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CONTEXT-SPECIFIC SPATIAL REPRESENTATIONS BY LATERAL SEPTAL CELLS

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Abstract—To test whether the location coding of lateral septal cells is dependent on cue constellations, we examined single units in two different recording arenas on alternating days. Repeated recordings of lateral septal neurons in the same arena revealed that matching locations are encoded on separate days by about one third of the cells. The cells typically showed location-selective firing in only one of the two recording arenas and initially showed unrelated patterns when tested in a different recording arena. When tested for a second time in each recording arena, the initially dissimilar patterns were modified towards increased similarity between arenas. Simultaneously recorded hippocampal principal cells showed distinct place fields for each recording arena throughout the recording sequence. These results indicate that the initial reorganization of the lateral septal location coding may occur as a direct consequence of the hippocampal reorganization. Further septal reorganization is then partially independent of established place fields in the CA1 and CA3 area.

Location-selective cells in cortical areas that receive projections from hippocampus proper (i.e. the subiculum and the entorhinal cortex) have not been shown to encode differences between recording arenas. Although some characteristics of this generalized coding scheme have also been found for location-selective lateral septal cells, the encoding of context information was generally preserved in the subcortical target cells of projections from the CA1 and CA3 area. © 2002 IBRO. Published by Elsevier Science Ltd. All rights reserved.

Key words: septum, hippocampus, place fields, remapping.

Allocentric space is encoded by the firing rate of neurons in multiple subregions of the hippocampal formation including the CA1 area, the CA3 area, the dentate gyrus, the subiculum, and the entorhinal cortex (O'Keefe, 1976; Barnes et al., 1990; Mizumori et al., 1992; Quirk et al., 1992; Sharp and Green, 1994). Neurons in these subregions show localized increases in firing rates when a rodent occupies the section of the arena floor that is referred to as the place field. The size of the fields and their peak firing rates above baseline levels show pronounced variability for different cells within and, in particular, between different hippocampal subregions. In addition to variability for the same recording arena, cells in the hippocampal formation also show a spectrum of responses when tested in a second recording arena.

The most common changes that are seen for cells in the CA1 and CA3 area in a modified arena are increased or decreased background firing rates in addition to altered spatial firing patterns such as the onset, offset, and shift of location-specific neuronal activity (Hill, 1978; Kubie and Ranck, 1983; Muller and Kubie, 1987; Thompson and Best, 1989; Wilson and McNaughton, 1993). If shifted, the altered firing patterns are typically not related to each other by a rotation or translation (Kubie and Ranck, 1983; Muller and Kubie, 1987; Bostock et al., 1991; Quirk et al., 1992; Tanila et al., 1997; Leutgeb and Mizumori, 1999; Sharp, 1999). The reorganization of field relations with respect to allocentric space and with respect to their nearest neighbors can be described as remapping the hippocampal rate code to a different arena surface (Muller and Kubie, 1987). The onset of remapping can be immediate (Hill, 1978; Wilson and McNaughton, 1993; Kentros et al., 1998), but may be incomplete and delayed when recording arenas show a high degree of ambiguity or similarity (Muller and Kubie, 1987; Bostock et al., 1991; O'Keefe and Burgess, 1996; Tanila et al., 1997). In contrast, patterns that can be matched have consistently been found for the place fields of entorhinal and subicular cells. For example, when a round arena is compared to a square arena, the areas of increased firing remain in the same direction from the center (Quirk et al., 1992; Sharp and Green, 1994). Furthermore, when the size of the arena is doubled, subiculum cells show fields along corresponding walls (Sharp, 1999).

The lateral septum receives direct, convergent projections from the CA3 area, the CA1 area, the subiculum, and entorhinal cortex (Swanson and Cowan, 1977, 1979; Swanson et al., 1981; see Amaral and Witter, 1995;

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Abbreviations: AP, anterioposterior; Fam1/Fam2, first and second recording sessions in the familiar arena; L, lateral; New1/New2, first and second recording session in a new arena.

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Jakab and Leranth, 1995; Freund and Buzsaki, 1996; Risold and Swanson, 1997 for review). Distinct information (i.e. from CA3 and CA1) as well as generalized information (i.e. from subiculum and entorhinal cortex) about different contexts may therefore be processed in the lateral septal nuclei. Spatial selectivity has been reported for lateral septal cells, but previous recordings were limited to recording sessions in one apparatus (Zhou et al., 1999). To establish whether lateral septal cells have some of the coding properties that have been described for the different areas of the hippocampal formation, we tested the response properties of lateral septal cells repeatedly in a familiar recording apparatus as well as in a modified arena that was initially new to the animal. For direct comparisons with the coding properties of hippocampal pyramidal cells, we also describe the single-unit activity of hippocampal place cells that were recorded in parallel.

EXPERIMENTAL PROCEDURES

Young adult, 7–9 months old, male Long–Evans rats ($n = 5$) were obtained from Simonson Laboratories (Gilroy, CA, USA). The animals were individually housed and food deprived to a minimum of 80% of their initial body weight (350–450 g). Training and recording sessions were performed only during the light phase of a 12 h light/12 h dark cycle.

Surgical procedures

The surgical procedures were performed according to NIH guidelines and have been described elsewhere in detail (Leutgeb and Mizumori, 1999). In brief, animals were deeply anesthetized with an initial dose of pentobarbital (45 mg/kg, i.p.; Nembutal, Abbott Laboratories, Chicago, IL, USA). The level of anesthesia was monitored continuously and additional doses (10 mg/kg, i.p.) were given as needed. After removing the skull and dura above the areas of interest, electrodes were lowered through cortex and placed dorsal to the lateral septal area (anterioposterior (AP) 0.5 to 1.0, lateral (L) 0.0 to 0.5) and hippocampus (AP −3.0 to −5.0, L 1.5 to 2.5). Additional recording electrodes were lowered towards the mamillary/ventral tegmental area (AP −5.3 to −6.0, L 0.0 to 0.5). All efforts were made to limit the number of animals used and their suffering. Only recordings from septal and hippocampal electrodes are described in this report.

Recording electrodes were manufactured as stereotrodes by twisting two 20-μm lacquer-coated tungsten wires (California Fine Wire, Grover City, CA, USA) and dipping them in Epoxylite. The stereotrodes were then inserted into a 30-gauge stainless steel cannula and cut with sharp scissors to extend about 1.5 mm beyond the distal end of the cannula. Microdrives were constructed by mounting an amphenol connector onto two steel screws (McNaughton et al., 1989) and by attaching two stereotrodes to each microdrive. A stainless steel reference electrode (114 μm) was lowered into the corpus callosum and secured to the skull along with the microdrives using dental cement and stainless steel screws. One of the screws served as an electrical ground. Penicillin G (1 ml; 300 000 units/ml, i.m.; Bicillin, Wyeth Laboratories, Philadelphia, PA, USA) was given as an antibacterial prophylactic at the end of surgery, and the animals were allowed free access to food and water for 1 week before again being placed on a food-restricted schedule.

Behavioral procedures

An elevated maze with a center platform (19.5 cm in diameter) and eight arms (57.5 cm long) was used for behavioral testing. Each maze arm was equipped with a small motor, which lowered the proximal half of the arm and restricted access to the end of the arm. The maze was positioned in a square enclosure defined by black curtains. Four visually distinct 30 cm by 50 cm posters (with horizontal stripes, vertical stripes, diagonal stripes, and a checkerboard pattern, respectively) were posted inside the curtains. The arrangement of these landmarks remained stable during training and recording sessions except for days when testing in new arenas was scheduled.

The animals were first trained to retrieve chocolate milk from each arm of an eight-arm maze when presenting one arm at a time. A pseudorandom sequence of arms was chosen for each trial. The rat was confined to the center platform for an interval of 2 min before starting the next sequence of eight arms. Using this forced choice procedure, the animals were pretrained before surgery until they performed eight trials of the task for 5 consecutive days. Maze training resumed 10 days after surgery and the forced choice task was changed to a spatial working memory task. The animals were trained to perform the spatial memory task for at least 5 days before conducting recording sessions in new environments.

Table 1. Summary of septal and hippocampal cells that were recorded in a familiar and a new arena

Animal	Manipulation[a]		Lateral septal cells		Hippocampal cells	
	Room	Layout	Total	Loc. spec.	Total	Loc. spec.
A	B	square	2	2	1	1
B[b]	A	rect.			1	1
C	B	square	3	2	2	2
	A	rect.	4	0	2	1
	B	rect.	4	1	3	2
D	A	rect.	2	1		
E	A	rect.	4	2		
	B	square	6	1	4	3
	B	rect.	5	1	2	2
	B	square[c]	2	1		
Total			32	11	15	12

[a]Each recording sequence consisted of alternating recording sessions in a familiar arena (room A, square) and one of several new arena configurations (room A, rectangular (rect.); room B, square; room B, rect.). Each arena configuration was associated with its distinct set of visual cues.

[b]The septal recording was from the medial septum.

[c]The visual cues that were posted inside the curtains were different from any of the other cue sets used.

The animals were screened daily for clearly isolated single units while they were confined to the center platform of the eight-arm radial maze. The signal on all recording channels was examined by using an audio monitor and an oscilloscope. When units were not identified during the initial screening, the electrodes were advanced for a maximum of 90 μm/day. All septal units were initially recorded in the familiar environment in standard sessions (i.e. eight trials) or in sessions that also included four trials in darkness. The data from these recording sessions will be reported separately.

Up to four new arenas, each with a different set of cues, were used for each animal. In addition to the distant visual cues, these arenas were also distinct from each other by posting the cues in (a) a rectangular instead of a square enclosure, (b) a square enclosure in a different recording room with a second eight-arm maze or (c) a rectangular enclosure in the second recording room (Table 1). In addition to the cues within the recording arena, each arena configuration was also associated with a particular path (i.e. direct or circuitous) and mode of transportation (i.e. cage covered or uncovered) from the housing room to the recording room.

Testing with a new cue configuration was conducted during 10 recording sequences for septal cells (Table 1). Each of these sequences consisted of daily sessions of eight trials, which were conducted on alternate days in either the familiar arena (Fam1, Fam2) or an arena that was initially new to the animal (New1, New2). Four recording sequences commenced in the familiar arena (Fam1–New1–Fam2–New2) and six sequences in the new arena (New1–Fam1–New2–Fam2). The new arena of each recording sequence had not been used for previous behavioral testing of the animal. All recording sessions in the new environment commenced within 5 min after the animal had been introduced into the room. During that time, the animal was restricted to the center platform of the maze. All recording sessions that are referred to as familiar were in the room that had previously been used for a minimum of 15 training and recording sessions.

Electrophysiological procedures

Signals from each of the recording electrodes were preamplified by an array of unity gain FET amplifiers. A headstage held the preamplifiers as well as a double diode system. The front array of six to eight infrared light-emitting diodes was centered above the animal's head and an additional diode was placed about 15 cm behind the head. Only position data that were obtained from front diodes were considered when analyzing the present data. The position of the animal was identified with a spatial resolution of 256×256 and a sampling frequency of 20 Hz. The x–y coordinates of the animal's position on the maze were time-stamped and stored along with single-unit data. Incoming signals from the recording electrodes were amplified 2000–10 000 times by a differential amplifier (Neuralynx, Tucson, AZ, USA), band-pass-filtered between 600 and 6000 Hz, and transmitted to an analog-to-digital board in a Pentium-based computer. The data acquisition program (Datawave Technologies, Longmont, CO, USA) recorded a 1-ms sequence of each signal that exceeded a preset threshold at a sampling frequency of 26–32 kHz per channel. Spike discharges of individual units were separated by using an on-line spike separation software (Datawave Technologies) that generated scatterplots of spike waveform parameters (e.g. amplitude, width) recorded on each of the two stereotrode wires. Discharges of individual units were identified manually by first outlining the cluster of spike discharges on the plot showing the relative peak amplitudes and then refining the boundaries with additional parameters (e.g. spike width). The data were replayed off-line and clusters were reexamined by using amplitude, spike width, peak time difference, phase angle, and waveform templates as parameters to separate single units. Phase angle was defined as the arctangent of the ratio of the spike heights on the two channels. Only clusters with consistent cluster boundaries throughout the recording session were included in the data analysis.

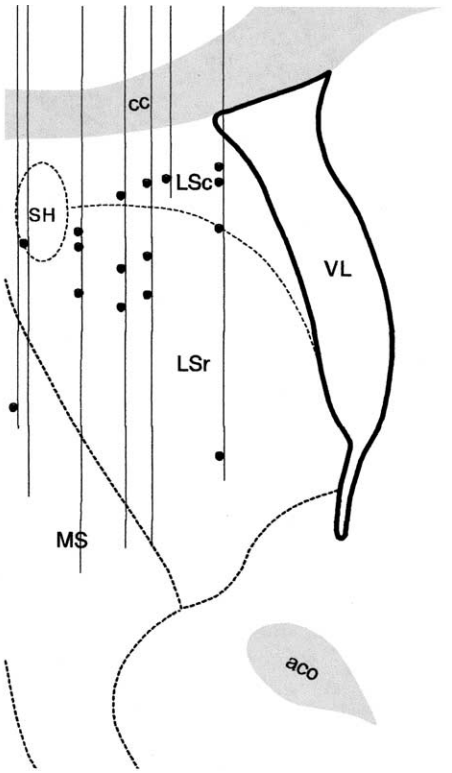

Fig. 1. The electrode tracts in the septum are shown for all animals ($n = 5$) along with the calculated depth of the electrode tip (filled circles) during each recording sequence. The tracts from different antero-posterior planes were projected onto a single atlas section (adapted from Swanson, 1992; Risold and Swanson, 1997). All recording sites but one were found to be located in the lateral nuclei. The remaining site was in the medial septal nucleus. aco, anterior commissure; cc, corpus callosum; LSc, lateral septal nucleus, caudal part; LSr; lateral septal nucleus, rostral part; MS, medial septum; SH, septohippocampal nucleus. VL, lateral ventricle.

Unit classification

Units were classified according to the anatomical location of the electrode tract (Fig. 1) and, for hippocampus, also by using discharge and spike characteristics that corresponded to principal neurons (i.e. complex spike cells) (Fox and Ranck, 1975; Shen et al., 1997; Leutgeb and Mizumori, 1999). The identity of single units across several days was assured by using amplitude and waveform characteristics of the extracellular spikes. These criteria clearly identified all of the septal units that were recorded for several days and additional criteria were not required. A different set of septal units was recorded during each of the 10 recording sequences that involved the transfer to a new recording room. Each septal unit was therefore recorded in a sequence of sessions that included a transfer to a room that was initially new to the animal (i.e. New1).

To maximize the number of hippocampal cells that were recorded simultaneously with septal cells, hippocampal units were in some animals recorded during successive recording sequences without moving the hippocampal electrodes. The reason for recording the maximum number of hippocampal cells simultaneously with lateral septal cells was to verify that we were recording lateral septal neurons under conditions that induce reorganization of hippocampal place fields. The hippocampal tissue movement that occurred because of lowering the septal electrodes (or for any unknown reason during the period of more than 1 week between recording sequences) may have been sufficient to move the hippocampal electrodes within the pyramidal cell layer to record from different cells during each

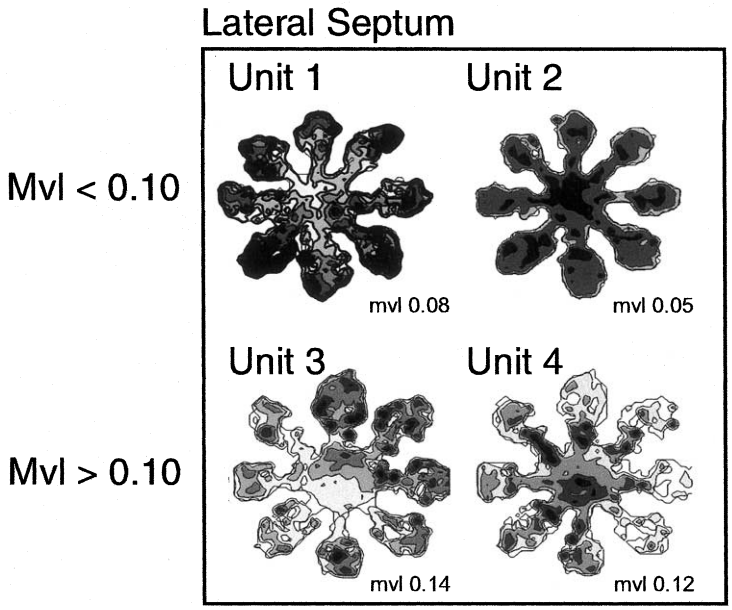

Fig. 2. The mean vector length (mvl) is calculated from vectors with a length corresponding to the average firing rate for each arm and a direction equal to the arm direction. A minimal mvl is considered a prerequisite for obtaining meaningful results when calculating spatial correlation coefficients, but not meant to indicate that a cell shows location-specific firing. The additional criterion (i.e. mvl < 0.10) is of particular importance for excluding cells that fire throughout the maze. The examples also show that cells with broad fields (mvl > 0.10) are retained for further analysis. The range of mean vector lengths for all lateral septal cells ($n = 32$) was 0.02–0.93 with a median of 0.08.

recording sequence. Visual inspection of plots that showed the location-specific firing in the familiar environment was therefore used as an additional criterion to verify that identical cells were not recorded between recording sequences and, conversely, also used to verify that identical cells were recorded within a recording sequence. It has been firmly established that the spatial firing of hippocampal single-unit activity does not usually change in cue-controlled environments during repeated recordings (Thompson and Best, 1990; reviewed in Eichenbaum et al., 1999).

Histology

The electrode tracts were identified in Cresyl Violet stained material. The final location of the recording electrode was marked by a small lesion (20 μA for 2 s). Recording sites along the electrode tract were identified by comparing the depth measurement for each recording session with the final position of the electrode. All single-unit recordings from sites that were anatomically confirmed to be located in the lateral septal nuclei were included in the data analysis (see Fig. 1).

Data analysis

Recording sessions were analyzed by dividing each session into trials and eliminating data that were recorded during intertrial intervals. There were five analysis routines applied to the data. (1) The mean firing rate of each cell in the familiar arena was calculated by averaging two sessions (Fam1, Fam2) and by expressing the discharge in the new environment as a percent of the mean discharge in the familiar arena. Cells with rates of less than 0.1 Hz were excluded from the calculation of percentages. (2) Location-specific single-unit firing was measured using individual spatial bins (64×64 pixels, each pixel corresponding to 2.4×2.4 cm on the maze). Rate maps were obtained by counting the number of spikes at each location and by dividing the spike count by occupancy time. Locations on the maze that were occupied for less than 200 ms were not further considered. The rates in identical locations between the two sessions were used to calculate pairwise correlation coefficients. Not averaging across neighboring pixels before calculating the correlation coefficients resulted in comparatively low numerical values (see Results) compared to an earlier study using the eight-arm maze (Markus et al., 1995). Correlation coefficients were calculated for the first compared to the second recording session in the familiar arena (Fam1–Fam2) and the first compared to the second session in the new arena (New1–New2). For each cell, the maximum of these two comparisons was considered the maximum correlation coefficient for the same arena (Max_{same}). (3) Correlation coefficients between different arenas were calculated by rotating one of the rate maps in 90° steps around the maze center. The 90° steps were chosen to account for fields that may be aligned with the square (or rectangular) layout of the recording room. The maximum of these four comparisons was then considered the correlation coefficient for comparisons between different environments. Using this method, the first session in the familiar arena was compared to the first session in the new arena (Fam1–New1) and the second session in the familiar arena was compared to the second session in the new arena (Fam2–New2). The maximum for all comparisons was then considered the maximum correlation coefficient for different arenas (Max_{diff}). (5) For each session, vectors with a length corresponding to the average firing rate for each arm and a direction equal to the arm direction were calculated. The mean vector length (mvl) was then calculated from these rate vectors. A mean vector length of more that 0.10 was considered indicative for radial asymmetry of unit activity (Fig. 2). (6) Fields were identified as continuous areas of at least 10 pixels (i.e. 57.6 cm^2) with a rate of more than two times the overall mean rate of the cell. Pixels were considered continuous through borders and corners to also reliably identify fields that are located on maze arms that have a diagonal orientation to the pixel grid. The minimum size of a field on the eight-arm maze was chosen to be smaller than that previously used for the open field (Zhou et al., 1999) to account for the incomplete sampling of space by restricting the animal's movement to the maze arms.

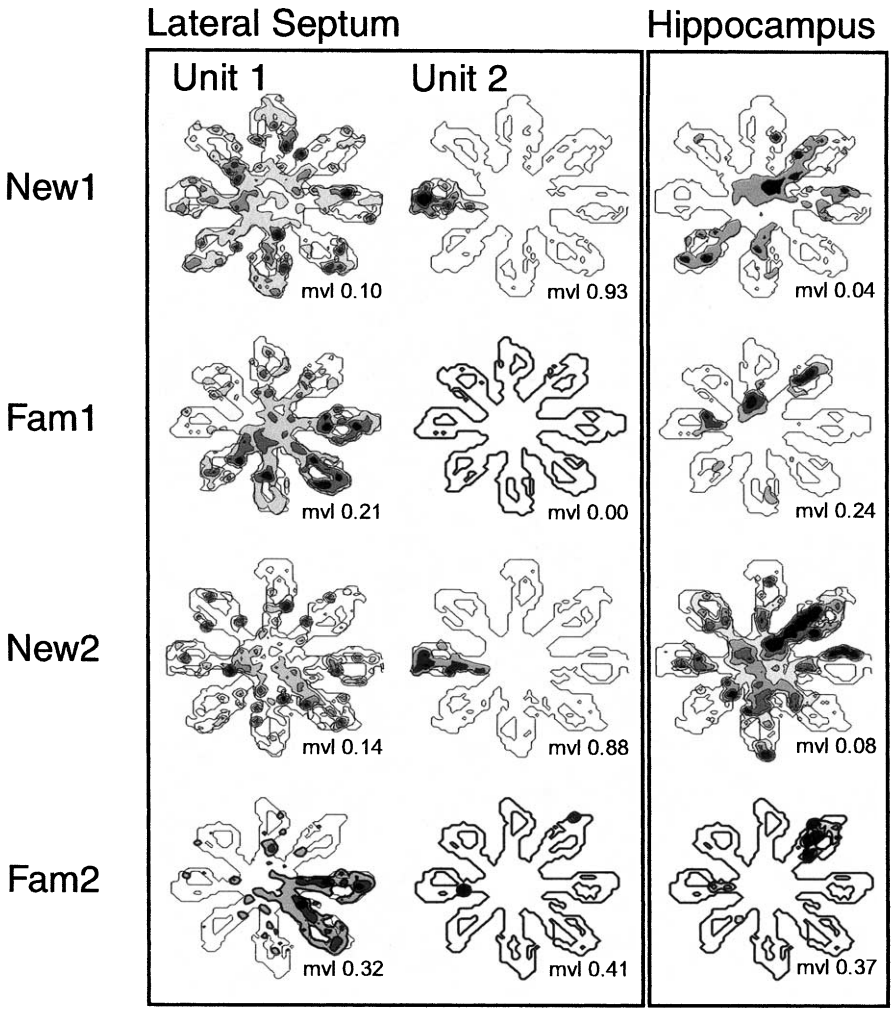

Fig. 3. Two simultaneously recorded lateral septal cells (Units 1 and 2) and a hippocampal cell that were tested in the familiar (Fam1, Fam2) and a new recording arena (New1, New2) for four consecutive days. Each of the septal cells had a field in one of the two arenas and initially showed an unrelated pattern when tested in the second arena. When tested for a second time in each recording arena, the initially non-selective patterns were modified towards increased similarity with the original field. Light gray, dark gray, and black areas correspond to areas with firing rates of more than 25%, 50%, and 75% of the maximum rate. mvl, mean vector length.

Statistical comparisons

Non-parametric tests were used for comparing the mean rates between recording sessions, the correlation coefficients of identical single units between recording sessions, and the correlation coefficients of septal and hippocampal units. The results of all statistical comparisons are reported at a significance level of 0.05.

RESULTS

Data for alternating recording sessions (one per day) in two different recording arenas are presented (Table 1). One of the recording arenas was familiar to the animal and the second recording arena was characterized by cues that were initially unknown to the animal. Thirty-two lateral septal cells were recorded during two sessions in the familiar arena as well as during an intervening recording session in the new arena. Twenty-six of these cells were also recorded during a second session in the new arena and 21 cells during a third session in the new arena. An example of two lateral septal cells that were recorded simultaneously for four consecutive days is shown in Fig. 3. These cells are representative for those that are defined below as location-selective.

The firing rates of the lateral septal cells ranged from the absence of discharges in one arena to a maximum of 125.5 Hz (mean ± S.E.M.: 8.7 ± 3.0 Hz; median: 3.9). Although pronounced differences between individual septal cells were observed, each cell showed approximately similar firing rates in the familiar and the new environment (range: 64.1–221.6%). However, the rates during the first session in the new environment increased in 21/29 cells ($P < 0.05$, 34.5 ± 10.3%). The increase during the second session in the new environment was not significant (15/26 cells, +12.9 ± 7.9%).

To distinguish location-selective firing from other behavioral correlates that have been described for lateral septal cells (Ranck, 1973; Zhou et al., 1999), we rea-

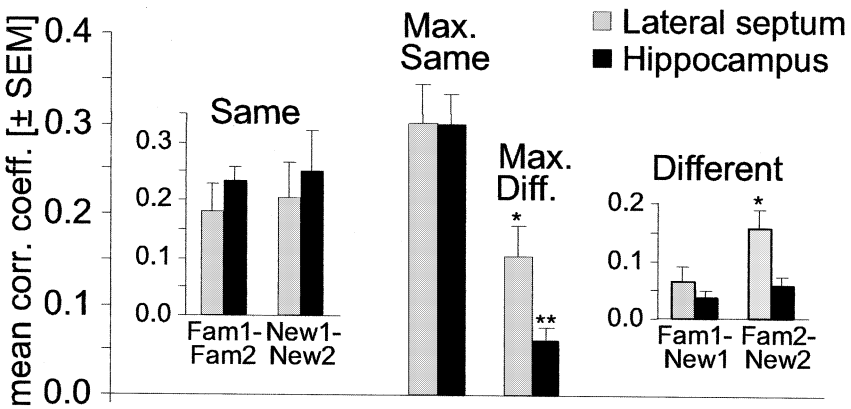

Fig. 4. The mean correlation coefficients (±S.E.M.) for pairwise comparisons of the firing rates in identical spatial bins are shown. (Center) For location-specific lateral septal cells and hippocampal principal cells, the maximum correlation coefficient for comparisons between recording sessions in the same arena (Max_{same}) was higher than the maximum correlation coefficient for comparisons between different arenas (Max_{diff}; septum: $n=11$, $Z=2.22$, $P<0.05$; hippocampus: $n=12$, $Z=3.06$, $P<0.01$). (Left insert) Fields that were recorded repeatedly in the familiar arena (Fam1–Fam2) show a similar correspondence (i.e. correlation coefficient) as fields that were recorded repeatedly in an arena that was initially new to the animal (New1–New2). (Right insert) For different arena comparisons of lateral septal cells, the correlation coefficients between the initial sessions (Fam1–New1) are lower than between the second sessions (Fam2–New2; $n=10$, $Z=2.19$, $P<0.05$). *Pairwise comparison significantly different at $P<0.05$. **Pairwise comparison significantly different at $P<0.01$.

soned that the radial symmetry of the behavior on the eight-arm maze (i.e. running outbound, retrieving the food reward, turning, running inbound) results in radial symmetry of unit firing on each arm for non-spatial correlates. Conversely, asymmetric firing patterns are expected from units with location selectivity. By using a mean vector length for unit firing on each arm of greater than 0.10 (see Fig. 2), we identified 13 cells with asymmetric firing patterns. These cells were further tested for corresponding unit activity in identical locations by calculating the correlation coefficient for firing in identical spatial bins between sessions (Fam1–Fam2, New1–New2, Fam1–New1, and Fam2–New2). Eleven of the 13 asymmetric cells showed corresponding patterns (i.e. the correlation coefficient exceeded 0.10) for at least one of the comparisons and these cells were considered location-selective. The firing rates of all 11 location-selective cells were below 6.7 Hz. During simultaneous recordings of multiple lateral septal cells (see Table 1), we observed that location-selective cells were recorded along with non-selective cells in seven of nine cases. The remaining two recording sessions consisted of one case with only location-selective lateral septal cells and one case with only non-selective cells.

A comparison of the maximum correlation coefficient for identical arenas (Fam1–Fam2 or New1–New2) with the maximum correlation coefficient for different arenas (Fam1–New1 or Fam2–New2) showed that the spatial firing patterns were corresponding better for sessions in the same compared to different arenas (Fig. 4; 10 of 11 cells; $Z=2.22$, $P<0.05$). The comparatively low scores for either the Fam1–Fam2 or the New1–New2 comparison (Fig. 4, left insert) compared to the maximum score for same arena comparisons indicates that many cells showed consistent location-specific firing in only one of the two recording arenas. In addition, when comparing the first (Fam1–New1) with the second (Fam2–New2) pair of sessions in the new and familiar environment, an increase in similarity for encoding the two environments was observed for nine of 10 location-selective cells (Fig. 4, right insert; $Z=2.19$, $P<0.05$; Fig. 5). The similarity with the familiar environment did not further increase on the third day in the new environment (data not shown). The described pattern of results can be seen for all lateral septal cells shown in Figs. 3 and 5. Location-selective firing is initially only observed in one of the two recording arenas. The pattern is then clearly repeated during the second session in the same arena and to a lesser extent also during the second session in the arena that did initially not show location-selective firing.

We compared our selection criterion for location-selective cells with one that has previously been used for defining lateral septal cells as spatially selective (Zhou et al., 1999). Identifying spatial selectivity by a minimum size (i.e. 57.5 cm^2) of the area where the firing rate exceeded two times the average resulted in the identification of 16/32 cells. These cells showed a spatial correlation coefficient of 0.20 ± 0.05 between sessions in identical environments, a spatial correlation coefficient of 0.12 ± 0.02 between different environments ($Z=1.76$, not significant). In our sample ($n=32$), the size criterion identified all cells with low firing rates (<3.8 Hz) and none with higher rates. This bias resulted in the identification of a large fraction of cells (7/16), which did not show consistent location-specific firing between sessions (i.e. the correlation coefficient for identical spatial bins was less than 0.1).

The criterion that was set in this study for lateral septal cells identified 12 of 15 hippocampal principal cells as location-selective (mean correlation coefficient: 0.30 ± 0.03). The spatial discharge patterns of these hippocampal cells in the new arena were unrelated to the familiar environment (Fig. 4, $Z=3.06$, $P<0.01$). The dissimilar-

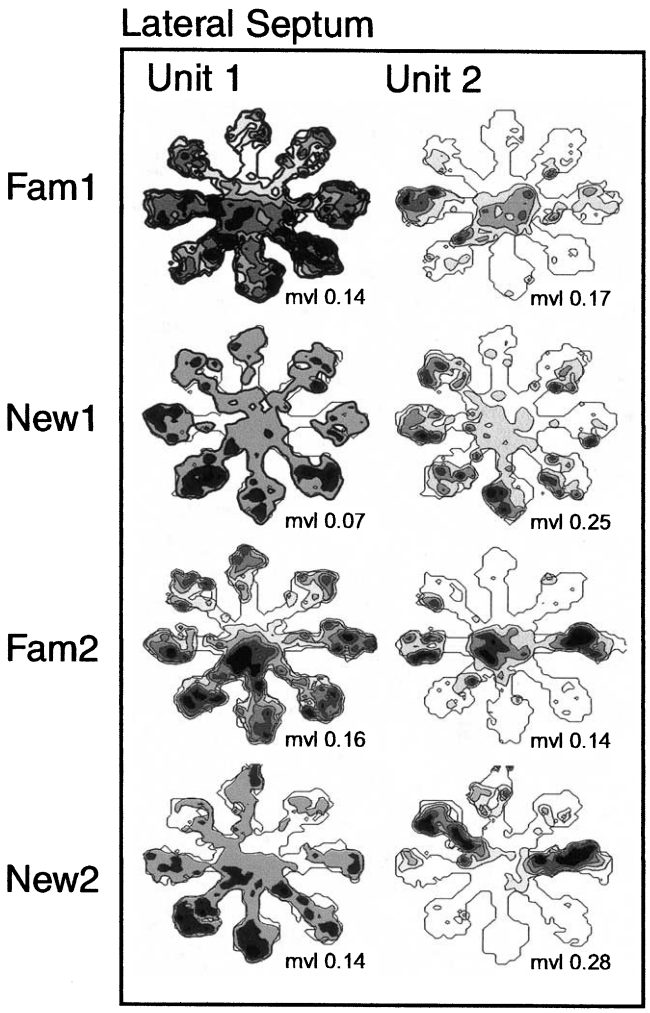

Fig. 5. Examples of lateral septal cells that showed an increased correspondence to the familiar arena on the second day of recording in the new arena. Unit 1: The initial field in the new environment was distinct from the spatial discharge pattern in the familiar room, but more similar fields were found during later sessions. Unit 2: A field that partially resembled the field in the familiar room emerged during the second session in the new environment. Similarity between recording arenas (i.e. firing on the east arm) as well as distinct subfields (i.e. firing on the northwest rather than the west arm) can be observed. mvl, mean vector length.

ity between the familiar and new arena was observed when comparing either the first or the second pair of sessions (Fig. 4, right insert). The fields of the hippocampal cells were not only different on average, but comparisons between sessions in identical arenas resulted for all cells in higher correlation coefficients than comparisons between sessions in different arenas. These results indicate that the sensory cues in the new environment were effective for reorganizing the hippocampal representation of space during all recording sequences with hippocampal cells ($n = 7$).

DISCUSSION

Location-selective lateral septal cells encoded matching locations when a recording session was repeated in the same arena after 2 days. The same cells encoded unrelated spatial patterns when initially tested in a different recording arena. When tested for a second time in the second recording arena, the location coding showed an increased similarity with the original location-selective pattern. The similarity did not reach the maximum level that was observed for comparisons between sessions in the same environment. In contrast, simultaneously recorded hippocampal principal cells showed distinct place fields for each recording room during the first as well as the second session. Remapping the allocentric space to a different set of location-selective cells was thus seen both in hippocampus (Hill, 1978; Kubie and Ranck, 1983; Muller and Kubie, 1987; Thompson and Best, 1989; Wilson and McNaughton, 1993) and lateral septum. However, lateral septal remapping is not as complete as observed for hippocampus. Accordingly, the overall pattern of location-selective firing of lateral septal cells can be described as in-between hippocampal and subicular/entorhinal characteristics.

Subicular and entorhinal place fields are characterized by matching patterns for different environments (Quirk et al., 1992; Sharp and Green, 1994; Sharp, 1999). Dif-

ferences in the extent of the change in the visual environment must be considered when comparing the present results for lateral septal cells to subicular and entorhinal cells. Manipulations that were used in previous studies either involved different sensory cues within the same recording room or a different size or geometry of the same recording room. One of the new environments that we used here consisted of a different set of cues in the same recording room (see Table 1). The changes in location-selective discharges that were observed with this lesser modification of sensory cues were not qualitatively different from recordings in a different room. These data indicate that lateral septal representations show reorganization when subicular and entorhinal representations would be expected to be consistent. However, it is currently not known whether subicular and entorhinal coding for space is already generalized during the initial recording session in a different environment or whether similarities may develop more gradually.

Irrespective of what is assumed for subiculum and entorhinal cortex, it can be inferred from the present results that hippocampal projections are initially effective in contributing to reorganization in the lateral septal location representations. Further processing in either the hippocampal formation or the lateral septum then results in a partial divergence from the pattern of reorganization in hippocampus proper. For example, combined input from entorhinal cortex, subiculum, and hippocampus proper (see Risold and Swanson, 1997) may explain why some of the lateral septal cells did not sustain the distinction between environments as readily as the hippocampal cell population. The direction of change that is observed in the septum is opposite from what has been reported for hippocampus proper. CA1 and CA3 neurons may in some instances not show initial place field reorganization, but they maintain a reorganized pattern once the new fields have been established (Bostock et al., 1991).

The current experimental design is not able to define the subset of cues that defines the firing patterns of lateral septal cells. The broad location selectivity of lateral septal cells indicates that the cells respond to patterns that are beyond the range of those in a single visual field. In addition, the pattern of reorganization that was observed in the present set of recordings further suggests that lateral septal location-specific correlates are not directly dependent on a limited set of visual cues. Reorganization was observed despite some common features between the rooms (e.g. the geometry of the maze, the behavior on the maze). Conversely, a limited degree of similarity was observed in the presence of different visual cues. Although one could adopt the view that stable location coding is dependent on the cues that are shared between environment and that altered location coding is dependent on the cues that were exchanged, this certainly does not account for the increased similarity with the familiar environment on the second compared to the first day of recording. Direct dependence of lateral septal neurons on a single sensory cue is also unlikely based on the projections to the lateral septal nuclei, which are predominantly of subicular or hippocampal origin (Swanson and Cowan, 1977, 1979; Swanson et al., 1981; see Jakab and Leranth, 1995; Risold and Swanson, 1997 for review).

The integration of multiple sensory cues corresponds to what has been described for hippocampal place cells, which are among the prominent source of highly integrated sensory information to the lateral septum. It seems therefore likely that location-selective discharge in the lateral septum is dependent on these projections. Although the information that is afferent to a brain region can be taken as an indication of information that is processed, it is insufficient for predicting single neuron firing patterns. A comparison of what has been described for subiculum and lateral septum suggests that the same type of afferent information can result in the encoding of the environment with a diverging emphasis. These differences can either emerge from the different pattern of afferent projection or by further processing of the information within the area. The pattern of projections is predominantly convergent in the lateral septum (i.e. receiving afferents from multiple subregions of the hippocampal formation) and predominantly sequential within the hippocampus (i.e. from CA3 to CA1 to subiculum). In addition, the intrinsic circuits of lateral septum are different from those of cortical areas. The majority of lateral septal neurons is inhibitory while most cortical neurons are excitatory (DeFrance, 1976; Köhler, 1985; Douglas and Martin, 1990; Freund and Buzsaki, 1996; Risold and Swanson, 1997).

Inhibitory connections within the septum would be a candidate mechanism that can contribute to the context-specific encoding of the environment by lateral septal cells despite the highly convergent projections from hippocampal pyramidal cells and despite the presence of a subset of projections without context-specific encoding (i.e. from subiculum). Taken together with findings that the lateral septal nuclei contribute to working and reference memory (M'Harzi and Jarrard, 1992; Leutgeb and Mizumori, 1999) and contextual fear conditioning (Garcia et al., 1997; Vouimba et al., 1998, 1999; Sparks and LeDoux, 2000), these coding properties suggest that the lateral septum could be an effective output pathway from hippocampus, in particular for providing information about the current context.

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