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Tracking Route Progression in the Posterior Parietal Cortex

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Summary

Quick and efficient traversal of learned routes is critical to the survival of many animals. Routes can be defined by both the ordering of navigational epochs, such as continued forward motion or execution of a turn, and the distances separating them. The neural substrates conferring the ability to fluidly traverse complex routes are not well understood, but likely entail interactions between frontal, parietal, and rhinal cortices and the hippocampus. This paper demonstrates that posterior parietal cortical neurons map both individual and multiple navigational epochs with respect to their order in a route. In direct contrast to spatial firing patterns of hippocampal neurons, parietal neurons discharged in a place- and direction-independent fashion. Parietal route maps were scalable and versatile in that they were independent of the size and spatial configuration of navigational epochs. The results provide a framework in which to consider parietal function in spatial cognition.

Introduction

Located between visual and motor regions of the cortex, the parietal cortex receives direct input from cortical and subcortical structures critical to spatial information processing. Deficits in spatial cognition are common to parietal lesions in rats, monkeys, and humans, and they reveal impairments in coordinating action sequences across space (Kolb and Walkey, 1987; Kesner et al., 1991; Save et al., 1992; Save and Moghaddam, 1996; Li and Andersen, 2001; Newsome and Pare, 1988; Mesulam, 1981). Neurophysiological work in monkeys has generated an abundance of data suggesting that neuronal ensembles of the parietal cortex comprise stable mappings for the spatial loci of attention, sensory stimuli, and/or motor plans (Duhamel et al., 1992; Colby and Goldberg, 1999; Buneo et al., 2002; Snyder et al., 1998; Andersen et al., 1985). Parietal cortex in rodents may perform similar functions, since parietal-lesioned rats exhibit deficits in recognizing changes in the spatial distribution of objects (Save et al., 1992; DeCoteau and Kesner, 1998). Taken together, these data suggest that the parietal cortex may provide continuity between otherwise spatially segregated sites of action and/or environmental stimuli.

Most parietal neuron recording experiments, however, have been performed with two potentially important factors held relatively constant. The first is the subject's position in the environment (also termed the "allocentric" position). This variable is a particularly strong determinant of discharge in the hippocampus, which is connected via entorhinal cortex to the parietal cortex (O'Keefe and Dostrovsky, 1971; Reep et al., 1994; Witter, 1993). Certainly for rats and possibly primates, restraint is likely to suppress the dynamic range of neurons sensitive to allocentric position (Berthoz, 1997; Jarosiewicz and Skaggs, 2004; Foster et al., 1989; Czurko et al., 1999). The second factor is the presence or absence of whole-body motion. In the absence of free movement, low, or at least constant, discharge rates would be expected from neurons responsive to self-motion information derived from proprioception, vestibular afferents, and/or motor efference copy. The integration of motion information is likely an important function of the parietal cortex, given the density of anatomical projections from thalamic nuclei that receive vestibular information (Fukushima, 1997) and the responsiveness of parietal neurons to passive limb movements (Mountcastle et al., 1975).

Recent experiments suggest that both allocentric position and self-motion information can, in fact, drive parietal cortical activity patterns in monkeys (Snyder et al., 1998; Ilg et al., 2004; Kawano et al., 1980; Klam and Graf, 2003). Evidence for an interaction between these two factors in driving neuronal activity in area MST has also been presented (Froehler and Duffy, 2002). Furthermore, studies in rats found that parietal neurons fired in conjunction with particular locomotor actions, such as turns, and provided initial evidence that such behavior-correlated discharge is modulated by movement direction and spatial position (McNaughton et al., 1994; Chen et al., 1994). Thus, like monkey parietal neurons, rat parietal neurons appear to be sensitive to spatial position, movement direction, and type of behavior. Notably, these same variables are also important determinants of discharge in other brain regions, such as the hippocampus and entorhinal cortex, that are implicated in spatial cognition (McNaughton et al., 1983; Frank et al., 2000; Fyhn et al., 2004; Hafting et al., 2005).

Thus, a more complete understanding of parietal cortical function may require the characterization of parietal neuron discharge properties under conditions entailing extensive, self-initiated motion through an environment. To this end, the present study addressed the following issues: (1) whether the responses of parietal cortical neurons are largely determined by one variable, such as type of behavior, movement direction, or spatial position or instead reflect an integration of these variables as is observed in the hippocampus; and (2) whether salient components, or epochs, of navigational behavior such as traversal of particular path segments or execution of a behavioral sequence are represented in the activity of parietal cortical neurons.

Single-unit recordings were collected as rats traversed multiple, complex routes on a labyrinth-style maze. Variations in route configurations and their spatial position in the recording area were implemented to demonstrate that parietal neuron activity is informative of progress through behavioral sequences. Parietal activity patterns were independent of movement direction

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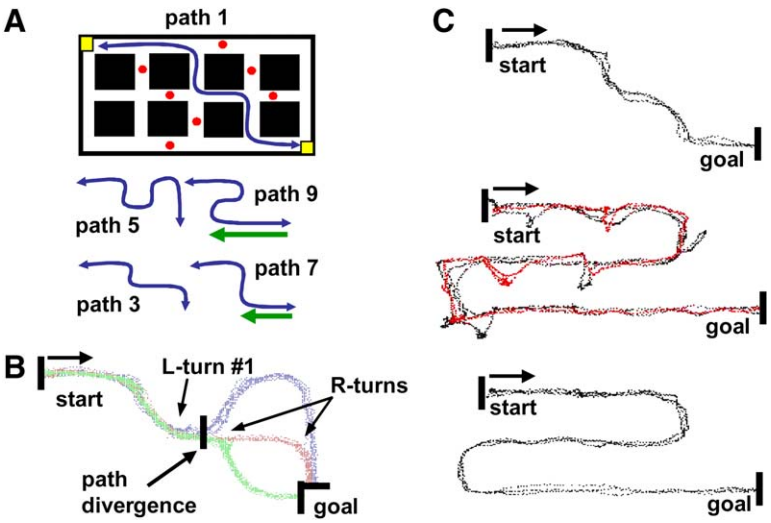

Figure 1. Design of Route Traversal Experiments

(A) Schematic of the maze-running experimental paradigm. Rats traversed paths between two food-reward sites (yellow squares). Black squares depict holes in the maze surface. But for sites where passage was blocked by small blocks (red circles), nearly the entirety of the maze was accessible. The maze surface was 61 × 122 cm. The maze and blockades were black. The arrangement of blocks defined single direct paths along which rats could shuttle between the fixed reward sites (depicted in blue is path #1). Below, four other commonly used paths are depicted (half-size). Animals always entered and exited the maze at the northwest corner. Traversals from this corner to the southeast corner were considered "outbound" and return paths "inbound."

(B) In some experiments, rats ran three different paths in succession (10 to 20 full lap blocks of each). These overlapped in part, but diverged for outbound traversals and converged for inbound traversals. Colored traces depict actual paths taken by an animal during a recording session (outbound traversals for paths 1, 3, and 5 are shown).

(C) Rats quickly learned new pathways between two food reward sites. Depicted is tracking data for an animal on a trained (top) path as well as the first (middle) and last (bottom) few laps across an untrained path. Traversal of the trained path is highly stereotyped. When forced to learn the untrained path, the animal first attempts to use the previous path (middle, red trace) and makes frequent off-path turns. Later (bottom), a stereotyped running pattern is established.

and spatial position and scaled with changes in the distance between the execution points of succeeding behaviors. The findings suggest that activity patterns of the parietal cortex are ideally suited to establishing continuity between succeeding behaviors under a wide variety of circumstances.

Results

One hundred and ninety-nine neurons (n = 7 rats) within the posterior parietal region of the rat cortex were recorded during performance of the task detailed in Figure 1. Most neurons (86%) were recorded during traversal of at least two pathways. For all neurons, sections along a pathway that were or were not associated with significant increases in spike discharge over a reference (immobility) rate were determined (see Experimental Procedures for details). As observed by McNaughton et al. (1994), what initially stood out were apparent relationships between discharge increases of individual neurons and maze locations where particular behaviors, such as turns or forward locomotion, were executed. For any given path, such activity patterns were reliable across recording sessions separated by at least one half hour and were not dependent on visual input (see Figure S1 in the Supplemental Data available online). For the large majority of neurons (74%), significant discharge increases were observed for multiple behaviors when discharge correlates were assessed during traversal of at least two paths (Figure 2). Thus, parietal neuron discharge is typically not specific to any single locomotor behavior. Furthermore, discharge rates during performance of particular behaviors exhibited significant variation according to the animal's position in the environment as a whole (i.e., the "allocentric" position), direction of travel, and overall navigational context (i.e., the particular route being traversed, see supporting analyses summarized in Figures S2 and S3). In light of this, the possibility that parietal neurons integrate multiple variables relevant to navigation through the entirety of a given path was considered.

Parietal Neuron Discharge as a Function of Navigational Context

Navigational context strongly impacted the discharge patterns of posterior parietal cortical neurons. The term "navigational context" used here refers to the route-specific sequence of behaviors, such as turns, and the distances between the execution points of those behaviors, which permits the animal to proceed from start to goal. One might expect to find, for instance, that increased discharge during forward locomotion might depend on where in the full sequence of behaviors that behavior occurs.

To examine this possibility, neuronal activity across the full length of path traversals was compared for paths identical in shape and in the sequence of behaviors executed, but opposite in the order of spatial positions encountered and directions of movement (Figure 3 and Figure S4). Sensitivity to navigational context was tested in 33 neurons recorded as animals (n = 7) ran path number 7 (see top of Figure 3). On this path, the behavioral sequence leading from start to goal was identical for outbound and inbound traversals. Each involved forward locomotion along 61 cm maze segments separated by a right and subsequent left turn. The results of this analysis were compared with those for CA1 hippocampal neurons, which, like parietal neurons, are well known for their sensitivity to allocentric position and movement direction. However, based on published data, CA1 neurons were expected to exhibit discharge better related to spatial position in the recording room as opposed to position in the behavioral sequences associated with path 7 outbound and inbound journeys.

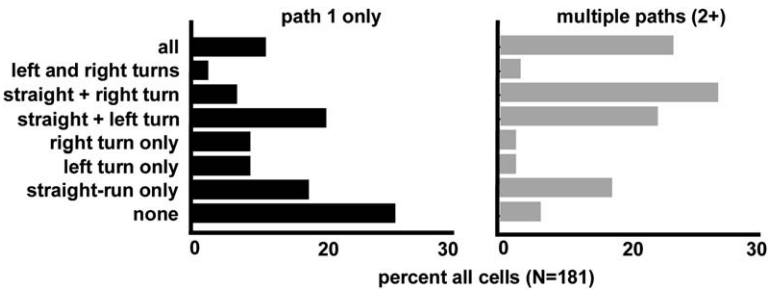

Figure 2. Behavioral Correlates of Parietal Neuron Discharge

Significant discharge increases were matched with the concurrent behavior (left turn, right turn, or straight-run) for 181 parietal cortical neurons recorded during traversal of path 1 and at least one other pathway. Depicted is the percent of all neurons exhibiting discharge restricted to no behavior, single behaviors, or multiple behaviors.

Figure 3A depicts outbound and inbound activity patterns for three parietal neurons recorded simultaneously during traversal of this path. For the three neurons depicted, the correlation between the outbound and inbound activity vectors (r-beh) was very high when they were aligned according to behavioral sequence (i.e.,

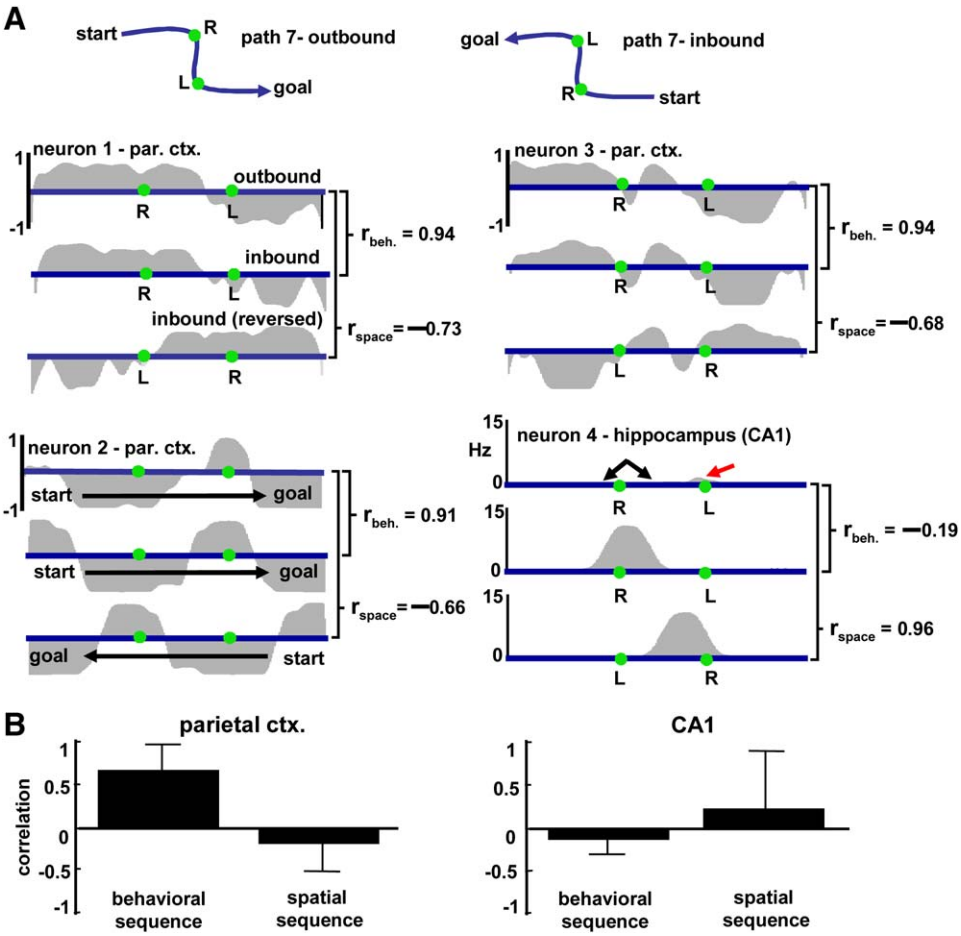

Figure 3. Navigational Context Modulates Parietal Neuron Discharge

(A) Plots of firing rate normalized to the reference (immobility) rate for three parietal neurons and a CA1 hippocampal neuron recorded during traversal of path 7. The true outbound and inbound path shapes and behavioral sequences are given above. In each case, the path was linearized (see Experimental Procedures for details of this process). "R" and "L" designate sites of right and left turns. y axis values of −0.5 and +0.5 correspond, respectively, to 300% decreases and increases in rate relative to the reference rate (see Experimental Procedures for further details). For this path, outbound and inbound behavioral sequences were symmetrical, but directions of movement and the sequence of spatial positions encountered were reversed. For each neuron, the first and second activity traces (gray contours) correspond to outbound and inbound traversals. For these, alignment is to the starting point for each traversal, though the start site was actually at opposite ends of the maze for outbound and inbound traversals. In this way, left to right positions on the x axis for the two traces correspond to the same point relative to start, goal, and turn sites (i.e., the same point in the behavioral sequence). The third trace is the inbound firing rate trace flipped horizontally such that points along the x axis now correspond to the same spatial positions (in the recording room) as those for the outbound activity trace. For parietal neurons, high correlations were observed between outbound and inbound unit activity vectors aligned according to behavioral sequence (first versus second traces = r_{beh}), but were negative when aligned according to the sequence of spatial positions encountered (first versus third traces = r_{space}). The opposite pattern was observed for the CA1 hippocampal neuron.

(B) Plots of mean values (±SD) for all correlations between outbound and inbound firing rate vectors aligned by behavioral sequence and by spatial sequence.

start through goal as shown in Figure 3A, this correlation is based on the first and second traces for each neuron). When the outbound and inbound activity vectors are aligned by spatial position (i.e., by horizontally inverting the inbound activity vector, see first and third trace for each neuron), the vector correlations (r-space) were negative. Neuron 1, for example, exhibited high discharge rates during forward locomotion and during right turns across the first halves of both outbound and inbound traversals despite the fact that the spatial positions associated with these halves were completely nonoverlapping and the directions of movement opposite.

Overall, the median correlation for outbound and inbound activity vectors aligned according to behavioral sequence (i.e., by "navigational context") was 0.64, with 24 of 33 neurons exhibiting a statistically significant positive correlation (Figure 3B). When the same vectors were aligned by spatial position, the median correlation was significantly lower overall, with negative correlation values registered for most (61%) of the neurons tested and with only 3 of 33 neurons yielding significant positive correlations (median r-space = −0.15; Wilcoxon matched-pairs signed ranks test, $p < 0.001$, $n = 33$). Thus, for the parietal neuron population as a whole, discharge according to the ordering of behaviors and the distances between them (i.e., discharge according to navigational context) was found to predominate over discharge according to movement directions as well as the ordering of spatial positions encountered.

Firing patterns for 32 hippocampal CA1 neurons (n = 3 rats) recorded during traversal of the same path reflected, as in parietal cortex, an integration of allocentric position and direction of movement. However, the form this integration took was different than that of parietal cortex. Neuron 4 of Figure 3A, for instance, exhibited discharge almost exclusively across the space encompassing the first turn (a right turn) and first third of the inbound journey's middle section. If, as was the case for parietal cortical neurons, this neuron discharged according to behavioral sequence, one would expect to see a similarly large increase in activity in the analogous region of the outbound journey (indicated by black arrows). Instead, on the outbound journey, this region was associated with a complete lack of discharge. Low-level discharge was found near the second turn (a left turn, see red arrow) of the outbound journey. This region shared the same spatial position as that associated with the larger activation on the inbound journey. Thus, the activity pattern of this neuron was consistent with previous accounts of hippocampal CA1 neurons, in that activity was restricted to a particular spatial region (i.e., a "place field") but with high sensitivity to the direction of movement (McNaughton et al., 1983). Accordingly, the correlation between the outbound and inbound activity vectors aligned by behavioral sequence was low (r-beh = −0.19). When the inbound activity vector was flipped horizontally such that outbound and inbound activity vectors were matched for position in the recording room (see first and third activity trace of neuron 4), the correlation was high (r-space = 0.96).

Similar results were observed for nearly all hippocampal CA1 neurons recorded. However, directional selectivity at the site of place-specific firing fields was even more pronounced for many neurons, and a few neurons exhibited place-specific firing fields for outbound and inbound journeys that were unrelated in terms of spatial position as well as position in the behavioral sequence (Figure S5). For such neurons, both the correlation by behavioral sequence and spatial position (r-beh and r-space, respectively) were low.

Overall, correlation for alignment by behavioral sequence was negative for the majority (23 of 32) of CA1 neurons (median r-beh = −0.09 ± 0.17). Only a single CA1 neuron registered a statistically significant positive correlation. Correlation by spatial position was positive for the majority (18 of 32) of CA1 neurons, with 10 bearing statistically significant positive correlations (median r-space = 0.2 ± 0.38). Opposite the pattern found for parietal cortical neurons, r-space for CA1 neurons was found to be significantly greater than r-beh ($p < 0.005$). Finally, mean r-beh and r-space values for CA1 hippocampal neurons were significantly different than the same values for parietal cortical neurons ($p < 0.001$ in each case).

Parietal Neuron Discharge Scales with Path Segment Size

The foregoing data indicate that the progression of the animal through a particular epoch or epochs of a given route can drive the activity of parietal neurons. Given this finding, one might also expect parietal neuron discharge to reflect perturbations in the spatial structure of navigational epochs. To test this, the distance over which a given neuron could be shown to discharge robustly and reliably between the execution of two behaviors (e.g., a left turn followed by a right turn) was compared for pathways wherein two identical behavior sequences were initiated at the same place and covered the same movement trajectories, but the distance between the execution points of the two behaviors varied by a factor of 1.5, 2, or 3. The criterion for inclusion of a neuron in this analysis was that it exhibit a significant increase in discharge across some portion of the route at or between the sites where the pair of behaviors were executed. Figure 1B depicts position-tracking data for one such experiment. The green traces correspond to a set of path 1 outbound traversals. Red traces correspond to path 3 outbound traversals (note that much of the path 3 tracing is hidden by the overlapping path 1 traces). For path 3, the distance between the first left turn and the subsequent right turn is double (or "2X") that of path 1. For other path pairings, the distance between the execution points of two behaviors differed by a factor of 1.5 or 3. In Figure 1A, the distance between the start and initial right turn for inbound traversals of path 9 is 1.5 times that of path 7 (see green arrows representing the length and direction of each navigational epoch). Similarly, the distance between the start and first right turn of path 9 inbound journeys was three times that for path 1.

For many of the neurons tested (n = 122, only one comparison was made for any given neuron), the distance over which continuous discharge occurred in the space between the behaviors in question was proportional to the length of that space. Data from one neuron included in this analysis are depicted in Figure 4A. Here, discharge rate is color mapped as a function of space for all outbound (upper images) and inbound (lower

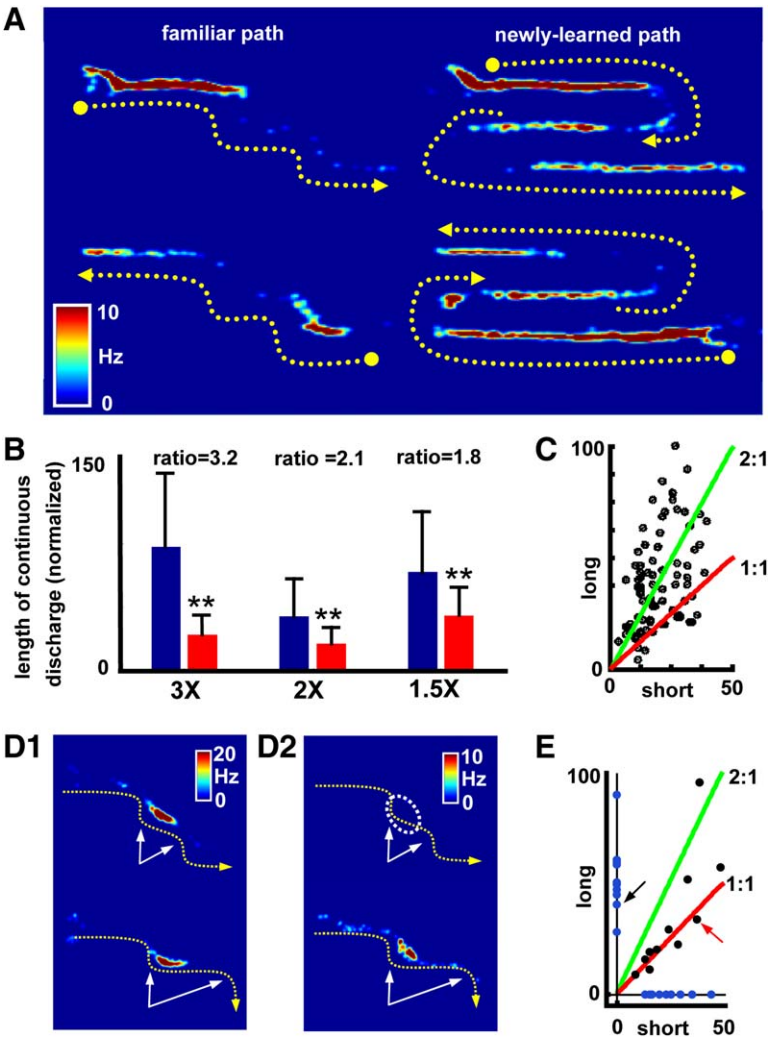

Figure 4. Parietal Neuron Discharge Scales with Path Segment Size

(A) Discharge rate-maps of a parietal neuron for outbound (upper plots) and inbound (lower plots) traversals of a familiar (left) and newly learned (right) path (full paths and direction of travel are shown with broken yellow lines). For each of the four traversal types, this neuron exhibited discharge along each path's entire first segment (ranging in length from 30.5 to 122 cm).

(B) Distance over which parietal neurons discharged significantly (see Experimental Procedures for explanation) on a given path segment varying in length by a factor of 3 (n = 17), 2 (n = 85), or 1.5 (n = 20) across two different paths (discharge distance for shorter segments in red, longer in blue, ±SD, the ratio of the means is given above). On average, parietal neurons discharge over distances roughly proportional to the length of a path segment (**$p < 0.001$).

(C) Scatter plot of discharge distances (in cm) over analogous segments of two different paths across which the segment length differed by a factor of two. Each point corresponds to the distance over which significant discharge was observed. 42 of 85 neurons exhibited a doubling of discharge distance on the longer epoch. Their points lie on or above the green line representing discharge distances across the longer epoch that are double those for the shorter. A small proportion of neurons (16/85) maintained similar discharge distances for both paths. Their points lie at or below the red line representing equal discharge distances on the two paths.

(D) Discharge rate-maps for two CA1 hippocampal neurons recorded during traversal of paths 1 and 3 (upper and lower ratemaps, respectively). The neuron shown in (D1) exhibited a firing field in the path segment separating the first left turn and second right turn for each path (marked by white arrows). For path 3, this path epoch is twice the length of the analogous epoch of path 1, yet the firing field length was nearly identical in size. Other CA1 neurons exhibited the pattern of the neuron depicted in (D2). For this neuron, discharge over the same path epoch was found for path 3, but absent for path 1.

(E) Discharge distances over short versus long path epochs are given for all CA1 neurons (n = 32). Points for the neurons shown in (D1) and (D2) are marked by the red and black arrows, respectively. Many CA1 neurons differentiated two paths by discharging on only one. Points for these neurons lie at zero on either the x or y axis. Other CA1 neurons discharged on both paths, but did not scale with path epoch size.

images) traversals of two different paths. This neuron tended to have highest discharge during forward locomotion across all four initial path epochs (i.e., between the start, where forward motion was initiated, and the first right turn), irrespective of the length of those epochs.

Quantitative analysis of this phenomenon was made from experiments in which the distances between the behaviors in question varied by a factor of 1.5, 2, or 3. Distance over which significant discharge occurred in these three conditions is summarized in Figure 4B, where, on average, the length of continuous discharge significantly increased during traversal of the longer path segment. For the parietal neuron population as a whole, the mean increases in discharge distance scaled with the changes in the length of the path segment. Figure 4C plots the length of continuous discharge for short (x axis) versus long (y axis) path segments, which differed by a factor of 2 (n = 85). The extent to which discharge distance increased to match the length of the longer segment ran on a continuum between "matching" values (those values near the green line) and "nonmatching" (those values near the red line).

Unlike parietal cortical neurons, CA1 hippocampal neuronal activity did not scale with the size of navigational epochs. Instead, a high percentage of CA1 neurons (19 of 31, or 61%) exhibited activity patterns that differentiated the two routes. Discharge rate as a function of space for one such neuron is color mapped in Figure 4D2. During traversal of path 3 (lower image), this neuron exhibited a firing field between the second turn (a left) and the third turn (a right). The distance between the analogous two turns on path 1 is half that for path 3. When traversing this shorter epoch on path

1, the same neuron did not discharge at all in this region of the path (indicated by the white oval). Other CA1 neurons maintained firing fields in both situations, but unlike parietal cortical neurons, the space over which robust and reliable discharge occurred did not scale to the size of the navigational epoch. The length of the firing field for the neuron depicted in Figure 4D1, for instance, was similar in size for traversals of path 1 and path 3, despite the doubling of distance between turns 2 and 3 on path 3.

The distances over which hippocampal CA1 neurons discharged robustly and reliably are given in Figure 4E. The overall distribution of discharge distances across short (x axis) and long (y axis) navigational epochs reflects the patterns of the two individual neurons described in Figure 4D. Blue-colored points correspond to neurons of the first type, which exhibited a lack of discharge on either the short or long epoch (the black arrow corresponds to the neuron depicted in Figure 4D2). There were no parietal cortical neurons of this type (see Figure 4C). Black points correspond to neurons that exhibited discharge for both epochs (the red arrow corresponds to the neuron depicted in Figure 4D1). The points for nearly all of these neurons lie near or below the red line signifying equal discharge distance for the long and short epochs.

Directional Tuning of Parietal Neuron Discharge Is Context Specific

The foregoing data indicate that parietal neurons discharge according to the progression of the animal through single or multiple epochs of a full route. Such patterns were independent of position in the environment and movement directions. However, a frequently observed outcome of monkey parietal recording experiments is directional tuning of discharge (Andersen et al., 1985; Duhamel et al., 1992; Snyder et al., 1998; Colby and Goldberg, 1999; Buneo et al., 2002; Crowe et al., 2004). An explanation for this apparent contradiction between properties of parietal cortex in the rat and monkey may lie in the fact that parietal neurons in the present study were recorded under conditions of minimal restraint. As already suggested in the introduction, this can be expected to increase the dynamic range of parietal afferents carrying information related to allocentric position and self-motion. In consideration of this, parietal neurons were examined for potential correlation to movement direction under conditions in which the type of self-motion (forward locomotion) and allocentric position could be held constant.

Consistent with previous accounts of directional tuning of parietal neurons in monkeys, direction of movement strongly impacted rat parietal neuron discharge when the type of locomotor behavior and allocentric position were held constant. Figure 5A depicts outbound and inbound activity patterns of a parietal neuron during traversal of path 1. This neuron increased discharge during straight-running along the first outbound path segment (upper panel). During straight-running across the same space, but in the opposite direction, discharge was minimal (lower panel, the area between the dotted lines is the same for the outbound and inbound paths). Outbound and inbound activity rates were compared for 81 neurons that exhibited significant discharge increases within the maze area between the dotted vertical lines in Figure 5A. The higher of the two firing rates (outbound or inbound) for each neuron was divided by the lower. These ratios were capped at 10 and are plotted in Figure 5B. With few exceptions, very high ($\geq$10) values were obtained, indicating a strong dependence on movement direction. Consistent with previous reports (McNaughton et al., 1983), a high percentage of hippocampal neurons (13 of 20, 65%) exhibited at least a doubling of discharge in the preferred direction, though this percentage was somewhat lower as compared to the parietal neuron population (77 of 81, 95%).

The impact of movement direction on discharge rate was specific to the context given by particular route locations. Tuning of parietal neuron discharge to a specific movement direction was not consistently observed when activity across the full space of the maze was

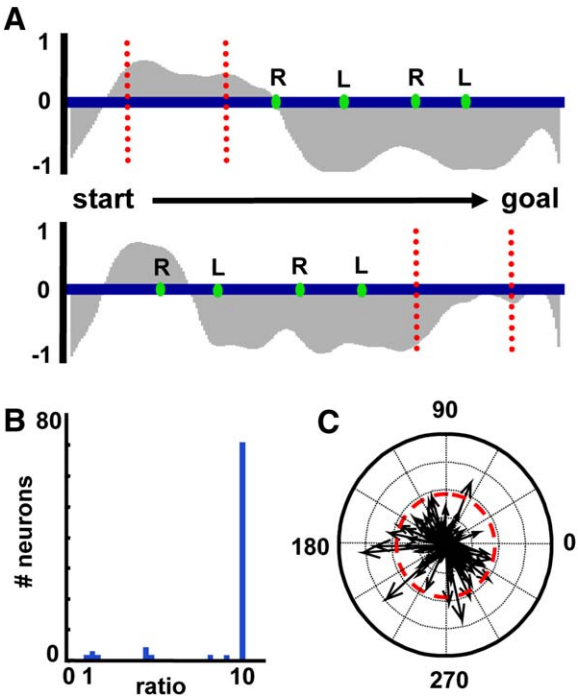

Figure 5. Movement Trajectory Modulates Parietal Neuron Discharge

(A) Discharge rate (normalized to reference rate observed during immobility, see Experimental Procedures for details) across path 1 traversals in the outbound (upper plot) and inbound (lower plot) directions. Green dots indicate points on the linearized path where turn peaks occurred (L, left turn; R, right turn). This neuron exhibiting a near tripling of discharge rate during outbound forward locomotion across the first path segment (upper plot), but near-baseline rates for the same maze region (bracketed by dashed red lines in both plots) during inbound forward locomotion in the opposite direction (lower plot).

(B) Distribution of outbound-inbound firing rate ratios for the space indicated by dashed red lines in (A) (the higher of the outbound and inbound rates was divided by the lower; ratios were capped at 10). The distribution is dominated by very high (10+) ratios indicating large differences in outbound versus inbound firing rates.

(C) Directional tuning (mean angle and length with length normalized to values between 0 and 1) of discharge activity during path 1 traversals (n = 199, outer circle = 1). The number of neurons with significant tuning (arrows exceeding in length the radius of the dashed red circle at 0.41) was barely above that expected by chance.

considered. Figure 5C summarizes the results of an analysis considering the possibility that parietal cortical neurons are directionally tuned for movement trajectory alone. First, movement trajectory was determined across time periods 166 ms in duration centered on each position-tracking point recorded during uninterrupted traversals of path 1 (note that this method excludes portions of recordings with little or no movement). Trajectories were then binned to one of 18 categories corresponding to 20º intervals. Finally, mean discharge rate for each trajectory bin was determined, a mean vector calculated, and the mean vector length subjected to Rayleigh's test for uniformity (Fisher, 1993). Using a probability cutoff of 0.05, only 10 of the 181 neurons (5.5%) analyzed were found to exhibit significant directional tuning. Similar results (data not shown) were observed during traversal of paths 3 and 5.

The analysis was taken one step further to consider the possibility that parietal cortical neuron discharge is tuned to upcoming or just-executed trajectories. To do this, directional tuning vectors were also determined using firing rates from 33 different time periods preceding and succeeding each position-tracking point by 0–400 ms in 25 ms steps. Again, no evidence that movement trajectory, in and of itself, drives parietal cortical neuron discharge was observed. No greater than 6.8% of all neurons were found to have statistically significant directional tuning vectors for any temporal offset between discharge and movement trajectory. Furthermore, across all neurons, there was no tendency for directional tuning vectors to be larger at any of the possible 33 temporal offsets. Thus, directional tuning of discharge is a feature of parietal cortex in rats as it is in monkeys. However, the specific direction to which discharge is tuned varies depending on position in a route.

Discussion

Previous work in both the rat and monkey has suggested that parietal cortical neuron discharge is modulated by the type of behavior performed (McNaughton et al., 1994; Buneo et al., 2002), the direction of motion (Steinmetz et al., 1987; Chen et al. 1994), and body position in the environment (Snyder et al., 1998; McNaughton et al., 1994). The navigational task employed in these experiments permitted parietal neuron activity to be formally related to each of these variables, and to consider the possibility that parietal cortical activity is organized according to other features of efficient route traversal, such as the state of progression through a route.

Direction of motion, spatial position, and type of locomotor behavior all impacted the discharge of parietal cortical neurons. Reversing the direction of forward locomotion through a given subregion of the environment greatly affected the discharge rates of nearly all neurons (Figure 5). Similarly, comparison of discharge across like turns (lefts or rights), which covered the same trajectories but occurred in different spatial positions, revealed a robust sensitivity to spatial position for the majority of neurons (Figure S2). Finally, discharge patterns for some parietal neurons were found to discriminate between the three locomotor behaviors considered (left turns, right turns, and forward locomotion; Figure 2).

However, like hippocampal neurons, most parietal neuron discharge reflected a complex convergence of directional, spatial, and behavioral influences. This is indicated by the inability of any of these variables to, on their own, predict discharge rates when the remaining variables were not held constant. For instance, when firing rates were considered across all directions of motion, only the number of neurons expected by chance were found to exhibit statistically significant directional tuning (Figure 5C). This indicates that directional tuning of parietal neurons depends on the context of spatial position and locomotor behavior. This finding is consistent with recent findings in monkeys (Crowe et al., 2004) where directional tuning of discharge varied randomly across behavioral contexts. Similarly, metrics for spatial tuning of discharge were not suggestive of the place-specific discharge seen in hippocampal neurons (Figure S2). Finally, most parietal neurons discharged in relation to at least two behaviors, with nearly 30% of all neurons discharging across both right and left turns (Figure 2). In addition, discharge in relation to any single behavior was, for most neurons, strongly modulated by direction of movement, spatial position, and navigational context (Figure S3). This is consistent with data from the monkey inferior parietal lobule (Fogassi et al., 2005) where discharge was differential for the same act when that act was embedded in different behavioral sequences.

Thus, as suggested by the diversity of inputs converging on the parietal cortex, the activity of most neurons can be said to reflect an integration of not one, but several types of information relevant to spatial cognition as it pertains to navigation. Notably, the integration of these variables is not a property unique to the parietal cortex, but is a feature common to many areas implicated in spatial cognition. However, the form that integration of these variables takes can differ greatly. Hippocampal neurons are unique in their tendency to discharge in single discrete regions of an environment, yet such activity is often modulated by speed and direction of movement (Czurko et al., 1999; McNaughton et al., 1983; O'Keefe and Burgess, 1996; Cacucci et al., 2004). Subicular, presubicular, and parasubicular neurons integrate direction of movement with spatial position, but in a manner that can be clearly distinguished from hippocampal neurons (Sharp, 1999; Cacucci et al., 2004). Finally, neurons of the dorsocaudal medial entorhinal cortex integrate direction, position, and distance traveled, but produce grid-like discharge patterns (Fyhn et al., 2004; Hafting et al., 2005).

Since the spatial discharge patterns of subicular, hippocampal, and entorhinal cortical neurons are organized in different ways, it was expected that parietal neurons would also exhibit a unique form of spatial tuning. What proved unique to parietal neurons is strong sensitivity to the animal's position in a route. Activity mapped individual or multiple epochs of route traversals defined by points of change in locomotor behaviors such as forward motion, turns, and initiation and termination of path running. Remarkable similarity in discharge patterns was found for paths differing completely in the ordering of environmental positions encountered and directions of motion, but identical in the ordering of behaviors executed and the spatial

distances between them (Figure 3 and Figure S4). This aspect of parietal cortical discharge proved to be different than that of a population of CA1 hippocampal neurons recorded under the same conditions (Figure 3 and Figure S5). The unique properties of parietal neuron activity lead to the hypothesis that an important function of parietal cortex is to form route representations that can be applied to multiple spatial settings.

In other path-running experiments, hippocampal neurons exhibit place-specific discharge, or lack thereof, depending on the type of preceding or subsequent behavior or direction of motion leading to that place (Frank et al., 2000; Wood et al., 2000; Ferbinteanu and Shapiro, 2003). Thus, sensitivity to behavioral sequence is also found in other brain regions implicated in spatial cognition. However, the presence or lack of place-specific discharge in these experiments refers to single, small subregions of the overall path where the direction of motion is unchanged. Thus, modulation of hippocampal discharge by the ordering of behavior is nevertheless dependent on place and direction of motion. In contrast, order-dependent discharge in the parietal cortex is independent of place and direction of motion. This is consistent with recent findings indicating that similar populations of deep-layer parietal cortical neurons express Arc following traversal of identical paths in different environments (Burke et al., 2005).

Parietal discharge patterns did bear some resemblance to those of deep-layer lateral entorhinal neurons exhibiting "path equivalent" discharge (Frank et al., 2000). Here, firing fields occurred in the same positions of paths bearing the same lengths. In some cases, such paths covered different spaces in the environment but bore the same behavioral and directional sequences. In others, path-equivalent discharge was, unlike parietal cortex, independent of the behavioral sequence utilized. This suggests that some regions of the entorhinal cortex may form representations intermediate to place- and direction-dependent representations in the hippocampus and place- and direction-independent representations in the parietal cortex.

Parietal neurons were not only sensitive to the position of the animal in the path as a whole, but also to the distances between the execution points of behaviors that defined navigational epochs. Altering the spatial distance between two behaviors produced, for most neurons, corresponding changes in the distance over which discharge occurred (Figure 4). Thus, activity patterns expanded across space to faithfully map the position of the animal between a pair of behaviors. Hippocampal CA1 neuronal activity did not scale with the size of navigational epochs, but, instead, most often differentiated epochs of different sizes by discharging on only one. Thus, hippocampal CA1 neuronal activity patterns were informative of which route the animal was to traverse, while parietal cortical neurons were informative of the animal's position in the route. In the present work, the spatial relationships between intra- and extra-maze cues were constant. However, CA1 neuron firing fields do adapt to path length when self-motion and environmental cues are mismatched (Gothard et al., 1996). This suggests that, under some circumstances, output of the parietal cortex may influence CA1 discharge patterns to offset conflicting sources of spatial information.

Together, these findings lead to the conclusion that parietal neuron discharge does reflect information pertaining to the current position in space, direction of motion, and type of locomotor behavior, but that such information is largely secondary to the positioning of activity increases relative to that of navigational epochs that comprise a route. The latter property of parietal neuron discharge is potentially critical to the ability of the animals to efficiently run through convoluted paths between two points in space. In this respect, parietal neuron efferents could potentially bias motor control systems toward selection of appropriate behaviors and/or bias attention toward detection of specific sensory stimuli, such as maze corners, that guide navigational behavior. Since neuronal ensembles in both prefontal cortex and supplementary motor cortex contain sequence-specific representations of upcoming behaviors (Tanji and Shima, 1994; Averbeck et al., 2002; Baeg et al., 2003), a challenge for future work is to determine whether and how parietal cortical representations interact with these regions in the production of coordinated behavioral sequences.

Experimental Procedures

All procedures fell within the guidelines of the National Institutes of Health and approved Institutional Animal Care and Use Committee protocols.

Surgery

Custom-fabricated microdrives containing ten stereotrodes were implanted over the posterior parietal cortex. Target coordinates, relative to bregma, were posterior 3.8 mm, lateral 2.3 mm. A craniotomy was made over the target site, the dura excised, and the stereotrode tips moved into the brain to an initial depth of 0.5 mm. Rats were permitted to recover for 5 days after surgery.

Behavioral Training

Adult Sprague-Dawley rats (n = 7) were trained to traverse, in outbound and inbound directions, three "familiar" paths (paths 1, 3, and 5 of Figure 1) between two maze sites where food reward was made available. The maze was positioned in a fixed region of a curtained area in the recording room. To provide consistent spatial cues, the curtains were adorned with large, flat objects of various geometric shapes. Training took place over 2–3 weeks, with total path traversals being few the first few days of training, but increasing to approximately 50 over the last 1–1.5 weeks. Behavior was motivated by food restriction. Body weights were not permitted to drop below 80% of free-feeding weights and typically remained above 85%. Once an animal was proficient at traversing each path (all animals reached the criterion of ten or more uninterrupted traversals per day of each path.), 2–3 days of training in darkness was given. Following surgery and recovery of path-running behavior, four to six recordings (one per day) were made using the three trained paths. Afterward, the use of new paths was implemented and recordings continued for a period of 1–2 weeks.

Recordings and Single-Unit Discrimination

For recording experiments, the microdrive was connected to a headstage (NBLabs, Denison, TX) containing field effect transistors (for current amplification of signals) and a bank of small, red light-emitting diodes (LEDs). Signals were fed to amplifiers (Neuralynx, Tucson, AZ) and then to computers running the acquisition program AD (Matt Wilson, MIT; and Loren Frank, UCSF). Signals were filtered between 0.6 and 6 KHz, digitized at 32 KHz, and amplified 5000–30,000×. Overhead video was led to a Dragon Tracker system (Dragon Tracker, Boulder, CO), which detected the position (0.5 cm/pixel resolution), at 60 Hz, of the headstage-mounted LEDs.

Single-unit discrimination was performed using custom-built software (Matt Wilson, MIT) based on waveform parameters and their

differential values between the two wires of each stereotrode (Figure S6). Discrimination procedures were the same as described in Nitz and McNaughton (2004).

For parietal neuron analyses, data from seven animals were utilized. No animal contributed more than 29% of neurons used in any analysis. CA1 recordings were obtained from three of the seven animals, with each contributing nearly equal numbers of neurons.

Histology

Rats were perfused under deep anesthesia with formalin and the brain dissected for analysis. Coronal sections were examined for detection of tracks left by stereotrodes. Parietal cortex recordings were made deep to cortical layer 3, between 3.5 and 4.5 mm posterior to bregma and between 2 and 4 mm lateral to the midline. This region corresponds to that described by Kolb and Walkey (1987), which, similar to the primate posterior parietal cortex, receives input predominantly from the lateral dorsal and lateral posterior thalamus (Figure S7). A combination of histological analysis, the presence of ripple events in field potentials, and complex spikes from single units were used to identify principal cells of the CA1 region of the hippocampus.

Selection of Path Traversals for Analysis

To simplify data analyses, the path of the animal was linearized, and outbound and inbound laps were separately defined. The initial step in the linearization process was to define uninterrupted path traversals. Using a guided user interface in Matlab, position records were examined on a lap-by-lap basis. Uninterrupted traversals lacked evidence for reversal of direction or a full stop of any duration. In practice, this meant that data used from paths not included in the presurgery training regimen corresponded to time points after the animal had learned the new path well enough to traverse it multiple times with no interruption. For all paths, a minimum of six uninterrupted path traversals was required for inclusion of the recording data in analyses. Overall, 60.7% ± 20.9% of traversals along trained paths were judged to lack interruption. A smaller percentage (53% ± 14.6%) of uninterrupted traversals was found for new paths. More traversals of newly trained paths were required to obtain the minimum number of uninterrupted traversals (mean 34.9 ± 13.4 traversals per recording versus 24.9 ± 7.5 for trained paths).

Detection of Turn Peaks and Path Linearization

The onsets and ends of uninterrupted traversals were defined by when the animal crossed fixed coordinates situated just inside the maze positions at which reward was delivered. Defining such points permitted the analysis of only those portions of path traversals where behavior was relatively stereotyped.

A combination of procedures was used to define the time at which the apex of each turn was reached. First, the apex of each turn was electronically marked by fixing the crosshairs of a target on the perceived point of each turn with the greatest change in trajectory. A sequence of position points surrounding this point was then rotated until the first and last points were equal in the horizontal plane. Final identification of the turn apex was derived by selecting the position point with the highest value in the vertical plane. Each tracking point could then be defined relative to the distance between the onset and first turn, the distance between succeeding turns, or the distance from the last turn to the path end (Figure S8). This ensured that mean discharge rates more accurately reflected the animal's position along a path given that slight differences in individual path trajectories relative to the maze were inevitable.

Movement trajectory was calculated for time periods of 166 ms centered on each position point recorded during path running. Each trajectory was taken as the angle between the position points corresponding to the beginning and end of each time period.

Defining Points of Increased Discharge

The activity of each neuron was normalized to its own average firing rate across all periods of immobility occurring at path endpoints where food consumption took place. Immobility was defined as movement speed of less than 2 cm/s. This cutoff excluded exploratory behaviors such as whisking and peering over the maze ends that sometimes preceded path traversals. Next, firing rates during path-running were calculated for time intervals (16.67 ms) centered on each position-tracking point (position was tracked at 60 Hz). For each interval, the difference between the firing rate and the reference rate was divided by the sum of the firing rate and the reference rate (McNaughton et al., 1994; Ferrera et al., 1994). Values for this ratio range between −1 and 1. Values of −0.2 and 0.2 correspond to 50% decreases and increases in discharge rate relative to the immobility reference rate. Values of 0.33 and 0.5 correspond, respectively, to a doubling and tripling of discharge rate.

Discharge increases were defined for those portions of the maze where firing rates exceeded by 50% or more the reference rate. In assembling the full set of data, it became clear that large increases in discharge for some neurons did not consistently appear at a given position across multiple traversals and that some small increases were highly regular in nature. Therefore, discharge increases were not considered reliable (and not considered further) unless the mean rate was significantly greater than the reference rate (t test with probability cutoff of 0.05 and a requirement that six consecutive position bins exceed the cutoff to greatly reduce the possibility that perceived increases reflect the expected random variability). Discharge increases defined by this method were used to assign behavioral correlates (straight-run, left turn, or right turn) and to subdivide the full dataset into groups of neurons appropriate for particular analyses. Discharge increases categorized as turn-related were those that occurred within 12.7 cm of a turn peak that corresponds to the halfway point between the most closely spaced turns. Discharge increases categorized as straight-run corresponded to the middle half of 61 cm path segments. By excluding the first and last quarters of such segments, confusion with points of turn behavior was avoided.

Supplemental Data

The Supplemental Data for this article can be found online at http://www.neuron.org/cgi/content/full/49/5/747/DC1/.

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