Task-Dependent Representations in Rat Hippocampal Place Neurons

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Kobayashi, Tsuneyuki, Hisao Nishijo, Masaji Fukuda, Jan Bures, and Taketoshi Ono. Task-dependent representations in rat hippocampal place neurons. J. Neurophysiol. 78: 597–613, 1997. It is suggested that the hippocampal formation is essential to spatial representations by flexible encoding of diverse information during navigation, which includes not only externally generated sensory information such as visual and auditory sensation but also ideothetic information concerning locomotion (i.e., internally generated information such as proprioceptive and vestibular sensation) as well as information concerning reward. In the present study, we investigated how various types of information are represented in the hippocampal formation, by recording hippocampal complex-spike cells from rats that performed three types of place learning tasks in a circular open field with the use of intracranial self-stimulation as reward. The intracranial self-stimulation reward was delivered in the following three contexts: if the rat 1) entered an experimenter-determined reward place within the open field, and this place was randomly varied in sequential trials; 2) entered two specific places, one within and one outside the place field (an area identified by change in activity of a place neuron); or 3) entered an experimenter-specified place outside the place field. Because the behavioral traits during navigation were more constant in the second task than in the first task, ideothetic information concerning locomotion was more relevant to acquiring reward in the second task than in the first task. Of 43 complex-spike cells recorded, 37 displayed place fields under the first task. Of these 37 place neurons, 34 also had significant reward correlates on place field. Although reward and place correlates of the place neuron activity did not change between the first and second tasks, neuronal correlates to behavioral variables for locomotion such as movement speed, direction, and turning angle significantly increased in the second task. Furthermore, 6 of 31 place neurons tested with the third task, in which the reward place was located outside the original place field, shifted place fields. The results indicated that neuronal correlates of most place neurons flexibly increased their sensitivity to relevant information in a given context and environment, and some place neurons changed the place field per se with place reward association. These results suggest two strategies for how hippocampal neurons incorporate an incredible variety of perceptions into a unified representation of the environment: through flexible use of information and the creation of new representations.

INTRODUCTION

Data demonstrating that the activity of complex-spike cells in the hippocampal formation increases when a rat or a monkey is in a specific location in the environment (Eichenbaum et al. 1987; McNaughton et al. 1983; Muller et al. 1987; Nishijo et al. 1997; O’Keefe and Burgess 1996; O’Keefe and Dostrovsky 1971; Olton et al. 1978; Ono et al. 1991, 1993; Quirk et al. 1990; Wible et al. 1986; Wiener et al. 1989; Wilson and McNaughton 1993, 1994), combined with memory deficit after lesion of the hippocampal formation (e.g., Bunsey and Eichenbaum 1996; Mishkin 1978; Olton et al. 1979; Zola-Morgan and Squire 1990), have contributed to the understanding of functions of the hippocampal formation (Eichenbaum et al. 1992; McNaughton and Nadel 1989; O’Keefe and Nadel 1978). These complex-spike cells are called “place cells,” and areas of the environment associated with firing increment are called “place fields.” Spatial correlates of place cell activity can be influenced by controlling environmental cues (Breese et al. 1989; Gothard et al. 1996; Muller and Kubie 1987; Muller et al. 1987; O’Keefe and Conway 1978; O’Keefe and Speakman 1987) that affect the place cell activity. Place cell activity may also be modulated by movement direction, speed, and turning angle as a rat moves through a place field (Breese et al. 1989; McNaughton et al. 1983; Wiener et al. 1989). In such studies rats approached reward locations through rather restricted trajectories in an eight-arm radial maze (McNaughton et al. 1983; Muller et al. 1994) or a square chamber (Breese et al. 1989; Wiener et al. 1989). On the other hand, Muller et al. (1987, 1994) showed relatively low directional selectivity in a behavioral paradigm in which rats searched for small food pellets scattered at random in a cylindrical apparatus. This discrepancy might be attributed to differences in the testing environments, because it has been suggested that the hippocampal neurons encode only salient cues (Muller and Kubie 1987; O’Keefe and Speakman 1987), local views (Leonard and McNaughton 1990; McNaughton et al. 1991), or structure of the maze (Muller et al. 1994). Furthermore, not only these sensory and/or motor factors but also cognitive factors such as behavioral context might affect place cell activity (Knierim et al. 1995; Kubie and Ranck 1983; Markus et al. 1995; Nishijo et al. 1997). Previously, we reported that monkey hippocampal neurons responded differently to the same percept (presentation of the same spatial cues and the same object) with the same behavioral response (go/no-go responses) when the object was presented in different contexts or situations (Eifuku et al. 1995; Nishijo et al. 1993; Ono et al. 1995). However, effects of context on neuronal correlates of rat place cells to movement variables (speed, direction, and turning angle) have not yet been tested in the same environment, except in a recent study that reported changes in neuronal correlates to direction between two different behavioral contexts (Markus et al. 1995). Reward availability might be also an important determinant of place cell activity. Two studies focused on whether or not place field shifted when the location of the reward was changed, and came to different conclusions: Breese et al. (1989) recorded place fields in rats as the rats explored a platform to obtain rewards available at five locations. When reward delivery was restricted, most of these place fields shifted to a single location. In contrast, Speakman and O’Keefe (1989)
demonstrated that, after relocation of the goal, only 2 of 19 place fields changed, but the others retained their locations relative to cues in a cue controlled environment.

Despite discrepancies among the studies cited above, the evidence indicates, at least, that the hippocampal formation processes diverse types of information. The diverse information is suggested to be conjunctively or relationally implicated in the hippocampal formation to represent the environment in a unified manner (Eichenbaum 1993; Eichenbaum et al. 1992; Knierim et al. 1995; McNaughton et al. 1989; Young et al. 1994). The question is how the hippocampal formation encodes the ever-changing and surprising variety of perceptions to represent the environment. There are at least two strategies. The first strategy is that representation in the hippocampal formation remains unaltered when an animal is confronted with modest changes in sensory information within an environmental or a behavioral context. The lesion studies reported that rats with lesions in the hippocampal formation or fornix were impaired when they were confronted with a new situation in the Morris water maze or a stimulus-stimulus association task, and suggest that the hippocampal formation is important for processing information effectively and flexibly (Bunsey and Eichenbaum 1996; Cohen and Eichenbaum 1993; Eichenbaum et al. 1990). Unit recording studies indicate that some hippocampal neurons could maintain their place field after darkening the experimental room (O’Keefe and Speakman 1987; Quirk et al. 1990). The rats probably switch information to be processed in the hippocampal formation from visual in light to proprioceptive and/or vestibular sensation in darkness (Knierim et al. 1995; McNaughton et al. 1991). This first strategy for the hippocampal formation to process information, i.e., flexibility in selection of information, suggests that the hippocampal neuronal correlates would be susceptible to adapting to new relevant cues if a given context changes, even in the same environment. This change in sensitivity to movement variables should be tested in the same environment, because some changes in the environment can influence place cell activity (Muller and Kubie 1987; Quirk et al. 1990). The second strategy is that representation in the hippocampal formation completely changes when an animal is confronted with a relatively large change in an environmental or behavioral context. This second strategy corresponds to creation of a new representation, or “complete remapping” (creation of a new place field) (Muller and Kubie 1987; Quirk et al. 1990) in the hippocampal formation. Theoretical studies assert that sparse and conjunctive coding enables the hippocampal formation to represent a variety of episodes with relatively little overlap (McClelland et al. 1995; McNaughton and Morris 1987; O’Reilly and McClelland 1994). Previous studies propose that the extent of remapping reflects the magnitude of the difference between two environments (Muller and Kubie 1987; Quirk et al. 1990), although a recent study reported significant effects of behavioral contexts on the place fields in the same environment (Markus et al. 1995).

Recently, we developed a protocol for the study of place neuron activity in rats that combines rewarding intracranial self-stimulation with video monitoring of the subject’s movement and location (Fukuda et al. 1992). The use of intracranial self-stimulation as a reward (Shizgal 1989) offers the following advantages over food or water rewards: 1) rapid learning of a task, 2) lack of satiation, and 3) absence of visual and olfactory information regarding the reward. This protocol enables us to perform many trials under different conditions within a short time and in a well-controlled environment. In the present study, using this paradigm, we identified the place fields of hippocampal place neurons in rats as they explored a circular open field to obtain an intracranial self-stimulation reward. To investigate the two strategies in the hippocampal formation noted above, we analyzed spatial, behavioral, and reward correlates of hippocampal place neurons of rats in the different behavioral and reward tasks but in the same environment. It should be noted, however, that changes in behaviors might falsely result in behavioral correlates of place neurons due to a sampling bias (Muller et al. 1994). For example, if the rat tends to exhibit a certain behavior (type X) in the place field of a place neuron, where neuronal activity is high, and another behavior (type Y) outside the place field, where neuronal activity is low, then correlation between the neuron activity and the type X behavior would be falsely high (“distributive hypothesis” of Muller et al. 1994). Therefore we further compared actual behavioral correlates of place neurons with predicted behavioral correlates (i.e., false behavioral correlates) based on the distributive hypothesis, in which neuronal correlates to behaviors are ascribed to the difference in time spent by the rat in different portions of the firing field of the place neurons in different behaviors. Finally, we assessed the plasticity of place neuron activity under conditions in which intracranial self-stimulation was delivered only outside the place field.

Preliminary reports of some of the data in this paper have been published in abstract form (Kobayashi et al. 1992, 1996).

**METHODS**

The methods used for the behavioral aspects of the present experiments using rewarding intracranial self-stimulation were substantially the same as those described in our methodological paper (Fukuda et al. 1992). The general methods are described below.

**Subjects and surgery**

Seventeen male albino Wistar rats were used. The rats weighed 270–320 g at the time of surgery, and were individually housed with food and water available ad libitum. All rats were treated in strict compliance with the US Public Health Service Policy on Human Care and Use of Laboratory Animals and the National Institutes of Health Guide for the Care and Use of Laboratory Animals.

Each rat was anesthetized with pentobarbital sodium (40 mg/kg ip) and implanted bilaterally with monopolar stimulating electrodes (enamel insulated, 200 μm diam, stainless steel) aimed at the medial forebrain bundle at the level of the lateral hypothalamus (4.3 mm caudal to the bregma, 1.6 mm lateral to the midline, and 8.8–9.0 mm ventral to the skull surface) according to the atlas of Paxinos and Watson (1986). Electrodes were attached to the skull with dental acrylic and stainless steel screws, one of which also served as the indifferent electrode for stimulation.

After 1 wk of recovery, the rats were screened for self-stimulation in an operant chamber and trained to perform place-related tasks in a circular open field (see below in detail). After this training, a recording electrode assembly was implanted above the CA1 layer of the dorsal part of the hippocampal formation (3.6 mm caudal to the bregma, 3.0 mm lateral to the midline, and 2.8
mm below the skull surface) under pentobarbital sodium anesthesia (40 mg/kg ip). This coordination allowed us to record neuronal activity not only in the CA1 but also CA3 layers. The recording electrode assembly consisted of a bundle of four or eight wires (Formvar insulated, 20 µm diameter, nichrome) encased in a stainless steel cannula (25-gauge), a small platform, and two screws. The recording electrode assembly was advanced slowly while the neuronal activities from all of the recording electrodes were monitored. If a complex-spike cell, indicating a pyramidal neuron, was found, the assembly was left in that position for 20–30 min to verify stability, and the two screws were then mounted on the skull with dental acrylic. The acrylic formed a shoulder in a lubricated groove in the screw to enable future adjustment of the recording electrode assembly.

**Apparatus**

Spatial behavior was investigated in a 150-cm-diam circular open field with a 45-cm-high wall, painted black on the inside (Fig. 1Aa). The experimenter could manually move or rotate the field on casters attached to the bottom. The open field was enclosed by a black curtain (180 cm diam and 200 cm high). The ceiling of the enclosure contained four small speakers mounted near the circumference, spaced 90° apart, four light bulbs individually mounted near the inner edge of each speaker, and a video camera (Behavioral Tracking Analyzer, BTA-2A, Muromachi Kikai, Tokyo) at the center (Fig. 1Ab). Usually a light bulb was turned on at the 3 o’clock position, and a speaker continuously emitted white noise at the 9 o’clock position. A small light bulb was mounted on the head of the rat. The video camera converted a real video image signal to a binary signal, and tracked the two-dimensional (horizontal) motion of the small bulb. A laboratory microcomputer (PC-9801, NEC, Tokyo) received the X and Y coordinates of the position of the head through an RS-232C serial port at 20 frames per second. A program delimited circular areas (reward places) in the open field, and triggered the delivery of current for intracranial self-stimulation when the rat entered the reward place. The experimenter monitored the locations of the reward place and the rat on a display screen, but no distinctive local cues marked the reward place for the rat.

**Behavioral training**

**SELF-STIMULATION SCREENING.** The rats were screened to self-stimulate in an operant chamber (30 × 30 × 33 cm) equipped with a lever on one wall. Each lever press triggered the delivery of an 0.5-s train of 0.3-ms negative square-wave pulses at 100 Hz. The current intensity for intracranial self-stimulation was determined to produce 40–70 lever presses per minute in the operant chamber. A stimulating electrode that produced stable lever pressing at a low current intensity was selected for each rat. The rats were trained to self-stimulate in daily 30- to 60-min sessions for 5–10 days until stable lever pressing was achieved. The current intensity, which was determined in this period for each rat, ranged from 100 to 250 µA, and was used throughout the following place tasks in the open field.

**PLACE TASK TRAINING.** After the implantation of the recording electrodes, the rats were trained to perform a spatial behavior in the open field. In the first condition, current for intracranial self-stimulation was delivered when the cumulative distance traveled by the rat reached a given distance. The initial distance was 80 cm, and this was increased progressively to 120 or 160 cm. The rats were usually trained for ~1 h/day for 2–4 days until they learned to travel the open field continuously. They were then trained in the following three kinds of place tasks.

1) Random search task: in this protocol a reward place (72 cm diam) was delimited; its center was chosen at random within a square circumscribed around the open field. The rat was rewarded with intracranial self-stimulation when it entered the reward place, which was then made inactive. After a 5-s interval to minimize the effect of intracranial self-stimulation per se on neuronal activity, the reward place was moved to a different location and reactivated (Fig. 1Ba).
2) Place learning task 1: two 40-cm-diameter reward places were located diametrically opposite one another in the open field (Fig. 1Bb). The rat was rewarded in both reward places when it returned to one of them after a visit to the other one. After this shuttle behavior had been acquired, the rat was trained to remain in the reward place for a predetermined time, which was gradually increased from 0.5 to 2.0 s in 0.5-s steps, before receiving the intracranial self-stimulation. This delay was intended to ensure that the rat identified the reward place as such, and was not rewarded for simply being brought into the reward place by automatic locomotion.

3) Place learning task 2: two circular areas were positioned, as in place learning task 1, but the rat received reward in only one of them, as delineated by a thick circle, only after visiting the other circular area (Fig. 1Br). The other area thus became a nonrewarded place, delineated by a thin circle, that still had to be visited to receive a reward in the reward place.

At the start of a session, the small electric bulb on the head of the rat was turned on, and a train of current for intracranial self-stimulation was delivered to activate the rat. Each session was terminated after 50 rewards had been delivered or 10 min had elapsed, whichever occurred first.

Recording procedures and data acquisition

After a few days of recovery from the implantation, the recording electrode assembly was driven at ~20–80 μm per day in 20-μm steps in the open field. If a complex-spike cell was found, the stability of the cell recording was tested by the running place tasks for 30–60 min. Neuronal activity was passed through a high-input impedance preamplifier made of a dual-channel field-effect transistor (2SK389, Toshiba Electric), amplified by a main amplifier, and converted to standardized pulses by means of a window discriminator. During intracranial self-stimulation, neuronal activity was isolated from the stimulus artifact by the window discriminator. The microcomputer summed the spikes (standardized pulses) over 50-ms intervals and combined this data with the X and Y coordinates of the head of the rat to construct a distribution map of the mean firing rate as a function of the position of the rat.

Data analysis

NEURONAL CORRELATES TO PLACE AND INTRACRANIAL SELF-STIMULATION. Place fields were delineated by a process used previously (Breese et al. 1989; Muller et al. 1987). Clusters of 4.5 × 4.5-cm pixels with firing rates exceeding twice the mean firing rate were identified. All pixels that did not satisfy this criterion were eliminated. A place field could be continued through any edge shared by two pixels meeting the criterion, but not through corners. If one or more neighboring pixels satisfied the criterion, the field was expanded to include the pixel(s). Each added pixel was then tested for the presence of a neighboring pixel that met the criterion. When no neighboring pixel satisfied the criterion, the limit of the field was identified. The minimum size for a place field was set at nine pixels. Boundaries of a place field were established by constructing a rectangle that had one diagonal connecting the minimum X and Y coordinates with the maximum X and Y coordinates.

For each 2.0-s period before and after onset of intracranial self-stimulation, the mean movement speed and mean firing rate were calculated every 100 ms; rates and speeds inside and outside the place field were calculated separately. To analyze neuronal correlates to reward, the periods were divided into four phases: 1) preintracranial self-stimulation (0.5 s before onset of intracranial self-stimulation) or predelay (0.5 s before delay time in place learning task 1), 2) delay for place learning task 1 (0.5, 1.0, 1.5, or 2.0 s), 3) intracranial self-stimulation (0.5 s), and 4) postintracranial self-stimulation (0.5 s after end of intracranial self-stimulation). The mean firing rates in these phases for each task were separately compared by one-way analysis of variance (ANOVA) with a significance level of P < 0.05.

NEURONAL CORRELATES TO BEHAVIORAL VARIABLES. We examined the behavioral correlates of the place neuron activity within the place field according to the procedure described by Wiener et al. (1989). The instantaneous direction of movement at each location within the place field was calculated along the vector between sequential locations 100 ms before and after passing through the point observed (Fig. 1C, αj). The direction of movement was determined only for the tokens located at which the rat traveled at a rate >5 cm/s. We examined the relationship between movement direction and neuronal activity by averaging firing rate samples within 45° angular bins. The directions whose firing rates were above the mean firing rate for all directions were defined as preferred directions. The instantaneous turning angle at each location within the place field was estimated as the arc subtended by two vectors connecting a location point and the points passed through 100 ms before and after the point observed (Fig. 1C, βj). The turning angle was determined only for those locations through which the rat traveled at a rate >5 cm/s. We examined the relationship between the turning angle and neuronal activity by averaging firing rate samples within 45° angular bins. The turning angles whose firing rates were above the mean firing rate for all turning angles were defined as preferred turning angles. The speed of movement at each location in the place field was calculated from the distance traveled in the same 200-ms interval used for the direction determination. The firing rate at each location was calculated as the number of spikes in each 50 ms. Preferred speeds were defined as those whose firing rates were above the mean firing rate for all speeds. The relation between movement speed and firing rate was plotted in 20-cm/s bins. The statistical reliability of each movement variable was evaluated by χ² analysis of the firing rate at various speeds, directions, and turning angles on the basis of at least five observations.

To numerically measure breadth of responsiveness (tuning) of each place neuron to each behavioral variable, entropy value was calculated on the basis of the formula by Smith and Travers (1979), which was derived from the equation for entropy based on information theory (Shannon and Weaver 1949). For each neuron, the breadth of responsiveness to each behavioral variable (i.e., speed, direction, and turning angle) was separately calculated from the following formula (Smith and Travers 1979)

\[ H = K \sum_{i=1}^{n} p_i \log p_i \]

where \( H \) is breadth of responsiveness, \( K \) is a scaling constant, and \( p_i \) is the relative response to each parameter of speed, direction, or turning angle. The value of \( K \) was adjusted so that \( H = 1.0 \) when \( p_i = 1/n \). On the basis of this definition, \( H = 0 \) means that the activity of a given neuron is highly tuned to one specific parameter, whereas \( H = 1 \) means that activity of a neuron is broadly tuned to all of the parameters in each variable. Entropy measures of breadth of responsiveness between the random search task and place learning task 1 were compared by paired t-test (\( P < 0.05 \)).

Muller et al. (1994) proposed a distributive hypothesis, in which neuronal correlates to direction are ascribed to the difference in time spent by the rat in different portions of the firing field of the place cells in different direction sectors. Because the behavioral trails during navigation were more constant in place learning task 1 than in the random search task, the changes in the entropy measurements of breadth of responsiveness from the random search task to place learning task 1 might be ascribed to a distributive error. To examine this issue, we calculated the predicted firing in each parameter of speed, direction, and turning angle, with the use of the data within place fields and on the basis of the formula by Muller et al. (1994) in which place neurons are supposed to...
have no correlation to speed, direction, and turning angle of movements. The predicted firing rate at a parameter of \( \phi \) in the pixel, and \( n \) is the number of pixels within the place field.

**Histology**

After the recording electrodes were advanced below the hippocampal formation, the locations of the recording and stimulating electrodes were identified histologically. The rats were deeply anesthetized with pentobarbital sodium (50 mg/kg ip), and the stimulating site was marked by an iron deposit, created by passing a 20-\( \mu \)A positive current through the stimulating electrode for 30 s. The recording site was marked by an electrolytic lesion, created by passing a 20-\( \mu \)A negative current through the recording electrodes for 30 s. Each rat was then perfused through the heart with 50 ml of 0.9% saline containing heparin followed by 200 ml of 10% buffered Formalin-containing 2% potassium ferricyanide. The brain was removed and fixed in Formalin for \( \approx \) 48 h. Sections (75 \( \mu \)m) were cut on a freezing microtome and were then stained with cresyl violet.

**RESULTS**

**Identification of place fields and behavioral correlates of place neuron activity by the random search task**

The activity of 43 complex-spike cells was recorded from the CA1 (\( n = 22 \)) and the CA3 (\( n = 21 \)) subfields of the hippocampal formation of rats as they performed the random search task. Thirty-seven (86.9%) had place fields (CA1, 19; CA3, 18). The remaining six (CA1, 3; CA3, 3) had no place field that met the criterion described in METHODS. Figure 2 shows an example of a CA3 place neuron. Figure 2A shows an example of the trajectory and sites of application of intracranial self-stimulation (each dot) for a recording session, and the corresponding place field of the place neuron in the random search task. The rat traveled 20165.7 cm and obtained 50 rewards in 533.5 s. The trail and intracranial self-stimulation almost uniformly covered the open field (Fig. 2A, left). The firing rate map shows a place field as a rectangle in the center of the open field (Fig. 2A, right).

**Figure 2.** Example of spatial, reward, and behavioral correlates of place neuron activity during random search task. A: trail of exploration (left) and map of firing rate (right). This neuron increased its activity near center of open field. Large rectangle: place field of neuron (see detail in METHODS). Dots in trail map: locations of reward delivery. B: curve of average movement speed (top) and histogram of average firing rates (bottom), which are time locked to onset of intracranial self-stimulation within (Ba) and outside (Bb) place field. Horizontal bar below abscissa: duration of reward. C: relation between neuronal activity and speed (Ca), direction (Cb), and turning angle of movement (Cc) within place field. In Cb, 0° corresponds to direction of vector extending from center to 12 o’clock. In Cc, turning angles greater than and < 0° correspond to right and left turns, respectively. H, numerical measure of breadth of hippocampal neuronal responses to each behavioral variable. A–C are from same neuron.

Because a trial was terminated if 50 intracranial self-stimulation rewards had been delivered in one session, the insignificant reward correlates in these three neurons were ascribed to low numbers of total intracranial self-stimulation rewards inside the place fields. The low numbers of total intracranial self-stimulation rewards resulted in a low degree of freedom in the statistical analysis, which in turn resulted in an insignificant reported difference. However, it should be emphasized that no place neurons consistently had reward correlates both inside and outside the place field. Furthermore, changes in movement speed before and after delivery of intracranial self-stimulation were very similar inside and outside the place field, as shown in Fig. 2B, top. These findings indicated that the effects of intracranial self-stimulation on place neuron activity were due neither to the direct effects of intracranial self-stimulation nor to the direct effect of movement speed.

**Figure 2C** shows the activity of the place neuron shown in A and B at various speeds (Ca), directions (Cb), and turning angles (Cc) of movement inside the place field. The neuronal activity was significantly modulated by speed (\( \chi^2 = 86.3, df = 5, P < 0.01 \)), preferred speed (50–90 cm/s), direction (\( \chi^2 = 64.3, df = 7, P < 0.01 \)), and preferred...
direction = 0–135°), and turning angle ($\chi^2 = 53.0$, df = 7, $P < 0.01$; preferred turning angle = $-45°$–$45°$) over a wide range. Of the 37 place neurons, 28 had significant direction-dependent responses (CA1, 13; CA3, 15), 24 had significant speed-dependent responses (CA1, 11 neurons; CA3, 13), and 21 had significant turning-angle-dependent responses (CA1, 9; CA3, 12). To quantitatively assess the breadth of responsiveness to each behavioral variable, a numerical measure of the breadth of responsiveness was introduced. Although the neuron in Fig. 2 demonstrated significant behavioral variable-dependent responses, numerical measures of breadth of neuronal response to each behavioral variable were rather high ($H \approx 0.96$).

Spatial and reward correlates of place neuron activity during the random search task and place learning task 1

To compare the spatial and reward modulation of place neuron activity in different behavioral tasks, a place field was initially identified in the random search task, and the activity of the same neuron was then tested in place learning task 1, in which one of the two reward places was located in the place field. Figure 3 shows examples of the spatial and reward correlates of a CA3 place neuron activity in the random search task and place learning task 1 with 0- and 1.0-s delay. The neuron had one large and two small place fields located at 1–3 o'clock during the random search task (Fig. 3Aa). The mean firing rate of the neuron in the pixels inside the three place fields was $5.6 \pm 0.3$ spikes/s, and the mean firing rate outside the place field was $0.5 \pm 0.1$ spikes/s. The firing rates during the preintracranial self-stimulation, intracranial self-stimulation, and postintracranial self-stimulation phases were significantly different inside the large place field [ANOVA, $F(2,11) = 19.01$, $P < 0.01$], and decreased during reward delivery (Fig. 3Ab). The post hoc test indicated that the firing rate during the preintracranial self-stimulation phase was significantly higher than the firing rate during the intracranial self-stimulation phase (Newman-Keuls test, $P < 0.05$). However, there was no significant difference in neuronal activity among the three phases outside the place field [ANOVA, $F(2,28) = 1.23$, $P > 0.05$; Fig. 3Ac]. During place learning task 1, the activity of the neuron corresponded spatially with the activity observed in the random search task (Fig. 3, Ba and Ca). In place learning task 1 with 1.0-s delay, the same effects of intracranial self-
stimulation on neuronal activity as shown in the random search task were observed. In place learning task 1 with delay, the activity of the neuron was significantly influenced by intracranial self-stimulation delivered in the reward place inside the place field [ANOVA, \( F(3,23) = 32.04, P < 0.05 \); Fig. 3Cb] but was not influenced by intracranial self-stimulation delivered outside the place field [ANOVA, \( F(3,23) = 0.76, P > 0.05 \); Fig. 3Cc]. The post hoc test indicated that the firing rate during the preintraocular self-stimulation phase was significantly higher than the firing rate during the intracranial self-stimulation phase inside the place field (Newman-Keuls test, \( P < 0.01 \)). In place learning task 1 without delay, the neuronal activity was not significantly influenced by the intracranial self-stimulation inside [ANOVA, \( F(2,20) = 0.70, P > 0.05 \); Fig. 3Bb] or outside [ANOVA, \( F(2,20) = 2.11, P > 0.05 \); Fig. 3Bc] the place field. Although the effects of intracranial self-stimulation reward were not statistically significant in place learning task 1 without delay, the activity changes were very similar to those in the random search task and place learning task 1 with delay. Thus the activity of the neuron inside the place field for all three tasks (random search task, and place learning task 1 with or without delay) was higher before intracranial self-stimulation than during intracranial self-stimulation.

The relatively high firing rates 2–4 s before and after delivery of intracranial self-stimulation outside the place field in place learning task 1 with and without delay in Fig. 3, Bc and Cc, were attributed to the rat’s being located inside or near the place field. The low firing rates around delivery of the intracranial self-stimulation in Fig. 3, Bc and Cc, were due to the rat’s being located outside the place field, rather than to inhibition by intracranial self-stimulation. To analyze the spatial correlates of the CA3 place neuron described above in greater detail, 2.0-s periods before and after reward delivery inside the place field were examined in four segments of 1.0 s each in place learning task 1 with 1.0-s delay; the spatial correlates in each time segment were reconstructed (Fig. 4). In the first and second segments before reward delivery, the neuron fired at a higher rate, with spatial correlates that corresponded to the place field observed in the random search task (Fig. 4, Ba and Bb). In the third and fourth segments, the rat entered the place field of the neuron, but the neuronal activity was lower than in the random search task (Fig. 4, Bc and Bd); during intracranial self-stimulation it became very low, reaching zero at one time. Thus the effects of intracranial self-stimulation on this neuron were similar in both the random search task and place learning task 1. Inside the place field, the neuronal activity gradually increased before delivery of intracranial self-stimulation, continued to increase during the delay time, and stopped increasing immediately after the reward delivery. However, no differences of neuronal activity between these phases were observed outside the place field (not shown). These results indicated that the neuron had both place and reward correlates.

Figure 5 shows another type of a CA3 place neuron with different reward correlates. This place neuron had two distinct place fields located at 6 and 8–10 o’clock in the random search task (Fig. 5Aa). The mean firing rate in the pixels inside the two place fields was 4.1 ± 0.3 spikes/s, and the mean firing rate outside the place field was 0.8 ± 0.1 spikes/s. In the random search task, neuronal activity was not significantly influenced by intracranial self-stimulation reward inside [ANOVA, \( F(2,3) = 1.50, P > 0.05 \); Fig. 5Ab] or outside [ANOVA, \( F(2,25) = 2.41, P > 0.05 \); Fig. 5Ac] the place field. In the random search task, neuronal activity was not significantly influenced by intracranial self-stimulation reward inside [ANOVA, \( F(2,3) = 28.62, P < 0.01 \); Fig. 5Bb] but the neuronal activity did not significantly change outside the place field before or after the intracranial self-stimulation [ANOVA, \( F(2,23) = 1.00, P > 0.05 \); Fig. 5Bc]. The insignificant reward correlates inside the place field in the random search task seem to be due to relatively few intracranial self-stimulation rewards inside the place field (i.e., \( n = 4 \) in this case), as described in the former section. The neuronal activities in the 15 bins of the summed histogram before, during, and after the intracranial self-stimulation were significantly correlated between the random search and place learning task 1. Inside the place field, the neuronal activity gradually increased before delivery of intracranial self-stimulation, continued to increase during the delay time, and stopped increasing immediately after the reward delivery. In the random search task, neuronal activity was not significantly influenced by intracranial self-stimulation inside [ANOVA, \( F(2,23) = 0.76, P > 0.05 \); Fig. 3Cc] or outside [ANOVA, \( F(2,20) = 2.11, P > 0.05 \); Fig. 3Bc] the place field. Although the effects of intracranial self-stimulation reward were not statistically significant in place learning task 1 without delay, the activity changes were very similar to those in the random search task and place learning task 1 with delay. Thus the activity of the neuron inside the place field for all three tasks (random search task, and place learning task 1 with or without delay) was higher before intracranial self-stimulation than during intracranial self-stimulation.
FIG. 5. Another example of spatial and reward correlates of place neuron activity during random search task and place learning task 1. A–C: trail of rat, reward locations, and spatial distribution of neuronal activities in random search task (A), place learning task 1 without delay for intracranial self-stimulation (B), and place learning task 1 with 1.0-s delay (C). During random search task, place neuron had place fields at 6 o’clock and at 8–10 o’clock (Aa). During place learning task 1 without (B) and with (C) delay time, neuron increased its activity during and after reward delivery in reward place within place field (Bb and Cb) but not outside place field (Bc and Cc). A–C are from same neuron. Other conventions as for Figs. 2 and 3.

task and place learning task 1 without delay (Pearson’s correlation coefficient = 0.601, P < 0.05). This indicated that the effects of intracranial self-stimulation reward on neuronal activity were similar in both the random search task and place learning task 1 without delay. In place learning task 1 with 1.0-s delay, intracranial self-stimulation significantly modulated neuronal activity in the reward place inside the place field [ANOVA, $F(2,23) = 10.9$, $P < 0.01$; Fig. 5Cb] but not outside the place field [ANOVA, $F(2,23) = 0.72$, $P > 0.05$; Fig. 5Cc]; this is the same as in place learning task 1 without delay.

Figure 6 shows a detailed analysis of the spatial correlates of the same CA3 place neuron shown in Fig. 5 during place learning task 1 with 1.0-s delay. The neuronal activity was very low before reward delivery and during the fourth segment, although the rat was in the place field identified during the random search task (Fig. 6, Ba, Bb, and Bd). In the third segment, activity increased during and after the intracranial self-stimulation, and the spatial correlates were similar to those observed in the random search task (Fig. 6Bc). This characteristic increase in neuronal activity during and after the intracranial self-stimulation was also observed in the other two conditions (Fig. 5Ab and Bb). Thus spatial and reward correlates of this neuron did not change among these three conditions.

Of the 37 place neurons, 21 (CA1, 10; CA3, 11) had significant reward correlates, as shown in Fig. 3 (type 1), and 15 (CA1, 9; CA3, 6) had significant reward correlates, as shown in Fig. 5 (type 2), in at least one of the three tasks (i.e., random search task, and place learning task 1 without and with delay). When the neurons had reward correlates, the effects of reward were only evident inside the place field, as shown in Figs. 3 and 5.

Behavioral correlates of place neuron activity during the random search task and place learning task 1

The neuronal correlates of the hippocampal place neurons to behavioral variables (speed, direction, and turning angle of movement) were analyzed only inside the place field identified during the random search task, and were compared within three tasks (random search task, and place learning task 1 without and with delay). Figure 7 shows the neuronal correlates of the same place neuron shown in Figs. 3 and 4 to the behavioral variables. In the random search task, the neuronal activity was significantly modulated by speed...
(χ² = 38.3, df = 4, P < 0.01; preferred speed = 30–90 cm/s; Fig. 7Aa), direction (χ² = 85.6, df = 7, P < 0.01; preferred direction = 0° and 90–180°; Fig. 7Ab), and turning angle (χ² = 53.79, df = 7, P < 0.01; preferred turning angle = −45–0–180°; Fig. 7Ac) over a wide range. However, neuronal correlates to some behavioral variables became more evident in place learning task 1. In place learning task 1 without delay, the neuronal activity was significantly modulated by speed (χ² = 37.8, df = 4, P < 0.01; preferred speed = 10–30 cm/s; Fig. 7Ba), direction (χ² = 20.7, df = 7, P < 0.01; preferred direction = 135–180° and 315°; Fig. 7Bb), and turning angle (χ² = 12.47, df = 7, P < 0.01; preferred turning angle = 45°, 135–180°, and −45°; Fig. 7Bc). A comparison of the numerical measures of the breadth of responsiveness to behavioral variables between the random search task and place learning task 1 without delay indicated that the breadth of responsiveness in speed (H = 0.80) in place learning task 1 without delay became smaller than the breadth of responsiveness in speed in the random search task (H = 0.99), whereas there were no changes in the breadth of responsiveness in direction (0.98 vs. 0.98) and only a slight increase in the breadth of responsiveness in turning angle (0.98 vs. 0.99).

The similar reduction in the numerical measures of the breadth of responsiveness was also observed in place learning task 1 with 1.0-s delay. In place learning task 1 with 1.0-s delay, the neuronal activity was significantly modulated by speed (χ² = 73.0, df = 5, P < 0.01; preferred speed = 10–70 cm/s; Fig. 7Ca), direction (χ² = 119.5, df = 7, P < 0.01; preferred direction = 315–0–180°; Fig. 7Cb), and turning angle (χ² = 11.62, df = 7, P < 0.01; preferred turning angle = 45°–90° and −45°; Fig. 7Cc). The numerical measures of the breadth of responsiveness to speed (H = 0.89) and direction (H = 0.95) in place learning task 1 with 1.0-s delay became smaller than those in the random search task (Fig. 7, A and C). However, it should be emphasized...
that these changes in breadth of responsiveness were observed only inside the place field, but not outside the place field (not shown).

Figure 8 shows the neuronal correlates inside the place field to the behavioral variables of the same CA3 place neuron shown in Figs. 5 and 6. In the random search task, the neuron had no significant speed modulation ($\chi^2 = 4.8$, df = 5, $P > 0.05$; Fig. 8Ab), but the directional ($\chi^2 = 46.2$, df = 7, $P < 0.01$; preferred direction = 45–180°; Fig. 8Ab) and turning angle ($\chi^2 = 10.97$, df = 7, $P < 0.01$; preferred turning angle = 90–135° and –90°; Fig. 8Ac) modulation were significant over a wide range. In place learning task 1 without delay, the neuronal activity developed significant speed ($\chi^2 = 35.3$, df = 5, $P < 0.01$; preferred speed = 10–70 cm/s; Fig. 8Ba), directional ($\chi^2 = 69.5$, df = 6, $P < 0.01$; preferred direction = 45–135° and 225°; Fig. 8Bb), and turning angle ($\chi^2 = 17.86$, df = 6, $P < 0.01$; preferred direction = 45°, 135–180°, and –45°; Fig. 8Bc) modulations that narrowed to more limited ranges. In place learning task 1 with 1.0-s delay, the neuronal activity was significantly modulated by speed ($\chi^2 = 20.0$, df = 5, $P < 0.01$; preferred speed = 30–90 cm/s; Fig. 8Ca), direction ($\chi^2 = 46.7$, df = 7, $P < 0.01$; preferred direction = 45–180°; Fig. 8Cb), and turning angle ($\chi^2 = 20.86$, df = 7, $P < 0.01$; preferred direction = 90°, 180°, and –135°; Fig. 8Cc). Although the neuronal correlates to the behavioral variables, except for the speed in the random search task, were evident in all three conditions, a comparison of the breadth of responsiveness indicated that all three numerical measures of the breadth of responsiveness for speed, direction, and turning angle became smaller in place learning task 1 than in the random search task (Fig. 8). In accordance with the place neuron shown in Figs. 3, 4, and 7, the breadth of the neuronal responses changed only inside the place field.

The optimal behavioral variables in speed, direction, and turning angle of the random search task, place learning task 1 without delay, and place learning task 1 with delay did not change systematically. Most hippocampal neurons tended to respond more to high-speed movement in the random search task, but not in place learning task 1 with or without delay, as shown in Figs. 7 and 8.

**Effects of task difference on breadth of responsiveness**

We analyzed the breadth of responsiveness of 21 place neurons (CA1, 9; CA3, 12) that were tested in three tasks in the same way. Because there was no significant difference between the mean breadth of responsiveness of the CA1 and CA3 place neurons for each behavioral variable (Student’s $t$-test, $P > 0.05$), the data from both CA1 and CA3 place neurons were analyzed together. First, we compared the entropy measurements of breadth of responsiveness, calculated from actual responses to each parameter of the behavioral variables, with those calculated from the predicted responses to each parameter according to the formula by Muller et al. (1994) (Fig. 9). In all three tasks (the random search task, place learning task 1 without delay, and place learning task 1 with delay), the entropy measures of breadth of responsiveness calculated from actual responses (filled columns) were significantly smaller than those calculated from predicted responses (open columns) to each of three parameters (paired $t$-test, $P < 0.01$ or 0.05). These results indicate that actual neuronal tuning to behavioral variables in all three tasks was significantly more selective than the neuronal tuning that was predicted according to the assumption that place neurons have no correlation to speed, direction, and turning angle of movements.

Second, effects of task difference on breadth of respon-
siveness were analyzed with the use of actual responses (filled columns). The breadth of responsiveness to movement speed in three tasks (random search task, place learning task 1 without delay, and place learning task 1 with delay) was 0.84–1.00 (0.96 ± 0.01), 0.56–0.99 (0.87 ± 0.02), and 0.66–0.97 (0.86 ± 0.02), respectively, and the breadth of responsiveness to direction in these three tasks was 0.72–0.99 (0.92 ± 0.01), 0.47–0.98 (0.84 ± 0.03), and 0.41–0.97 (0.84 ± 0.03), respectively. The mean breadth of responsiveness to movement speed and direction in place learning task 1 with and without delay was significantly smaller than that in the random search task (paired \( t \)-test, \( P < 0.01 \); filled columns in Fig. 9, A and B). The breadth of responsiveness to turning angle in three tasks (random search task, place learning task 1 without delay, and place learning task 1 with delay) was 0.75–0.99 (0.92 ± 0.01), 0.52–0.99 (0.89 ± 0.03), and 0.54–0.99 (0.86 ± 0.03), respectively. Similarly, a reduction of the mean breadth of responsiveness to turning angle in place learning task 1 was statistically significant (paired \( t \)-test, \( P < 0.05 \); filled columns in Fig. 9C). These results indicate that the neuronal correlates to behavioral variables became more evident in place learning task 1 than in the random search task.

Third, net effects of task difference on breadth of responsiveness were analyzed when the contribution of distributive errors was taken into account (hatched columns in Fig. 9). For this purpose, difference in breadth of responsiveness between predicted and actual responses for each neuron was calculated (i.e., predicted breadth of responsiveness minus actual breadth of responsiveness; hatched columns). A two-way ANOVA (task \( \times \) behavioral variable) revealed a significant main effect of task \( [F(2,180) = 6.625, P < 0.02] \). There was no significant main effect of behavioral variable \( [F(2,180) = 1.028, P > 0.05] \) or the task \( \times \) behavioral variable interaction \( [F(4,180) = 0.419, P > 0.05] \). The post hoc test indicated that mean difference between predicted and actual breadth of responsiveness in place learning task 1 with delay was significantly larger than that in the random search task (Newman-Keuls test, \( P < 0.05 \)), and larger than that in place learning task 1 without delay (Newman-Keuls test, \( P < 0.05 \)). The results demonstrated significant effects of task difference on breadth of responsiveness of place neurons even after the contribution of distributive errors was eliminated. Taken together, these results indicated that neuronal correlates of movement speed, direction, and turning angle significantly increased in place learning task 1.

**Plastic changes of the spatial correlates of the place neuron activity in place learning task 2**

Initially, the place fields were identified by the random search task in two or three sessions. Place learning task 1 was tested with and without delay in four or five sessions, and place learning task 2, in which the reward place corresponding to the place fields was changed to a nonreward place, was tested in four or five sessions. The changes in place field were analyzed in relation to reward place. We defined the place field changes as follows: 1) if a new place field during and/or after place learning task 2 moved away from the circular area where an initial place field was located during place learning task 1, which was the reward place in
place learning task 1 and nonreward place in place learning task 2; and 2) only if the new place field did not overlap with that circular area. The place fields of the place neurons were very stable during both the random search task and place learning task 1. No place neurons shifted place fields during the random search task and place learning task 1, before place learning task 2 was introduced. During place learning task 2 and subsequent place learning task 1, 6 of 31 (19.4%) place neurons identified by the random search task and place learning task 1 developed new place fields associated with a reward place located outside the place fields that were initially identified by the random search task and place learning task 1. The other 25 (80.6%) did not change place fields. It must be emphasized that there were no relations between the place field changes and total numbers of sessions for all three tasks, and that all six place neurons shifted their place fields during or after place learning task 2.

Figure 10 shows an example of a CA3 place neuron that retained its spatial correlates when the reward place contingency was changed. This neuron had two place fields, located at 1 and 9–11 o’clock, in the random search task (Fig. 10A). In place learning task 1, where areas inside and outside the place fields were associated with intracranial self-stimulation reward, the neuron fired in the 9–10 o’clock point in the place field where the rat received intracranial self-stimulation (Fig. 10B). In place learning task 2, where only an area outside the place fields was associated with the intracranial self-stimulation reward, the neuron retained its original spatial correlates in the first and fourth sessions of place learning task 2 (Fig. 10, C and D).

Figure 11 shows an example of a CA1 place neuron that developed a new place field while it retained an original place field identified in the random search task, when the reward delivery location was changed in place learning task 2. The place field of this neuron was located between 5 and 6 o’clock in the random search task (Fig. 11A). A similar spatial correlate was maintained in place learning task 1 (Fig. 11B). The activity of the same neuron was then recorded during place learning task 2, in which no reward was given at the reward place at 5 o’clock in the place field. In the first session of place learning task 2, the neuron increased its activity predominantly around the reward place outside the place field at 11 o’clock, and slightly in the nonreward place at 5 o’clock (Fig. 11C). In the fourth session, the neuron increased its activity in both the reward and the nonreward places at 5 and 11 o’clock (Fig. 11D).

Figure 12 shows an example of a CA1 place neuron that completely changed its spatial correlates when the reward delivery location was changed. The place field of this neuron was located at 6 o’clock in the random search task (Fig. 12A). The spatial correlates were retained in place learning task 1 (Fig. 12B). The same neuron was then tested in place learning task 2, where the nonreward place was set with the place field at 6 o’clock. In the first session of place learning task 2, the neuron increased its activity predominantly around the nonreward place (Fig. 12C). In the fourth session, the place field shifted along the rat’s path toward the reward place, partly remaining in the departure sector of the previously determined place field (Fig. 12D). Immediately after that session, the neuron was recorded in place learning task 1 with 1.0-s delay, and its place field then appeared on the same pathway but closer to the reward place at 12 o’clock (Fig. 12E). In the second session of place learning task 1, the place field of the neuron was concentrated in the area at 12 o’clock (Fig. 12F), where it had rarely fired in the random search task and place learning task 1. Figure 12G shows how the centers of the place field gradually shifted toward the reward place at 12 o’clock.

**Recording sites**

The approximate anatomic locations at which the place neurons were recorded are shown in Fig. 13. These sites were determined histologically from small lesions made in the hippocampal formation after recording. The place neurons recorded were located in the CA1 and CA3 subfields of the hippocampal formation.

**DISCUSSION**

**Effects of reward on place neuron activity**

In the present study, intracranial self-stimulation reward influenced the neuronal activity of most place neurons only inside the place fields, and the effects of intracranial self-stimulation reward were essentially similar in three different
tasks: random search task, place learning task 1 without delay, and place learning task 1 with delay. Speakman and O’Keefe (1990) suggested that the reward would work as a sensory cue or a landmark. This indicated that the place neurons in the present study might develop a spatial reference frame relative to the reward place. This does not appear likely from the results of the present study. First, the difference between random and fixed reward deliveries in the random search task and place learning task 1 did not affect the spatial correlates of the place neurons in both tasks. Second, the change in neuronal activity before or after delivery of intracranial self-stimulation was similar in both the random search task and place learning task 1 although locations of delivery of intracranial self-stimulation were different between the random search task and place learning task 1. In the random search task the animals could not use reward delivery as a landmark because it was delivered in random locations, but in place learning task 1 the animals could use it as a landmark because it was delivered in fixed locations (i.e., reward places). Therefore the similarity of changes in neuronal activity aligned with reward delivery in both tasks strongly suggests that the neuronal activity reflected the motivational aspects rather than the spatial significance of the intracranial self-stimulation reward. The effects of intracranial self-stimulation were also not ascribed to other coincidental factors such as behavioral changes, because the results

**FIG. 11.** Example of place neuron that developed new place field in place learning task 2 while it retained place field in random search task. A: place field was located at 5–6 o’clock in random search task. B: spatial correlates were retained in place learning task 1, where 1 reward place was located in place field observed in random search task. C: spatial correlates at 5 o’clock were retained, but new spatial correlates appeared at 11 o’clock in 1st session of place learning task 2, where reward was delivered only in reward place at 11 o’clock. D: spatial correlates at 5 o’clock were retained, but new spatial correlates at 11 o’clock persisted in 4th session of place learning task 2. A–D are from same neuron. Other conventions as for Fig. 2.

**FIG. 12.** Example of place neuron that completely shifted its place field during sessions of 2 place learning tasks. A: place field was located at 6 o’clock in random search task. B: in place learning task 1, reward was presented in place field observed in random search task. C: 1st session of place learning task 1, in which reward was delivered only in reward place at 0 o’clock. D: 4th session of place learning task 2. E and F: 2 successive sessions of place learning task 1 after place learning task 2. G: gradual changes of center of place field. Random search task (1), place learning task 1 (2), 1st–4th sessions of place learning task 2 (3–6), and 1st–3rd sessions of place learning task 1 after place learning task 2 (7–9). A–G are from same neuron. Other conventions as for Fig. 2.
from the three different behavioral tasks were consistent. 
Therefore no spatial, behavioral, or reward factors could account for all of the activity of a place neuron, because intracranial self-stimulation only influenced the activity inside the place field. These results suggest that the activity of a place neuron is determined by a constellation of all of the factors.

In nonspatial paradigms, hippocampal neuron activity has been associated with cue stimuli and responses in classical conditioning tasks, delayed matching and non-matching to sample tasks (Hampson et al. 1993; Otto and Eichenbaum 1992; Sakurai 1990; Wible et al. 1986), odor discrimination tasks (Eichenbaum et al. 1987; Wiener et al. 1989), and a nonspatial radial maze task (Young et al. 1994), as well as with reward delivery (Hampson et al. 1993). Little attention was focused on the neuronal correlates to the reward itself in those studies. The present experiments show two types of neuronal responses synchronous with reward delivery in the place field during the random search task and place learning task 1. Neurons fired most 1) from the time of arrival in the place fields until the onset of reward (type 1) and 2) from the onset of reward until the start of approach to the opposite reward place (type 2). The type 1 neurons might correspond to the approach-consummate cells (Ranck 1973) and goal-approach cells (Eichenbaum et al. 1987) that fired when the rat approached the food/water or goal. Because type 1 neurons continued to fire during the delay period before delivery of intracranial self-stimulation, they might also correspond to the approach-consummate mismatch cells (Ranck 1973), or to the misplace cells (O’Keefe 1976) that fired when a food reward was not found at the goal. The type 2 neurons might correspond to the hippocampal neurons, such as motion punctuate cells (Ranck 1973), and cup-approach cells (Wiener et al. 1989), that fired at the end of approach movements, or to consummatory cells that fired during consummatory behaviors (Ranck 1973).

Effects of behavioral tasks on spatial and behavioral correlates of place neuron activity

The random search task and place learning task 1 had a common association structure, in which intracranial self-stimulation reward was associated both with the place field and with multiple locations in the random search task and with a zone diametrically opposite the place field in place learning task 1. The same spatial and reward correlates were consistently observed in both the random search task and place learning task 1. These results suggest that spatial correlates do not change if the tasks share a common place reward association. In the random search task, intracranial self-stimulation was delivered if the rat entered areas that were randomly located on the open field, but only after a certain distance was traversed. Because the rat could not locate a fixed locus of intracranial self-stimulation, it seemed to explore the open field uniformly with no particular orienting directions. In place learning task 1, the rats’ constant trails over several sessions suggest that behavioral factors such as a specific speed, direction, and turning in a specific place were important to accomplish the task effectively. Each behavioral variable during locomotion was less relevant in the random search task than in place learning task 1; place neurons, with relatively broad movement tuning in the random search task, became more selective in place learning task 1. The difference in behavioral requirements between the random search task and place learning task 1 resulted in an increased correlation of the place neuron to specific behavioral variables.

In the random search task, the rats received a reward when they incidentally entered the reward place, located at random. The random search task is similar to the behavioral paradigm used by Muller and Kubie (1987) in which they reported that the firing of hippocampal place neurons was about the same when the rat moved in opposite directions inside the place field. The present results, in which the place neuron activity was nondirectional, or had broad directional correlation in the random search task, are similar to the results of Muller and Kubie (1987) and Muller et al. (1994), and suggest that the place neuron activity is poorly correlated with the direction of rats’ movement when the rats randomly move in all directions.

Place learning task 1, in which a shuttle behavior was required, is similar to the task used by McNaughton et al. (1983), Breese et al. (1989), Wiener et al. (1989), and Muller et al. (1994). McNaughton et al. (1983) tested place neurons in an eight-arm radial maze, and found place neurons that increased their firing rates only when the subject was passing through an arm of the maze in one direction. Breese et al. (1989) and Wiener et al. (1989) used square chambers in which reward was available in each corner, and reported place neuron activity correlated with the movement speed, direction, and turning angle of the animal. These results suggested that place neuron activity is correlated with the directional parameter when rats move linearly (Muller et al. 1994). Recently, Markus et al. (1995) also reported an increase in neuronal correlates to direction in a directed search task in comparison with a random search task in the hippocampal formation. However, some are differences between our results and those of Markus et al. The increase in neuronal correlates to direction was largely ascribed to creation of new directional place fields rather than changes in neuronal correlates in the same place fields (Markus et al. 1995), whereas neuronal correlates to direction increased in the same place fields in the present study. The present results indicate that, even in the same environment,
neuronal correlates not only to direction, but also to speed and turning angle, flexibly increase according to behavioral requirement in the tasks.

The changes reported in the present study indicate that neuronal correlates of various variables are not fixed. Behavioral and reward correlates of place neuron activity as well as the flexible changes were observed only inside the place field. These results suggest the existence of active information selection mechanisms in the hippocampal formation, and suggest that a place field acts as a window through which relevant information is focused. Previous unit recording studies reported that the hippocampal place cells of rats became less responsive to environmental cues when rats were disoriented, because disorientation caused the rats to disregard relevant environmental cues for spatial recognition (Knierim et al. 1995). Passive displacement of the restrained animals greatly reduced the place correlates of the hippocampal neurons (Foster et al. 1989). This reduction in place correlates may be attributed to disturbed or decreased attention to environmental cues. A monkey’s active intention to move the cab that it drove was important to the formation of place-related activity by hippocampal neurons; passive movement of the monkey cab greatly reduced place-related activity (Nishijo et al. 1997). Furthermore, the amplitudes of sensory evoked potentials responding to auditory, visual, and somatosensory cues in the human hippocampal formation were markedly reduced when the subject’s attention was directed elsewhere (McCarty et al. 1989). These observations from other studies also suggest the existence of active information selection in the hippocampal formation.

Plastic change of place neuron activity

The present study shows that, during several sessions of place learning task 2, ~20% of the place neurons shifted place fields to locations newly associated with intracranial self-stimulation rewards; these neurons displayed no increase in activity in the random search task and place learning task 1. The intracranial self-stimulation was associated with both place field and non-place field regions in the random search task and place learning task 1, but was only associated with a region outside the original place field in place learning task 2. However, the change of reward place alone cannot account for the shifting of the place field, because reward availability was not the sole determinant of hippocampal neuron activity (see above). Although most of the place fields identified during the random search task retained their locations in place learning task 2, some place fields shifted to the reward place in place learning task 2, and the locations of place fields changed gradually. The neurons did not demonstrate the original place field when the task was reversed from place learning task 2 to place learning task 1. These findings indicate that complete remapping can occur in the same behavioral task and environment, and suggest that former experience (insertion of place learning task 2) influenced the place field because it was stable during place learning task 1 if place learning task 2 was not imposed during recording.

Breese et al. (1989) and Speakman and O’Keefe (1990) focused their attention on the plasticity of spatial correlates of place neuron activity in relation to reward. Speakman and O’Keefe (1990) found that shifting the goal in a four-arm elevated plus maze by 180° relative to controlled cues elicited a goal-related change of place field in only 2 of 19 place neurons. Breese et al. (1989) showed that place fields were established during a place task in which a water reward was available at five loci on a rectangular platform. In 40 of 47 neurons, the old place fields disappeared and new place fields emerged at a single locus where reward was available. Winer et al. (1989) compared the spatial and behavioral correlates of hippocampal complex-spike cell activity in spatial and nonspatial paradigms, and showed that of 52 complex-spike cells 41 demonstrated place fields at a different location during a place task than from an odor task performed on the same platform. Consistently, Markus et al. (1995) also reported that place fields changed under different behavioral tasks. These studies indicate that hippocampal place cells behave differently as animals perform different tasks.

The most striking difference between these studies is the location of place fields. According to Speakman and O’Keefe (1990), place fields were located in various parts of the apparatus; according to Breese et al. (1989), most place fields were located near the cups from which a water reward was delivered before testing, and new place fields emerged at a single locus where reward was available. These differences might be due to differences in the behavioral requirements of the two tasks. The behavioral task by Speakman and O’Keefe (1990) was a spatial reference memory task, in which the position of the rat, in a frame of reference to extramaze spatial cues, was important to the accomplishment of the task. In the behavioral tasks by Breese et al. (1989), the rats might determine their positions by using a local maze-based frame; here, the relation of intramaze cues to a specific cup associated with reward delivery was probably more relevant than extramaze cues.

It has been demonstrated that experience, or learning-dependent changes in neuronal responsiveness, occurs in various brain areas (Allard et al. 1991; Bichot et al. 1996; Kirkwood et al. 1996). The present results, along with an earlier study (Markus et al. 1995), add evidence of learning-dependent changes in the place fields of the place neurons in the hippocampal formation. It has been suggested that ensemble, or population neuron, but not single-neuron, coding in the hippocampal formation effectively represents space (Wilson and McNaughton 1993), or various task-relevant features (Deadwyler et al. 1996). Therefore, if the population neuron coding of space is considered, an increase in the number of place neurons with reference to a reward area after place learning task 2 may contribute to more precise representation of the new reward area or the path integration to the new reward area.

Hippocampal function in path integration

It has been suggested that place cells are primarily involved in path integration (Knierim et al. 1995; McNaughton et al. 1991). In the present study, the place neurons did not alter the locations of their place fields when the paths to the reward loci changed from random (i.e., random search task) to fixed places (i.e., place learning task 1). Although these results seem to contradict the path integration hypothesis, they do not refute it. For one thing, the mere existence of place cells may contribute to path integration. A computational study suggested that the entire synaptic connection
along a chain of place cells, the initial and last two place cells of which represented start and goal locations, was comparable with path integration, and that this synaptic connection would be refined by learning or experience so that there would be a minimum number of place cells in the chain (Mulder et al. 1996). The stability of the place fields between the random search task and place learning task 1, as shown in the present study, is a prerequisite for this computational hypothesis. Second, the increase in the breadth of tuning of place neuron responses in place learning task 1 indicated that the hippocampal place neurons became more sensitive to behavioral variables in place learning task 1 than in the random search task. Behavioral variables were more relevant and path integration was more important in place learning task 1 than in the random search task. These results strongly suggest that place neurons more effectively encode information regarding behavioral variables for path integration in place learning task 1, because ideothetic information regarding behavioral variables (i.e., internally generated sensation such as proprioceptive and vestibular sensation in contrast to externally generated sensation such as visual and auditory sensation) is the primary information to be processed for path integration (Knierim et al. 1996; McNaughton et al. 1991).

Conclusions

The present study elucidates important characteristics of the hippocampal place neurons: they flexibly encode diverse and relevant information such as space, reward, behavioral variables, and former experience to create a new representation. The place field might work as a window to focus attention on relevant information to be processed in the hippocampal formation. The results also suggest that spatial (place), as well as other task-relevant information, is relationally (Cohen and Eichenbaum 1993; Eichenbaum 1993; Eichenbaum et al. 1990, 1992; Young et al. 1994) or conjunctively (Knierim et al. 1995; McNaughton et al. 1989) encoded in the hippocampal formation, because hippocampal neuronal correlates of relevant information were associated with a specific area (i.e., place field) in the present study. These findings correspond to the neurophysiological bases of human episodic memory suggested by theoretical and computational studies (McClelland et al. 1995; McNaughton and Nadel 1989). We thank Drs. R.G.M. Morris and S. I. Wiener for valuable comments. This work was supported in part by Japanese Ministry of Education, Science and Culture Grants-in-Aid for Scientific Research 08408036, 08279105, 08279215, 08234209, 07244103, and 08680884, and by Funds for Comprehensive Research on Aging and Health.

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REFERENCES


McClelland, J. L., McNaughton, B. L., and O’Reilly, R. C. Why there are complementary learning systems in the hippocampus and neocortex: insights from the successes and failures of connectionist models of learning and memory. Psychol. Rev. 102: 419–457, 1995.


