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Neuronal Activity Related to Visually Guided Saccades in the Frontal Eye Fields of Rhesus Monkeys: Comparison With Supplementary Eye Fields

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SUMMARY AND CONCLUSIONS

1. The purpose of this study was to analyze the response properties of neurons in the frontal eye fields (FEF) of rhesus monkeys (*Macaca mulatta*) and to compare and contrast the various functional classes with those recorded in the supplementary eye fields (SEF) of the same animals performing the same go/no-go visual tracking task. Three hundred ten cells recorded in FEF provided the data for this investigation.

2. Visual cells in FEF responded to the stimuli that guided the eye movements. The visual cells in FEF responded with a slightly shorter latency and were more consistent and phasic in their activation than their counterparts in SEF. The receptive fields tended to emphasize the contralateral hemifield to the same extent as those observed in SEF visual cells.

3. Preparatory set cells began to discharge after the presentation of the target and ceased firing before the saccade, after the go/no-go cue was given. These neurons comprised a smaller proportion in FEF than in SEF. In contrast to their counterparts in SEF, the preparatory set cells in FEF did not respond preferentially in relation to contralateral movements, even though most responded preferentially for movements in one particular direction. The time course of the discharge of the FEF set cells was similar to that of their SEF counterparts, except that they reached their peak level of activation sooner. The few preparatory set cells in FEF tested with both auditory and visual stimuli tended to respond preferentially to the visual targets, whereas, in contrast, most set cells in SEF were bimodal.

4. Sensory-movement cells represented the largest population of cells recorded in FEF, responding in relation to both the presentation of the targets and the execution of the saccade. Although some of these sensory-movement cells resembled their counterparts in SEF by exhibiting a sustained elevation of activity, most of the FEF sensory-movement cells gave two discrete bursts, one after the presentation of the target and another before and during the saccade. Like their counterparts in SEF, the sensory-movement cells tended to be tuned for saccades into the contralateral hemifield, but this tendency was more pronounced in FEF than in SEF. The FEF sensory-movement cells discharged more briskly, with a shorter latency relative to the presentation of the target, than their counterparts in SEF. In addition, the FEF sensory-movement neurons reached their peak activation sooner than SEF sensory-movement neurons. Most FEF sensory-movement cells exhibited different patterns of activation in response to visual and auditory targets.

5. The pause-rebound cells that were identified in SEF were not observed as commonly in FEF. No further analysis was therefore possible.

6. Presaccadic movement neurons that discharged before goal-directed saccades were encountered in FEF. These cells comprised a similar proportion to that found in SEF. The presaccadic movement cells in FEF appeared to have smaller movement fields that were more restricted to the contralateral hemifield than were their counterparts in SEF. The temporal discharge characteristics of the presaccadic eye movement cells in FEF and SEF were not distinguishable, however.

7. Postsaccadic movement cells discharged specifically after saccades had been initiated. These comprised a significantly larger proportion than in SEF. They tended to respond best for targets in the contralateral hemifield. In addition, the onset of activity after the saccade was later in FEF than in SEF.

8. No cells were recorded in this study of FEF that were modulated according to eye position.

9. Although low-intensity (<50 μA) electrical microstimulation of SEF as well as of FEF evokes saccadic eye movements, the elicited eye movements have markedly different characteristics. Saccades evoked by microstimulation of FEF do not vary with eye position, whereas those evoked from SEF do. In addition, whereas prolonged stimulation of FEF often elicits a series of saccades all of the same vector, prolonged stimulation of most sites in SEF elicits a single saccade to a particular orbital position followed by maintained fixation.

10. No cells were encountered that discharged specifically in no-go trials that required withholding the saccade. However, preparatory set cells and sensory-movement cells in FEF exhibited patterns of differential modulation in no-go trials that were not observed in SEF. Many of these neurons exhibited sustained activation after the no-go cue until the reward was delivered. In addition, the visual responsiveness of the phasic sensory-movement cells was attenuated if the no-go cue was presented simultaneously.

11. The results of this investigation indicate that, although there may be specific substantial differences between FEF and SEF, the two cortical areas also have much in common. On the one hand, it seems clear that FEF and SEF serve in parallel in generating goal-directed but not spontaneous saccades. On the other hand, both single-unit and microstimulation data suggest that SEF represents eye position in a more explicit fashion than FEF. Although there were several pieces of evidence showing that FEF responds more robustly and specifically to visual and auditory stimuli, it does not seem correct to make a rigid distinction between these two regions in terms of externally versus internally guided saccades. However, the results are consistent with the speculation that SEF may be more involved in regulating when a goal-directed saccade will occur, whereas FEF may be more involved in targeting and initiating the gaze shift.

INTRODUCTION

At least two regions in frontal cortex are involved in generating visually guided eye movements—the prearcuate frontal eye field (FEF) (reviewed by Bruce 1990; Goldberg

TABLE 1. *Cell types recorded in FEF*

Cell Type	Monkey *M*	Monkey *Q*	Total	%
Sensory	21	16	37	17
Preparatory set	5	7	12	5
Sensory movement	30	62	92	41
Pause-rebound	2	1	3	2
Presaccadic	29	21	50	22
Postsaccadic	11	19	30	13
Eye position	0	0	0	0
Suppressed	11	1	12	
Modulated but unclear	32	21	53	
Unmodulated/inactive	17	3	20	

Sensory cells responded to the visual and/or auditory stimuli. Preparatory set cells discharged from the appearance of the target until the presentation of the cue to execute or withhold the movement. Sensory-movement cells discharged in association with both the appearance of the target and the execution of the saccade. Seventy percent of these were transient sensory-movement cells, which exhibited 2 discrete bursts—1 for the target and 1 for the saccade. The remainder were sustained sensory-movement cells, which displayed a sustained elevation from the target until the saccade. Pause-rebound cells are suppressed at the appearance of the target and discharge at the saccade. Presaccadic cells burst before and during saccades. Postsaccadic cells discharged after saccades had been initiated. Eye position cells would be those for which discharge varied according to position of eye in orbit. Suppressed cells showed reduced activity during a trial but could not be otherwise characterized. Modulated but unclear cells showed some apparently systematic modulation during the trial, but insufficient data were collected to allow further analysis. Unmodulated/inactive cells did not discharge or did not modulate their activity during trial. FEF, frontal eye fields. Percentages represent values of task-specific modulated neurons.

and Segraves 1989; Schall 1991a) and the dorsomedial supplementary eye field (SEF) (Mann et al. 1988; Schall 1991b; Schlag and Schlag-Rey 1987). The presence of these two fields implies that each makes a unique contribution to visuomotor behavior. The first step in delineating the specific role of each area is to compare the patterns of neuronal activation in both regions. Thus this paper will report the results of a direct comparison between neuronal activity in FEF and SEF of rhesus monkeys making visually and auditory-guided saccadic eye movements under the same task conditions.

A preliminary report of some of these data has appeared (Schall et al. 1987).

METHODS

Two juvenile male rhesus monkeys (*Macaca mulatta*) provided the data for this investigation. They will be referred to as *M* and *Q*. These monkeys were also used for the SEF/supplementary motor area (SMA) recordings reported in the preceding paper. The animals were cared for in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals and the guidelines of the Massachusetts Institute of Technology Committee on Animal Care. The details of training, surgery, and data collection and analysis are described in the preceding paper. The reaching task was not used because preliminary results indicated that, at least in this paradigm, neural activity in FEF is not modulated any differently in relation to saccades made with or without forelimb movements.

RESULTS

A total of 85 penetrations into prearcuate cortex yielded 309 cells, 224 of which exhibited activity modulated in relation to some component of the task. The cells could be separated into various groups on the basis of their modulation in relation to the different events. The number of cells identified in the different groups is given in Table 1.

The locations of the penetrations made in the FEF that encountered visually responsive and saccade-related neurons in *monkeys M* and *Q* are shown in Fig. 1. Visually responsive neurons were found over a widespread area of the prearcuate gyrus, as observed previously (e.g., Suzuki and Azuma 1983). Presaccadic movement-related units were encountered over the same region, although they tended to be concentrated in the anterior bank of the arcuate sulcus, where low-intensity microstimulation evoked contraversive saccades. These results are in agreement with recent work that delimits FEF to the rostral bank of the arcuate sulcus (e.g., Bruce and Goldberg 1985; Bruce et al. 1985). However, neurons that discharged in association with saccadic eye movements were found on the crown of the gyrus.

Sensory cells

Sensory cells were distinguished by their discharge in response to visual or auditory stimuli combined with a lack of activation associated with the saccade. The neuron illustrated in Fig. 2 responded specifically to stimuli falling in

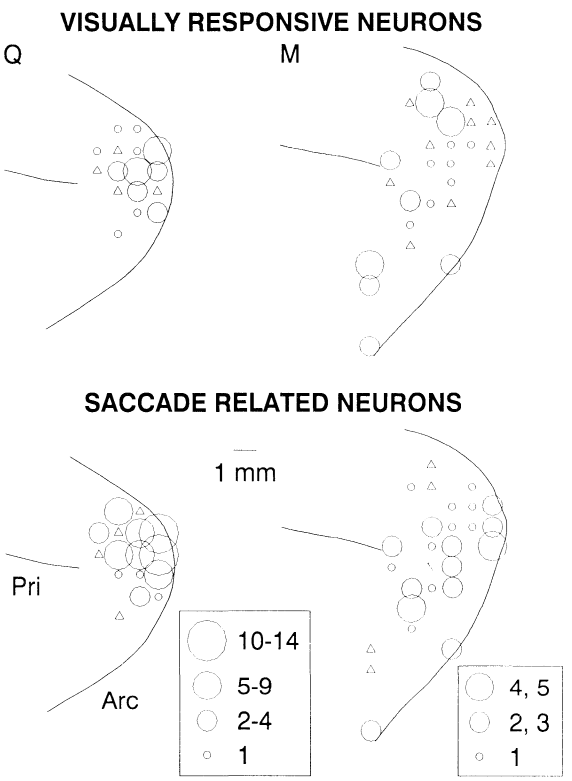

FIG. 1. Location of electrode penetrations in *monkeys M* (*right*) and *Q* (*left*). Arc, arcuate sulcus; Pri, principal sulcus. Rostral is *left* and lateral is *down*. Location of each penetration that encountered phasic and tonic visually responsive neurons is illustrated in the *top 2 panels*. Locations of penetrations that encountered neurons with a presaccadic burst are illustrated in the *bottom 2 panels*. Sizes of circles indicate numbers of units recorded at each site according to the respective legend for each monkey; triangles indicate penetrations in which none of these particular cell types were recorded.

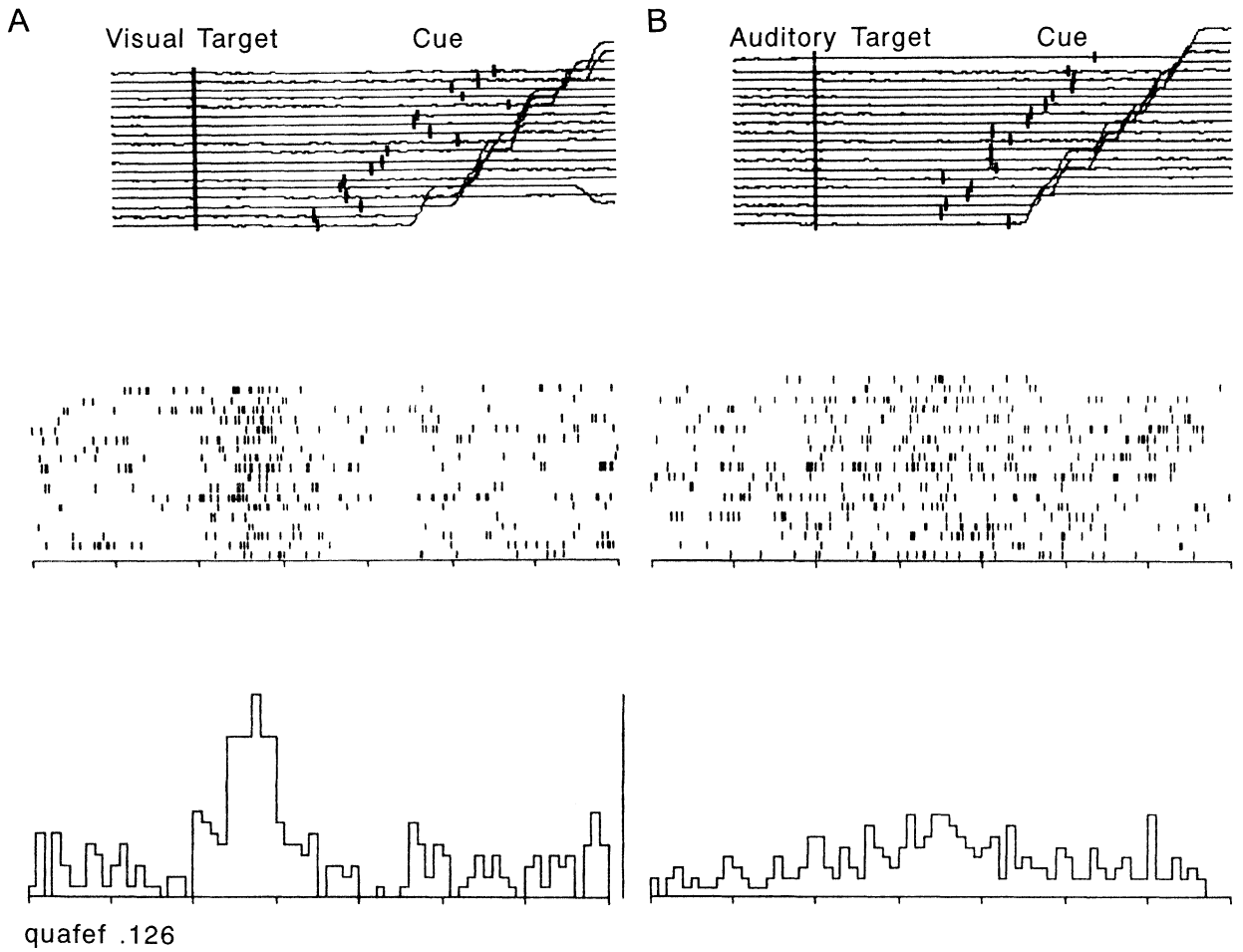

FIG. 2. Sensory visual cell. Responses to the contralateral visual (*A*) and acoustic (*B*) target are shown. Neuronal activity is illustrated in a raster and histogram of firing frequency. Eye position traces, raster, and histogram are aligned on the time of presentation of the target, indicated by the 1st tick mark in the eye position trace. The 2nd tick mark indicates the time of occurrence of the go cue, and the inflection in the eye movement trace is the saccade to the appropriate target. Each tick mark on the time scale represents 200 ms, and the histogram scale bar represents 50 Hz. Trials have been sorted for display according to the interval between presentation of the target and execution of the saccade.

the contralateral hemifield and was only minimally activated by the auditory stimulus. Also notice the consistency of the response compared with its more variable counterpart in SEF (Fig. 3 of Schall 1991b). Seventeen percent of the task-related cells recorded in FEF were sensory, which was similar to the 16% observed in SEF. Fourteen of the sensory cells included the fovea in their receptive field, and 10 of these did not respond to the peripheral targets, which indicates that their receptive fields extended <8° from the fovea.

Quantitative measures of FEF sensory cell responses are shown in Fig. 3. The relative responsiveness of the units to the targets in the different directions is shown in Fig. 3*A*. Cells with receptive fields restricted to the central light-emitting diode, of course, did not exhibit directional tuning. The mean ± SE response direction bias of these units was 0.07 ± 0.02. Although a few sensory cells with peripheral receptive fields were omnidirectional, most responded preferentially to the target in one direction. The mean response direction bias for the FEF sensory cells with peripheral receptive fields was 0.42 ± 0.04, which was not significantly different from the SEF sensory cells with peripheral receptive fields. The FEF sensory cells that did exhibit significant directional tuning tended to prefer the contralateral targets (mean angle = 173°, V test $u = 5.08$, df = 26, $P < 0.0001$) (Fig. 3*B*). This tendency was not different between sensory cells in FEF and SEF (Watson $U^2 = 0.175$). These results indicate that sensory cells in FEF and SEF emphasize the contralateral hemifield to the same extent.

The mean response latency for sensory cells in FEF was 77 ± 8 ms (Fig. 3*C*). Although apparently shorter, this distribution was not significantly different from the onset times observed for sensory cells in SEF. The time between the onset of activity and the peak of activity, the rise time, for FEF visual cells (Fig. 3*D*) averaged 48 ± 7 ms, which was significantly shorter than the corresponding value for SEF sensory cells ($t = 3.65$, df = 94, $P < 0.001$). The time of response cessation for the FEF sensory units is shown in Fig. 3*E*; its mean value was 215 ± 16 ms, which was also significantly shorter than that of SEF sensory cells ($t = 3.25$, df = 94, $P < 0.01$). Thus, in response to visual stimuli, both SEF and FEF initiate activity at essentially the same time, but neurons in FEF respond more quickly and more briefly than their counterparts in SEF.

The response to visual and auditory stimuli was tested in only five sensory cells in FEF. Just one cell had a visual/au-

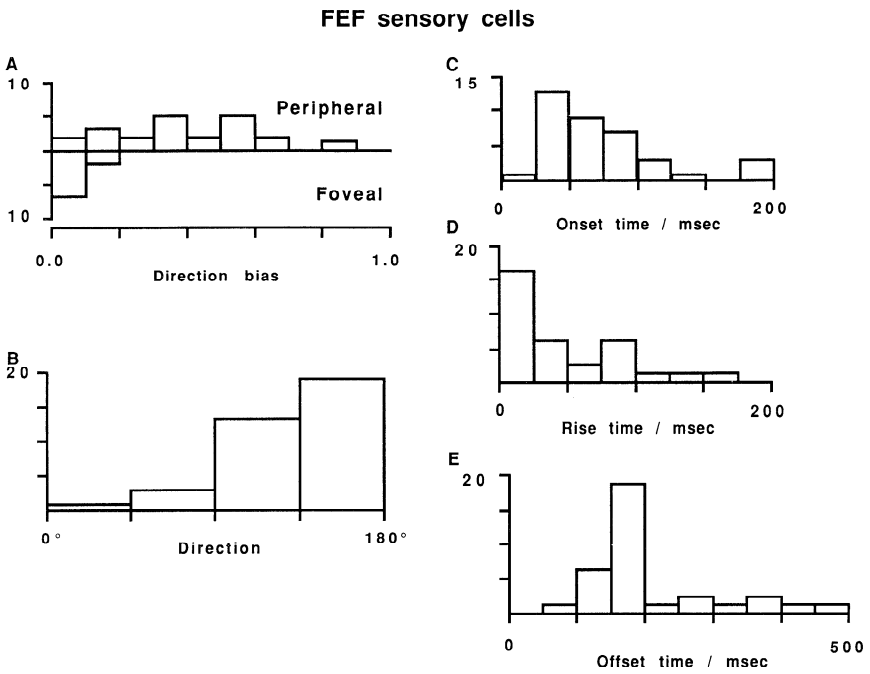

FIG. 3. Quantitative measures of sensory cell responses. *A*: distribution of direction bias, which measures the relative response to targets in each direction; it can range from 0 to 1, with 0 signifying equal responses for all directions. *Top*: neurons with receptive fields that did not include the fovea; *bottom*: foveal receptive fields. *B*: distribution of preferred direction. An angle of 0° represents ipsilateral, and 180° represents contralateral to the hemisphere in which the unit was recorded. Only cells with direction bias >0.1 are illustrated. *C*: distribution of onset times, which are times of inflections in the cumulative sum of spikes relative to the presentation of the target. *D*: distribution of rise times, which are times between the onset and peak of activity, which was defined by the steepest slope of the cumulative sum. *E*: distribution of response termination times, which are times of 2nd inflections in the cumulative sum of spikes after target presentation.

ditory response contrast ratio of 0.0, and it had a foveal receptive field. The remainder were either predominantly visual (n = 3) or predominantly auditory (n = 1). These limited data, although certainly not irrefutable, are consistent with the interpretation that sensory cells in FEF are more modality specific than their counterparts in SEF.

Preparatory set cells

This class of cell was specifically active during the period when the eye movement can be programmed but was not yet executed, i.e., after the target was presented until the go/no-go cue was given (Fig. 4). Although tonic neurons have been reported in FEF (Bruce and Goldberg 1985), this particular pattern of modulation has not been described before. The cell illustrated in Fig. 4, even though it appeared to have a moderately high spontaneous discharge rate, displayed elevated activity after the target appeared. The level of activation was the same whether the target was visual or auditory. The activity of this neuron decayed after the go cue was given, and the cell was essentially silent 50 ms before the saccade was initiated. This population comprised a smaller percentage of the modulated units recorded in FEF (5%) than in SEF (12%).

To identify preparatory set cells, it was necessary to delay the initiation of the movement relative to the presentation of the target. Figure 5 illustrates the pattern of activity of another set neuron when the delay between presentation of the target and of the cue was long and when it was short. The decay of activity in the long delay condition (Fig. 5, *A* and *B*) appeared the same for this neuron as it did for the one shown in Fig. 4. When the cue was presented immediately after the target (Fig. 5, *C* and *D*), however, this unit seemed to burst just before the saccade. Close inspection of Fig. 5*D*, though, indicates that the duration of activation was correlated with the saccade latency. Also, whereas in the long-delay case the activity of this unit had decayed considerably within 100 ms before the saccade, in the short-delay case the activity was more abruptly reduced at the initiation of the saccade.

A quantitative analysis of preparatory set cell activity is shown in Fig. 6. Set cells in FEF tended to respond preferentially for targets in one direction; the mean response direction bias was 0.36 ± 0.05, which was not significantly different from that observed for set cells in SEF. However, in this small population there was no tendency to respond preferentially for any particular direction (Rayleigh test for randomness r = 0.15, df = 11, P = 0.788). Thus, although the set cells recorded in FEF were as well tuned for saccade direction as were those in SEF, unlike in SEF there was not a significant tendency to respond best for contraversive movements.

Three FEF set cells displayed anticipatory activity, discharging from 25 to 100 ms before the stimuli were presented. In SEF a higher proportion of the set cells exhibited anticipatory activity. The average response latency for the FEF set cells that discharged after the target was presented was 93 ± 13 ms (Fig. 6*C*). This was not different from the latency of FEF sensory cells or SEF set cells. The rise time of the FEF set cells (Fig. 6*D*), which was quite variable, averaged 117 ± 29 ms; this was significantly longer than that of FEF sensory cells (t = 3.42, df = 47, $P < 0.01$) but was significantly shorter than the rise time of SEF set cells (t = 2.46, df = 58, $P < 0.02$).

The time at which their activation was terminated was the key feature of preparatory set cells that distinguished them from the other tonic neurons in FEF, the sustained sensory-movement cells (see below). Whereas set cells stopped firing after the cue but before the movement, sensory-movement cells stopped firing after the movement. The times of termination of activation after presentation of the go cue (Fig. 6*E*) had a mean value of 147 ± 12 ms, which was not different from that of SEF set cells. Figure 6*F* illustrates the distribution of times of cessation relative to the initiation of the saccade; the average value was −115 ± 19 ms which was not significantly different from the corre-

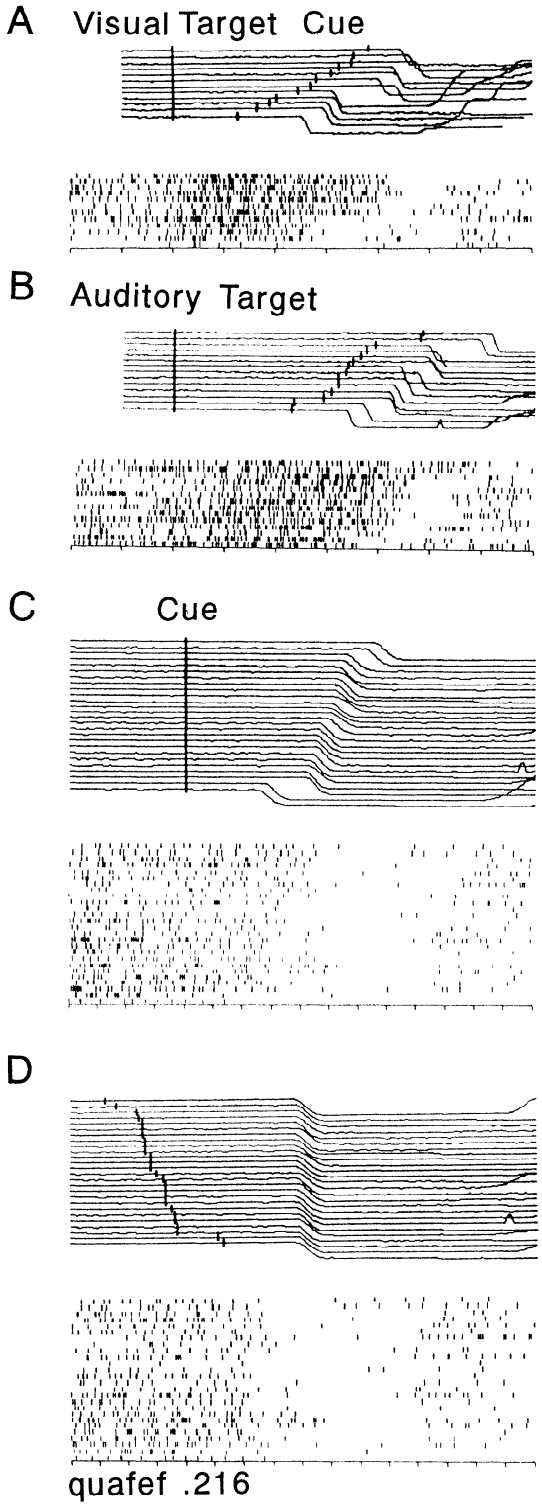

FIG. 4. Preparatory set cell. Eye position traces and rasters are aligned on the time of presentation of the visual target (*A*), the auditory target (*B*), the go cue (*C*), or the execution of the saccade (*D*). Time scale in *A* and *B* is 200 ms, whereas that in *C* and *D* is 50 ms. Although there was moderately high spontaneous activity, presentation of either the visual or the auditory target elicited a clear elevation in the discharge rate. This neuron ceases firing after the cue and before the saccade, after which there is a period of suppressed activity.

sponding value for SEF set cells. Comparing this distribution with that shown in Fig. 10*A5* reveals the fundamental distinction between preparatory set cells and the sustained sensory-movement cells described below. Set cells had quit firing by the time the saccade was initiated.

To summarize, preparatory set cells in FEF begin to respond at the same time as their counterparts in SEF as well as the sensory cells in FEF or SEF. The FEF set cells reach their peak activation faster than SEF set cells but slower than FEF sensory cells; and they stop discharging at the same time, after the cue but before the saccade, as those in SEF.

Only seven set cells were analyzed in blocks of no-go trials (Fig. 7). The mean time that the discharge terminated for this subpopulation of cells after the go cue was 112 ± 50 ms, whereas the average after the no-go cue was 291 ± 50 ms. Thus, when a saccade must be withheld, the set cells in FEF continued to fire for longer than if a saccade were to be generated. This is different from what was observed in the population of SEF set cells, which ceased firing as soon as either the go or the no-go cue was presented.

Four set cells were recorded with both visual and auditory targets. Three were predominantly visually responsive, and the remaining cell responded equally to the visual and auditory targets. This limited data does not permit any conclusions about the modality specificity of FEF preparatory set cells.

Finally, all the set cells were activated specifically during the task. None of these units were modulated to the same degree for saccades in the intertrial interval, although a few of the neurons exhibited a measure of activation in relation to occasional saccades in the intertrial interval.

Sensory-movement cells

The largest group of the modulated neurons recorded in FEF discharged in association with both the presentation of the target and the execution of the saccade. This population constituted a higher proportion of the modulated cells in FEF (41%) than in SEF (28%). Examples of these cells are shown in Figs. 8 and 9. Two subtypes could be distinguished: sustained sensory-movement cells discharged continuously from the appearance of the target until the execution of the saccade (Fig. 8), whereas transient sensory-movement cells exhibited two discrete bursts, the first after the presentation of the target and the second before the execution of the saccade (Fig. 9). These two subpopulations were most clearly distinguished in trials in which the presentation of the cue to move was delayed relative to the presentation of the target; otherwise, both groups of cells displayed a single elevation of activity. The pattern of two transient bursts was never observed in SEF, where, instead, all of the sensory-movement neurons exhibited a single sustained elevation of activity. In FEF these two patterns of modulation probably represent ends of a continuum; that is, it was not uncommon to find sensory-movement neurons that exhibited clearly defined bursts while also having an elevated discharge rate throughout the trial. In the following analysis, however, units showing additional discrete bursts for the target and the saccade, representing 70% of all the sensory-movement cells, were distinguished from the remainder that gave a single period of activation.

The quantitative analysis of the activity of FEF sensory-movement neurons is shown in Fig. 10. Most of the sen-

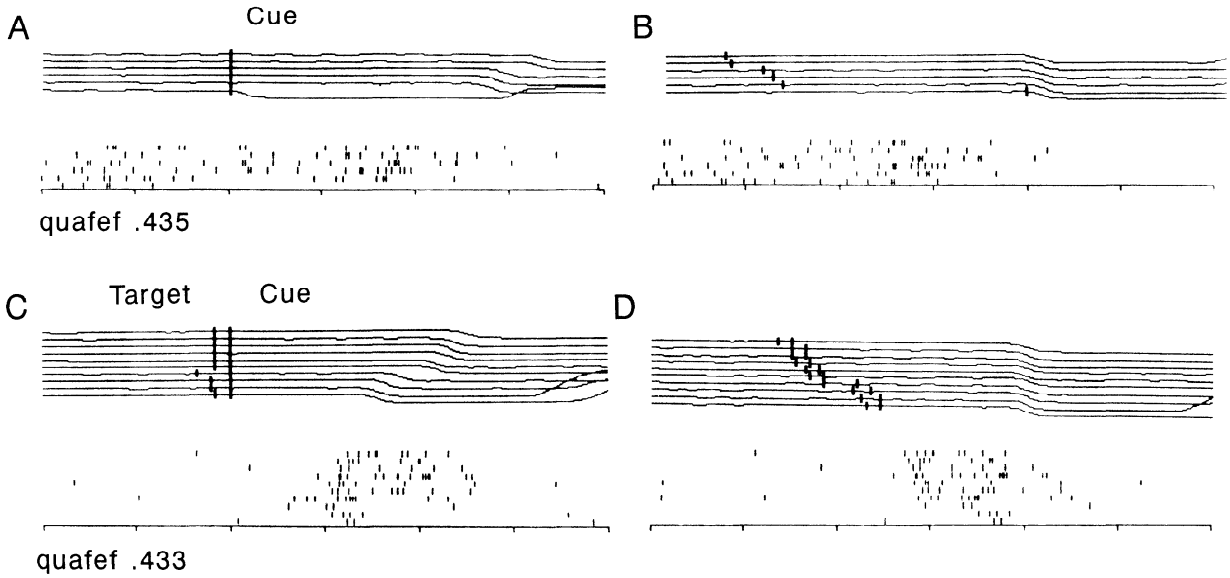

FIG. 5. Preparatory set cell activity with long and short target-cue delays. *A* and *C* are aligned on the presentation of the cue; *B* and *D* are aligned on the saccade. Time scale is 100 ms. *A* and *B* were collected with a long delay between presentation of the target and delivery of the go cue; the neuron ceases firing after the cue but before the saccade. *C* and *D* were collected with short target-cue delays. In this case the cell began to discharge ~100 ms after the target was presented and quit firing when the saccade was initiated.

sory-movement cells responded preferentially for targets in one direction; the mean response direction bias for sustained sensory-movement cells (0.34 ± 0.04) was not significantly different from the response direction bias for transient cells (0.38 ± 0.02), and neither was different from SEF sensory movement cells. Both sustained and transient sensory-movement cells tended to respond best in association with saccades to the contralateral hemifield (sustained: mean angle = 169°, u = 1.39, df = 25, $P < 0.1$; transient: mean angle = 172°, u = 3.25, df = 60, $P < 0.001$). The tendency of FEF sensory-movement cells to respond preferentially in association with contralateral saccades was more pronounced than that in SEF (U^2 = 0.615, $P < 0.001$). Thus, although the sensory-movement cells in FEF and SEF appear to have the same degree of spatial tuning, FEF

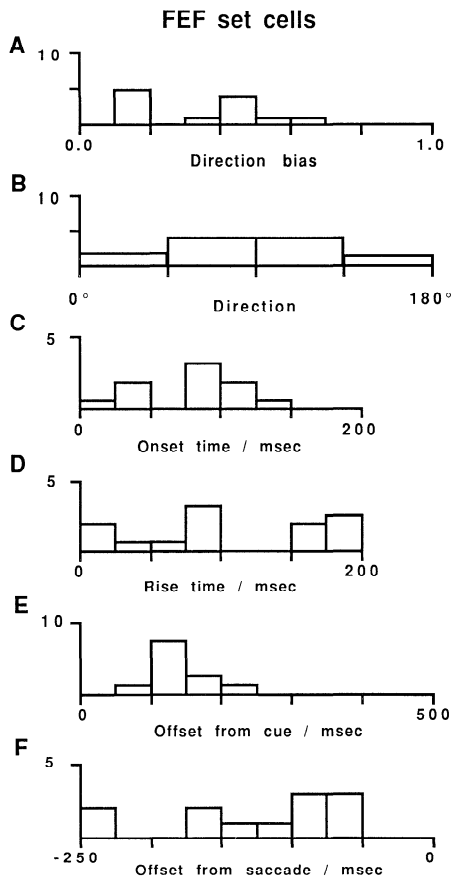

FIG. 6. Quantitative measures of set cell. Conventions as in Fig. 3, except that 2 distributions of response termination time are shown. *E*: distribution relative to the time that the cue was delivered; *F*: distribution of times relative to the time that the saccade was initiated.

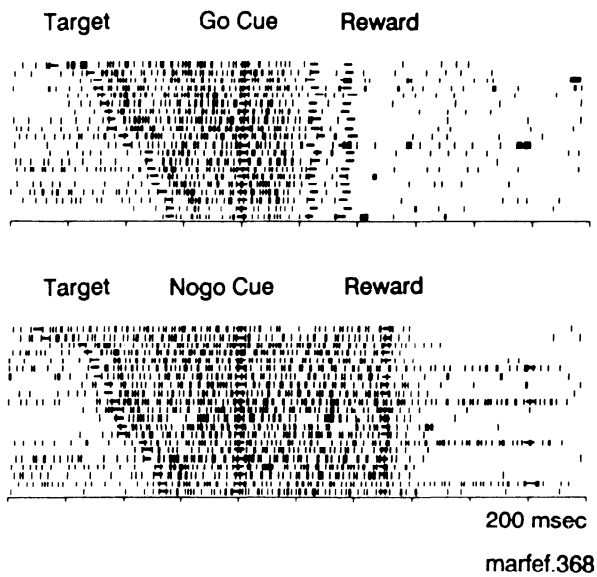

FIG. 7. Comparison of preparatory set cell activity in go and no-go trials. Horizontal tick marks in the raster display indicate the time of occurrence of the labeled event. Tick mark between Go cue and Reward represents the saccade. Contrast the decay of activity before the saccade in go trials with the prolonged activity in no-go trials, lasting until the stimuli were turned off when the reward was given. Note the especially protracted discharge in the 4 trials numbered 6, 10, 15, and 20 from the *top* raster.

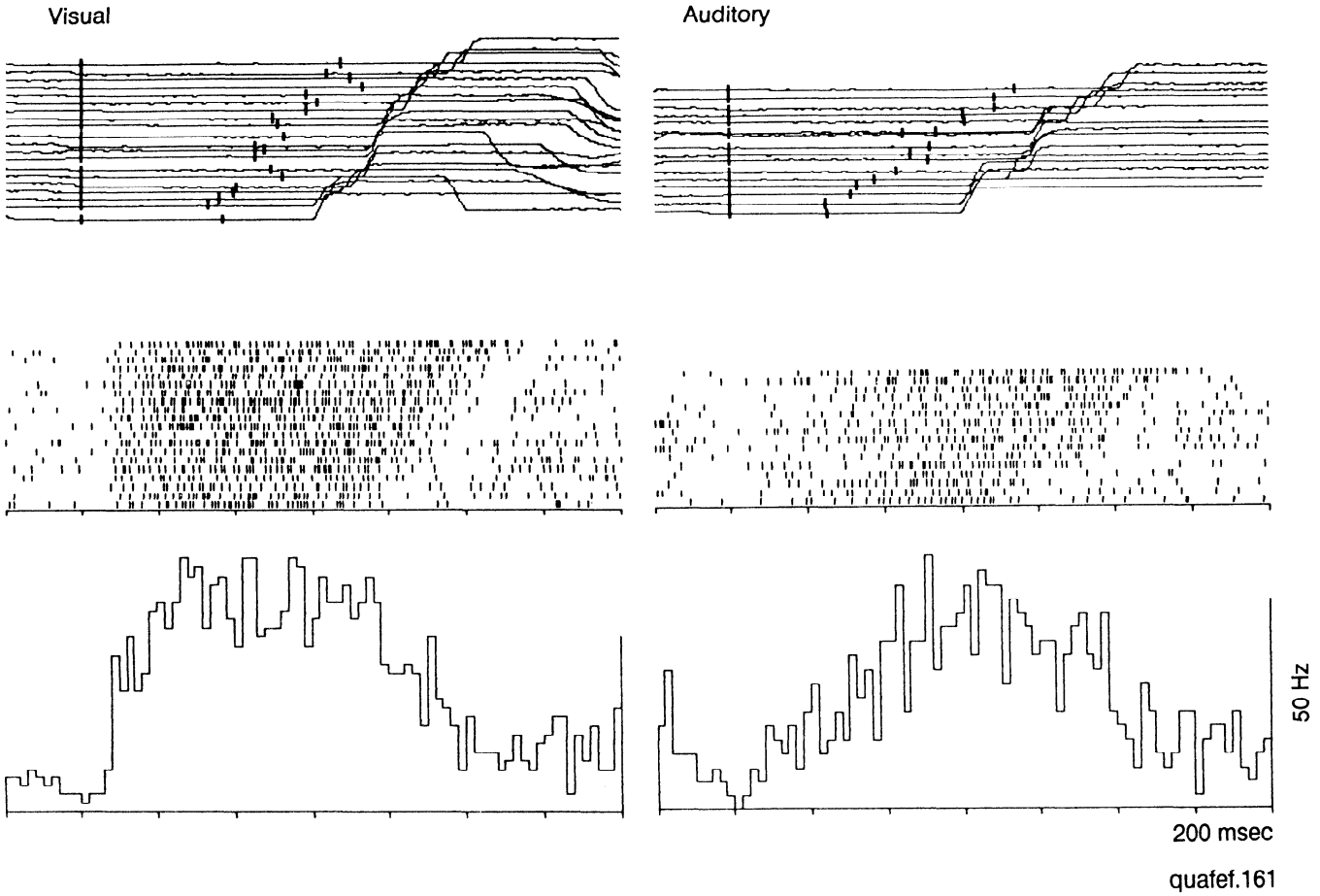

FIG. 8. Sustained visuomovement cell. Eye position traces, rasters, and histograms are aligned on the time of presentation of the visual (*left*) and auditory (*right*) targets. After the visual target, this cell showed a sustained elevation of activity, which decayed after the saccade was in flight. After delivery of the acoustic target, the sensory component of the response was diminished, even though a rise in activity preceded the saccade.

sensory-movement cells are more likely to respond to stimuli in the contralateral hemifield and less likely to respond to ipsilateral stimuli.

One sustained and six transient sensory-movement cells exhibited activity before the appearance of the target; these cells discharged from 20 to 100 ms before the target. The incidence of anticipatory activity in FEF was lower than that in SEF sensory-movement cells. The mean response latency of the sustained sensory-movement cells with positive response latencies, 98 ± 9 ms, was significantly longer than the onset time of the transient sensory-movement cells, 65 ± 4 ms ($t = 3.78$, df = 80, $P < 0.001$). However, the latencies of the sustained and of the transient sensory-movement FEF cells were not statistically different from the FEF sensory cell response latency. On the other hand, the onset time of the transient but not of the sustained FEF sensory-movement cells was significantly shorter than the onset time of the SEF sensory-movement cells ($t = 5.63$, df = 158, $P < 0.001$).

Not surprisingly, the rise time of sustained sensory-movement FEF neurons, 104 ± 17 ms, was significantly longer than that of the transient sensory-movement cells, 56 ± 6 ms ($t = 3.37$, df = 90, $P < 0.01$). The rise time of transient sensory-movement FEF cells was not different from the rise time of the FEF sensory cells, but the rise time of the sustained FEF sensory-movement cells was longer than that of the FEF sensory cells ($t = 3.28$, df = 63, $P < 0.01$). Finally, the rise times of both the sustained and the transient sensory-movement FEF cells were shorter than that of the SEF sensory-movement cells (worst case, $t = 4.96$, df = 131, $P < 0.001$).

To summarize these results on the activation of the visually responsive neurons in FEF and SEF, Table 2 presents the sequence of activation of the different cell types in the two areas. It should be noted that these values can vary according to where the stimuli fall relative to the most sensitive part of each unit's receptive field. Still, two points seem worthy of attention. First, the FEF has a consistent lead in responding to the visual target. Second, although the initial response latency for each cell class is rarely >100 ms, the delay until each population of cells is fully activated is considerably longer.

Two measures of response termination time were determined: the first was measured relative to the presentation of the target for the transient sensory-movement cells and the second relative to the saccade for both sensory-movement types. The cessation time for the first burst of the transient sensory-movement FEF cells relative to the presentation of the target averaged 208 ± 11 ms, which was not significantly different from the termination time of the FEF sensory cells but was significantly shorter than that of the SEF sensory cells ($t = 4.43$, df = 120, $P < 0.0001$). Hence, the

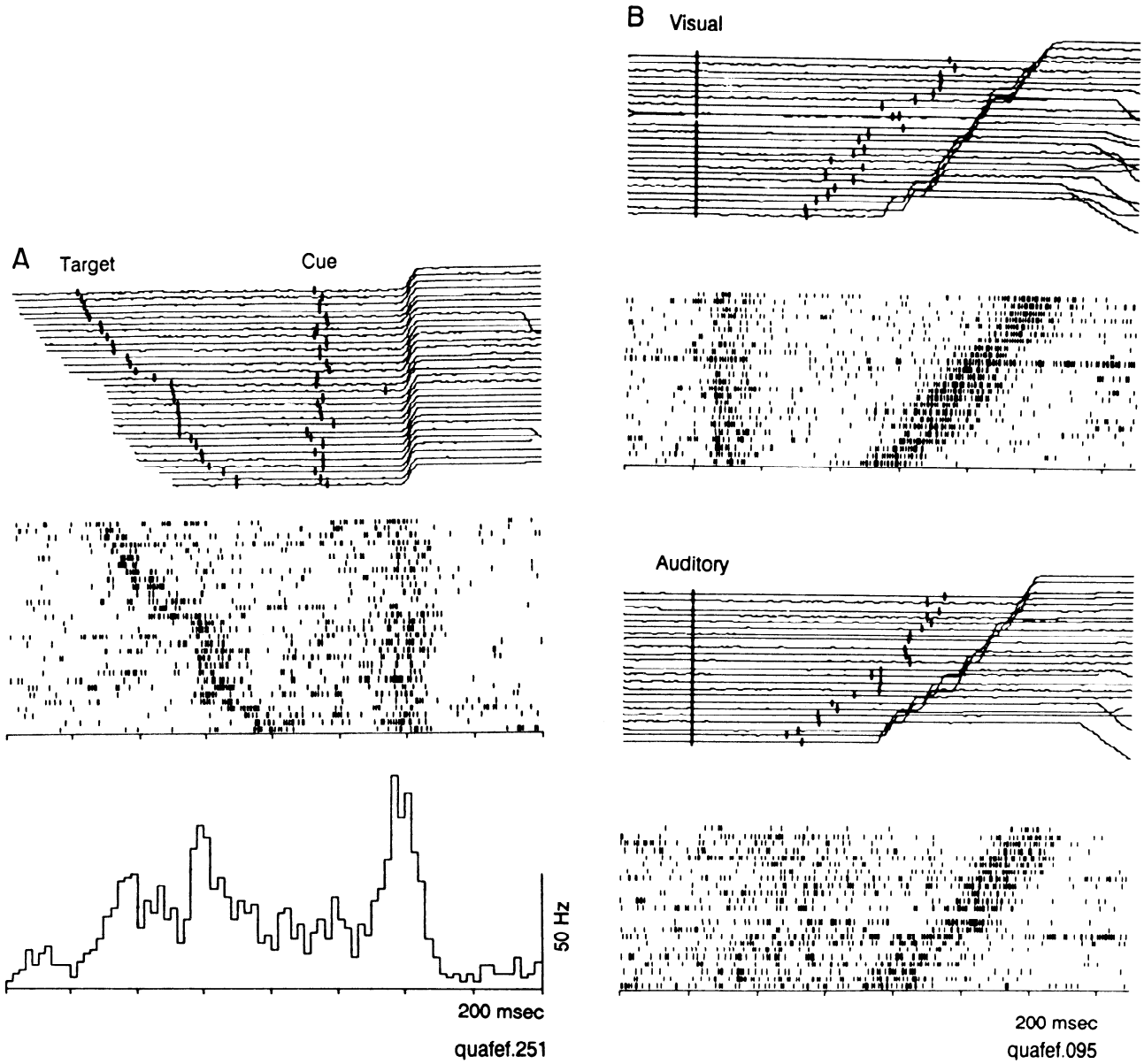

FIG. 9. Transient sensory movement cells. *A*: eye position traces, raster, and histogram are aligned on the saccade. Note the 2 discrete bursts associated with presentation of the target and execution of the saccade. *B*: eye position traces and rasters are aligned on the presentation of the visual (*top*) or auditory (*bottom*) target. Note that, although this cell exhibited 2 discrete bursts associated with visually guided saccades, the 1st burst was replaced by an indistinct activation preceding the saccade-related burst for auditory-guided saccades.

phasic visual response in FEF is briefer than that in SEF.

The sustained sensory-movement FEF cells ceased firing, on average, 92 ± 13 ms after execution of the saccade. The second burst of the transient sensory-movement FEF cells was concluded 87 ± 7 ms after the saccade was initiated; these values were not significantly different from one another or from the mean termination time of SEF sensory-movement cells.

The different subpopulations of sensory-movement cells responded in a variety of ways in no-go trials. A sufficient amount of data to analyze was collected in go and no-go trials for 15 sustained sensory-movement cells. Most (10/15) of the sustained sensory-movement cells continued to discharge after the no-go cue until the reward was delivered. This is illustrated in Fig. 11*A*. These units ceased firing when the first posttrial saccade was initiated. The remaining five sustained sensory-movement cells ceased to discharge on average 88 ± 31 ms after the no-go cue, in contrast to their termination at 364 ± 31 ms after the go cue. Thus only a fraction of the sustained sensory-movement cells in FEF resembled their counterparts in SEF during no-go trials. The prolonged activation that was observed in most of the sustained sensory-movement cells in FEF was rarely if ever seen in SEF.

Sufficient data were collected in 35 transient sensory-movement to compare responses in go and no-go trials. Three of these sensory-movement units had a sustained component to their response, and these cells displayed the same prolonged activation that was described above. In all of the remaining transient sensory-movement cells there was little if any response after the no-go cue, as illustrated in Fig. 12.

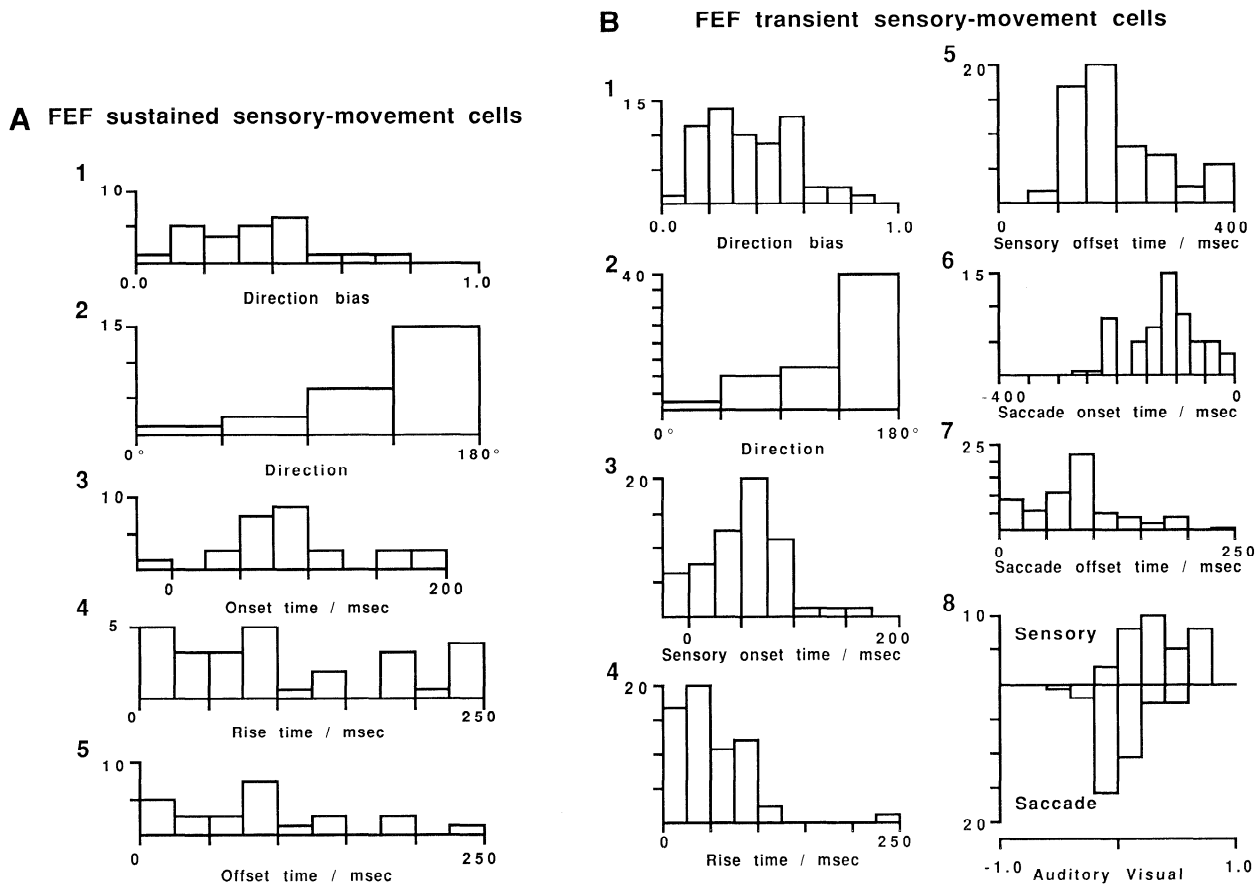

FIG. 10. Quantitative analysis of sustained (*A*) and transient (*B*) sensory-movement cells. Conventions as in Fig. 3. In addition, a measure of the relative responsiveness to visual and auditory stimuli is shown. Values can range from −1 (exclusively auditory) to +1 (exclusively visual). *B8, top*: ratio for the phasic target response; *bottom*: ratio for the saccade-related response.

In 12 of these transient sensory-movement cells, data were collected in no-go trials with no delay between appearance of the target and presentation of the cue. In these trials the go/no-go distinction was made evident at the same time that the target was presented. The response of 10 of these neurons to the target varied according to whether the simultaneous cue was go or no-go. As illustrated in Fig. 12*B*, the response to the target in no-go trials was attenuated relative to that observed in go trials. Of all of the units subjected to this analysis, the cell illustrated in Fig. 12*B* initially gave the most robust response in no-go trials. Still, it is of interest to note that in successive no-go trials the visual response of this unit was reduced until, in the final no-go trials of this block, there was no visual response. It should be noted that there was also some reduction in response to the target + go cue during this same block of trials. Even so, the response attenuation was much more pronounced when the target was paired with the no-go cue. The remaining two transient sensory-movement cells had a sustained component, and their target response was not attenuated in no-go trials with simultaneous target and cue presentation. This lack of attenuation was also observed in all of the sustained sensory-movement cells tested in this fashion (Fig. 11*B*).

TABLE 2. *Sequence of activation of visually responsive cells in FEF and SEF*

Cell Type	Response Latency, ms	Rise time, ms	Time to Peak Activation, ms
FEF transient sensory-movement	65	121	186
FEF sensory	77	125	202
SEF sensory	92	176	268
FEF set	93	210	303
FEF sustained sensory-movement	98	202	300
SEF set	106	293	399
SEF sensory-movement	116	335	451

Values are averages and are listed in rank order. FEF, frontal eye fields; SEF, supplementary eye fields.

The responses of FEF sensory-movement cells to visual and auditory stimuli proved interesting and varied. Unlike in SEF, where most of the sensory-movement cells responded equally to visual and acoustic stimuli, none of the sustained sensory-movement cells in FEF were bimodal; all but one responded preferentially for visual stimuli (as illustrated in Fig. 8). In trials in which the auditory target was presented, there was no sensory response, although these neurons gradually became activated before the saccade. In contrast, one sustained sensory-movement cell responded exclusively for auditory-guided saccades (Fig. 13), but unlike its visual counterpart in FEF, this cell had no saccade-related activation. This modality specificity is in general

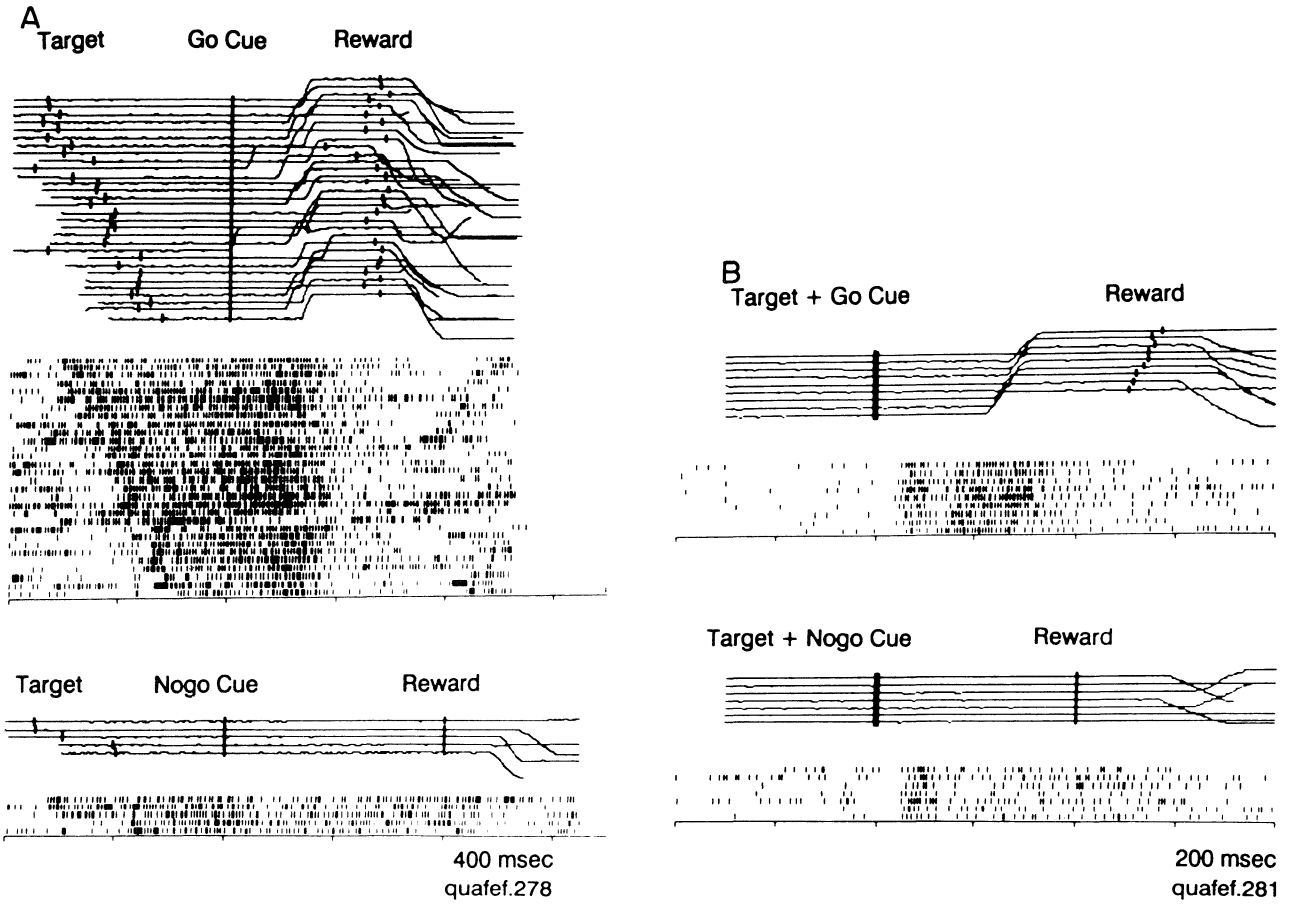

FIG. 11. Response of a sustained sensory-movement cell in go and no-go trials. *A*: eye position traces and rasters are aligned on the presentation of the go cue (*top*) or no-go cue (*bottom*). Contrast the prolonged activation in no-go trials until the reward is delivered to the abrupt decay after the saccade in go trials. *B*: eye position traces and rasters are aligned on the simultaneous presentation of the target and the go cue (*top*) or no-go cue (*bottom*). Contrast the robust visual response followed by the perisaccadic burst in go trials with the equally robust visual response followed by weak modulation until the reward in no-go trials.

different from the population of sensory-movement cells recorded in SEF, although visual and auditory specific examples were encountered in SEF.

The transient sensory-movement cells tended to respond preferentially to visual targets, with only weak and inconsistent activation after the auditory target (Fig. 9*B*). At the same time, the saccade-related component of the response did not distinguish visual from auditory guidance. It was possible to determine a value for the visual/auditory response ratio contrast for both the sensory and the motor component of the response of transient sensory-movement cells. The average sensory visual/auditory response contrast ratio was 0.33 ± 0.06, which was significantly different from 0.0 ($t = 5.92$, df = 33, $P < 0.001$), indicating a visual bias. On the other hand, the visual/auditory response contrast ratio of the motor component was 0.02 ± 0.04, which was not different from 0.0. This result shows that, although the sensory component of these neurons' response is modality specific, the motor component is not.

All of the sensory-movement cells recorded in FEF were either exclusively or significantly more active in relation to the goal-directed saccades made in performance of the task than in relation to spontaneous saccades executed in the intertrial interval.

Pause-rebound cells

Only three neurons were recorded in FEF that exhibited a biphasic pattern of modulation resembling the pause-rebound cells that were observed more frequently ($n = 18$) in SEF. The small number prohibited further analysis.

Presaccadic movement cells

A presaccadic movement neuron from FEF is illustrated in Fig. 14. This type of unit was characterized by its discharge associated solely with and beginning before the execution of the saccade. Twenty-two percent of the modulated neurons sampled in FEF fell into this category; this was comparable with the incidence in SEF (17%).

The quantitative analyses of presaccadic movement activity are illustrated in Fig. 15. Presaccadic movement cells in FEF tended to respond preferentially for movements in one direction. The mean direction bias, 0.38 ± 0.03, was significantly greater than that of SEF presaccadic movement cells ($t = 3.87$, df = 93, $P < 0.001$) but not different from the direction tuning of the other FEF cell types. The presaccadic movement units exhibited a significant tendency to

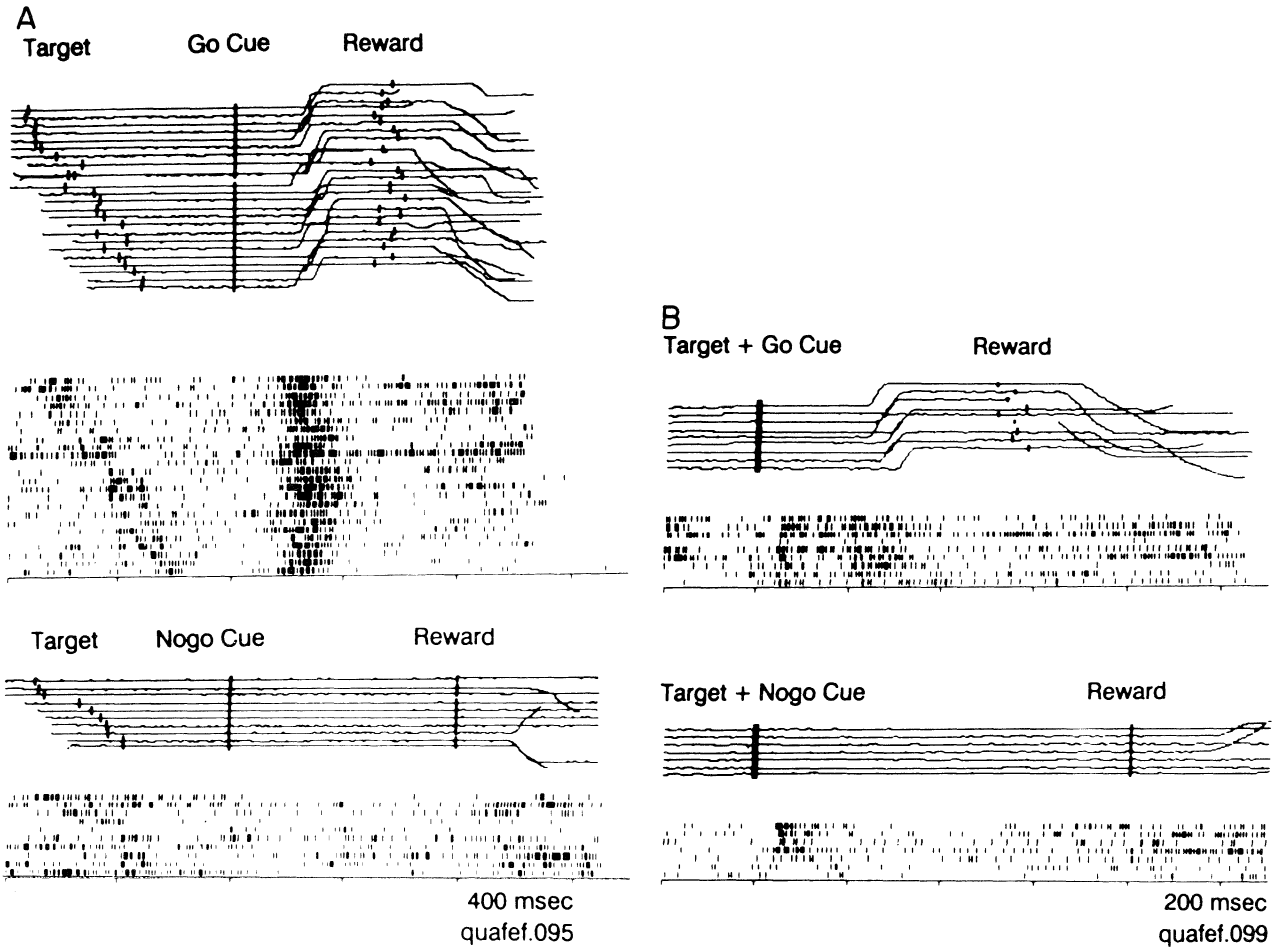

FIG. 12. Response of a transient sensory-movement cell in go and no-go trials. Conventions are as in Fig. 11. *A*: contrast the strong perisaccadic burst after the go cue with the absence of activity after the no-go cue. *B*: these trials were not sorted for display but instead are shown in the relative order of occurrence from *top* to *bottom*. Interleaved trials with other targets are not shown. Contrast the consistent visual and perisaccadic burst after the target + go cue with the progressively attenuated visual response after the target + no-go cue. In the final 2 no-go trials there was no visual response.

prefer contralateral eye movements (mean angle = 188°, $u = 5.14$, df = 40, $P < 0.0001$), which was more pronounced in FEF than in SEF ($U^2 = 0.412$, $P < 0.001$). Taken together, these results indicate that the presaccadic movement cells in FEF have more restricted movement fields that are more likely to be confined to the contralateral hemifield than their counterparts in SEF.

The onset time of the presaccadic burst was determined relative to saccade initiation. The mean onset time for the FEF presaccadic movement neurons was 126 ± 13 ms, and some cells began to discharge >300 ms before the saccade. This was not different from the onset time of the presaccadic component of the transient sensory-movement cells (130 ± 12 ms) or the SEF presaccadic movement cells (144 ± 7 ms). Hence, both FEF and SEF generate a saccade command signal at the same time.

The average time that the FEF presaccadic movement burst concluded after the saccade was launched was 106 ± 12 ms, which was not different from that of transient sensory-movement cells (87 ± 7 ms) or SEF presaccadic movement cells (103 ± 112 ms). However, the times of termination of activity were distributed differently for FEF and SEF presaccadic movement cells. The most common time of cessation of discharge for FEF presaccadic movement cells was 75–100 ms, whereas the most common termination time in SEF was 0–50 ms. The saccade duration ranged from 45–55 ms in this data. Thus, whereas SEF presaccadic movement cells ceased firing at the initiation of the saccade, FEF presaccadic movement cells discontinued firing after the termination of the saccade.

Postsaccadic cells

A number of the units recorded in FEF discharged specifically after the initiation of the saccade (Fig. 16). In FEF 13% of the cells were postsaccadic, whereas in SEF only 2% were. The FEF postsaccadic cells were preferentially responsive after saccades in a particular direction; the mean response direction bias was 0.36 ± 0.03. Furthermore, the postsaccadic cells tended to respond best for contralateral saccades (mean angle = 184°; $u = 1.87$, df = 24, $P < 0.05$). The average onset time for FEF postsaccadic cells was 41 ± 7 ms, which was later than that of their SEF counterparts ($t = 2.51$, df = 37, $P < 0.02$). The time that the discharge concluded was 221 ± 14 ms after the saccade, which was not different from that of the SEF postsaccadic units.

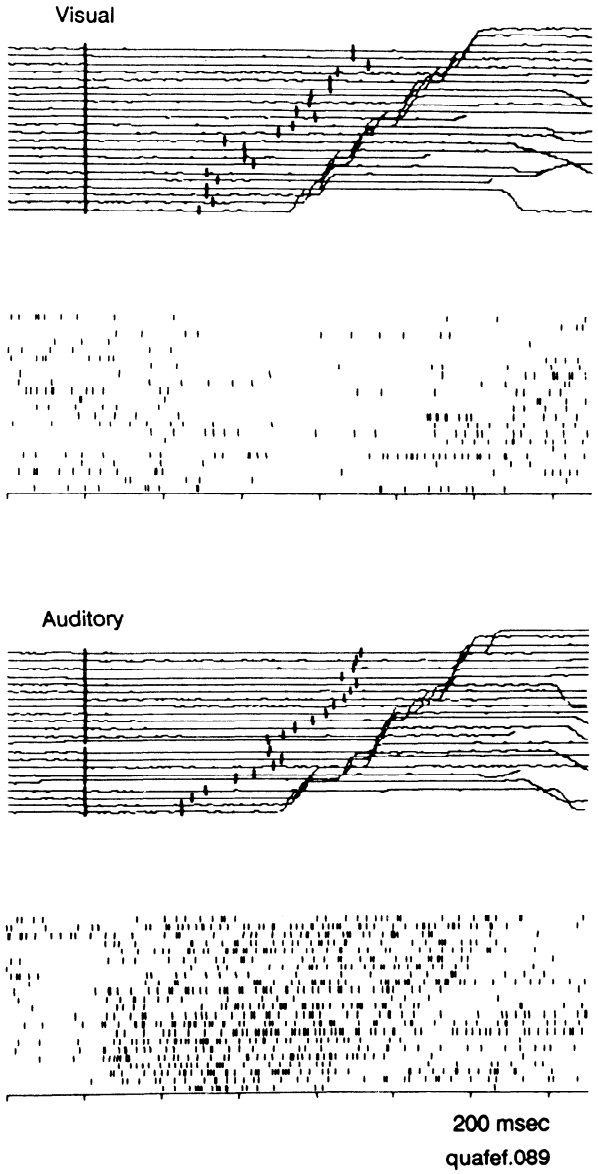

FIG. 13. Auditory-movement cell. Eye position traces and rasters are aligned on the visual (*top*) or auditory (*bottom*) target.

To summarize these data, the sequence of activation in FEF and SEF relative to a goal-directed saccade is given in Table 3. It should be noted that the precise values can vary according to whether the saccade was directed to the most sensitive point of each unit's movement field (e.g., Sparks 1975). Nevertheless, it is evident that the presaccadic burst is issued by both FEF and SEF at essentially the same time. It is interesting that the discharge of the pause-rebound neurons in SEF occurs so much later than that of the presaccadic movement neurons. The postsaccadic cells in SEF appear to fire after the initiation of the saccade, whereas the postsaccadic cells in FEF appear to fire around the conclusion of the saccade.

Eye position cells

In this investigation of FEF no units with activity related to eye position were recorded, unlike previous studies (Bizzi 1968; Bizzi and Schiller 1970; Bruce and Goldberg 1985). In contrast, a small number were observed in SEF of the same monkeys. Unfortunately, this experiment was not designed to look specifically for eye position effects on neural responses.

Microstimulation-evoked saccades

Additional evidence that an eye position signal is more prominent in SEF than in FEF is provided through intracortical microstimulation, which is illustrated in Fig. 17. As observed many times before (Bruce et al. 1985; Marrocco 1978; Robinson and Fuchs 1969; Schiller 1977; Schiller et al. 1979), the amplitude and direction of saccades evoked by stimulating FEF does not vary with initial orbital position. The lack of dependence on orbital position of the electrical stimulation elicited saccades is evident in Fig. 17, *B* and *D*, which plots the eye movements from a common starting position. Note the significant overlap in the eye position traces for each stimulation trial; also notice that a saccade was elicited in every trial. Another characteristic of FEF microstimulation is that prolonged stimulation (500 ms) often results in multiple saccades, all of the same amplitude and direction. In the example shown in Fig. 17, *A* and *B*, a sequence of two leftward saccades was elicited from all initial positions except the most leftward one.

In marked contrast to these data from FEF, stimulation of many sites in SEF tends to elicit saccades that bring the eyes to a specific location in the orbit (see also Mann et al.

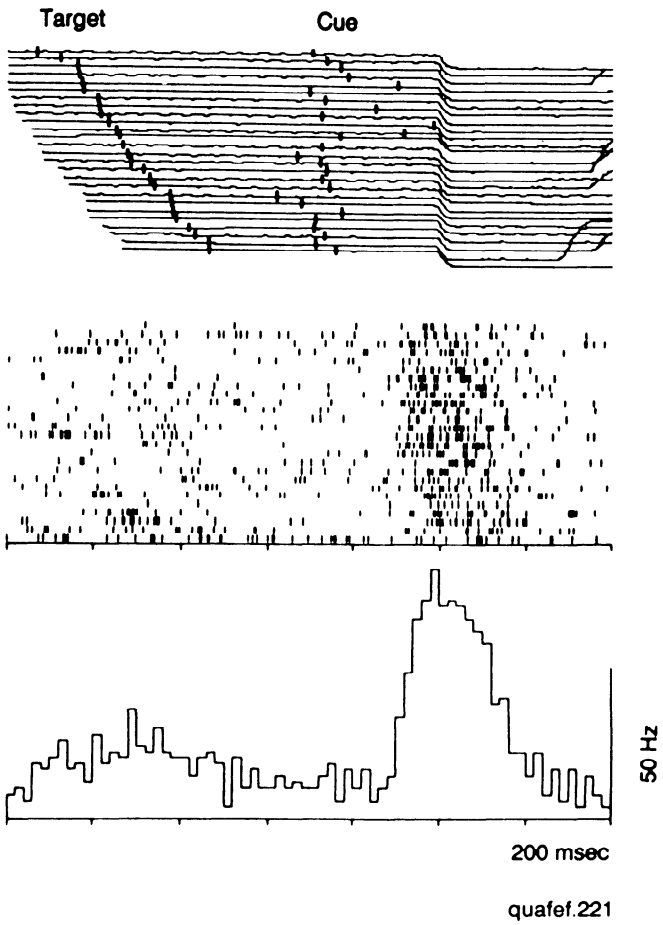

FIG. 14. Presaccadic movement cell. Eye position traces, raster, and histogram are aligned on the saccade.

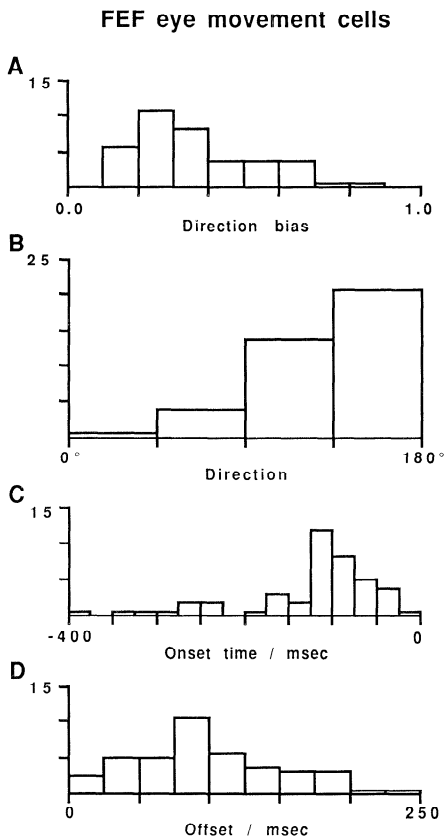

FIG. 15. Quantitative analysis of presaccadic movement cells. Conventions as in Fig. 3.

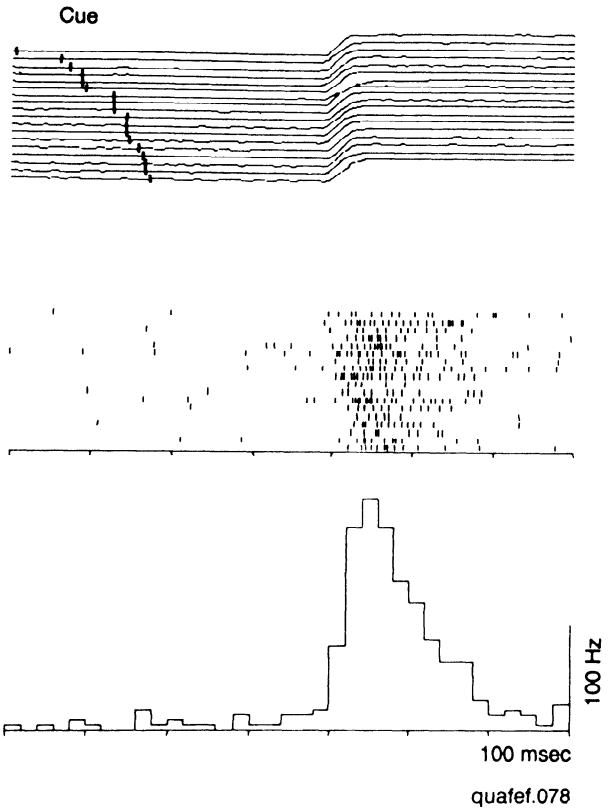

FIG. 16. Postsaccadic cell. Eye position traces, raster, and histogram are aligned on the saccade, and the time scale is expanded.

1988; Mitz and Godschalk 1989; Schlag and Schlag-Rey 1987). Consider first Fig. 17, *E* and *F*. The dependence on orbital position of the saccades elicited by stimulation of this SEF site is made evident in Fig. 17*F*, which plots the eye movements from a common starting position; the spatial arrangement of the initial positions appears replotted in the arrangement of final positions. When the eyes were at the right initial position, a horizontal-leftward saccade of ~30° amplitude was elicited in eight of eight trials in this particular block. When the eyes were at the top initial position, a down-leftward saccade of ~15° amplitude was elicited in eight of eight trials. Similarly, when the eyes were at the bottom initial position, an up-leftward saccade of ~15° amplitude was elicited in seven of seven trials. When the eyes were at the central initial position, a leftward saccade of slightly <15° amplitude was elicited in six of seven trials; however, in one trial no saccade was evoked from this position. Finally, when the eyes were at the left initial position, within the region to which the eye was moved by stimulation from other initial positions, then the same stimulation elicited no saccade in seven of seven trials.

Contrast this pattern of results with that obtained from FEF, shown in Fig. 17, *C* and *D*. The saccades were of ~40° amplitude. Even when the eyes were fixated on the leftward target, a saccade was elicited. Whereas stimulation at many sites in SEF fails to elicit a saccade if the eye is at a particular location, in no case does stimulation of an effective site in FEF fail to evoke a saccade.

Figure 17, *G* and *H*, illustrates this last observation in a more exaggerated fashion from another site in SEF. In 35 out of 36 trials when the eyes were at the top, center, bottom, and left targets, no saccade was elicited. In contrast, leftward saccades were evoked by stimulation of this site when the monkey was fixating the right target in nine of nine trials. In one trial with the initial fixation directed at the left target, the saccade evoked was in the opposite, ipsilateral direction.

In further contrast with FEF, prolonged stimulation of SEF rarely evokes multiple saccades. The duration of electrical stimulation of the SEF sites, illustrated in Fig. 17, was 800 and 1,000 ms. Stimulation of this duration in FEF consistently elicits "staircase" saccades. As illustrated for SEF, however, this period of stimulation serves only to keep the eye fixed at a particular orbital position.

Other cells

Three other classes of cells were identified. One class was suppressed throughout the trial, from when the monkey

TABLE 3. *Sequence of activation of perisaccadic cells in FEF and SEF*

Cell Type	Onset Time, ms
SEF presaccadic	−144
FEF transient sensory-movement	−130
FEF presaccadic	−126
SEF pause-rebound	−38
SEF postsaccadic	17
FEF postsaccadic	41

The average values of onset time relative to saccade initiation are shown in rank order; negative values indicate presaccadic discharge. Abbreviations, see Table 2.

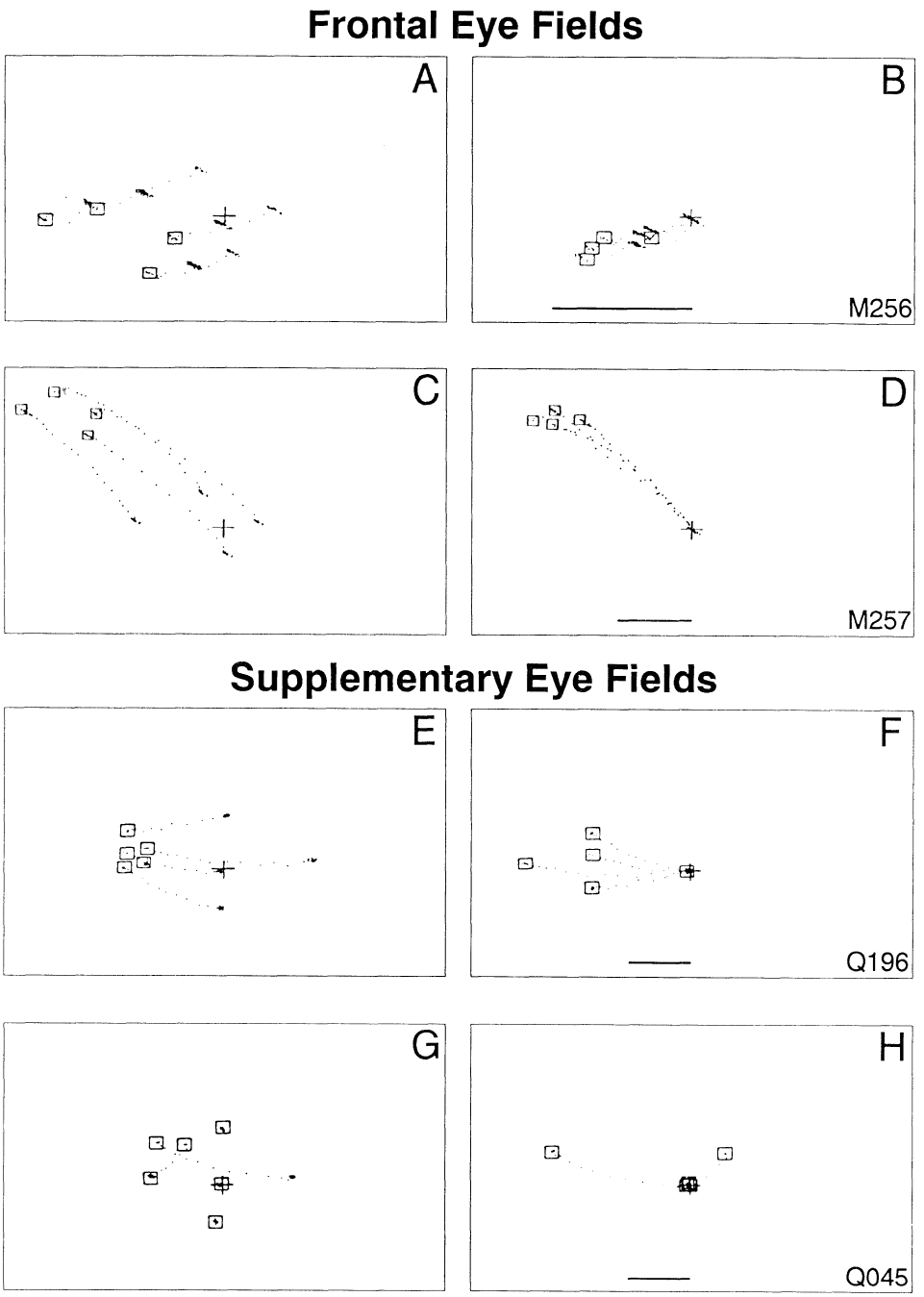

FIG. 17. Eye movements elicited by intracortical microstimulation of FEF (*A–D*) and SEF (*E–H*). *A*, *C*, *E*, and *G*: absolute eye position; *B*, *D*, *F*, and *H*: eye position relative to a common starting point. Cross represents the central fixation spot. Horizontal bar in *B*, *D*, *F*, and *H* represents 10°. A square is drawn around the final eye position. Initial positions correspond to the locations of the 1 central and 4 peripheral LEDs. *A* and *B*: saccades evoked from 1 site in FEF; stimulation was 40 μA for 500 ms. Prolonged stimulation elicited a sequence of 2 leftward saccades from each initial position except the most leftward one, from which a single leftward saccade resulted. As shown in *B*, the direction and amplitude of each saccade were essentially the same. *C* and *D*: saccades elicited from stimulation of another site in FEF (40 μA, 500 ms). Multiple saccades were not evoked, presumably because the saccades were of such large amplitude. Although there is a degree of curvature in the trajectories, *D* shows that the saccades were essentially all of the same amplitude and direction. *E* and *F*: saccades evoked from a site in SEF (90 μA, 1000 ms). Prolonged stimulation elicited a single saccade from each initial position except the leftward one. Direction and amplitude of the saccades varied in such a manner that the eye tended to be moved to 1 general orbital position. *G* and *H*: saccades evoked from another site in SEF (20 μA, 800 ms). Prolonged stimulation elicited a leftward saccade from the right initial position. In contrast, no saccades were evoked when the eye was at the top, central, or bottom initial positions, as indicated by the square around a constant fixation eye position in *G* and by the number of squares around the central point in *H*. Two trials are illustrated with the eye at the left initial position. In the typical trial illustrated, no saccade was elicited. However, in a single trial a reversal, right-upward saccade was evoked from the left initial position.

fixated the central spot until after the saccade. The fixed nature of the stimuli (limited number of embedded LEDs) prohibited further evaluation of these cells. Some of this group seemed to be responsive for saccades of larger amplitude than were required by the task. Units that were clearly modulated during the task, but for which insufficient data were obtained, were grouped in the modulated but unclear category. This designation was in contrast to the final class, which was either inactive or unmodulated during the trial. Presumably this last population would have been active had the task required the additional element of behavior that these cells subserve.

DISCUSSION

This study has described the discharge properties of a number of neuronal types in the FEF (summarized in Fig. 18). The present results will be compared with previous studies of FEF. Then the similarities and differences between FEF and SEF will be highlighted.

Relation to previous work

There have been a number of single-unit recording studies of FEF in monkey (Bizzi 1968; Bizzi and Schiller 1970; Bruce and Goldberg 1985; Goldberg and Bushnell 1981; Mohler et al. 1973; Pigarev et al. 1979; Segraves and Goldberg 1987; Wurtz and Mohler 1976). Within the limits of differences in experimental design, the results of the present study are in good agreement with this previous work.

The percentages of the major cell types that were observed in this study were similar to those reported by Bruce and Goldberg (1985) and Segraves and Goldberg (1987) using similar tasks. However, differences in experimental

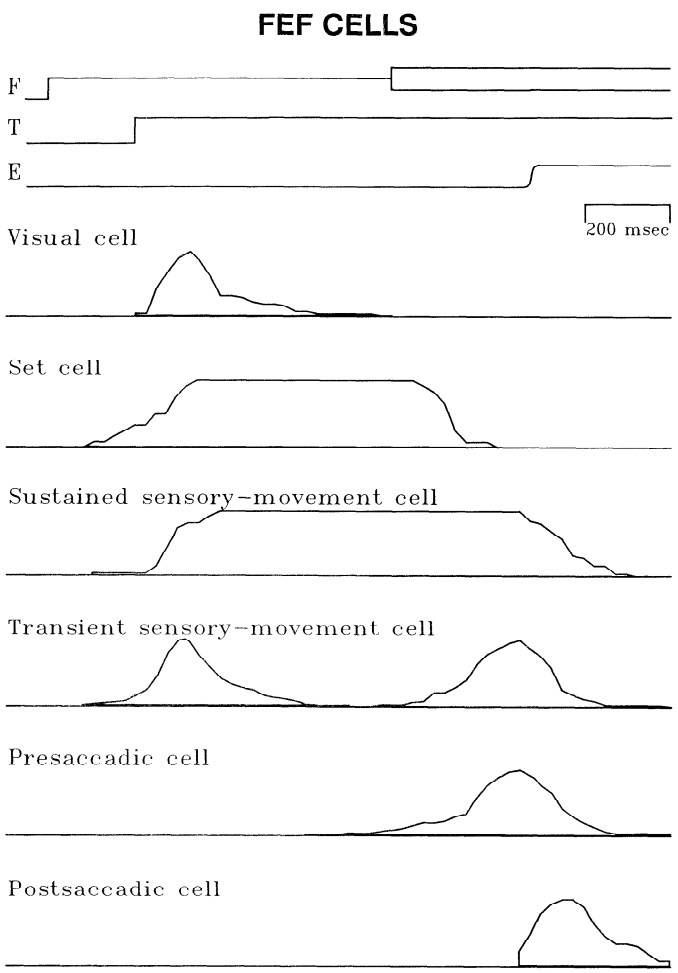

FIG. 18. Summary of FEF cell types. *Top*: traces for the fixation spot (F), target (T), and eye (E). Cumulative times for the onset and termination of activity of the different cell types are illustrated. Magnitude of response is not reflected in this figure.

paradigm allowed these previous studies to identify neurons that were not found in this experiment (for example, pursuit-related and eye position cells). At the same time, certain neurons were described for the first time in this investigation.

Although they were rarely encountered, the preparatory set cells have not been described as such in FEF before. Bruce and Goldberg (1985) described neurons that were tonically activated by the target for the saccade, but differences in experimental paradigm make comparison of their results with the present ones difficult. On the one hand, by having their monkeys generate a goal-directed saccade with no visual target, Bruce and Goldberg were able to distinguish tonic visual cells from visuomovement cells. Such a task condition was not used in this study, so it is likely that some of the units identified with sustained activity in the present study would have been characterized as tonic visual cells by Bruce and Goldberg. On the other hand, in the delayed-saccade task used by these investigators, they did not identify cells that stopped firing after the fixation spot turned off but before the saccade was initiated.

In the present study an attempt was made to provide various quantitative measures to characterize the spatial and temporal response properties of the different populations. Because the present experiment was limited in design by having four immovable visual stimuli, the spatial tuning of the cells was grossly underestimated relative to the data of Bruce and Goldberg (1985). Thus this element of these data is difficult to compare with the corresponding measures obtained with stimuli that could be positioned arbitrarily. Nevertheless, because the same stimulus configuration was used in recordings from SEF, the comparison between areas in this study is acceptable.

The present report includes more quantitative data on the temporal properties of the different FEF cell types than has been published heretofore. The possibility that the stimuli may not have always been stimulating the most sensitive spot in each unit's receptive field might introduce some additional variability in the temporal response numbers. Nevertheless, the values of visual response latency found in this study are in agreement with those observed previously (Bruce and Goldberg 1985; Goldberg and Bushnell 1981; Mohler et al. 1973; Pigarev et al. 1979). The measure of how quickly cells reached their peak level of activation was not previously studied. This value of rise time varied across the different visually responsive subpopulations; in general, the more phasic the response, the faster the rise time. This measure of activity is important for providing a complete description of the time course of activation of the different populations of cells. Such information is necessary to understand how the buildup in neural activity in these areas is related to saccade latency (see Carpenter 1981; Reulen 1984; Schall 1988).

Auditory responses were noted in this study and have been observed before in prearcuate cortex (Azuma and Suzuki 1984; Bruce and Goldberg 1985; Newman and Lindsey 1976; Vaadia 1989; Vaadia et al. 1986). These earlier investigations have demonstrated that the incidence of auditory responses increases as one explores more medially in prearcuate cortex, in regions representing more peripheral receptive fields and longer saccades. The incidence of auditory-responsive neurons, identified in this study, appears lower than what has been reported previously. One reason for this is that most of the penetrations in FEF in this study were aimed at regions representing smaller eccentricities because of the placement of the stimuli.

New observations were made in the present study of sensory-movement units that responded in different fashions to the visual and auditory stimuli. For example, some visuomovement units did not discharge when an acoustic target was presented and began to fire only before the saccade (Fig. 9). In contrast, other units fired in a prolonged fashion specifically for auditory-guided saccades but not for visually guided saccades (Fig. 13). Similar modality-specific response patterns have been observed in the superior colliculus (Jay and Sparks 1987a). Furthermore, recent results have demonstrated that the receptive field of auditory cells in FEF shift with gaze (Russo and Bruce 1989) in a fashion similar to that observed in the superior colliculus (Jay and Sparks 1987b). The behavior of SEF cells in such a paradigm requires testing.

Previous physiological investigations of FEF have not used a go/no-go task. Evidence from ablation studies implicates prearcuate cortex in the performance of such tasks (e.g., Van Hoesen et al. 1980). In addition, no-go–specific activity has been recorded in prearcuate prefrontal cortex

(Sasaki and Gemba 1986; Watanabe 1986). Two basic results were observed in the present study during no-go trials. First, neurons with tonic activation like preparatory set cells and sustained sensory-movement cells exhibited prolonged activity after the no-go cue until the reward was delivered. The second result in no-go trials was found in transient sensory-movement cells that, not surprisingly, failed to discharge after the no-go cue when no saccade was executed, even though they displayed the same target response. In contrast, these phasic cells tended to show an attenuated response when the target was presented simultaneously with the no-go cue. This result seems to be simply the converse of the saccade-related enhancement of visual responses described previously (Goldberg and Bushnell 1981; Wurtz and Mohler 1976). An interesting element of this particular finding is the fact that even though the go and no-go trials were not in blocks but were interspersed, the initial response of most of the phasic cells in these trials distinguished the go and no-go trials. In other words, the transient sensory-movement cells did not respond to the target in their receptive field when it was presented simultaneously with the no-go cue. Moreover, this modulation appears to be specific to the phasic and not the tonic visual cells. Further work is required to substantiate this result and clarify the mechanism.

Similarities between FEF and SEF

The limited comparative data available indicate that these two cortical areas share much in common, in terms of both connectivity (most recently, Huerta and Kaas 1990; Huerta et al. 1986, 1987; Shook et al. 1990, 1991; Stanton et al. 1988a,b) and physiological properties. The results of the present experiment show that SEF and FEF both contain a number of cell types, including sensory, sustained sensory-movement, presaccadic eye movement, and postsaccadic eye movement.

The sensory cells represented approximately the same proportion of the task-related population in each area. The receptive field size and tendency to be localized in the contralateral hemifield were the same in each area. In addition, even though the mean response latency in FEF was less than that in SEF, the distributions of response onset times were not statistically different. This result suggests that both areas might share a common source of visual input. In fact, both regions receive intracortical afferents from extrastriate visual areas in the superior temporal sulcus and inferior parietal lobule (Huerta and Kaas 1990; Huerta et al. 1987), as well as thalamic nuclei, including medial dorsal, ventral anterior, and intralaminar (Huerta and Kaas 1990; Huerta et al. 1987), where visual activity has been recorded (Schlag and Schlag-Rey 1984).

A hallmark observation of the visual cells in FEF is that their response is enhanced if the stimulus is the target for a saccade (Goldberg and Bushnell 1981; Wurtz and Mohler 1976). The present experiment did not perform this test, so it was not possible to discriminate the visual cells in FEF from their counterparts in SEF on this basis. It will be very interesting to determine whether visual cells in SEF exhibit the saccade-related response enhancement or, indeed, the attention-related enhancement that is seen in posterior parietal cortex (Bushnell et al. 1981) but not in FEF.

Neurons were recorded in both FEF and SEF that showed a sustained elevation of activity after the presentation of the target. In SEF two subpopulations of these cells were identified on the basis of the time that their activity terminated; preparatory set cells quit firing 50–100 ms before the saccade, whereas sensory-movement cells continued to discharge until after the saccade. The same distinction could be made in FEF. The directional tuning of set cells in FEF and SEF was not distinguishable. Also, whereas the mean onset time in FEF was slightly shorter than that in SEF, the distributions of response latencies were not different. Finally, the time of activity decay relative to both the cue and the saccade was not different.

Sustained sensory-movement cells were recorded in both FEF and SEF. They had similar visual response latencies, and the directional tuning was similar in the two areas. Also the time of activity decay after a saccade was not different between FEF and SEF in this population. This pattern of modulation has been observed in a number of other structures—including nucleus reticularis tegmenti pontis (Crandall and Keller 1985), superior colliculus (Mays and Sparks 1980), the substantia nigra pars reticulata (Hikosaka and Wurtz 1983b), caudate nucleus (Hikosaka et al. 1989), inferior parietal lobule (Gnadt and Andersen 1988), and prefrontal cortex (Funahashi et al. 1989; Joseph and Barone 1987)—in association with saccades to remembered locations or with saccades to the second of a double-step target. Because neither of these tasks were included in this investigation, it is not possible to distinguish members of this cell class in FEF and SEF on these grounds.

Presaccadic bursting neurons were found in both areas. The temporal characteristics of the presaccadic eye movement cells in the two areas were not different. These units in both areas begin to discharge 100–400 ms before a goal-directed saccade made by a motivated monkey but not before spontaneous saccades. This contingency has been reported in a number of other preoculomotor structures, including the substantia nigra pars reticulata (Hikosaka and Wurtz 1983a), the caudate nucleus (Hikosaka et al. 1989), and certain units in the superior colliculus (Mohler and Wurtz 1976). Thus it appears that a command is generated in both FEF and SEF for intentional saccades. This is consistent with the fact that low-intensity intracortical microstimulation elicits saccades from both FEF (e.g., Bruce et al. 1985) and SEF (e.g., Schlag and Schlag-Rey 1987). However, this data from SEF must be reconciled with the earlier observation that combined ablation of FEF and the superior colliculus results in an essentially complete loss of eye movements (Schiller et al. 1980). Evidently the saccade command generated in SEF must be combined with that from FEF or the superior colliculus. Preliminary data indicate that saccades can be evoked from SEF after either unilateral FEF or superior colliculus ablation (Schall et al. 1987).

Differences between FEF and SEF

Certain cell types were found to be somewhat unique to each area in this study. SEF contained pause-rebound cells, preparatory set cells, and eye position cells that were observed less frequently in FEF. In addition, modulation that was apparently specifically related to withholding the saccade in no-go trials seemed more evident in SEF than in

FEF. In contrast, the transient sensory-movement cells found in FEF had no counterpart in SEF. The double-burst pattern of modulation that characterized the transient sensory-movement cells has been observed in a number of other structures, including nucleus reticularis tegmenti pontis (Crandall and Keller 1985), substantia nigra pars reticulata (Hikosaka and Wurtz 1983a), superior colliculus (Mays and Sparks 1980; Mohler and Wurtz 1976; Wurtz and Goldberg 1972), extrastriate visual area V4 (Boch and Fischer 1983), the inferior parietal lobule (Andersen et al. 1987, 1990b), and prefrontal cortex (Boch and Goldberg 1989). An understanding of the significance of the absence of this particular cell type in SEF awaits an understanding of its role in saccade generation. Finally, postsaccadic cells were much more common in FEF than in SEF. Clearly, much more experimental work is needed to ascertain what role the different neuron classes might serve in saccade generation; even so, the fact that there are different neuron classes in these two areas indicates that they do indeed contribute to different aspects of saccade generation. At present, however, it is possible only to speculate about possible functional differences.

ORBITAL VERSUS RETINAL COORDINATES. One of the most compelling differences that might distinguish FEF and SEF is the evidence for a representation of eye position in SEF that is absent or less pronounced in FEF. This observation is based on two results.

First, as reported already (Mann et al. 1988; Mitz and Godschalk 1989; Schlag and Schlag-Rey 1987), the saccades evoked by microstimulation of many sites in SEF tend to converge on a particular orbital position, whereas the saccades evoked from FEF are of a fixed vector. It should also be noted in this context that microstimulation of the posterolateral inferior parietal lobule also evokes saccades that vary with initial eye position (Shibutani et al. 1984). The possibility must be considered that the orbital dependence that is apparent with microstimulation of SEF may be due simply to the constraints of the movement of the globe at extreme angles (see Segraves and Goldberg 1984). Although the existing data do not exclude this possibility, stimulation of many sites in SEF brings the eye to a position in the orbit that is not very eccentric (compare Fig. 17, *C* and *E*). More compelling evidence for different coordinate systems in FEF and SEF is obtained using long stimulus trains. Prolonged stimulation of FEF as well as of superior colliculus elicits successive staircase saccades, all of the same direction and amplitude (Robinson 1972; Schiller and Stryker 1972; Schiller et al. 1979). In marked contrast, evidence was presented in this paper as well as by Schlag and Schlag-Rey (1987) that such protracted stimulation of many sites in SEF elicits a single saccade, which brings the eye to the specific orbital position, followed by sustained fixation until the electrical stimulation is turned off. Furthermore, if the eyes happen to be in the vicinity of the specified endpoint when the stimulation is delivered, then no eye movement is elicited.

The second piece of evidence for an eye position signal in SEF is that neurons with activity modulated according to orbital position have been identified there. Such units in SEF were described in the preceding paper (Schall 1991a); they have also been identified by Schlag and Schlag-Rey (1985, 1986). These SEF units discharged before saccades directed to a particular range of endpoints; they also discharged during tracking eye movements that had the same endpoints as well during attentive fixation in the appropriate direction. As detailed in the previous paper, this constellation of properties has not been reported before for either the fixation and tracking units of posterior parietal cortex (Erickson and Dow 1989; Komatsu and Wurtz 1988; Lynch et al. 1977; Robinson et al. 1978; Sakata et al. 1980, 1983), for prefrontal fixation units (Suzuki and Azuma 1977), or for the eye position units originally described in FEF (Bizzi 1968; Bizzi and Schiller 1970; Bruce and Goldberg 1985). Having identified these neurons in SEF, however, we must note that recent recordings in FEF have located units with these properties—but such units are less common than in SEF (J. Schlag and M. Schlag-Rey, personal communication). To summarize, then, SEF appears distinct from FEF in having a greater proportion of neurons signally eye position, those neurons firing before gaze shifts that move the eyes into the appropriate orbital position.

It is notable that anatomic evidence is accumulating that is consistent with these physiological observations. Specifically, SEF but not FEF receives input from the central superior lateral thalamic nucleus (Huerta and Kaas 1990), where Schlag-Rey and Schlag (1984) reported a high incidence of eye position cells. Moreover, those sites in SEF from which fixed-vector saccades were elicited by microstimulation were reciprocally connected to such sites in the intralaminar nuclei, whereas sites in SEF from which convergent saccades were elicited were connected to functionally corresponding thalamic sites (Schlag-Rey et al. 1987).

If further work validates the existence of an eye position signal in SEF, this would have important implications for our understanding of the neural basis of saccade generation. There is now compelling evidence that the position of the eye in the orbit must be accounted for by the saccade generation mechanism (e.g., Hallet and Lightstone 1976; Sparks and Mays 1983). Exactly how this is done is unknown; indeed, an explicit eye position signal in the forebrain has been somewhat elusive. However, there is now evidence for an eye position–related modulation of perisaccadic and visual activity in extrastriate visual area V3A (Galletti and Battaglini 1989) and in the inferior parietal lobule (Andersen et al. 1985b, 1987, 1990a,b; Andersen and Mountcastle 1983; Lynch et al. 1977; Robinson et al. 1978; Sakata et al. 1980), as well as in central thalamus (Schlag and Schlag-Rey 1984; Schlag-Rey and Schlag 1984). It has been argued that a combination of the activity of a number of neurons with responses that vary with eye position can serve to guide saccades accurately (Andersen et al. 1990b; Zipser and Andersen 1988). It will be interesting to see whether a similar scheme might be appropriate for understanding SEF cell properties.

On the other hand, an alternate point of view holds that an explicit spatial coordinate system is not necessary but that, instead, a combination of the present saccade vector with the next target vector maintains the spatial accuracy; cell activity consistent with this scheme has been described in FEF (Goldberg and Bruce 1990). One key neuronal element in the hypothesis of Goldberg and Bruce is the post-

saccadic cells, which are suggested to signal the vector of the last saccade. In this light, it is interesting to note that the incidence of postsaccadic cells in FEF was significantly higher than that in SEF. It is possible that eye position is registered in the inferior parietal lobule, FEF, and SEF all using different mechanisms.

SELF-GENERATED VERSUS EXTERNALLY CUED MOVEMENTS. Another framework within which to understand the functional differences between FEF and SEF is by analogy to the comparative organization of the postarcuate premotor area (reviewed by Wise 1985) and the SMA (reviewed by Goldberg 1985). It has been suggested that the SMA is responsible for self-generated limb movements, whereas the postarcuate premotor area is responsible for externally-triggered sensory-guided movements. By analogy it might be that corresponding roles are played by the SEF and FEF for eye movements.

In some respects the present results might be consistent with this hypothesis. For example, FEF cells responded more consistently and robustly to the visual or auditory stimuli than did their counterparts in SEF. In addition, the fact that the tonic neurons in FEF continued to discharge after the cue was given in no-go trials indicated that they were responding to the stimulus in their receptive field, whether or not it was still the target for a saccade. By contrast, their counterparts in SEF quit firing once the no-go cue was delivered, even though the stimulus was still present in their receptive field. Besides this, there were three other pieces of evidence showing that at least some of the neurons in SEF that appeared to be visually responsive were not actually stimulus-bound, that is, that their response was not necessarily linked to the actual physical presentation of the target. First, a higher proportion of the cells responding to the target in SEF than in FEF exhibited anticipatory activity. Second, some preparatory set and sensory-movement cells in SEF became activated in specific trials in which the target never appeared. Third, whereas most of the preparatory set and sensory-movement cells in SEF responded equally to the visual or auditory targets, most of the set and sensory-movement cells in FEF responded preferentially for visual or auditory stimuli.

Thus on these grounds it could be argued that FEF more faithfully represents the sensory input, whereas SEF may reflect more of an internally generated signal that combines stimulus location with whether it is the target for a saccade. This statement is not inconsistent with the well-documented enhancement of the visual response of FEF cells to stimuli that are the target for an eye movement (Bruce and Goldberg 1985; Goldberg and Bushnell 1981; Wurtz and Mohler 1976); indeed, it will be important to determine whether the same behavior is seen in SEF. Furthermore, the aforementioned findings are consistent with anatomic observations that afferents from visual cortical areas are denser to FEF than to SEF, while at the same time SEF receives heavier input from prefrontal cortex and the mediodorsal thalamic nucleus (Huerta and Kaas 1990; Huerta et al. 1987).

Three independent experiments have been performed to test the hypothesis under consideration directly in the SMA and postarcuate premotor area (Kurata and Wise 1988; Okano and Tanji 1987; Romo and Schultz 1987). Although there may be some bias in the responses seen in the two areas consistent with the hypothesis, neurons were recorded in both areas that were active before both self-generated and externally triggered movements. Similar results have also been obtained in both FEF and SEF. Bruce and Goldberg (1985) showed that the presaccadic burst cells in FEF discharge before both self-generated and visually guided saccades, provided a reward is contingent on their performance. For SEF, Schlag and Schlag-Rey (1987) showed that presaccadic units are activated before rewarded, self-generated saccades, and the results reported in the previous paper (Schall 1991b) showed that such cells also fire in relation to visually guided saccades. Therefore the distinction between FEF and SEF on these grounds is probably not the most fruitful point of view.

REGULATING INITIATION VERSUS GUIDANCE OF SACCADES. Models of the brain stem saccade generator require two descending inputs, one being target location and the other a trigger signal (reviewed by van Gisbergen and van Opstal 1990). In the search for a reasonable functional difference between these regions, it might be useful to consider the distinctions between the mechanisms responsible for selecting the target, those for initiating a saccade, and those for regulating when the gaze shift will be launched (e.g., Carpenter 1981). Now, it has long been recognized that the SMA does not play a role in the low-level programming of movements. Instead, data have accumulated showing that SMA is important in organizing sequences and regulating patterns of movement (reviewed by Goldberg 1985). Consistent with this, lesions of SMA in humans do not adversely affect visually guided saccades, antisaccades, or even single memory-guided saccades; instead these patients are impaired in generating a sequence of remembered saccades (Gaymard et al. 1990). In light of this finding, it is important to note that there is evidence that saccades can be generated as planned sequences (Zingale and Kowler, 1987). Moreover, a recent report has shown that some neurons in SMA are specifically activated in relation to movements that are part of a sequence (Mushiake et al. 1990).

Evidence from the present study about the respective roles of FEF and SEF in regulating saccade initiation was obtained by comparing the patterns of responses in go trials, requiring execution of a saccade, with the patterns of activation in no-go trials, requiring withholding of a saccade. Whereas the tonic neurons in SEF (preparatory set and sensory-movement) ceased firing after the no-go cue was given, the tonic neurons in FEF continued to discharge in no-go trials until the stimuli were turned off at the conclusion of the trial. Furthermore, a number of units in SEF were specifically or differentially activated after the no-go cue. One interpretation of these results is that the activity of the SEF cells may signal target location only when a saccade is impending. Thus their response could represent not only stimulus location but also movement intention. In contrast, the response of the FEF cells appeared to be more of a pure sensory activation. These results suggest that one way to functionally distinguish FEF from SEF is that the latter

structure has more to do with regulating saccade initiation, i.e., serving as a high-level control over when a gaze shift should occur.

Although much more information about the connections of these two regions is necessary, unfortunately, the anatomic data collected to date neither confirm nor refute this idea. For example, it appears that both SEF and FEF have direct projections to the nucleus raphe interpositus (Huerta and Kaas 1990; Huerta et al. 1987; Shook et al. 1990; Stanton et al. 1988b), which consists of the omnipause neurons (Büttner-Ennever et al. 1988) that appear to be responsible for ultimately initiating saccades. Also, evidence has accumulated for a "triggering circuit" involving the caudate nucleus, substantia nigra, and superior colliculus (reviewed by Hikosaka and Wurtz 1989); and recent work has shown that FEF and SEF send only partially overlapping projections to the striatum (Parthasarathy et al. 1990; Shook et al. 1991). The projections from SEF to striatum tended to be distributed somewhat rostrolaterally relative to those from FEF. In suggestive correspondence with these data is the observation that units in the striatum responding in relation to memory-guided saccades and units exhibiting a gradual elevation of activity preceding saccades tended to be localized rostrolaterally relative to the neurons in the striatum that discharged in relation to visually guided saccades (Hikosaka et al. 1989).

Other evidence that SEF may have relatively more than FEF to do with the regulating the time of initiation of a saccade is obtained from relating neuronal discharge rates directly to saccade latency on a trial-by-trial basis. In the delayed saccade task used for this study, there was a significant reduction in saccade latency as the foreperiod increased. To determine what role the tonic neurons in SEF and FEF played in generating saccades, we performed an analysis relating the level of activity of preparatory set and sensory-movement neurons during the foreperiod to the subsequent saccade latency. Preliminary evidence indicates that on a trial-by-trial basis the level of activity of any single unit in SEF or in FEF does not predict saccade latency (Schall 1988). However, further analysis of these data indicates that the time course of the reduction in saccade latency is correlated with the time course of activation of the preparatory set and sensory-movement cells in SEF but not those in FEF (unpublished observation). The observation that preparatory set cells are more numerous in SEF than in FEF is also consistent with the hypothesis that the activity of the tonic units in SEF regulates when a saccade that has been targeted by FEF can be initiated.

Conclusion

The presence of two regions in the frontal lobe that are involved in generating saccadic eye movements begs for an explanation more profound than redundancy. The results of this comparative study intimate substantial differences in the functional organization of FEF and SEF. Still, it seems that the most revealing experiments have yet to be done. It is to be hoped that the information provided in these papers will aid in the design of these studies.

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