode and simultaneously with the HD unit. Sinusoidal 7–8 Hz (theta) waves are a characteristic hippocampal EEG pattern. (B) ISI and autocorrelation (AC) histograms of a single unit that was recorded within 50 μm of the HD unit. The central peak and the second peak at ~120 ms in the AC histogram are characteristic for hippocampal principal cells (i.e. complex spike cells). In addition, the raw traces of the signals were representative of this cell class and different from those of the HD cell (as shown in the middle). The vertical and horizontal scale bar correspond to 100 μV and 500 μs, respectively.

ratio was considerably higher than in retrosplenial cortex,[5] similar to lateral dorsal thalamic nucleus,[27] and lower than reported for ATN and postsubiculum.[3,43,44] The small signal amplitudes of hippocampal HD units may have resulted in higher than usual relative noise levels, meaning that the estimated peak-to-baseline ratio should be regarded as a lower limit.

Persistent head direction signals during visual cue removal and rotation

Previously described HD cells in retrosplenial cortex, ATN and postsubiculum maintained their approximate preferred direction after the room lights were turned off or after a prominent visual cue was removed.[6,22,45] The same result was seen for three of four hippocampal units and for all three cingulate units tested in darkness (Fig. 3). The peak rate in the dark condition compared with the light condition was 86.8 ± 12.4% for hippocampal units and 95.5 ± 2.5% for cingulate units [$t(5) = -0.59$, $P > 0.5$]. Although the variance for the per cent change between light and dark was higher for hippocampal units than for cingulate units, the difference did not reach significance [$F(5,5) = 4.2$, $P > 0.09$].

In the room that had been used for behavioral training and the majority of the recording sessions (room 1), control of the preferred direction by non-visual cues was suggested in sessions that began in darkness (Fig. 4B). When the animal was introduced into the room with the lights off, all tested hippocampal HD units ($n = 4$) immediately established a preferred direction that corresponded to that observed in sessions with standard illumination. In contrast, in a room (room 2) in which the animals had limited experience (<12 recording sessions) the tested hippocampal HD units ($n = 2$) did not establish a stable preferred direction during the period of dark testing. Restoring the illumination in room 2 resulted in a consistent directional preference that corresponded to standard testing conditions. Visual cue control was also not observed in room 1 when hippocampal HD units were tested after rotating the cues by 180°. Cue rotations in room 1 did not result in a shift of the preferred direction for any of the

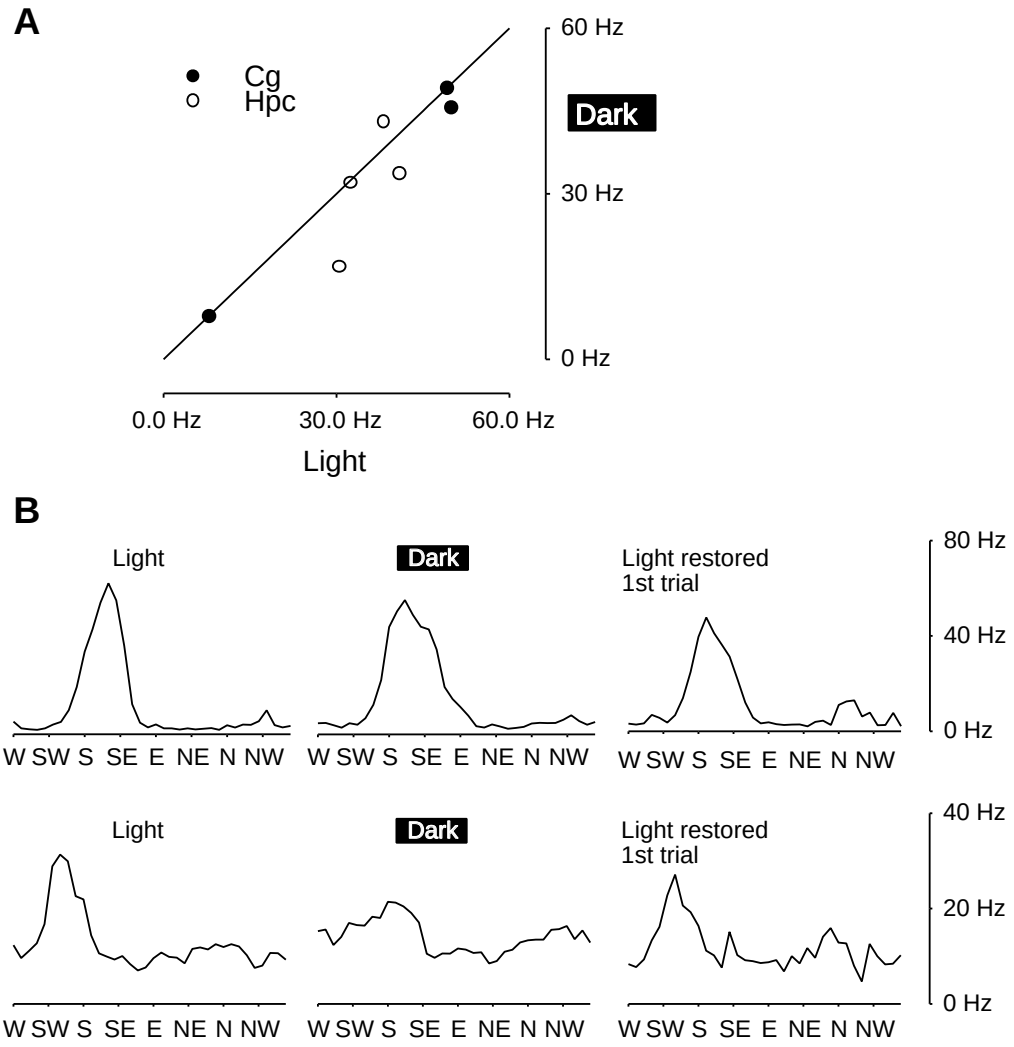

Fig. 3. Visual tests of HD tuning. Testing HD units in the absence of ambient illumination revealed that peak rate (A) and preferred direction (B) were similar in darkness and standard light conditions in six of seven cells. Significant differences in the response of hippocampal and cingulate units to darkness were not observed [$t(5) = -0.59$, $P > 0.5$]. Tuning curves for each testing condition are shown in (B) for one of the hippocampal HD units that retained its preferred direction (top) and the hippocampal HD unit that showed the most pronounced change in darkness (bottom). Examining individual trials of the recording session indicated that the peak rate at the preferred direction progressively decreased in darkness and was promptly re-established after the lighting was restored.

hippocampal HD units tested ($n = 4$). All units retained their preferred direction with respect to the coordinate system of the recording room.

Experience-dependent use of visual cues for controlling the preferred direction of hippocampal head direction units

Unlike what was observed following cue rotation in room one, a shifted preferred direction (of 180°) was observed in two of three hippocampal HD units tested in room 2 after rotating the visual cues by 180° (Fig. 4A). For one of these HD units, the cue rotation session was the second recording session in room 2. For the second unit, new visual cues were used for the cue rotation session. The new set of cues had been introduced during the previous session after seven recording sessions with the original cues. The preferred direction of the HD units shifted with the visual cues in both cases, indicating that the cues were effective in controlling the preferred direction after they had been associated with the environment for <1 h. The third unit was tested during the first recording session in room 2. Its preferred direction remained in accordance with the room coordinates during the cue rotation condition.

Differences in the preferred direction with respect to compass orientations were observed when hippocampal units ($n = 3$) were tested in both recording rooms. The angular deviation across environments for each of the units was 90°, 135° and 180°. The preferred direction in each room was stable throughout the period of standard testing (up to 16 days in room 1 and up to 13 days in room 2). Visual cue manipulations were performed while recording two of the hippocampal HD units. The original visual cues were replaced with a new set of cues in room 1 for one unit and in both recording rooms (during two separate series of manipulations) for the second unit. The preferred direction of the first unit did not change after the visual cues were replaced in room 1. In contrast, introducing an entirely different set of visual cues into each of the rooms shifted the preferred direction of the second unit by 90° in room one and 45° in room 2 (Fig. 4C). Using two sets of visual cues,

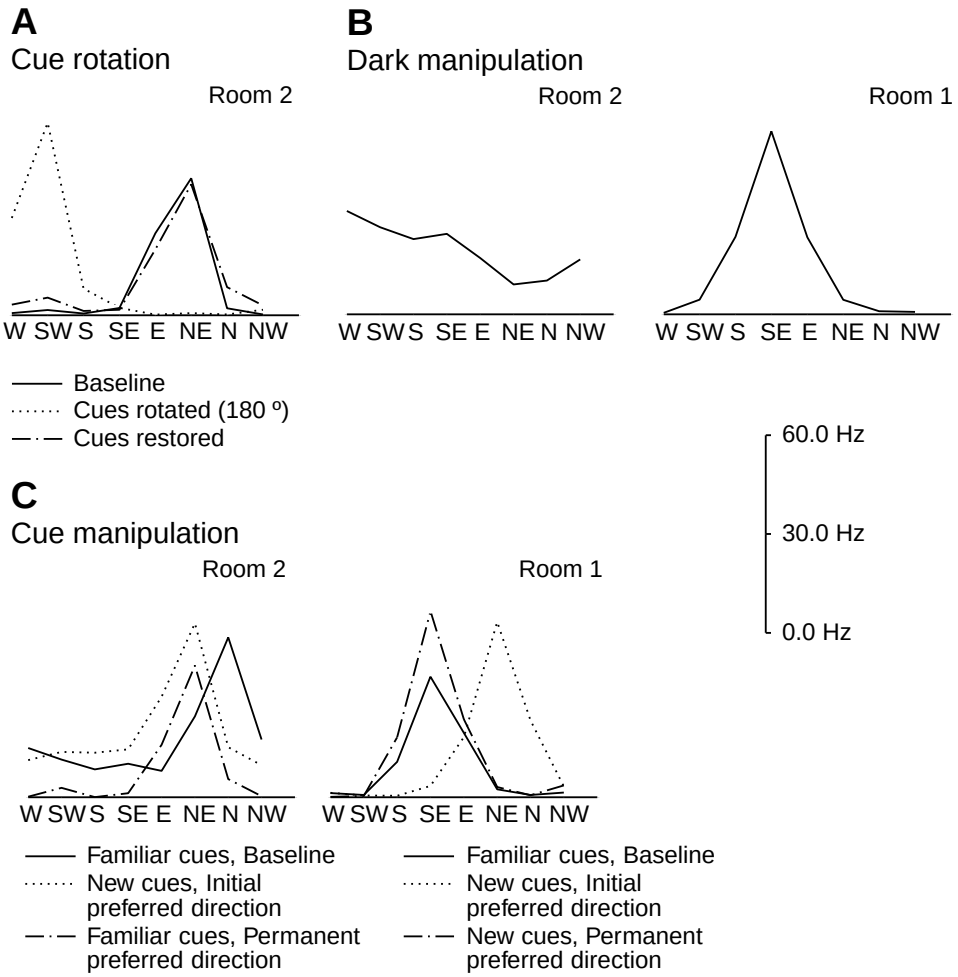

Fig. 4. Experience dependence of hippocampal HD tuning. Visual cue manipulations revealed that cue control of hippocampal HD units is experience dependent. (A) The preferred direction rotated with the visual cues in a room in which the animal had limited experience (room 2). Reintroducing the animal into room 2 after rotating the cues by 180° resulted in a corresponding 180° shift of the preferred direction of the hippocampal HD unit. The animal had limited (<1 h) experience with the cues that were used for the recording session. A shifted preferred direction was never observed when the same manipulation ($n = 4$ units) was performed in a more familiar room (room 1, not shown). (B) Differences in the dependence of hippocampal HD units on visual as opposed to non-visual cues were also seen when the units were tested in recording sessions that started in darkness. Left: Starting the recording session in darkness in room 2 resulted in the absence of a preferred direction (top). Restoring the illumination re-established the tuning that was observed in standard conditions [as shown in (C)]. Right: Starting the recording session in darkness in the familiar room (room 1) did not result in any decrement of the peak rate or the directional tuning of the hippocampal HD cells. (C) Introducing an entirely different set of visual cues into a recording environment resulted in conflicting preferred directions for the same environment. After the animal had been repeatedly tested with both sets of cues, the preferred direction stabilized to baseline in room 1 and to the new orientation in room 2.

which are associated with different preferred directions, in an otherwise identical recording environment resulted in a conflict with background and stable non-visual cues. The cue conflict was resolved after the units were repeatedly tested with both sets of cues. In one case (room 1), the preferred direction for the new cues changed to correspond to the preferred direction that was seen in the presence of the original set of cues. In the second case (room 2), the preferred direction for the original set of visual cues changed to the preferred direction that was initially only established in the presence of the new cues. Introducing the new cues had therefore resulted in an altered relation between the original set of cues and their corresponding preferred direction. The permanent change in the preferred direction in room 2, however, did not alter the preferred direction of the HD unit in room 1.

DISCUSSION

Data presented here show that angular self-motion information is encoded in hippocampus independently of location information. Hippocampal HD units are distinct from principal neurons of hippocampus (i.e. complex spike cells) with regard to waveform characteristics, average discharge rates and rhythmic discharge patterns, suggesting that the extracellular signals were recorded from interneurons. The present hippocampal spikes were classified as being generated by small interneurons based on the following characteristics. First, the short-duration extracellular spikes at hippocampal sites corresponded to waveforms expected for interneurons (see Fig. 1B, case 3–6). Combined intracellular and extracellular recordings from hippocampal neurons have shown that extracellular signals closely correspond to the first derivative of the intracellular action potential. Using this method, the extracellular waveforms have been predicted from intracellular recordings of hippocampal interneurons,[31] and it has previously been confirmed that short-duration spikes are generated by different subclasses of interneurons.[8] At least six different

classes of interneurons can be distinguished in hippocampus,[12] each of which can be expected to be recorded with a probability that corresponds to its average cell size according to the direct relation between cell size and maximum extracellular spike amplitude.[19,31] In addition, dendrites can act as current sources during the depolarizing phase of the action potential and generate signals with an initial positive peak when the action potential backpropagates into dendritic regions.[8,19]

Second, the recorded extracellular spikes do not match the signal amplitude or waveform of spikes that would be generated in the vicinity of unmyelinated or myelinated axons. Central unmyelinated axons and nodes of myelinated axons generate extracellular spikes that are at least an order of magnitude smaller than the spikes of small neurons. For a 1-μm-thick axon, the estimated maximum signal amplitude directly adjacent to the membrane would be about 1 μV.[2,7,14,19,41] In addition to expected signal amplitudes below recording threshold, extracellular spikes of axons show a characteristic waveform when the electrode is located directly adjacent to the membrane (i.e. the nodal membrane for myelinated axons). The waveform is characterized by an initial positive peak followed by a negative peak. After the negativity, the signal either returns to baseline without a second positive peak or shows a second positive peak that is much less pronounced than the initial peak.[7,14,41] Significant deviations from this characteristic waveform are only expected at distances from central fibers where signals are not detectable. The absence of notable fiber projections from areas with head direction cells to layers (e.g. stratum pyramidale) where hippocampal head direction units were found[23,42,46] further suggests that signals recorded at hippocampal sites were not generated by axonal projections, but by hippocampal interneurons.

In contrast to the hippocampal spikes, cingulate cortex spikes were recorded in locations with a high density of fibers and showed waveforms with a prolonged signal duration after the negative peak. These considerations, along with the low stability of the signals that were recorded dorsal to hippocampus, suggest that cingulate spikes (Fig. 1B, case 1 and 2) could, in theory, have been generated by axons.[7,14,41] However, the much higher expected signal amplitudes at dendritic sites and the presence of a signal on the second stereotrode wire suggest that these recordings are more likely to be generated by dendritic regions than by the close proximity of a single stereotrode wire to a central axon. The uncertainty about the source of extracellular spikes is not unique to cingulate cortex and would apply to any brain area where neuron somata and fiber tracts are interspersed. Since it is not clear whether the present recordings at cingulate sites correspond to the previously reported cell populations,[5,6] we cannot be sure whether the recordings can be directly compared.

Although the present results provide evidence for location-independent HD cells in the CA1 region of hippocampus, the origin of the directional signal is uncertain. Direct retrosplenial projections to hippocampus are an unlikely source of HD information since the projections are restricted to the CA3 region[34] and have not been confirmed.[47] Hippocampal HD cells could receive their information directly from postsubicular projections to the CA1 region. Although these projections are sparse,[23,42,46] the presence of the signal in even a small number of interneurons could exert a powerful influence on the principal cell population.[12] Furthermore, since a subpopulation of CA1 interneurons projects back to CA3,[40] HD information would not need to be restricted to the CA1 region.

As an alternative hypothesis to the possibility that hippocampal interneurons receive HD codes directly, one could propose that the orientation of the rat in the environment is conveyed to hippocampus as a distributed code. Although entorhinal cortex receives projections from areas with HD information,[42,44,46] its cells do not directly code for heading direction.[1,28,35] Consistent spatial relations between the place fields of individual entorhinal units are retained across different environments[35] and could be used to compute directional vectors that convey the orientation of each environment. If received as a population code, HD information may either remain integrated with location signals or be converted to location-independent directional signals.

The control of hippocampal HD cells by external and idiothetic cues is similar to that of HD cells in other brain areas. The hippocampus may therefore directly receive functionally identical HD information that is present in other areas and combine the information with highly processed context-dependent information representing other aspects of the environment. Angular and linear self-motion representations may be an essential component of hippocampal function[9,36,48] and, when present along with place information, may importantly contribute to computing or correcting the cumulative signal for path integration.[16,26,49] In addition, mismatches between internally generated (i.e. idiothetic) information and external cues can result in the reorganization of hippocampal place representations.[20–22,39] The co-occurrence of HD and place cells within hippocampus would allow for strong synaptic interactions, which could be used for rapidly associating the directional heading with a new set of hippocampal place representations.

Although HD coding in primates has only been reported in postsubiculum and parahippocampal gyrus,[38] a significant proportion of principal cells in the primate hippocampus is motion sensitive.[33] Principal cells in primates may therefore have a broader role in representing movement-related information while interneurons seem to code for self-motion information in the rodent hippocampus.[36] It remains to be addressed whether representing these signals in different cell populations results in fundamentally different modes of hippocampal operation or whether similar computations can be performed by either cell type. Separate modes of processing are suggested by the different forms of long-term potentiation that are present in synapses between pyramidal cells compared with those between pyramidal cells and interneurons (reviewed in Ref. 25).

CONCLUSIONS

Recent theoretical considerations suggest that internally generated information may be represented in hippocampus distinctly from other sensory information in order to generate goal-directed behavior[4,13,37,49] or a metric for hippocampal representations.[26] According to the latter view, sensory cues in the environment are inserted into the self-motion representation during exploratory behavior. In contrast to a distinct role of idiothetic representations, the information may be

represented in hippocampus identically to other sensory information. Consequently, correlational learning in hippocampus would take place irrespective of the type of information and identify sensory as well as movement sequences as behavioral episodes.[11,30,50] Future theoretical speculations on the role of hippocampus will need to incorporate the fact that hippocampus encodes multiple aspects of behavior as well as external sensory information in principal cell and interneuron networks.

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