Neuronal Activity Related to Saccadic Eye Movements in the Monkey's Dorsolateral Prefrontal Cortex

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SUMMARY AND CONCLUSIONS

1. Single-neuron activity was recorded from the prefrontal cortex of monkeys performing saccadic eye movements in oculomotor delayed-response (ODR) and visually guided saccade (VGS) tasks. In the ODR task the monkey was required to maintain fixation of a central spot throughout the 0.5-s cue and 3.0-s delay before making a saccadic eye movement in the dark to one of four or eight locations where the visual cue had been presented. The same locations were used for targets in the VGS tasks; however, unlike the ODR task, saccades in the VGS tasks were visually guided.

2. Among 434 neurons recorded from prefrontal cortex within and surrounding the principal sulcus (PS), 147 changed their discharge rates in relation to saccadic eye movements in the ODR task. Their response latencies relative to saccade initiation were distributed between −192 and 460-ms, with 22% exhibiting presaccadic activity and 78% exhibiting only postsaccadic activity. Among PS neurons with presaccadic activity, 53% also had postsaccadic activity when the monkey made saccadic eye movements opposite to the directions for which the presaccadic activity was observed.

3. Almost all (97%) PS neurons with presaccadic activity were directionally selective. The best direction and tuning specificity of each neuron were estimated from parameters used to fit a Gaussian tuning curve function. The best direction for 62% of the neurons with presaccadic activity was toward the contralateral visual field, with the remaining neurons having best directions toward the ipsilateral field (7%) or along the vertical meridian (15%).

4. Most postsaccadic activity of PS neurons (92%) was also directionally selective. The best direction for 48% of these neurons was toward the contralateral visual field, with the remaining neurons having best directions toward the ipsilateral field (36%) or along the vertical meridian (16%). Eighteen percent of the neurons with postsaccadic activity showed a reciprocal response pattern: excitatory responses occurred for one set of saccade directions, whereas inhibitory responses occurred for roughly the opposite set of directions.

5. Sixty PS neurons with saccade-related activity in the ODR task were also examined in a VGS task. Forty of these neurons showed highly similar profiles of directional specificity and response magnitude in both tasks, 13 showed saccade-related activity only in the ODR task, and 7 changed their response characteristics between the ODR and VGS tasks.

6. The majority of PS neurons with saccade-related activity in the ODR task showed that activity only in conjunction with task-related saccades; comparable activity was not observed in association with saccadic eye movements made during the intertrial interval (ITI), even though both classes of saccades were performed in the dark. This context dependency was characteristic of both pre- and postsaccadic activity of PS neurons.

7. Among 53 frontal eye field (FEF) neurons tested in the ODR task, 26 had saccade-related activity, with 47% of these having presaccadic responses. All saccade-related activity in FEF was directionally selective, and 72% of their best directions were toward the contralateral visual field. All six FEF neurons also examined in a VGS task showed similar responses across tasks.

8. These results indicate that PS neurons participate in the control of purposive saccadic eye movements. Most saccade-related activity of PS neurons was postsaccadic, and such postsaccadic activity may be important in terminating the processes leading to memory-guided saccades. Their presaccadic activity, although a smaller proportion of the total, could help initiate and guide saccadic eye movements in the ODR task.

INTRODUCTION

Neuronal activity in the dorsolateral prefrontal cortex of monkeys has been examined during performance of a wide variety of paradigms, including spatial delayed response (Fuster 1973; Kojima and Goldman-Rakic 1982; Kubota et al. 1974; Niki 1974c; Niki and Watanabe 1976), spatial delayed alternation (Kubota and Niki 1971; Niki 1974b), visual discrimination (Fuster et al. 1982; Kubota et al. 1980; Quintana et al. 1988; Rosenkilde et al. 1981; Yajeya et al. 1988), go/no-go tasks (Komatsu 1982; Watanabe 1986), reaction time procedures (Sakai 1974; Sawaguchi 1987), and visual tracking tasks (Funahashi 1983; Kubota and Funahashi 1982). The behavioral responses required in all of these tasks are manual, i.e., either lever pressing and release or flexion-extension arm and hand movements. Many prefrontal neurons exhibit movement-related activity during performance of these tasks, activity that usually begins before the initiation of the index response and that often persists during its execution. Moreover, this activity is often "differential" (Fuster et al. 1982; Niki 1974c) or "directional" (Kojima and Goldman-Rakic 1982; Kubota and Funahashi 1982), i.e., neuronal activation occurs for one direction of movement and only weakly or not at all for other directions of movement. On the basis of these findings, it has been argued convincingly that neuronal activity in the dorsolateral prefrontal cortex during behavioral tasks is related to the initiation or execution of the manual response (Fuster 1989; Kubota 1978).

The question now arises whether the involvement of prefrontal neurons in motor control extends beyond the domain of arm movements. It is known that the frontal eye fields (FEF), located in the anterior bank of the arcuate sulcus at the posterior border of the prefrontal cortex, have activity closely related to the execution of purposeful saccadic eye movements (Bruce 1988; Bruce and Goldberg 1985). Similarly, it is also known that the supplementary eye fields (SEF), located within the supplementary motor...
area, also have activity related to saccadic eye movements (Schlag and Schlag-Rey 1987). However, despite anatomic connections of the prefrontal cortex within and surrounding the principal sulcus (PS) with the superior colliculus (Goldman and Nauta 1976; Leichnetz et al. 1981), the F-F-F (Barbas and Mesulam 1981; Huerta et al. 1987), and the SEF (Huerta and Kaas 1990), the possible contribution of the PS region to oculomotor control has received little attention.

Recently, neuronal activity in the prefrontal cortex has begun to be examined in oculomotor paradigms, and there are indications that neurons in the frontal cortex outside FEF and SEF may also participate in the execution of saccades. For example, Boch and Goldberg (1989) reported activity of PS neurons during visually guided saccades (VGSs), activity that is similar in some ways to that of FEF neurons; and other studies have reported both pre- and postsaccadic activity in the prefrontal cortex (Barone and Joseph 1989; Joseph and Barone 1987; Kojima 1980). However, it is not clear from these previous studies how many PS neurons show pre- or postsaccadic activation; whether the presaccadic activity is substantially different from the postsaccadic activity in terms of directional selectivity, response magnitude, tuning specificity, etc.; and how such activities depend on visual stimulation.

Therefore, to understand further the saccade-related activity in the PS cortex, especially under conditions excluding visual influences, we have examined saccade-related activity in an oculomotor delayed-response (ODR) task requiring purposive memory-guided saccades in the dark. For comparison with the activity in PS and elsewhere that has previously been examined during VGSs, we also analyzed neuronal activity in VGS tasks in which the monkey’s saccadic eye movements were externally guided.

METHODS

Subjects and experimental setups

The four rhesus monkeys (Macaca mulatta, 3.2–5.3 kg) that served as subjects for this study are the same as in our previous reports (Funahashi et al. 1989, 1990). The experimental apparatus, surgical procedures, recording procedures, and basic methods of data analysis are described in detail in those reports. Briefly, the monkey sat in a primate chair during the experiment with his head fixed in position facing a 19-in. monochrome cathode ray tube (CRT) (RCA, TC 1119), where visual stimuli were presented by a computer graphics card (Pacific Binary Systems, Graph11). There was no background illumination on the CRT, and the monkey was in darkness when the visual stimuli were off. The magnetic search coil technique was used to obtain the monkey’s eye position and movements. An on-line computer system (PDP-11) presented visual stimuli, monitored eye position, and rewarded correct oculomotor behavior with a 0.2-ml drop of lightly sweetened water. Water was not available in the monkey’s home cage during the recording period; instead they worked to satiety during the daily 2- to 4-h recording sessions and were given ad lib chow and fruit on return to their home cage.

ODR task

Figure 1A shows a schematic drawing of the ODR task. After a 5-s intertrial interval (ITI), the fixation target (a small white spot, 0.1" in diam) appeared at the center of the CRT. The monkey looked at the fixation target and maintained fixation for 0.75-s (the fixation period), whereupon the visual cue (a filled white square, 0.7 × 0.7") was presented for 0.5-s (the cue period) at one of four or eight peripheral locations (13° eccentricity). Stimulus location was randomized over trials so that the monkey could not predict where the cue would appear on any given trial. A crucial feature of the task was that the monkey had to maintain fixation throughout the cue period and also throughout the subsequent delay period (usually 3.0-s). At the end of the delay, the fixation target was extinguished; this was the “go” signal to make a saccade. If the monkey made a correct saccadic eye movement within the next 0.5-s (the response period), it was immediately rewarded with a drop of water. A correct saccade was defined as an eye movement that ended within a circular window (6° in diam) around the location where the cue had been presented.

FIG. 1. Schematic drawings of behavioral paradigms. A: oculomotor delayed response (ODR) task. B: visually guided saccade I (VGS-I). C: visually guided saccade II (VGS-II). D: visually guided saccade III (VGS-III). Horizontal and vertical eye positions, timing of visual stimulus presentations (fixation target, visual cue, saccade target), and reward delivery are shown for each task.
VGS tasks

Activity related to VGSs was examined with the use of one of three VGS tasks described below. These VGS tasks were applied only to neurons that showed saccade-related responses in the ODR task. The change in task condition was not indicated by any explicit signals except the different size of the fixation target used in the two tasks (VGS-I and -II), but the VGS and ODR tasks were always run in blocks of ≥40 trials.

VGS-I (Fig. 1B). After a 3.0-s ITI, the fixation target (a filled square, 0.7 X 0.7") appeared at the center of the CRT. If the monkey looked at it and maintained fixation for 2.0-s, the fixation target instantaneously moved to one of four or eight peripheral locations. The monkey was required to make saccadic eye movement to this peripheral target within 0.5-s to obtain a drop of liquid reward. The peripheral locations were the same as for the ODR task and were randomized across trials.

VGS-II (Fig. 1C). After a 4.0-s ITI, the fixation target (a filled square, 0.7 X 0.7") appeared at the center of the CRT. If the monkey initiated and maintained fixation for 1.5-s, the fixation target instantaneously moved to one of four or eight peripheral locations. In this version of the VGS task, the monkey was required to make a saccadic eye movement to the peripheral fixation target within 0.5-s and also to maintain fixation for 3.0-s to obtain a drop of liquid reward. Again, the locations of peripheral targets were the same as those of visual cues in the ODR task and were randomized across trials.

VGS-III (Fig. 1D). This task was almost identical to the ODR task, except that the peripheral visual stimulus remained on during the delay period as well as the response period. Therefore the monkey was simply required to make a VGS to the peripheral stimulus within a 0.5-s response period after the central fixation target disappeared.

Recording and analysis of single-neuron activity

Single-neuron activity was recorded with Parylene-coated tungsten microelectrodes (2-5 MΩ at 1 kHz, Micro Probe) or glass-coated cgljot microelectrodes (0.5-1.0 Ω at 1 kHz). We monitored both the raw activity signal and the output of a window discriminator (Model DS-1, BAK) simultaneously with an oscilloscope (5110, Tektronix) and an audio monitor. After analyzing the response properties of neurons, we sometimes microstimulated through the recording electrode while the monkey maintained fixation at the central target so that we could determine whether the recording site was in the FEF, according to criteria described by Bruce et al. (1985).

The on-line computer system, in addition to carrying out the behavioral paradigms, sampled neuronal and oculomotor signals and stored these data in relation to task events on magnetic media. Two types of data files were stored: event buffer files contained the time of every event that the computer had access to, including the time of each discriminated action potential and the time of events such as the appearance and disappearance of visual cues, and also the time, duration, direction, and amplitude of each saccade made. Individual event buffer files usually contained 50-100 trials. Analog buffer files contained multiple records (1- to 2-s epochs) of eye position and eye velocity signals, together with the discriminated action potentials and a code representing progress through the task paradigm.

Using the stored event buffer files, we examined rasters and histograms of neuronal activity for each cue location. For the present study, the rasters and histograms were made with different alignment points, including the start of the delay period, the start of the response period, and the initiation of saccadic eye movement. We also made cumulative histograms to determine the latency of saccade-related activity.

Neuronal activity in relation to spontaneous saccades during the ITI was also analyzed. To examine this activity, we set an amplitude tolerance (4-39") as well as a directional tolerance (±15") to select saccades made during ITI comparable with those performed in the response period of the formal tasks; we then made rasters and histograms of neuronal activity aligned at the initiation of these saccades.

Analysis of directional selectivity

To analyze quantitatively the directionality of neurons that showed directional saccade-related activity, we made tuning curves using the Gaussian function

\[ f(d) = B + Re^{-(d-DW-ci2} \]

where \(f(d)\) is discharge rate as a function of cue direction \((d)\). The constants are defined as follows: \(B\) is the spontaneous or background discharge rate for the neuron, \(D\) is the saccade direction yielding the strongest activity, and \(R\) is the response rate above background at the best saccade direction. Finally, \(T_d\) measures tuning with respect to saccade direction; specifically, \(T_d\) is the width of the tuning curve where the response is diminished to \(1/e (36.8\%)\) of the peak response. This Gaussian tuning curve method has previously been used to examine the memory fields and visual receptive fields of PS neurons (Funahashi et al. 1989, 1990) as well as visual receptive fields and movement fields of FEF neurons (Bruce and Goldberg 1985; Bruce et al. 1985). In the present study the data to be fit were, for each cue direction, the maximum discharge rate over any 100 ms portion of the 1-s period after the fixation target disappeared. The fit was implemented by iteratively searching for the \(B, R, D,\) and \(T_d\) combination that minimized the sum of the squared deviations between the data and the curve.

![FIG. 2. Latencies of saccade-related activity for principal sulcus neurons (A) and frontal eye field neurons (B). Latency for each neuron was measured from cumulative histograms at the cue direction yielding its maximum response.](image-url)
FIG. 3. A: directional presaccadic activity of a principal sulcus neuron during the oculomotor delayed-response task. This neuron (7074.0, right hemisphere) had a phasic excitatory presaccadic response when the monkey made saccades to the upper left visual field (90, 135, and 180° directions), as well as a phasic excitatory postsaccadic response when the monkey made saccades to the lower right visual field (0, 270, and 315° directions). It also had a phasic cue-period activity for the 90 and 135° directions. Visual cues were randomly presented at 1 of the 8 locations indicated in the central diagram. All cue eccentricities were 13° and all delay periods were 3 s. C, D, and R correspond to cue, delay, and response periods, respectively. Histogram binwidth is 40 ms. B: activity aligned at the initiation of saccades in the response period of the 135° and 315° trials. Response latency was ∼60 ms as judged by the inflection of the cumulative histogram at the 135° cue position. Histogram binwidth is 15 ms. C: activity in conjunction with spontaneous saccades made during the intertrial interval (ITI) and having the 135 ± 15° or 315 ± 15° directions. Although the histograms represent 19 saccades for the 135° direction and 27 for the 315° direction, raster lines are shown only for the last 14 saccades of each. Histogram binwidth is 15 ms.
A Activity during the ODR task

This neuron (5215.1, left hemisphere) had a strong phasic postsaccadic response when the monkey made saccades to the left visual field (135°, 180°, and 225° directions). Visual cues were randomly presented at 1 of the 8 locations indicated in the central diagram. All cue eccentricities were 13° and all delay periods were 3 s. C, D, and R correspond to cue, delay, and response periods, respectively. Histogram binwidth is 40 ms. B: activity aligned at the initiation of saccades in the response period of the 180° trials. Response latency was 110 ms as judged by the inflection of the cumulative histogram. Histogram binwidth is 15 ms. C: activity in conjunction with spontaneous saccades made during the intertrial interval (ITI) and having the 180° ± 15° directions. Although the histograms represent 44 saccades, raster lines are shown only for the last 14 saccades. Histogram binwidth is 15 ms.

B Rewarded saccades in task

C Spontaneous saccades in ITI

FIG. 4. A: directional postsaccadic activity of a principal sulcus neuron during the oculomotor delayed-response task. This neuron (5215.1, left hemisphere) had a strong phasic postsaccadic response when the monkey made saccades to the left visual field (135°, 180°, and 225° directions). Visual cues were randomly presented at 1 of the 8 locations indicated in the central diagram. All cue eccentricities were 13° and all delay periods were 3 s. C, D, and R correspond to cue, delay, and response periods, respectively. Histogram binwidth is 40 ms. B: activity aligned at the initiation of saccades in the response period of the 180° trials. Response latency was 110 ms as judged by the inflection of the cumulative histogram. Histogram binwidth is 15 ms. C: activity in conjunction with spontaneous saccades made during the intertrial interval (ITI) and having the 180° ± 15° directions. Although the histograms represent 44 saccades, raster lines are shown only for the last 14 saccades. Histogram binwidth is 15 ms.
FIG. 5. A: directional post-saccadic activity of a principal sulcus neuron during the oculomotor delayed-response task. This neuron (5232.0, left hemisphere) had phasic excitatory post-saccadic responses when the monkey made saccades to the upper right visual field, as well as phasic inhibitory post-saccadic responses when the monkey made saccades to the lower left visual field. Visual cues were randomly presented at 1 of the 8 locations indicated in the central diagram. All cue eccentricities were 13° and all delay periods were 3 s. C, D, and R correspond to cue, delay, and response periods, respectively. Histogram binwidth is 40 ms. B: activity aligned at the initiation of saccades in the response period of the 0° and 225° trials. Response latency was 0-ms as judged by the inflection of the cumulative histogram at the 0° cue position. Histogram binwidth is 15 ms. C: activity in conjunction with spontaneous saccades made during the intertrial interval (ITI) and having the 0 ± 15° or 225 ± 15° directions. Although the histograms represent 28 saccades for the 0° direction and 18 for the 225° direction, raster lines are shown only for the last 14 saccades of each. Histogram binwidth is 15 ms.
FIG. 6. Directional tuning of saccade-related activity for 5 principal sulcus neurons in the oculomotor delayed-response task. Plots show discharge rate during the response period for the 8 different cue directions, with a Gaussian function fit to the data. Rate for each saccade direction was measured during the 100 ms period starting at the neuron’s response latency for its best direction. Visual cues were presented at 1 of the 8 directions randomly, always at 13° eccentricity, and each data point represents the average of 6–10 trials. A: directional tuning for 2 principal sulcus neurons with presaccadic activity. Neuron 5210.0 (left hemisphere) has narrowly tuned (T_d = 17°) excitatory presaccadic activity with its best direction at −78°. Neuron 7093.2 (right hemisphere) has broadly tuned (T_d = 56°) excitatory presaccadic activity with its best direction at 127°. B: 3 examples of directional tuning for principal sulcus neurons with postsaccadic activity. Neuron 5270.0 (left hemisphere) has narrowly tuned (T_d = 19°) excitatory postsaccadic activity with its best direction at −26°. Neuron 5078.0 (right hemisphere) has moderately tuned (T_d = 36°) excitatory postsaccadic activity with its best direction at 119°. Neuron 5258.0 (left hemisphere) has broadly tuned (T_d = 86°) excitatory postsaccadic activity with its best direction at 0°.
Histology

After 2–8 mo of nearly daily recording sessions, the monkeys were killed with an overdose of pentobarbital sodium and perfused with saline followed by buffered Formalin. The brains were photographed. Frozen coronal sections were taken and stained with thionin. Individual recording sites that had been marked with electrolytic lesions (20 μA, 10–15-s, tip negative) or iron deposits (tip positive for elgiloy electrodes) were identified. However, the long duration of recording and large number of electrode penetrations precluded identification of most penetrations, and their locations in the brain were estimated from their microdrive coordinates relative to identified penetrations.

RESULTS

General

The activity of 434 PS and 53 FEF neurons recorded from six hemispheres of four rhesus monkeys was quantitatively analyzed. At some sites the FEF classification was confirmed by low thresholds (<50 μA) for eliciting saccadic eye movements by microstimulation (Bruce et al. 1985). Data for PS and FEF neurons are presented separately. Among 434 PS neurons, 147 (34%) exhibited saccade-related responses while monkeys performed the ODR task. We classified as saccade-related activity any excitatory or inhibitory activity occurring within the 0.5-s response period of the ODR task or during the period up to 0.5-s after the termination of the saccadic eye movement made in the response period. Because such activity was almost always directionally selective, as will be described below, it is almost certainly related to the saccadic eye movement. If such activity were only related to the disappearance of the fixation target, to the impending reward delivery, to the sound of the reward, or to the reward itself, it would likely be omnidirectional. When omnidirectional saccade-related activity was observed, we always ascertained whether or not the same response occurred in relation to free rewards to exclude purely reward-related activity from this sample.

The latencies of the 147 PS neurons with saccade-related activity were analyzed by constructing cumulative histograms aligned at the initiation of the eye movement. The response latency was defined as the time from the initiation of the saccadic eye movement to the start of the activity. Figure 2A shows the distribution of latencies, according to the cue direction yielding the largest response for each neuron. These latencies were distributed from -192 to 460 (85 ± 130-ms, mean ± SD; median, 72-ms). On the basis of these latencies, PS neurons with saccade-related activity were classified into two groups: neurons with presaccadic activity (latency <0-ms) and those with postsaccadic activity (latency ≥0-ms). However, the distribution appears to be unimodal and its mode is 0–50-ms, indicating that many PS neurons classified as having postsaccadic activity actually begin responding during the saccade (perisaccadic).

Presaccadic activity

Among 147 PS neurons having saccade-related activity in the ODR task, 33 (22%) began responding before the initiation of the saccadic eye movements and, therefore, were classified as having presaccadic activity. Of the 33 PS neurons with presaccadic activity, 29 showed excitation and 4 showed inhibition. The mean presaccadic latency was -73 ± 43 (SD) ms (n = 33) with a median of -57 ms.

All but 1 of the 33 PS neurons with presaccadic activity exhibited directional selectivity in that they had significantly different response magnitudes for different directions of saccadic eye movements. The remaining PS neuron was omnidirectional, exhibiting similar activity for all saccade directions.

Figure 3 is an example of a PS neuron with presaccadic activity in the 90°, 135°, and 180° trials. Its latency was -60-ms at the 135° direction (Fig. 3B). The same neuron also had excitatory post-saccadic activity in the 0, 45, 270, and 315° trials, these directions being approximately opposite to those with presaccadic activity. Such opposing pre- and postsaccadic activation was observed in 17 (53%) PS neurons with presaccadic activity.
A Pre-saccadic activity

B Post-saccadic activity

FIG. 8. A: polar plots of the best directions of presaccadic activity in the oculomotor delayed-response task for 13 principal sulcus neurons. B: polar plots of the best directions of postsaccadic activity in the oculomotor delayed-response task for 61 principal sulcus neurons. Best directions were determined by the parameter \(D\) of the Gaussian function tuning curve fit. Best directions of right hemisphere neurons were transformed into mirror-image directions, as if all neurons were recorded from the left hemisphere. Notice the contralateral bias, especially for the presaccadic data.

DIRECTIONAL SELECTIVITY. To quantitatively analyze the directional selectivity of presaccadic activity, we constructed, by their best fit to the Gaussian function, tuning curves of 13 PS neurons that showed directional presaccadic activity under the eight-cue condition in the ODR task. Figure 6A shows the tuning curves of two PS neurons: a narrowly tuned neuron (5210, \(T_d = 17^\circ, D = -78^\circ\)) and a broadly tuned neuron (7093, \(T_d = 56^\circ, D = 127^\circ\)). For all PS neurons, tuning indexes \((T_d\) in the formula) were distributed from 17 to 130\(^\circ\), the median index was 48\(^\circ\), and the mean \pm SD was 51 \pm 35\(^\circ\) (Fig. 7A).

The tuning curves also provided estimates of each neuron’s best direction for saccade-related activity (\(D\) in the formula). Figure 8A shows polar plots of best directions for 13 PS neurons with presaccadic activity in the ODR task. Best directions of eight PS neurons (61\%) were directed toward the visual field contralateral to the recording hemisphere. Three PS neurons had best directions ipsilateral to the recording hemisphere, and the other two PS neurons had best directions along the upper (90 \pm 10\(^\circ\)) and lower (270 \pm 10\(^\circ\)) meridian. This contralateral bias was not statistically significant.

Postsaccadic activity

Most PS neurons with saccade-related activity exhibited postsaccadic responses. As mentioned above, 17 expressed both pre- and postsaccadic activity in approximately opposite directions (Fig. 3); however, a much greater number (114 PS neurons, 77\% of all saccade-related neurons), exhibited only postsaccadic activity. The mean postsaccadic response latency was 131 \pm 109 (SD) ms and the median was 122 ms.

As with presaccadic activity, most (105, 92\%) of the 114 PS neurons with solely postsaccadic activity showed directional postsaccadic activity, with the remaining 9 (8\%) having omnidirectional postsaccadic activity. The neuron shown in Fig. 4 had phasic excitation only after saccades to the 135, 180, and 225\(^\circ\) directions. The latency for the 180\(^\circ\) direction was 110-ms (Fig. 4B), and the response latencies at the 135 and 225\(^\circ\) directions were similar.

Of 114 PS neurons with only postsaccadic activity, 75 showed only excitation and 18 showed only inhibition. However, the other 21 neurons showed a reciprocal response in their directional activity: excitatory postsaccadic responses occurred for some directions, whereas inhibitory postsaccadic responses occurred at roughly opposite directions. Figure 5 is an example of a PS neuron that exhibited phasic excitation after the initiation of 0, 45, 90, and 315\(^\circ\) saccades, with maximum activity at the 0\(^\circ\) direction and a mean latency of 0-ms (Fig. 5B). The same neuron showed an inhibition after saccades in the 225 and 270\(^\circ\) directions.

TABLE 1. Comparison of directional selectivity among cue-, delay-, and response-period activity

<table>
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<tr>
<th></th>
<th>Contralateral</th>
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<th>Vertical</th>
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<td>7</td>
<td>62</td>
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<tr>
<td>Delay period</td>
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<td>13</td>
<td>46</td>
<td>Funahashi et al. 1989</td>
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<td>Response period</td>
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<td>12</td>
<td>74</td>
<td>Present study*</td>
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<tr>
<td>Total</td>
<td>106</td>
<td>44</td>
<td>32</td>
<td>182</td>
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</tbody>
</table>

* Sum of pre- and postsaccadic activity.
A ODR task

B VGS task

FIG. 9. An example of a principal sulcus neuron (5231, left hemisphere) that responded similarly in the oculomotor delayed-response (ODR) task and the visually guided saccade (VGS) task. A: directional post-saccadic activity during the ODR task. This neuron had phasic excitatory post-saccadic responses for the 180, 225, and 270° directions and also had phasic inhibitory post-saccadic responses for the 0 and 45°. Response latency was 95 ms after saccade initiation at the 225° direction. Histogram binwidth is 15 ms. B: activity during the VGS task. Although the responses were weaker, excitatory responses still followed saccades at the 180, 225, and 270° directions. However, the inhibitory post-saccadic responses for the 0 and 45° directions in the ODR task disappeared, and instead, weak excitatory presaccadic responses were present for the 0° direction. Rasters and histograms in both A and B are aligned at the initiation of saccades. In both tasks, visual cues were randomly presented at 1 of the 8 locations indicated in the central diagram, and all cue eccentricities were ±15°. Histogram binwidth is 15 ms.
1. ODR task

![Graphs showing activity patterns during ODR task](image)

2. VGS task

![Graphs showing activity patterns during VGS task](image)

3. ODR task

![Graphs showing activity patterns during ODR task](image)

Although the proportion of contralateral directions was slightly higher for the presaccadic activity, a $\chi^2$ test revealed that the proportions of contralateral, ipsilateral, and vertical directions did not differ significantly between the pre- and postsaccadic activity. However, there is an overall decrease in the proportion of contralateral directions across the three periods of the ODR task (cue, delay, and response), as shown in Table 1. For the response period data in Table 1, we combined pre- and postsaccadic samples. The cue and delay period data are taken from our previous papers (Funahashi et al. 1990 and 1989, respectively). We compared the directionality across all three periods, again using a $\chi^2$ test, and found a statistically significant difference in their distributions ($\chi^2 = 11.93$, df = 4, $P < 0.05$).

When the individual periods are compared with each other, the directionality of the cue period activity significantly differs from that in the response period ($\chi^2 = 6.36$, df = 2, $P < 0.05$). Comparisons of the delay period activity with the cue period activity that precedes it and with the saccade-related activity that follows it both fail to achieve statistical significance. Overall, it appears that the contralateral bias...
SACCade-RELATED ACTIVITY IN THE PREFRONTAL CORTEX

of the activity decreases with temporal distance from the visual cue.

Saccade-related activity in VGS tasks

Among the 147 PS neurons with saccade-related activity in the ODR task, 60 were also examined in one of the three VGS tasks (VGS-I, VGS-II, or VGS-III).

Forty PS neurons (5 with presaccadic activity and 35 with postsaccadic activity) exhibited similar saccade-related activity across tasks. For example, in the ODR task, the neuron shown in Fig. 9 had phasic excitatory responses after saccades to the 180, 225, and 270° locations and phasic inhibitory responses after saccades to the 0 and 45° directions. The response latency was 98-ms in both cases (Fig. 9A). However, in the VGS task, the phasic excitatory responses at 180, 225, and 270° were weaker, and the inhibitory responses at 0 and 45° disappeared (Fig. 9B).

Thirteen PS neurons (7 with presaccadic activity and 11 with postsaccadic activity) exhibited saccade-related activity only in the ODR task, and no saccade-related activity was observed for any direction in the VGS tasks. Figure 10 shows an example of a PS neuron in which directional saccade-related activity (\( D = 271°, T_d = 10° \)) was observed in the ODR task under the four-cue condition (Fig. 10, J and 3) but not in the VGS task (Fig. 10-2).

The remaining seven PS neurons had only postsaccadic activity in the ODR task but exhibited some presaccadic activity in the VGS task. These neurons tended to have visual responses to the cue in the ODR task.

DIRECTIONAL SELECTIVITY. To quantitatively assess the similarity in the directional selectivity of saccade-related activity between the ODR and VGS tasks, we constructed tuning curves for 35 PS neurons examined under the eight-cue condition in both tasks and compared their best direc-

FIG. 11. Top: comparison of the directional tuning of saccade-related activity in the oculomotor delayed-response (ODR) task vs. the visually guided saccade (VGS) task for 2 principal sulcus neurons. Plots show responses for the 8 different directions, with the Gaussian function fit to both sets of data. Response for each cue direction was measured by discharge rate during the 100-ms period beginning at the response latency of the neuron's best direction. A: this neuron (5231, left hemisphere) has very similar tuning specificity and best direction across tasks (ODR \( T_d = 35°, D = 219° \); VGS \( T_d = 47°, D = 213° \)). B: this neuron (5244, left hemisphere) has different best directions but similar tuning across tasks (ODR \( T_d = 18°, D = 286° \); VGS \( T_d = 23°, D = 0° \)). Bottom: scattergrams of best directions (C) and tuning indexes (D) for saccade-related activity in the ODR task and in the VGS task. Data were obtained via tuning curves for 35 principal sulcus neurons that had all been examined under the 8-cue condition for both tasks. The correlation for the best directions was strongly positive (\( r = 0.751 \)), that for the tuning indexes was not (\( r = 0.057 \)). E: scattergram based on the peak discharge rates (100-ms period) of saccade-related activity in the ODR task and those in the VGS task. Data were obtained via tuning curves for 35 principal sulcus neurons that had all been examined under the 8-cue condition for both tasks. There was a significant positive correlation (\( r = 0.587 \)) of the peak discharge rates between 2 tasks.
A ODR task (PS neurons)

B VGS task (PS neurons)

FIG. 12. A: polar plots of the best directions of both pre- and postsaccadic activities in the oculomotor delayed-response task for 74 principal sulcus neurons. B: polar plots of the best directions in the visually guided saccade task for 35 principal sulcus neurons. No clear contralateral bias of best directions was observed in either task. Best directions were determined by the parameter \( (D) \) of the Gaussian function tuning curve fit. Best directions of right-hemisphere neurons were transformed into their mirror-image directions, as if all neurons were recorded from the left hemisphere.

**Response Magnitude.** The magnitude of saccade-related responses in the ODR and VGS tasks was very similar. Magnitude of saccade-related activity for each task in individual PS neurons was defined as the maximum discharge rate over a 100-ms epoch of the 1-s period after the disappearance of the fixation target at the best response direction for the neuron during that task. Figure 11E is a scatter plot of the saccade-related response magnitudes in both tasks for 35 PS neurons examined; the positive correlation \( (r = 0.587) \) between the two activities was observed across neurons. The mean saccade-related response \( (36.7 \pm 21.9 \text{ spikes/s}) \) for 35 PS neurons in the ODR task did not differ significantly from that \( (34.3 \pm 25.0 \text{ spikes/s}) \) in the VGS task.

Saccade-related activity during spontaneous saccades in the ITI

An important issue in oculomotor control is the dependence of neuronal activity on the “meaning” or “purpose” of the response. To address this issue, we examined whether PS neurons with saccade-related activity in the ODR task showed comparable responses and directional selectivity during spontaneous saccades in the ITI. Note that both types of saccades are made in the dark. The amplitude tolerance \( (4-39^\circ) \) and the directional tolerance \( (-15^\circ) \) were chosen to select saccades made in the ITI comparable with those associated with the largest saccade-related activity in the response period of the ODR task, and then rasters and histograms of neuronal activity aligned with the initiation of the selected spontaneous saccades were constructed.

Forty-nine PS neurons with either pre- or postsaccadic activity were selected and examined with the use of this procedure. Neither neurons with presaccadic activity nor those with postsaccadic activity showed activity in relation to spontaneous saccades comparable with their saccade-related activity in the ODR task. As shown in Figs. 3C, 4C, and 5C, although some PS neurons exhibited response patterns for spontaneous saccades similar to those for rewarded saccades, their response magnitudes during spontaneous saccades were always weak compared with those observed during rewarded saccades. Figure 13 shows other PS neurons (e.g., neurons 3028 and 7093) with excitatory presaccadic activity in relation to rewarded saccades but with no discernible activity in relation to spontaneous saccades of the same direction. Similarly, neurons 3025 and 3006 in Fig. 13 had postsaccadic activity in relation to rewarded saccades but not in relation to spontaneous saccades.
FIG. 13. Activity of 4 principal sulcus neurons in relation to saccadic eye movements made in the response period of the oculomotor delayed-response (ODR) task (rewarded saccades) and to spontaneous saccades made during the intertrial interval (ITI). Rasters and histograms of rewarded saccades were constructed from trials for the cue direction having the best response in the ODR task. Rasters and histograms during spontaneous saccades were constructed from ITI saccades having comparable amplitude (6.5°–26°) and directed in the neuron's best directions (±15°). Histogram binwidth is 15 ms.
FIG. 14. Composite histograms for 2 principal sulcus neurons in conjunction with rewarded saccades (left) and spontaneous saccades during the intertrial interval (ITI, right). Composite histograms on the left represent 56 (neuron 5229) and 39 (neuron 5204) rewarded saccades. Those on the right represent 117 (neuron 5229) and 126 (neuron 5204) saccades in the ITI with comparable amplitudes (6.5-26°) as the rewarded saccades. Notice that neuron 5229 (left hemisphere) had presaccadic activity in conjunction with rewarded saccades, whereas neuron 5204 (left hemisphere) had postsaccadic activity. However, no response was observed in either neuron in conjunction with spontaneous saccades made during the ITI. Histogram binwidth is 15 ms.

Scored at the initiation of all spontaneous saccades in the ITI with amplitudes comparable with rewarded saccades (6.5-26°). As shown in Fig. 14, clear presaccadic (neuron 5229) or postsaccadic activities (neuron 5204) were observed when rewarded saccades were made but not in relation to spontaneous saccades. All 147 PS neurons with saccade-related activity in the ODR task were analyzed by this method, and no PS neuron showed comparable activity in relation to spontaneous saccades. Therefore it appears that PS neurons have substantial activity in relation to purposeful saccades but no or very weak activity in relation to spontaneous saccades.

Saccade-related activity in FEF

Of 53 neurons recorded from the FEF, 26 (49%) had saccade-related activity in the response period of the ODR task. Of these, 23 (89%) showed excitation and 3 (11%) showed only inhibition. The latency of FEF activity in relation to saccade initiation was distributed from -123 to 312 ms, as shown in Fig. 2. The overall mean latency was 70 ms, with 11 FEF neurons (42%) having presaccadic responses and the remaining 15 (58%) classified as postsaccadic. The mean latency of the FEF sample did not significantly differ from the mean latency of our PS sample (85 ms); however, the proportions of pre- and postsaccadic cells did differ significantly, indicating that FEF neurons are more likely than PS neurons to have presaccadic activity in the ODR task ($\chi^2 = 4.594$, df = 1, $P < 0.05$).

The saccade-related activity of all 26 FEF neurons was directional. Tuning indexes ($T_d$) of 18 FEF neurons that were tested under the eight-cue condition were distributed between 4° and 107° (Fig. 7). The mean $T_d$ was $36 \pm 27°$ (SD) and the median was 34°. Although the mean tuning index of FEF neurons was narrower than that of PS neurons (43°), the difference was not statistically significant. Most best directions ($D$) (13/18) were toward the visual field contralateral to the hemisphere from which the neurons were recorded; the best directions of 4 FEF neurons were toward the ipsilateral visual field, and the remaining FEF neuron had its best direction along the vertical meridian (270°). This contralateral bias was statistically significant ($\chi^2 = 4.765$, df = 1, $P < 0.05$).

Six FEF neurons with saccade-related activity were also examined under the VGS task. All six showed very similar saccade-related activity in the ODR and VGS tasks, with comparable best directions and tuning indexes across tasks.

Cortical distributions of neurons with pre- and postsaccadic activity

Figure 15 illustrates the locations of all penetrations and also depicts the approximate locations of neurons with pre- and postsaccadic activity in each of the six hemispheres.
Post-saccadic activity
Pre- and post-saccadic activity

FIG. 15. Tracings of the frontal cortex showing locations of electrode penetrations for the 4 monkeys (monkeys 2, 3, 5, and 7) studied. Perspective of the tracings is approximately normal to the dorsolateral prefrontal cortical surface, roughly midway between standard lateral and dorsal views. Black circles indicate surface locations of electrode penetrations where neurons with post-saccadic activity were found. Gray circles indicate surface locations where both neurons with pre- and post-saccadic activities were found. PS, principal sulcus; AS, arcuate sulcus.

Saccade-related activity in the prefrontal cortex

Historically, a rather large area of the prefrontal cortex was considered the FEF. For example, Wagman et al. (1961) elicited contralateral eye movements from virtually the entire PS as well as from the full extent of the arcuate sulcus. However, the prefrontal area, from which eye movements can be elicited with $\leq 50 \mu A$ intracortical stimulation, is a much smaller zone largely confined to the anterior bank of the arcuate sulcus (Bruce et al. 1985). Moreover, a high percentage of neurons in this region respond in conjunction with saccadic eye movements, with many having discharges that precede purposive saccades made with or without visual guidance (Bruce and Goldberg 1985). Consequently, recent studies (e.g., Huerta et al. 1987; Stanton et al. 1989) consider this low-threshold zone to be the true FEF. Schlag and Schlag-Rey (1987) provide a more historical view of this “shrinkage” of the FEF and introduce a zone of mesial frontal cortex, the SEF, which has physiological properties similar to those of the FEF, including low electrical thresholds for eliciting saccades.

The present study provides further evidence, however, that cortex in the PS and surrounding cortex also participates in oculomotor control, possibly by influencing FEF, with which it is connected (Barbas and Mesulam 1981; Huerta et al. 1987; Selemon and Goldman-Rakic 1988), and also through connections with SEF (Huerta and Kaas 1990), the posterior parietal cortex (Cavada and Goldman-Rakic 1989; Pandya and Kuypers 1969), the basal ganglia (Goldman and Nauta 1977; Selemon and Goldman-Rakic 1985), or the superior colliculus (Goldman and Nauta 1976; Leichnetz et al. 1981). Moreover, the present study also provides data concerning FEF activity during memory-guided saccades and thus helps clarify how, in the context of the ODR task, the activity of PS neurons is similar to that of FEF neurons, as well as how saccade-related activity in these two parts of prefrontal cortex differs.

Saccade-related activity related to mnemonic function

As mentioned in the INTRODUCTION, involvement of PS neurons in memory-guided manual responses is well established (for review, see Fuster 1989; Goldman-Rakic 1987). The present evidence clearly shows that the role of PS neurons in memory-guided behavior extends to the oculomotor system as well. As with manual delayed-response tasks, neurons in and around PS are selectively activated in rela-
tion to the visual cue (Funahashi et al. 1990), in relation to the delay (Funahashi et al. 1989) and, as shown in the present study, in relation to oculomotor behavior. Further, in manual delayed-response tasks, many neurons exhibit responses to more than one event in the task (e.g., Fuster 1973), and our present and previous analyses of neuronal activity reveal that a similar variety of activation patterns characterizes prefrontal neurons in relation to the ODR task. This degree of correspondence between the response characteristics of PS neurons in manual and oculomotor tasks is remarkable and provides a strong case for a comprehensive role of PS neurons in memory-guided behavior. These findings further suggest that the principles and mechanisms that apply to one task may generalize to the other. Nevertheless, the special features of the ODR task and associated data analysis systems we have employed allowed us to discover, among other things, several features of PS activity that previously were not readily accessible or prominent in studies employing manual paradigms. These include 1) a dissociation between pre- and postsaccadic activity, 2) a temporal relation between postsaccadic activity and the delay-period activity, 3) opponent response activation patterns in single neurons, and 4) context dependency. Each of these points is discussed in further detail below.

Context dependency in saccade-related activity of PS neurons

An important feature of saccade-related activity in PS neurons, and one that may be characteristic of PS, is that both pre- and postsaccadic activities are context dependent, i.e., PS neurons showed saccade-related responses only when the monkey performed purposive saccades leading to the reward. Both pre- and postsaccadic activities in PS neurons were much reduced or absent in relation to spontaneous saccades: neuronal responses were not comparable with those recorded in association with rewarded saccades in the ODR task. This contrasts with FEF neurons, which show context dependency only for presaccadic responses (Bruce and Goldberg 1985). Context-dependent presaccadic activity has also been reported in the posterior parietal cortex (area 7a) (Lynch et al. 1977), the caudate nucleus (Hikosaka et al. 1989), and the substantia nigra (Hikosaka and Wurtz 1983b). In all these structures, most neurons displaying presaccadic activity in conjunction with rewarded saccades respond weakly or not at all in conjunction with spontaneous saccades of the same direction and magnitude. As discussed earlier, PS is directly connected with each of these structures (for further review, see Goldman-Rakic 1988).

Few differences emerged in the activity patterns in conjunction with sensory-guided versus memory-guided saccades in the present study. The great majority of PS neurons exhibited postsaccadic activity with similar directional selectivity and response magnitude in relation to both types of saccade. This finding must be interpreted cautiously because our sampling procedure may have biased the results. We examined neuronal activity in the VGS tasks only if they exhibited saccade-related activity in the ODR task. Thus we did not test neuronal activity in both tasks randomly and probably undersampled neurons that were active only in the VGS tasks. As lesion studies show that the PS area is critical in memory-guided responses, we could expect that the saccade-related activity in PS neurons might be greater in memory-guided relative to sensory-guided tasks. On the other hand, because the caudal PS region is a component of a larger network of cortical areas, including FEF, SET, and the posterior parietal cortex (Selemon and Goldman-Rakic 1988), it is reasonable that PS neurons reflect activity patterns in the extended circuit without playing an obligatory or decisive role in sensory-guided behaviors. Finally, saccade-related activity may not be what best distinguishes the prefrontal cortex from other cortical or subcortical structures. A significant challenge for future studies will be to determine both the function and source of oculomotor signals of PS neurons.

Postsaccadic activity

Most PS neurons with response-period activity in the ODR task exhibited only postsaccadic activity, i.e., neuronal activation began at the same time or well after the initiation of saccadic eye movements. The median latency of postsaccadic activity was 122 ms. Because the mean duration of the saccadic eye movements in the ODR task was 44.9 ± 7.6 (SD) ms (Funahashi et al. 1989), most postsaccadic activity in PS commences >50 ms after the completion of the saccadic eye movements.

Postsaccadic activity has been neglected in many reports, possibly because this activity could not have a direct role in the initiation of saccadic eye movements. In fact, postsaccadic activity has commonly been considered evidence of a corollary discharge from the structures directly responsible for movement (McCloskey 1981). However, the context dependency of the saccade-related activity of PS neurons indicates that this activity is not a corollary discharge from oculomotor structures in the brain stem. Postsaccadic activity of PS neurons was observed only in relation to rewarded saccades and was either weak or absent in relation to spontaneous saccades. In contrast, neurons in the oculomotor nuclei proper, in the brain stem premotor nuclei (Hepp et al. 1989), and in the superior colliculus (Sparks et al. 1976; Sparks and Mays 1980) are active before and during every saccade into their response fields, regardless of whether it is rewarded or spontaneous. In this regard, the postsaccadic activity of PS neurons differs from postsaccadic activity in the inferior and lateral pulvinar (Robinson et al. 1986) and in the FEF (Bizzi 1968; Bizzi and Schiller 1970; Bruce and Goldberg 1985; Bruce et al. 1985); postsaccadic activity in these structures is more likely to be a corollary discharge because it occurs after every saccade into a neuron's response field.

A possible source of postsaccadic activity in PS neurons could be the feedback loop originating in the cerebral cortex, passing through the basal ganglia and the thalamus, and terminating in the corresponding cerebral cortex (Alexander et al. 1986). Saccade-related activity has been recorded both in the caudate nucleus and in the substantia nigra pars reticulata, and, like PS neurons, these neurons appear to be active only during purposive saccades (Hikosaka et al. 1989; Hikosaka and Wurtz 1983a,b). It is of interest that activity in nigral neurons is suppressed during saccadic eye movements (Hikosaka and Wurtz 1983a,b).
The suppression of nigral neurons during the saccade disinhibits cells in the superior colliculus and hence facilitates the initiation of saccades (Hikosaka and Wurtz 1983c). The substantia nigra also projects to the mediodorsal nucleus of the thalamus (Illinsky et al. 1985), which, in turn, has direct connections with PS (Giguere and Goldman-Rakic 1988; Goldman-Rakic and Porrino 1985; Tobias 1975). As in the case of the nigrocollicular circuit, suppression of nigral during saccades would disinhibit thalamic neurons and hence facilitate thalamocortical transmission (Buee et al. 1986). One possibility, therefore, is that postsaccadic activation of PS neurons is via this circuit.

Another source of postsaccadic activity in PS neurons could be other cortical structures that are similarly context dependent. Unlike postsaccadic activity, the presaccadic activity in FEF is context dependent (Bruce and Goldberg 1985). This is also the case in the posterior parietal cortex (Lynch et al. 1977). Therefore the context-dependent, saccade-related activity in PS neurons could derive, in part, from the context-dependent, presaccadic activity in the FEF and the posterior parietal cortex, assuming a transmission delay because the average latency of saccade-related activity in PS neurons is delayed relative to presaccadic activity in these structures.

Functional significance of postsaccadic activity in the delayed-response task

What is impressive about the postsaccadic activity of PS neurons recorded in the present study is that most of these were directional as well as context dependent. Such postsaccadic activity could clearly be important for correct performance in delayed-response tasks. In the ODR task, holding spatial information "on line" as directional delay-period activity is essential for the monkey to direct his eye movements correctly at the end of the delay (Funahashi et al. 1989). However, such directional delay-period activity is no longer necessary once a saccade eye movement has been made and may even be counterproductive if it persists into the next trial, because in delayed-response tasks the subject is required to refresh his memory on each new trial. As described in our previous report (Funahashi et al. 1989), both excitatory and inhibitory delay-period activities were actively terminated immediately after the subject made saccadic eye movements. Postsaccadic activation observed in PS neurons may be a neuronal signal from brain areas responsible for the initiation of purposive saccades and may play a critical role in terminating delay-period activity.

Comparison between pre- and postsaccadic activity

Surprisingly, the pattern of context dependency of the saccade-related activity of PS neurons found in the present study is quite different from that previously reported in FEF neurons. As described before, we found that all saccade-related activity of PS neurons, both pre- and postsaccadic activity, was highly context specific. The presaccadic activity in FEF is similarly context specific (Bruce and Goldberg 1985). However, the postsaccadic activity in FEF follows saccades into the neuron’s movement field in all contexts: spontaneous, visually guided, or memory-guided saccades (Bruce and Goldberg 1985; Bruce et al. 1985) and even in the quick phase of nystagmus (Bizzi 1968). Thus, although postsaccadic activity in FEF could well derive from a corollary discharge of oculomotor commands in the brain stem, our data indicate that postsaccadic activity in PS probably does not. However, the context-dependent saccade-related activity in PS neurons logically could derive from the context dependent presaccadic activity in FEF.

We cannot dismiss the possibility that the pre- and postsaccadic activity of PS neurons represent extremes of a single continuum activity rather than two distinct classes of responses. Apart from their difference in latency, they are very similar in most other respects: 1) they have similar directionality, both exhibiting a weak bias for contralateral directions; 2) despite our classification into pre- and postsaccadic activity, the latency distribution appears to be unimodal, and the saccade-related activity of many PS neurons actually commences during the saccade; and 3) pre- and postsaccadic activity are similarly dependent on behavioral context, as just discussed. Therefore, in contrast to the hypothesized separate functions and origins for pre- and postsaccadic activity of FEF neurons (e.g., Bruce 1990; Goldberg and Bruce 1990), our data leave open the possibility that the pre- and postsaccadic activity of PS neurons may have a common but temporally extended function that is not understood at present.

Directional selectivity of saccade-related activity

More than 90% of the PS neurons exhibiting pre- and postsaccadic activity were directional; each PS neuron had a different "best direction." Although the population of PS neurons in one hemisphere appeared to be responsive over the entire visual field (see Fig. 124), many of the best directions for both pre- and postsaccadic activities were toward the visual field contralateral to the hemisphere from which the neuron was recorded. Slightly stronger contralateral bias was observed in presaccadic activity than in postsaccadic activity (62 and 48%, respectively).

Directional selectivity and contralateral bias in saccade-related activity have been observed in other brain areas. The majority of neurons with presaccadic activity in FEF have contralaterally directed optimal saccades, and contralateral directions were represented in each hemisphere (Bruce and Goldberg 1985). Although our sample size is small, our FEF samples also showed significant contralateral bias. Contralateral bias in saccade-related activity has also been observed in SEF (Schlag and Schlag-Rey 1987), in the posterior parietal cortex (Andersen et al. 1987; Lynch et al. 1977), in the caudate nucleus (Hikosaka et al. 1989), and in the superior colliculus (Sparks et al. 1976; Sparks and Mays 1980; Wurtz and Goldberg 1972).

However, the contralateral bias of saccade-related activity of PS neurons is fairly weak in comparison with the overwhelming contralaterality of neuronal activity of oculomotor structures like the superior colliculus and FEF. Moreover, as documented in Table 1, the saccade-related activity of PS neurons is also less contralaterally biased than the cue-period and delay-period activity occurring earlier in the ODR task. Overall, there is a tendency for activity of PS neurons during the ODR task to become more bilaterally symmetrical as it progresses from the cue period, through
the delay period, and finally to the response period. In part, this could reflect an internal processing within the PS cortex, because there are strong callosal connections between the left and right PS (Goldman-Rakic and Schwartz 1982; Schwartz and Goldman-Rakic 1984). We suppose that the cue-period activity of PS neurons represents the registration of spatial task information, that the sustained delay-period activity represents a short-term memory for this information, and that the response-period activity represents a read-out of this information, including feedback from other brain areas confirming that such a readout took place. The progressive change in laterality at each stage reemphasizes that these are active processes that involve substantial communication between neurons in many areas, including communication across the two hemispheres. The diminishing laterality may also reflect the fact that the PS region is critical for the guidance of hand and arm movements, as well as oculomotor behavior, during the performance of spatial delay tasks and that PS is connected with the supplementary motor area (SMA), where such manual responses are bilaterally represented (Brinkman and Porter 1979). In this regard, we should also note that the directionality of the saccade-related activity agrees with earlier PS recordings during manual delayed-response tasks (Fuster 1973; Niki 1974c) insomuch as these investigators found relatively little contralateral bias of PS activity. Quantitative data on the laterality of PS activity in manual tasks involving multiple cue locations and control of fixation could clarify these issues.

**PS neurons with opponent responses for opponent directions**

Several PS neurons exhibited different responses for opposing saccade directions. One example was a subset of PS neurons that exhibited complementary pre- and post-saccadic activation at roughly opposite directions (e.g., Fig. 3). These neurons could initiate or trigger saccades to their best directions and also receive a feedback signal as post-saccadic activity when the monkey made saccadic eye movements to opposite directions. As the monkey usually made a subsequent saccade to the central location where the fixation target for the next trial would appear, it is possible that the post-saccadic activity for the opposite direction might be a presaccadic response for making an eye movement back to the fixation target. However, as shown in Fig. 3C, the saccade-related activity of PS neurons was very context dependent and weak or absent in conjunction with spontaneous saccades in ITI, and thus post-saccadic activity of these PS neurons is not likely to be presaccadic activity for making an eye movement back to the fixation target during ITI.

Another example was a subset of PS neurons with only post-saccadic activity that exhibited reciprocal responses; excitatory post-saccadic responses occurred for some directions, whereas inhibitory post-saccadic response occurred at roughly opposite directions (e.g., Fig 5). Such reciprocity has been observed in motor systems, in sensory systems, and even in mnemonic responses in the prefrontal cortex (Funahashi et al. 1989). Such complementary or reciprocal responses for opposite directions could be a widely distributed strategy in the nervous system and could play as important a role in higher cortical function as in motor control and sensory perception.

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**REFERENCES**


SACCADE-RELATED ACTIVITY IN THE PREFRONTAL CORTEX


NIKI, H. Prefrontal unit activity during delayed alternation in the monkey. II. Relation to absolute versus relative direction of response. Brain Res. 68: 197–204, 1974b.


