To investigate the role of the medial parietal region (MPR), comprising area 7m and the retrosplenial and posterior cingulate cortices, in spatial navigation, we analyzed the spatial aspect of the responses of the MPR neurons in monkeys while they actively performed a navigation task in a virtual environment. One-third of the analyzed MPR neurons were activated depending on the location of the monkeys in the environment, that is, showed place-selective responses. Some neurons showed varying responses based on the starting point (SP) or destination. We further investigated the responses of the place-selective neurons when the monkeys were shown animations of the entire navigation route, including the preferred field, and a segment of the route, including an area around the preferred field, and a still image of the preferred field. We observed that the responses of some place-selective neurons reduced when the monkeys viewed the preferred field in the segmented animation or in the still image compared with when they viewed the entire animation. These results suggested that the knowledge about the SP or destination, that is, context, is necessary to activate place-selective neurons. The effect of such contextual information suggests that the MPR plays decisive roles in spatial processing such as navigation.

Keywords: medial parietal cortex, navigation, posterior cingulate cortex, retrosplenial cortex, virtual environment

Introduction

While navigating to a destination in a large-scale environment, it is crucial to have information regarding the current location. Increase in the activity of place cells that are located in the hippocampus has been observed when an organism traverses a specific region in an environment; such studies have been reported in rodents (O’Keefe and Dostrovsky 1971; O’Keefe and Nadel 1978), macaque monkeys (Matsumura et al. 1999; Hori et al. 2005), and humans (Ekstrom et al. 2003). The existence of place cells provides evidence that the hippocampus is crucially involved in navigation (O’Keefe and Nadel 1978; Poucet et al. 2003).

Human lesion studies (Bottini et al. 1990; Takahashi et al. 1997; Barrash 1998; Aguirre and D’Esposito 1999; Maguire 2001) and neuroimaging studies (Maguire et al. 1997, 1998; Maguire 2001; Spiers and Maguire 2006) have revealed that besides the hippocampus, the parietal cortex also plays a role in navigation. Animal lesion studies have revealed that lesions in the parietal cortex impaired spatial processing in rats (Goodrich-Hunsaker et al. 2005; Rogers and Kesner 2006) and maze learning in monkeys (Traverse and Latto 1986).

These studies suggest that both the hippocampus and the parietal cortex play crucial roles in navigation. Functional differences between these 2 areas of the brain have also been discussed in the literature (Arbib 1999; Berthoz 1999; Maguire 1999; Save and Poucet 2000). These studies suggest that place and self-movement information, both of which are crucial for navigation, are processed separately; the hippocampus processes allocentric place information, whereas the parietal cortex processes egocentric self-movement information.

In our previous study (Sato et al. 2006), we observed that the neurons in the medial parietal region (MPR) of monkeys were route selectively activated in a navigation task. The route-selective neurons were differently activated depending on the destination even if the movement and the place were the same. Moreover, when the MPR neurons were reversibly inactivated by muscimol injection, the monkey lost its sense of direction during the navigation task. We considered that these neurons integrated movement and place information. Thus, we speculated that the parietal cortex may be involved in the processing of both place as well as movement information. However, the mechanisms underlying the processing of place information in the MPR neurons and whether the mechanisms are the same as those in the hippocampus are yet unclear.

During navigation, the information of the current location is always processed with reference to that of the destination; thus, the information about the destination may function as a context. The importance of the same place may be different under a different context. For example, a particular place located along the route from an individual’s home to a school might have a different significance from that located along the route from that individual’s home to a hospital. Furthermore, the cumulative sequential information from a starting point (SP) to a particular location, which is provided by a system known as the path integration system (Redish and Touretzky 1997; Redish 1999), may also affect the information of the current location as a context. Thus, in this study, we defined the information of the SP and destination as contextual information and hypothesized that during navigation, the contextual information may play an important role in the processing of the information regarding the current location.

The present study has 2 aims. The first is to determine how place information is processed in the MPR neurons; this was analyzed by making the monkeys perform a navigation task in a virtual environment. In the previous study, we had only focused on how MPR neurons integrated place and movement information. The second aim is to examine how spatial responses in the MPR change depending on the context. By using the virtual reality technique, we were able to capture...
a portion of the entire route in the form of animated segments and still images. Using these stimuli, we examined the effect of context on the processing of spatial responses in the MPR neurons of monkeys.

Materials and Methods

Subjects
In this study, 2 male Japanese monkeys (Macaca fuscata) were used. They were cared for in accordance with the guidelines outlined in the “Guide for the Care and Use of Laboratory Animals” of the National Research Council of USA. This study was approved by the Ethics Committee of the Nihon University School of Medicine.

Navigation Task
We trained the monkeys to perform a navigation task (please also refer to our previous articles, Sato et al. 2004, 2006). During the experiment, the monkeys were seated on a primate chair with their heads fixed. A virtual environment generated by computer graphics (CGs) (hardware: SGI, Tokyo, Japan; software: Solidray, Yokohama, Japan) was projected stereoscopically on a 100-in. tangential screen using 2 liquid crystal projectors (Victor, Tokyo, Japan). The monkeys wore polarized glasses and were able to view the stereoscopic images. The monkeys manipulated a joystick that was attached to the chair to navigate through the virtual environment. The monkeys could only move their arms to manipulate the joystick. The chair was stationary. The position of one eye of each monkey was monitored routinely using an infrared eye movement recording system (sampling rate, 250 Hz; RMS, Hiroasaki, Japan).

A virtual building with 2 floors was created for this experiment (Fig. 1). The building had 8 rooms on the first floor and 7 rooms on the second floor. All the rooms had a door that opened into a corridor. An elevator connected the first and second floors. When a monkey entered the elevator, it automatically moved to the other floor. In addition, 2 starting points (SP A and SP B; Fig. 1b) and 5 goals were set. The routes from the SPs to the destination rooms were predetermined.

In each trial, the SP and the goal were selected pseudorandomly. After about 10-s intertrial interval, an image of the destination room was presented on the screen as an instruction cue. The cue image was turned off when the monkeys moved the joystick in any direction and the display immediately changed to that of the SP. Subsequently, the monkeys used the joystick to control their virtual movement from the SP to the destination room via a series of checkpoints (CPs). At each CP, the monkeys chose 1 of 3 joystick operations to move to the next CP: tilting the joystick forward, left, or right to move forward, left, or right, respectively. To keep moving forward, the monkeys had to tilt the joystick forward continuously. Thus, to move to a CP located at the right side, the monkeys had to first keep the joystick tilted toward the right so that the scene stopped rotating, release the joystick once, and again tilt it forward until the forward movement stopped, indicating that the monkeys had reached that CP. On successfully reaching the goal room, the monkeys were rewarded with juice. If the monkeys reached a wrong CP, that is, strayed off from the predetermined route, the trial was aborted, and a time-out period (10–30 s) was imposed. Such a trial was considered an error trial. The monkeys were allowed to try each route at least 5 times during a recording session. The 2 monkeys performed the task with approximately 87% and 94% accuracy (Sato et al. 2004, 2006).

Data Acquisition and Analysis

We recorded single unit activity in the MPR. A part of the data has been reported previously, and some neurons that were activated in this study were the same as those reported in the previous study (Sato et al. 2006). The recording site included area 7m and the posterior cingulate and retrosplenial cortices (Fig. 1c).

For the analysis, we divided the entire area of a floor of the virtual building into 20 × 17 square place blocks (Fig. 2b). Of all the place blocks, 49 were used in the navigation task (Fig. 1c). Next, we calculated the discharge rate of the neurons in each of the 49 place blocks. The monkeys moved through 7, 11, 15, 17, and 16 place blocks while moving from SP A and 10, 3, 7, 8, and 16 place blocks while moving from SP B to reach Goals I, II, III, IV, and V, respectively. On average, the monkeys required 1027 ms to cross 1 place block. Thus, the monkeys required approximately 8, 9, 17, 15, and 18 s from SP A and 5, 9, 10, 13, and 24 s from SP B to reach Goals I, II, III, IV, and V, respectively.

We recorded the activities of all isolated neurons to prevent sampling bias. First, we selected the neurons that showed statistically significant (paired t-test, P < 0.05) activity at a place block, at which the neuron showed the highest discharge rate among the 49 place blocks used (the best place block), compared with the baseline activity (mean discharge rate of the neurons during the 1-s period before cue presentation). Neurons showing significant discharge rates in this analysis were considered as responsive neurons. Next, we investigated the place selectivity of the responsive neurons. The discharge rates of the neurons across all the 49 place blocks were compared using the oneway analysis of variance (ANOVA), and the neurons that showed a statistical difference in activity (P < 0.05) were considered as place-selective neurons. For such neurons, post hoc tests were conducted (Tukey’s honestly significant difference [HSD] test) to determine the place blocks associated with the highest activity of the neurons (the best place block). The place blocks for which the discharge rate of the neurons was not statistically different (P > 0.05) from the discharge rate observed at the best place block were defined as the preferred fields. Thus, the minimal preferred field consisted of a single place block; however, if more than 1 successive few place blocks were depicted, such a cluster was considered as 1 preferred field.

To describe place selectivity in the MPR neurons, we calculated the selectivity index (SI) using the following formula.

\[
SI = \frac{R_i - R_{max}}{n - 1} \times 100
\]

Here, \(R_i\) is the mean discharge rate at each place block, and \(R_{max}\) is the mean discharge rate at the best place block, where a neuron showed the maximum discharge rate and \(n\) is the number of place blocks. This index usually takes a value between 0 and 1. A value of 0 indicates that a neuron shows identical activity at all place blocks, and a value of 1 indicates that a neuron shows activity at a particular place block but shows no activity at other place blocks. We also calculated the orientation and movement SIs using the same formula. For calculating the orientation SI, we used the mean discharge rate of the neurons when the monkeys faced 1 of 8 directions on the ground plane in the virtual environment. For calculating the movement SI, we used the mean discharge rate while the monkeys moved forward, turned left, or right, or remained stationary. In addition to calculating the SIs, we also computed the information conveyed by the neurons that showed selective responses, using the information measure introduced by Skaggs et al. (1993).

Passive Presentation of Animations and a Static Scene

We further examined the responses of some of the place-selective MPR neurons to passively presented animations of the navigational route and a static scene (Fig. 7). There were 3 test conditions: Passive (whole), Passive (segment), and Still image. For all the conditions, the joystick was removed from the primate chair, and the monkeys could not manipulate it. In the Passive (whole) condition, the image of the destination room was presented; the monkeys viewed the animation of the entire route from the SP to the goal, which included the preferred field of the neurons. In the Passive (segment) condition, the animation of a segment of the entire route (between neighboring CPs) was presented passively. In the Still image condition, a still image of the closest CP from the best place block was presented. By comparing the responses of the neurons between the Passive (whole) and the Passive (segment) conditions, we could determine whether the information of SPs and the destinations affected the responses of the place-selective neurons. Furthermore, by investigating the responses of the neurons to the still image, we could confirm whether the neurons responded when the visual scene of the preferred field was displayed. In the Passive (whole) condition, the monkeys were rewarded at the end of the animation (reached the goal in the animated scene). In the Passive (segment) and Still image conditions,
the monkeys were sometimes rewarded when the stimulus was turned off to keep the monkey’s attention.

**Results**

We recorded the activity of 580 neurons in the MPR of the 4 hemispheres while the monkeys performed the navigation task in the virtual reality building. Of these 580 neurons, 220 (38%) showed significant responses when the monkeys traversed a place in the virtual environment. Of these 220 neurons, 193 (88%) elicited different responses to different places (place-selective neurons). Thus, 33% of all the recorded MPR neurons (193/580) were place-selective neurons.

Figure 2 shows the responses of a representative place-selective neuron. This neuron was activated when the monkey reached an area in front of the elevator while moving toward Goal V (Fig. 2a–c). This neuron had 1 preferred field that consisted of 2 place blocks (Fig 2b, place blocks marked by red dots).
It was noteworthy that the activity of this neuron was maintained irrespective of whether the monkey was stationary or in motion (Fig. 2d, the period during which the monkey turned right after entering the preferred field and that during which the monkey started moving forward after turning right). Similar to this neuron, of the 193 place-selective neurons, 104 (54%) showed significant responses while the monkey remained stationary. Of the 104 neurons, 35 (34%) showed stronger responses at the preferred field while the monkeys remained stationary than while they were in motion.

Similar to the neuron in Figure 2, of the 193 place-selective neurons, 41 (21%) had a single preferred field. However, some neurons had more than 1 preferred field. The neuron shown in Figure 3 had 2 preferred fields. One was en route to Goal III, which was in the corridor on the first floor in front of the room of Goal II (Fig. 2b lower, consisted of 3 place blocks). The other was en route to Goal V, which was in front of the door of the Goal V room on the second floor (Fig. 2b upper, consisted of 1 place block).

We quantitatively analyzed the property of the preferred field. The total number of place blocks in the place fields of each place-selective neuron was relatively small. Of the 193 place-selective neurons, the preferred field of 21 neurons (11%) consisted of 1 place block. Of the 193 place-selective neurons, the preferred fields of 97 neurons (50%) consisted of less than 6 place blocks (the left part of the histogram marked with the dashed line in Fig. 4a). We regarded that the discontinuous place blocks belonged to different preferred

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**Figure 2.** Illustration of place-selective responses of an MPR neuron. (a) Neuronal activity while the monkey navigated to Goal V. The histogram and raster diagrams were aligned according to the arrival of the monkey at the preferred field (vertical blue line and arrowhead). The marks on the raster diagram indicate the timing of the start of the navigational phase (yellow circles) and that of entering 1 of the 49 place blocks in the virtual environment (orange diamonds, see text for details). The colored underline in each raster diagram indicates the period (in length) and direction (in color) of joystick operation: green, forward; red, left; and blue, right. The inset images are the scenes the monkeys saw during the period indicated in the raster diagram. This neuron was activated when the monkey traversed the place in front of the elevator. (b) Activity of the same neuron expressed by gradation in place blocks. Each floor of the environment was divided into $20 \times 17$ place blocks on the ground plane (dotted cyan lines). The area enclosed by the red line indicates the preferred field of the neuron. (c) Neuronal responses to the preferred places using the navigation task expressed in hue gradation. (d) Magnified view of the period indicated by the red bar under the histogram shown in (a). The red underlines in the raster diagrams indicate the time when the monkey was stationary, and the shaded red areas represent the static state of the monkey, which remained common in all the trials. 1F, 1st floor; 2F, 2nd floor.
fields. Thus, 60% (116/193) of the place-selective neurons showed less than 4 preferred fields (the left part of the histogram starting from the dashed line in Fig. 4b). The mean size of each preferred field was not statistically different depending on the number of preferred fields of each place-selective neuron ($F < 1$, Fig. 4c). In 46% (88/193) of the place-selective neurons, all preferred fields consisted of less than 6 place blocks and the number of the preferred fields was less than 4 (population within the shaded square column in Fig. 4d), which included all the place blocks used in the navigation task, that is, all the locations the monkeys visited during the navigation task (Fig. 4e). We calculated the percentage of the area occupied by the preferred field of each place-selective neuron. For example, a neuron whose preferred field consisted of 1 place block occupied 2% (1/49) of the entire route used in the navigation task. The median of the percentages of the 193 place-selective neurons was 10%.

To determine whether the MPR neurons contributed to the processing of other information related to navigation, we calculated the SI for different places and compared the values of place SI with those of orientation and movement SIs (see Materials and Methods). The mean place SI for the neurons with place-selective responses was 0.62 ± 0.16 (mean ± standard deviation, SD; Fig. 5a). The mean orientation SI for the neurons that showed statistically different responses ($P < 0.05$) when the monkeys faced different orientations on the ground plane was 0.41 ± 0.18 (Fig. 5a). The mean movement SI for the neurons that showed statistically different responses ($P < 0.05$) between the different types of movement was 0.41 ± 0.16 (Fig. 5a). A one-way ANOVA revealed that the SIs showed statistically significant differences ($F(2,477) = 287.06$, $P < 0.001$), and post hoc tests revealed that the place SI was significantly higher than both the orientation and movement SIs ($P < 0.001$).

Besides SIs, we calculated the information values conveyed by the neurons that showed selective responses for place, orientation, and movement. The mean information values conveyed by the neurons that showed place-, orientation-, and movement-selective responses were 1.36 ± 1.25, 0.55 ± 0.57, and 0.60 ± 0.93 bits/s (means ± SDs), respectively (Fig. 5b). A one-way ANOVA and post hoc tests revealed that the information conveyed by the place-selective neurons was significantly higher than that conveyed by the orientation- and movement-selective neurons ($F(2,477) = 34.86$, $P < 0.001$).

Figure 3. Another illustration of a neuron that showed place-selective responses. This neuron became active at 2 areas in the virtual environment (2 preferred fields). (a) Neuronal activities while the monkey navigated to Goal III (upper) and Goal V (lower). The inset images above the histogram indicate the scene in the virtual environment around the timing corresponding to the histogram. The activity of the same neuron is also expressed by gradation in place blocks (b) and hue graduation (c). The details are the same as those in Figure 2.
These results suggest that the MPR neurons represent place information with higher selectivity than information regarding orientation and movement in the virtual environment.

We found that the responses of some place-selective neurons varied depending on the SP. The neuron shown in Figure 6 was activated when the monkey traversed the place around the elevator en route to Goal V from SP A (Fig. 6a,b); thus, this place was the preferred field of this neuron. However, this neuron showed reduced responses at the same place when the monkey started from SP B (Fig. 6a,c). This suggests that place-selective responses of this neuron were dependent on the SPs of the navigation task. We also identified the neurons whose responses were affected by the destination. We analyzed the effects of SP and destination in 112 place-selective neurons. Of the 112 neurons, 43 (38%) showed variations in the responses at the best place depending on the SP and/or destination (12 neurons were affected by SP, 12 by destination, and 19 by both SP and destination). This suggests that the context, that is, where the monkeys started from or where their destination was, was important for the activation of the place-selective neurons (context-dependent place-selective neuron). This also suggested that the place-selective neurons did not merely respond to the visual features of the CGs.

In the case shown in Figure 6, the monkey entered the preferred place from the same direction regardless of the SP. However, in some other cases, the monkeys entered the preferred place from the opposite direction. We examined the differences in the responses of 51 neurons whose preferred field was the place where the monkeys entered from opposite directions and found that 40 neurons (78%) showed insignificant ($P > 0.05$) varying responses when the monkeys entered the preferred field from different directions. This suggested that the responses of these neurons were independent of the monkeys' direction in the virtual environment.

To further examine the effects of context on the responses of the place-selective neurons, we tested the activity of the neurons when the monkeys were shown animations and a static scene (Fig. 7). In the Passive (whole) condition, the monkeys were shown the animation of the entire route from the SP to the goal, which included the preferred field of the neuron. In the Passive (segment) condition, the monkeys were passively shown the animation of a segment of the entire route (between neighboring CPs). In the Still image condition, the monkeys were shown a still image of the nearest CP from the preferred field.

The preferred field of the neuron shown in Figure 7a was around the Goal I room (Fig. 7a; navigation task). The activity
of this neuron was observed at the same place (statistically insignificant compared with the activity during the navigation task) in the Passive (whole) condition; however, its activity significantly decreased in the Passive (segment) condition and no responses were observed in the Still image condition. Figure 7b shows another such neuron. The preferred field for this neuron was between the elevator and the Goal V room on the second floor (Fig. 7b, navigation task). In contrast to the activity of the neuron shown in Figure 7a, the activity of this neuron decreased significantly in the Passive (whole) condition. In addition, this neuron showed almost no responses in the Passive (segment) and Still image conditions (Fig. 7b). Thus, active navigation was important for activating this neuron. In both the cases, because the still image did not induce any responses, it could be considered that these neurons did not respond merely to the visual features of the CG. Furthermore, a decrease in the responses at the preferred field in the Passive (segment) conditions compared with the Passive (whole) condition suggested that the context of the entire route was important for activating these neurons.

In Figure 8 and Table 1, the responses of the neurons in the 3 conditions are summarized. We analyzed the responses of 47 neurons in the 3 conditions. In the Passive (whole) condition (Fig. 8a, left bar), the responses of 12 neurons (26%) reduced significantly (3/12) or were absent (9/12). In the Passive (segment) condition (Fig. 8a, middle bar), 26 neurons (55%) showed significant reduction in their responses (13/26) or failed to respond (13/26). In the Still image condition (Fig. 8a, right bar), the responses of 33 neurons (70%) were significantly reduced (7/33) or absent (26/33). A Cochran’s Q test revealed that there was a significant difference in the proportion of the neurons with reduced responses between the 3 conditions ($Q(2) = 23.66, P < 0.001$), and post hoc tests revealed that the proportion of neurons with reduced responses in the Passive (segment) and Still image conditions was higher than that in the Passive (whole) condition ($P < 0.005$). In accordance with these results, the normalized responses differed significantly among the 3 conditions ($H(2,46) = 7.70, P < 0.001$) (Fig. 8b).

The post hoc tests revealed that the responses in the Passive (whole), Passive (segment), and Still image conditions were significantly smaller than those in the navigation task ($P < 0.05$). These results imply that the place-selective neurons were nonresponsive to the visual features of the CG but were responsive to place information associated with context.

These neurons could be classified into several types. Compared with the responses of the neurons in the navigation task, those of 15 neurons of the 47 tested (28%) were significantly weaker in the Passive (segment) and Still image conditions but not in the Passive (whole) condition (Fig. 8c; the neuron shown in Fig. 7a was of this type). Of the 47 neurons, the responses of 9 (19%) were significantly reduced in all the 3 conditions compared with those in the navigation task (Fig. 8d; the neuron shown in Fig. 7b was of this type). As mentioned above, it was suggested that the context where the monkeys started their navigation from or the location of their destination affected on the responses of these types of neurons (context-dependent place-selective neurons). Of the neurons examined, 9 (19%) showed significantly weaker responses only in the Still image condition (Fig. 8e), and 9 neurons (19%) showed similar responses in all the 3 conditions (Fig. 8f). There was only 1 neuron that showed higher responses in the Passive conditions than that in the navigation task (2%).

In the navigation task, the final destination was instructed at the beginning of the task. This might have led to the development of a sequential list of the route knowledge from the SP to the destination (see Discussion and our previous paper, Sato et al. 2006). Thus, there is a possibility that the cue stimulus affects the responses of the place-selective neurons. Actually, 49% (94/193) of the place-selective neurons responded to the cue images, and 34 (36%) of those showed selectivity to the cues (Fig. 9). The mean cue SI for these neurons was 0.46 ± 0.14 (mean ± SD), which is significantly lower than the mean place SI ($f(33) = 5.78; P < 0.001$). Furthermore, in 11 (32%) of the 34 of abovementioned neurons, the route instructed by the preferred cue stimulus included the preferred field of that neuron (Fig. 9). Thus, the cue instruction may have some effect on the place information represented in the place-selective neurons.

We also analyzed the effects of eye movements on the responses of the 108 place-selective MPR neurons. First, we calculated the correlation coefficient between the number of saccades and the discharge rates at each place block for each neuron, and found that 98 neurons out of the 108 neurons investigated (91%) did not show significant correlation ($P > 0.1$).
Next, we investigated the effects of eye position. The visual field was divided into 4 quadrants and the bias of time spent on each quadrant was examined using the $\chi^2$ test. If there was any bias in the time spent, we could attribute the change in neuronal activity to the bias of the eye position. However, in 107 of the 108 neurons (99%), we did not find such tendency ($\chi^2$ test, $P > 0.1$). We also reanalyzed the data using an analysis of covariance (ANCOVA) with horizontal and vertical eye positions as covariates. However, of the 212 neurons examined, only 3 (1%) showed a difference in the results between the ANOVA and the ANCOVA. Thus, it is unlikely that the responses of the MPR neurons examined in our study can be explained only on the basis of their correlation to eye movement. In addition, we also examined the differences in the bias of eye position for the data in the context-based experiment. In all of the 47 neurons tested with the passive animations and static images, neither differences between the time spent on the quadrants nor differences in the proportions between the conditions were observed ($\chi^2$ test, $P > 0.1$), suggesting that the differences in the neuronal activity between the conditions of the context-based experiment are not due to the differences in the eye positions.

**Discussion**

We investigated the spatial aspect of the MPR neurons while the monkeys performed the navigation task in a virtual environment and found that 33% (193/580) of the analyzed MPR neurons showed varying responses depending on the location of the monkeys in the virtual environment, that is, place-selective responses. In the virtual environment used in this study, movements of the monkeys and of the primate chair were restricted; therefore, optic flow of the CG was the only self-movement cue. However, the properties of most place-selective neurons could not be explained only on the basis of responses to a specific optic flow pattern and/or to a scene of the CG (Figs. 6–8). Furthermore, the responses of some place-selective neurons at the preferred field depended...
on the SP or the destination (Fig. 6); we defined these neurons as the context-dependent place-selective neurons.

We further analyzed the responses of the place-selective neurons with 3 conditions: the Passive (whole), Passive (segment), and Still image conditions. In these conditions, the animation of the entire route (Passive (whole) condition), a segment of the route (Passive (segment) condition), and a still image of the route (Still image condition) were used as stimuli.

Figure 7. Results of the context-based experiment. (a) Activity of a representative neuron. Each row indicates the activity of the neuron in the navigation task and under each condition (Passive [whole], Passive [segment], and Still image conditions, see text for details). The format of the schemes is the same as those in Figure 2. This neuron was activated when the monkey traversed the place in front of the door to Goal I in the navigation task (first row). Almost similar response of the neuron to the animation of the same route was observed (Passive [whole] condition, second row). However, this neuron did not significantly respond to the segmented animation around the preferred field (Passive [segment] condition, third row left) nor to the still image of an area close to the preferred field (Still image condition, third row right). (b) Another representative neuron. This neuron was activated when the monkey traversed the place around the CP on the second floor in the navigation task (first row). The same neuron showed significantly lesser response in the Passive (whole) condition (second row) and did not respond in the Passive (segment) nor Still image conditions (third row).
In the Still image condition, 70% of the tested neurons showed weaker or no response compared with the responses observed during the navigation task, suggesting that place-selective neurons are not activated by simple visual cues. Although the animation of a route segment was a part of the entire route, the monkeys could not identify the SP and destination in these animations, because such a route segment was sometimes included in the other routes. The animation of the route segment did not contain contextual information (for definition, see Introduction). Hence, the difference in the responses of the neurons between Passive (whole) and Passive (segment) conditions could be because of the lack of contextual information, indicating that such information affects the responses of the place-selective neurons. In this study, 2 contexts were possible: a retrospective context, which was from the SP to the current location, and a prospective context, which was from the current location to the destination. However, it was unclear which of the 2 contexts had a stronger effect on the responses of place-selective neurons in the MPR. We plan to address this issue in the future.

Some place-selective neurons in the MPR selectively responded to the cue stimulus. Furthermore, in some of such neurons, the route to the goal indicated by the preferred cue included the preferred field. This may be an additional contextual effect, suggesting that the cue instruction activates the place-selective neurons. When the cue stimulus is presented, the knowledge about the route up to the destination (Sato et al. 2006) may be sequentially registered, that is, the context of that trail is created. Thus, the context that affects the activity of place-selective neurons could be a memorized one rather than an ongoing one.

We did not observe a specific relationship between the temporal pattern of eye movement and the activity of MPR neurons. Analyses of eye movements revealed that at least the number of saccades and eye positions did not affect the activity of almost all the MPR neurons. Thus, although further careful
examinations are required, it is unlikely that the activity of MPR neurons is associated with a specific eye movement.

We previously reported that MPR neurons showed route-selective responses; neurons responded to a specific behavior at a specific place to navigate along a route (Sato et al. 2006). The response properties of context-dependent place-selective neurons in this study seem to be similar to those of the route-selective neurons because both responded when the monkeys traced a particular route. In the previous study, we defined route-selective neurons as those that show activity during a specific behavior at a specific point on a specific route. In the previous study, because we were interested in understanding the neural processing of route selection at each CP (blanching point), we analyzed the neuronal activities during 1-s time intervals just after the monkeys operated the joystick at each CP. Thus, in the previous study, we analyzed the neuronal activity only when the monkeys were around the CPs (corresponding to 1 place block, as defined in this study). On the other hand, in the present study, because we were interested in neuronal responses to different places, we analyzed the neuronal activity at all the place blocks (49 place blocks). In addition, we analyzed the data only during the period when the monkeys were in motion in the previous study, whereas in this study, we analyzed the data during the period when the monkeys were stationary (i.e., when the animal received no optic flow). Nonetheless, half of the place-selective neurons were active even in the absence of movement, suggesting that movement cues hold less importance at least in the activation of place-selective neurons than in the activation of the route-selective neurons. Furthermore, most of the context-dependent place-selective neurons seem to differ from the route-selective neurons. Of the 43 context-dependent place-selective neurons, 27 (63%) did not show route-selective responses when we assessed the data with the same criteria of the previous study (Sato et al. 2006). The preferred field of the place-selective neurons not showing route-selective responses was not located near the CPs. Of the remaining 16 neurons that showed both the route-selective and the context-dependent place-selective responses, 11 were activated at the same place block on the same route. This suggests that the populations of both the types of neurons partly overlap.

The response properties of the MPR place-selective neurons seem to be similar to those of the hippocampal place cells in

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<td>Activity of the neurons in the context-based task with respect to that in the navigation task</td>
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| nd | + | — | 1 (2%) |
| nd | nd | — | 9 (19%) * 
| nd | nd | nd | 9 (19%) * |
| Total | 47 |

Note: —, the responses of the neurons in the context-based task were weaker than that in the navigation task; nd, no difference; +, the responses of the neurons in the context-based task were stronger than that in the navigation task. Superscripts c-f, activities corresponding to the response profile of the neurons shown in Figure 8c-f.

Figure 9. Representative MPR neurons that showed place- and cue-selective responses. (a) Neuronal activities when the monkeys navigated to Goal III. The details are the same as those in Figure 2. (b) This neuron responded to the cue stimulus that instructed the monkey to navigate to Goal III (image of the Goal III room was shown). The histogram and raster diagram were aligned with the onset of the cue stimulus presentation (vertical blue line and arrowhead). (c) Responses of the same neuron to the best place on each route (the highest discharge rate in each route, red circle) and to each cue stimulus (green square). The response profile of the neuron to the best place was similar to that of the cue stimuli. The response to the cue of Goal III (shaded) was significantly larger than that of the cues of Goal II and Goal IV (P < 0.05). The activity at the best place en route to Goal III was significantly larger than that of the other goals (P < 0.05). The responses to the cue stimulus were calculated on the basis of the discharge rate during the 1-s period after presentation.
several aspects. First, we found that some MPR neurons showed no or weakened activity when the monkeys passively traversed the preferred field (Figs. 7 and 8; Passive [segment] and Passive [whole]) and when the monkeys viewed the static image of the navigation route (Figs. 7 and 8; Still image). This occurred even though the visual features of the CG were the same as those when the monkeys actively traversed the navigation route. Hippocampal place cells were reported to have similar features (Foster et al. 1989); these cells also ceased to show activity when rats passively viewed the environment.

Secondly, hippocampal place cells are generally activated independent of the direction on the ground plane (O'Keefe and Nadel 1978). Similarly, most of the MPR neurons showed higher selectivity for place rather than direction on the ground plane in the virtual environment. However, some MPR neurons showed high selectivity for orientation (Fig. 5a; high SI for Orientation). This is consistent with the observations in the MPR neurons of rats (Chen et al. 1994; Cho and Sharp 2001). When rats were made to explore an environment with limited paths, some hippocampal place cells started showing directional tuning (McNaughton et al. 1983; Muller et al. 1994; Markus et al. 1995). In the present study, the monkeys also became familiar with the environment with limited routes, suggesting that this may cause higher orientation selectivity in some MPR neurons.

In addition, the effect of context on hippocampal place cells has also been reported (Frank et al. 2000; Wood et al. 2000; Ferbinteanu and Shapiro 2003). The remapping of a preferred field, that is, a shift in the preferred field, generally occurred when an animal was shifted to a different environment (Bostock et al. 1991; Lever et al. 2002); this phenomenon can be regarded as one of context-dependent place-selective responses. However, even in the same environment, remapping of the hippocampal place cells was observed when the goal was configured (scattered or specific) (Markus et al. 1995); similar goal-dependent response changes were also observed in human hippocampal neurons (Ekstrom et al. 2003). We also observed that the responses of the place-selective MPR neurons changed even in the same environment depending on the SPs or goal locations. In future, we intend to investigate whether neuronal remapping of the MPR neurons occurs in a novel or different environment.

Several neuroanatomical studies have shown direct connections between the hippocampus and the MPR (Leichnetz 2001; Kobayashi and Amaral 2003, 2007; Morecraft et al. 2004); thus, similarities in the neuronal response properties between the MPR and the hippocampus may be attributed to these anatomical connections. However, the hippocampus is suggested to be associated with the formation of new associations and/or with the development of recent memory regarding nonspatial (Wirth et al. 2003) as well as spatial information (Teng and Squire 1999). Thus, it is likely that the properties of the hippocampal place cells are associated with a more general memory processing, whereas the MPR neurons are involved in the spatial processing for navigation (Wolbers and Büchel 2005).

Moreover, anatomical connections between the MPR and cortical areas that contain neurons that respond selectively to optic flow patterns have also been reported (Leichnetz 2001; Kobayashi and Amaral 2003, 2007; Morecraft et al. 2004); the cortical areas include the medial superior temporal area (MST; Saito et al. 1986; Duffy and Wurtz 1991), ventral intraparietal area (Schaafsma and Duysens 1996; Bremmer et al. 2002), and area PeC (Battaglia-Mayer et al. 2001; Raffi et al. 2002). MPR neurons may receive optic flow information from these areas. In addition to MPR, some MST neurons have been reported to be associated with spatial information processing (Froehler and Duffy 2002). These parietal areas might be involved in transforming visual self-movement information into place information.

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Conflict of Interest None declared.

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References

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