Incomplete Suppression of Distractor-Related Activity in the Frontal Eye Field Results in Curved Saccades

Robert M. McPeek
The Smith-Kettlewell Eye Research Institute, San Francisco, California

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McPeek, Robert M. Incomplete suppression of distractor-related activity in the frontal eye field results in curved saccades. J Neurophysiol 96: 2699–2711, 2006. First published August 2, 2006; doi:10.1152/jn.00564.2006. Saccades in the presence of distractors show significant trajectory curvature. Based on previous work in the superior colliculus (SC), we speculated that curvature arises when a movement is initiated before competition between the target and distractor goals has been fully resolved. To test this hypothesis, we recorded frontal eye field (FEF) activity for curved and straight saccades in search. In contrast to the SC, activity in FEF is normally poorly correlated with saccade dynamics. However, the FEF, like the SC, is involved in target selection. Thus if curvature is caused by incomplete target selection, we expect to see its neural correlates in the FEF. We found that saccades that curve toward a distractor are accompanied by an increase in perisaccadic activity of FEF neurons coding the distractor location, and saccades that curve away are accompanied by a decrease in activity. In contrast, for FEF neurons coding the target location, there is no significant difference in activity between curved and straight saccades. To establish that the distractor-related activity is causally related to saccade curvature, we applied microstimulation to sites in the FEF before saccades to targets presented without distractors. The stimulation was subthreshold for evoking saccades and the temporal structure of the stimulation train resembled the activity recorded for curved saccades. The resulting movements curved toward the location coded by the stimulation site. These results support the idea that saccade curvature results from incomplete suppression of distractor-related activity during target selection.

INTRODUCTION

Natural visual scenes often contain many different objects that could serve as saccade goals. The selection of saccade goals has been studied in the laboratory using visual search tasks, in which a saccade target must be chosen from distractors. We have observed that saccades made in a color pop-out search task tend to show greater variations in curvature than saccades to single stimuli (Fig. 1; also see Arai et al. 2004; McPeek and Keller 2001, 2003). Other studies have also reported trajectory curvature of saccades in tasks with multiple stimuli, including double-step tasks (Findlay and Harris 1984; Minken et al. 1993; Van Gisbergen et al. 1987) and abrupt-onset paradigms in which an irrelevant distractor suddenly appears (Doyle and Walker 2001; Godijn and Theeuwes 2002; Ludwig and Gilchrist 2003; McSorley et al. 2004; Port and Wurtz 2003).

McPeek and Keller (2003) studied the neural correlates of curved saccades in color pop-out search. They found that saccades that curve toward a distractor are accompanied by an increase in the activity of superior colliculus (SC) neurons coding the distractor location. This distractor-related activity peaks around the time of saccade onset and is quenched during the course of the saccade. At the same time, the activity of neurons coding the target location continues unabated. To show that the distractor-related activity is causally related to saccade curvature, subthreshold microstimulation in the SC was used to reproduce the pattern of activity seen at the distractor site for curved saccades. This stimulation successfully induced systematic curvature in saccades made to single visual stimuli presented without distractors.

Port and Wurtz (2003) examined SC activity related to curved saccades using multiple microelectrodes. They simultaneously recorded the activity of two SC neurons coding different movement vectors during highly curved saccades in a task in which two stimuli appeared in rapid succession. These saccades were initially directed toward one stimulus, but their trajectories curved such that they ended near the location of the other stimulus. It was found that two separate pools of SC neurons are sequentially activated for these curved saccades: initially, neurons coding the first goal are active, but later, neurons coding the final saccade goal become active.

Together, these observations imply that curved saccades result when two competing populations of SC neurons are active near the time of saccade onset, with one population eventually winning and suppressing the other. This suggests that target selection and movement execution do not necessarily occur serially, in sequential stages of processing, and that a saccade can be initiated even while the process of target selection is continuing (Hooge and Erkelens 1996; McPeek and Keller 2001, 2002b; McPeek et al. 2000; Theeuwes et al. 1999; Viviani and Swensson 1982). Under this view, the increased saccade curvature that has been observed in these tasks is caused by competition between different saccade goals, occurring immediately before and during the saccade (McPeek and Keller 2001, 2003; Port and Wurtz 2003; Van der Stigchel et al. 2006; Walker et al. 2006).

As a further test of this idea, we studied the activity of neurons in the frontal eye field (FEF) during curved saccades in search. In contrast to the SC (Sparks 1978; Sparks and Hartwich-Young 1989; Sparks et al. 1990; Waitzman et al. 1991), activity in the FEF is normally poorly correlated with saccade dynamics (Segraves and Park 1993). However, like the SC (Basso and Wurtz 1998; Carello and Krauzlis 2004; Glimcher and Sparks 1992; McPeek and Keller 2002a, 2004), the
Saccades to Single Stimuli

Saccades in Search

10 deg

FIG. 1. Saccade trajectories made to visual targets appearing either alone or with distractor stimuli. Left: trajectories of saccades made from the central position to 4 different target locations. Each target appears alone on a blank background. Right: trajectories of saccades made to the same 4 target positions, when the target was presented along with 3 distractors. In each trial, an odd-colored target appears at 1 position, and distractors simultaneously appear at the other 3 positions. Saccades made in the presence of distractors exhibit much more curvature than saccades in the absence of distractors.

FEF is known to be involved in saccade target selection (Schall and Hanes 1993; Schall and Thompson 1999; Schiller and Tehovnik 2005). Thus if the increase in saccade curvature that is seen in the presence of distractors is related to target selection, we should see its correlates in the FEF. Understanding the pattern of activity that gives rise to saccade curvature is also important for interpreting curvature results in behavioral tasks. Many behavioral studies use saccade trajectory curvature as a proxy for the state of activity of the oculomotor system (Doyle and Walker 2001; Godijn and Theeuwes 2004; McSorley et al. 2004; Sheliga et al. 1994; Theeuwes et al. 2005). Thus knowing how activity in different oculomotor structures is related to saccade curvature provides essential information for understanding these results.

We tested the role of the FEF in producing curved saccades in two ways: first, we recorded FEF activity during curved and straight saccades in a visual search task to show that FEF activity is modulated in association with saccade curvature. Next, we stimulated in the FEF, eliciting predictable saccade curvature, to show that FEF activity can be causally linked with saccade curvature.

METHODS

Four male rhesus monkeys (Macaca mulatta) weighing between 4 and 7 kg were used in this study. All four monkeys (A–D) participated in the recording experiments, and two monkeys (A and D) participated in the stimulation experiments. All experimental protocols were approved by the Institutional Animal Care and Use Committee at the California Pacific Medical Center and complied with the guidelines of the U.S. Public Health Service policy on Humane Care and Use of Laboratory Animals.

A detailed description of the general methods and behavioral tasks has been published recently (McPeek and Keller 2003). Eye movements were measured using a magnetic coil system (Fuchs and Robinson 1966; Judge et al. 1980), and eye position and velocity were sampled and stored with a 1-kHz sampling rate. Under dim ambient illumination, monkeys were trained to perform head-restrained eye-movement tasks, for liquid reward, to stimuli presented on a cathode ray tube.

The FEF was accessed through a recording chamber positioned above the arcuate sulcus, implanted aseptically under isofluorane anesthesia. We used standard methods to record single neurons with tungsten microelectrodes. Action potentials were identified using a time-amplitude window discriminator, and spike occurrences were registered with a resolution of 1 kHz. The location of the recording and stimulation sites in the anterior bank of the arcuate sulcus was histologically confirmed in monkeys A–C. Monkey D is still participating in experiments.

In this study, we confined our analyses to visuo-motion neurons. These neurons were identified in the memory-saccade task and showed significant visual and saccade-related activity. We calculated mean visual activity over a period from 50 to 125 ms after target onset for stimuli in the cell’s response field (RF). Similarly, we calculated mean movement-related activity as the discharge over a period from 40 ms before saccade onset to 10 ms after saccade onset. We compared activity during these epochs with each cell’s mean baseline activity, over a period from 25 to 125 ms before target onset (during initial fixation). Cells showing significantly greater than baseline visual and movement activity in the memory-saccade task (P < 0.05 in the Wilcoxon signed-rank test) were included in the analysis.

Memory-saccade paradigm

During an initial fixation interval of 450–650 ms, monkeys fixated a white spot in the central position, subtending 0.25° in diameter with a luminance of 1.2 cd/m² against a homogenous dim background of 0.12 cd/m². At the end of this interval, a target stimulus was presented at a peripheral location while the fixation point remained illuminated. After 150 ms, the target stimulus was removed, and the monkeys had to continue fixating the central fixation point for an additional 500–700 ms. At the end of this “memory” interval, the central fixation point disappeared, and monkeys were rewarded for making a saccade, within 70–500 ms, to the location where the peripheral stimulus had been presented. The target stimulus was a red or green disc, with a luminance of 0.9 cd/m². The size of the target was M-scaled to keep its salience constant across different eccentricities (Rovamo and Virsu 1979). At an eccentricity of 15°, the target subtended 2° of visual angle.

Single-target paradigm

Trials began with a 450- to 650-ms fixation period as for the memory-saccade task. However, at the end of the fixation period, the fixation point disappeared, and an eccentric target stimulus was presented. The physical properties of the target were the same as in the memory-saccade task. In each trial, the target stimulus was randomly presented at one of four possible locations, which were all at the same eccentricity, but were separated from each other by angles of 90°. The four locations were adjusted for each neuron so that one of the locations fell near the center of the neuron’s RF, as determined in a preliminary on-line analysis. The monkeys were rewarded for saccading to the location of the target within 70–400 ms of the onset of the stimuli.

Search paradigm

The search task was identical to the single stimulus task described above, with the difference that three distractor stimuli were presented simultaneously with the target stimulus, at equal eccentricity from fixation, separated by angles of 90° (Fig. 2A). The distractors were identical to each other. They were isoluminant with the target and differed from the target only in color. In each trial, the color of the target was randomly chosen to be red or green, and the distractors were of the opposite color.

As shown in Fig. 2A, the data were separated in four groups, according to the location of the target: Into field (the target appeared in the RF of the neuron); Ipsilocation (the target appeared at the array location separated 90° in direction from the center of the RF, but in the same hemifield); Contra location (the target appeared at the array location separated 90° in direction from the center of RF, but in the opposite hemifield); and Opposite location (the target appeared at the array location diametrically opposite the RF).
FIG. 2. Schematics of the search (A) and stimulation (B) paradigms. Left: paradigm events vs. time. Right: spatial arrangements. A: in the search task, animals were rewarded for making a saccade to an odd-colored target presented with 3 distractors. Target appeared randomly in 1 of 4 locations, and distractors appeared in the other locations. Target positions were defined with respect to location of response field (RF) of each cell under study (shown here by the gray region): the Into field location was at the center of the cell’s RF; the Ipsi location was in the same hemifield as the RF, but shifted by 90° in direction; the Contra location was in the opposite hemifield, but shifted by 90° from the RF; the Opposite location was diametrically opposite the RF. Randomly, in 50% of trials, a subthreshold stimulation train began 30-80 ms after target appearance (30-80 ms). The frequency of pulses in the stimulation train began at 10 Hz and increased linearly over a period of 125 ms to a maximum frequency of either 200 or 250 Hz. The train ended, similar to what has been reported previously (Burman and Bruce 1997; Izawa et al., 2004a,b). Such sites were not studied because our goal was to examine the trajectory of saccades initiated in the midst of the accelerating stimulation train, and such responses were virtually absent at these sites.

Data analysis

Off-line analyses of the eye movement data were performed by algorithms using velocity and acceleration criteria to detect the beginning and end of saccades. The algorithm’s identification of saccades was inspected for every trial to verify its accuracy. The monkeys performed the search task correctly in 76% of trials, well above chance-level performance (25%) and comparable with human performance in a similar task (McPeek et al. 1999). Erroneous saccades to distractors were excluded from analysis, as were saccades that were directed toward the correct target but were inaccurate. Inaccurate saccades were defined as those landing outside a circular region centered on the target stimulus, with a radius equal to the greater of 2° or 15% of the mean saccade amplitude, where mean saccade amplitude was computed separately for each cell and each target location.

Saccade curvature and “corrected curvature”

Saccade curvature was measured as the maximum deviation from a straight-line trajectory, divided by the amplitude of the movement (Smit and Van Gisbergen 1990). Other measures of curvature have been proposed (see Ludwig and Gilchrist (2002) for an evaluation of different curvature measures), but using the maximum deviation allows the present results to be compared easily with previous experiments using the same task (Arai et al. 2004; McPeek and Keller, 2001, 2003). In analyses comparing neural discharge for curved and straight saccades (Figs. 3–5), curved saccades were defined as those with curvature values outside a range 0.75 SD from the mean curvature value computed. The mean curvature value was determined using accurate saccades made in the search task and was separately calculated for each of the four stimulus locations used with each neuron.

Saccades made to different parts of the visual field by different individuals can have idiosyncratic natural curvature values (Smit and Van Gisbergen 1990; Thomas and O’Beirne 1967; Viviani et al., 1977), and we also computed a “corrected curvature” measure (McPeek and Keller 2001, 2003), which allowed us to collapse data across different target positions and different monkeys. Briefly, for each cell or stimulation site, we computed the mean curvature for saccades made to each target location in the single-stimulus task. We used these means as the natural curvature values for saccades made to those locations. We then subtracted these means from each individual curvature value for saccades made to the same location by the same animal in the search or stimulation paradigms to obtain the deviation from the baseline natural curvature. We adjusted the sign of curvature so that saccades that curved toward the RF of the cell being recorded (or toward the FVS of the stimulation site) had positive curvature values and saccades that curved away from the RF (or FVS) had negative curvature values. We call this new curvature measure “corrected curvature,” to distinguish it from the raw curvature values.
RESULTS

FEF activity for curved saccades

We report here on the activity of 86 FEF visuo-movement neurons. Consistent with earlier studies (Arai et al. 2004; McPeek and Keller 2001, 2003), we found significantly greater saccadic curvature in the search task than in the single-stimulus task (mean unsigned curvature in search = 0.049, in single-stimulus task = 0.024; \( t \)-test: \( P < 0.001 \)). We examined the activity of each cell in the search paradigm for straight and curved saccades to each of the four target locations tested. Curved saccades could be curved in one of two directions (either clockwise or counterclockwise), and we analyzed the two directions of curvature separately. A factorial two-way ANOVA, with target location (Into field, Ipsi, Contra, and Opposite) and curvature direction as factors, indicated that there were no significant differences in the magnitude of unsigned corrected curvature among the different groups of curved saccades (all \( P > 0.21 \)), confirming that the groups were similar except for their directions of curvature and target locations.

Although the movement fields of FEF neurons are typically fairly large, saccade-related activity in FEF is known to depend on the endpoint of the movement being made (Bruce and Goldberg 1985). To minimize the likelihood that endpoint differences between curved and straight saccades would influence our findings, we excluded inaccurate saccades from analysis (see METHODS). As a further check, we measured the mean radial distance between the endpoints of the straight saccades and the saccades curved in each direction for each cell and each target location. The differences in endpoint were small (maximum difference for any cell = 1.6°; mean difference across cells = 0.6°), indicating that the saccades differed primarily in the trajectories they took to reach similar endpoints.

The activity of a representative FEF neuron for curved and straight saccades is shown in Fig. 3, aligned on the onset of the saccade. The approximate center of the cell’s RF (up and right) is shown by the gray region in the top panels. For saccades made into the cell’s RF (Fig. 3A), there is no difference in the cell’s discharge for straight saccades (shown in blue) versus saccades curved in either the counterclockwise (red) or clockwise (green) directions: for all three groups of saccades, the cell shows a similar increase in activity peaking around the time of movement onset.

The results are quite different for saccades made to the Ipsi target location (Fig. 3B). As expected, the cell shows an overall lower level of activity for saccades to this location than for saccades into the RF. Around the time of saccade onset, there is a gradual decrease in mean activity for straight saccades, because the selected saccade goal lies outside the RF. However, if curved saccades are caused by lingering competition between target and distractor goals, we expect that saccades that are curved toward this cell’s RF (in the counterclockwise direction) will be accompanied by a higher rate of activity in this cell. As shown in Fig. 3B, for saccades curved toward the cell’s RF (red trace), the cell’s activity immediately before the saccade is higher than for straight saccades, as predicted.

We also predict that saccades that curve away from the cell’s RF will not be accompanied by increased activity. In fact, for this cell, there appears to be a slight decrease in activity (green trace). We speculate that saccades curving away from the cell’s RF may be accompanied by greater discharge of neurons coding the stimulus in the Opposite location (diametrically opposed to the cell’s RF), because the saccades curve toward the Opposite location. It is possible that competition from these cells drives down the activity of the recorded cell.

We quantified the cell’s perisaccadic activity as the mean discharge rate during a 50-ms time window from 40 ms before to 10 ms after saccade onset. Because the continuous curvature parameter was binned to create three groups (curved toward, straight, and curved away), we used a linear contrast (Rosenthal et al. 2000) to test for a consistent trend in the cell’s activity across the three groups. For saccades to the Ipsi location (Fig. 3B), the contrast confirmed a significant linear trend in the cell’s activity (\( P < 0.001 \)), with higher perisaccadic activity for saccades curved toward the cell’s RF, and...
lower activity for saccades curved away from the RF. We performed a similar comparison for saccades made when the target was in the cell’s RF. Here, we compared perisaccadic discharge for straight, counterclockwise, and clockwise curved saccades (Fig. 3A) and found no significant linear trend ($P = 0.79$). Thus when saccades are made to the center of the RF, activity is not correlated with trajectory curvature.

Population activity in FEF for curved saccades

This pattern of results for curved and straight saccades is also apparent in the mean activity of our population of cells during the perisaccadic period (Fig. 4). Here, we only included the analysis of a particular target location for each cell if there were at least five saccades curved in each of the two directions (clockwise and counterclockwise) in the set of movements for that location. Typically, the number of movements curved in each direction included in each of the four directional sets was 9, and the number of straight movements was usually $\geq 35$.

To examine population activity, we first normalized the activity of each cell according to its maximum discharge rate for saccades made into its RF. This normalization procedure prevented the population activity from being dominated by cells with higher overall firing rates. Figure 4A shows that the mean population activity for saccades made into the RF is virtually identical for straight saccades and for saccades curved either clockwise or counterclockwise. We had sufficient data to
include 50 cells in the population estimates for this panel. A contrast revealed no significant linear trend \((P = 0.42)\) for activity during the perisaccadic period. On the other hand, for saccades made to the Ipsi location (Fig. 4B), perisaccadic activity is higher for movements curved toward the RF than for straight saccades, and lower for movements curved away from the RF (linear contrast: \(P = 0.0014\); 52 cells contributed to the population activity estimates). A similar, but less pronounced, pattern of results is seen for the Contra location (Fig. 3C): activity is slightly higher for saccades curved toward the RF than for straight saccades, and slightly lower for saccades curved away from the RF \((P = 0.037; n = 56)\). Finally, for the Opposite location, there is no apparent difference in activity for straight saccades and saccades curved in either direction \((P = 0.37; n = 58)\). This last result confirms that the modulations seen for curved saccades are not simply generalized changes in activity across all FEF neurons. Rather, curvature-related activity is spatially specific, occurring only when the direction of curvature is either toward or away from the cell’s RF.

Figure 5 shows scatterplots of the perisaccadic activity of each cell for curved and straight saccades made to each target location. Figure 5A compares activity for curved and straight saccades made to the center of the RF. Saccades curved in both the clockwise and counterclockwise directions are included here. We had sufficient data to include 62 cells in this analysis, and we found that there was no significant difference in activity across cells for curved versus straight saccades (paired \(t\)-test, \(P = 0.29\)). Figure 5B makes a similar comparison for saccades to the Opposite location. Again, we included saccades curved in both the clockwise and counterclockwise directions, and we had enough data to analyze 74 cells. As for the Into field location, we found no significant difference in perisaccadic activity between curved and straight saccades \((P = 0.73)\) for the Opposite location.

For saccades made to the Ipsi and Contra locations, if curvature toward the RF is caused by competition between the RF stimulus (distractor) and the target, we predict that saccades curved toward the cells’ RFs will be accompanied by greater activity than straight saccades. These comparisons are shown in Fig. 5, C and D. Figure 5C shows that the activity for saccades to the Ipsi location that are curved toward the RF is significantly higher than the activity for straight saccades \((n = 65; P < 0.005)\). For the Contra location, shown in Fig. 5D, there is also a significant increase in activity for saccades that curve toward the RF \((n = 69; P = 0.016)\). Similar comparisons for saccades to the Ipsi and Contra locations that curved away from the RF are shown in Fig. 5, E and F. For the Ipsi location (Fig. 5E), there was an overall lower rate of perisaccadic activity for saccades curved away from the RF \((P = 0.021)\). For the Contra location (Fig. 5F), the trend was not significant \((P = 0.17)\).

**Relationship between FEF discharge and amount of curvature**

If curvature is related to competition between target and distractor stimuli, stronger distractor-related activity should result in greater curvature toward the distractor location. In the preceding analyses, we simply categorized saccades as curved in one of two directions without regard to the magnitude of curvature. Here, we treat curvature as a continuous variable and examine the curvature of saccades as a function of the deviation of perisaccadic activity from the activity for straight saccades to the same location. Because of the limited number of curved saccades recorded for each neuron, this required us to pool data across neurons. For each cell, we first computed the mean baseline perisaccadic activity for straight saccades to each target location. For each saccade, we then calculated the deviation in mean perisaccadic activity from this baseline for saccades to the same target location. To pool across neurons with different maximum firing rates, we normalized these changes in perisaccadic activity by each cell’s mean activity level for accurate, straight saccades made into the RF. This prevented cells with higher maximal discharge rates from dominating the results. We plotted the mean normalized change in activity level as a function of curvature.

The results for the Ipsi target location are shown in Fig. 6A. The data are binned by curvature value, with the horizontal error bars showing the width of each bin. As curvature toward the RF increases (positive curvature values), FEF activity systematically increases above its normal baseline level for...
straight saccades made to the same location. On the other hand, when saccades are curved away from the RF, FEF activity declines below baseline, although this decrease in activity is less pronounced.

As a control measure, we performed a similar analysis for saccades to the Opposite location (Fig. 6B). Unlike the results for the Ipsi location, we do not predict any systematic change in activity as a function of the direction or magnitude of curvature for the Opposite location. However, this analysis provides a measure of the amount of noise inherent in the analysis. Here, positive curvature values denote curvature in the counterclockwise direction and negative curvature values denote curvature in the clockwise direction. As shown in Fig. 6B, there is no systematic change in activity as a function of curvature for the Opposite location. Overall, the data support the idea that greater perisaccadic activity at a distractor site, presumably because of ongoing competition between target and distractor stimuli, is associated with greater curvature toward the distractor.

We quantified these observations by testing for the presence of a significant correlation between curvature and normalized FEF activity pooled across cells at each of the four target locations. We found that the correlation between curvature and FEF activity was significant ($P < 0.001$) for the Ipsi and Contra locations (Pearson $r = 0.17$ and 0.11, respectively), but was not significant for the Into field or Opposite locations ($r = 0.017; P = 0.23$ and $r = 0.015; P = 0.31$, respectively). We also found that the correlation between curvature and FEF activity was significantly higher for the Ipsi location than for the Contra location ($P = 0.01$). Finally, across all locations, we found a significant correlation between saccade latency and curvature ($P < 0.01$), with greater curvature for shorter latency saccades, but the magnitude of this correlation was small ($r = 0.03$), consistent with our earlier findings (McPeek and Keller 2003).

To determine whether the apparent correlation between FEF activity and curvature is dependent on saccade latency, we fitted a linear regression model of normalized FEF activity that incorporated both corrected curvature and saccade latency as factors. By testing the significance of the regression coefficient for curvature, we found that, even accounting for saccade latency, curvature was a significant predictor of FEF activity for the Ipsi and Contra locations ($P < 0.002$ in both cases), but not for the Into field or Opposite locations ($P > 0.30$ in both cases).

Finally, we compared the strength of the correlation between FEF activity and curvature with that of the SC, by reanalyzing SC neural data that was collected under virtually identical experimental conditions to this study (McPeek and Keller 2003). We calculated Pearson correlation coefficients between corrected curvature and normalized mean perisaccadic firing rate for SC neurons in the same way that we did for FEF neurons. For both the Ipsi and Contra positions, SC activity was significantly correlated with saccade curvature (Ipsi, $r = 0.21$; Contra, $r = 0.15; P < 0.001$ in both cases), whereas there was no significant correlation for the Into field and Opposite locations (Into field, $r = 0.019$; Opposite, $r = 0.014; P > 0.29$ in both cases). Although the correlation coefficients for both the Ipsi and Contra locations were higher for the SC than the FEF, this difference was significant only for the Contra location (Ipsi, $P = 0.07$; Contra, $P = 0.03$).

**Saccade curvature caused by FEF microstimulation**

In the previous section, we found that curved saccades in search are associated with increased activity of FEF cells coding the distractor location toward which the saccade curves. We reasoned that if this activity is causally linked to saccade curvature, we should be able to induce curvature in saccades by applying appropriate microstimulation to the FEF. Figure 2B shows the stimulation paradigm, which is virtually identical to that used in an earlier study of SC activity and saccade curvature (McPeek and Keller 2003). After an initial fixation
period, a single visual target was presented at one of two locations, and monkeys were rewarded for making a saccade to the target. In randomly selected trials, electrical microstimulation was delivered before saccade onset. The temporal profile of the stimulation train was intended to resemble the pattern of activity that we recorded in FEF neurons coding distractor stimuli for saccades curved toward the distractor. Specifically, the train began before saccade onset and steadily increased in frequency, before being terminated upon saccade onset. The visual targets were randomly placed in each trial at either the Ipsilateral or Contra location relative to the movement vector coded by the stimulation site (see Fig. 2).

We applied this paradigm at 22 sites in two monkeys. Results from a representative site are shown in Fig. 7. We first determined the movement vector coded by the FEF site by applying suprathreshold stimulation (50 µA at 350 Hz) to produce what we refer to as FVS (Fig. 7A). We decreased the stimulation frequency to 250 Hz (the maximum frequency used in the curvature experiments) and lowered the stimulation current until saccades were no longer elicited (Fig. 7B). Using these subthreshold parameters, we carried out the curvature stimulation paradigm described above, presenting a single target at the Ipsilateral or Contra side and delivering microstimulation randomly in 50% of trials. We separately analyzed trials with and without stimulation, shown in Fig. 7, C and D, respectively. In the stimulation condition, many saccades to the visual target exhibited greater curvature than saccades made to the same location in the absence of stimulation. The direction of this curvature was consistently toward the FVS coded by the stimulation site. Thus it is as though the microstimulation acts as a "virtual" distractor, which competes with the saccade target, resulting in a deviation of the movement trajectory.

**Influence of “deadtime” on stimulation-induced saccade curvature**

The saccades produced in the subthreshold stimulation condition in Fig. 7C have a wide range of curvature values, from very little curvature to highly curved. We suspected that the amount of curvature induced by stimulation might be critically dependent on the timing of the stimulation train relative to the onset of the saccade. Indeed, we found such a relationship for stimulation in the SC (McPeek and Keller 2003). In the SC study, as in this experiment, the stimulation train was terminated 125 ms after it began, or as soon as a saccade was detected, whichever occurred first. We measured the time between the final stimulation pulse delivered and the onset of the saccade, which we called the deadtime. We examined saccade curvature for long versus short deadtimes. Results for a representative site are shown in Fig. 8. When the deadtime between the final stimulation pulse and saccade onset was large, very little curvature was observed (Fig. 8A). On the other hand, when stimulation occurred within ~30 ms of saccade onset, we typically observed a greater amount of curvature (Fig. 8B). For comparison, the randomly interleaved trials without stimulation are shown in Fig. 8C.

Summary data relating deadtime and the amount of curvature in the direction of the FVS across all 22 of our stimulation sites are shown in Fig. 9. In some trials, one or two stimulation pulses were delivered after saccade onset, because of unavoidable delays in detecting the saccade and in the real-time control of the stimulator. These trials were assigned negative deadtime values (at right side of abscissa), whereas trials in which the stimulation train stopped before saccade onset were assigned positive values of deadtime. The mean and SE of curvature in nonstimulated trials is shown by the symbol at the left side of the abscissa. In general, the pattern observed here for FEF stimulation resembles that seen for SC stimulation (McPeek and Keller 2003). Large values of deadtime were generated when the 125-ms stimulation train reached its maximum frequency and ceased before saccade onset. For these trials, there was little systematic curvature in the direction of the FVS, even though the stimulation train reached its highest frequency. On the other hand, robust curvature is seen for deadtimes of ~30 ms or less. Thus it seems that stimulation within ~30 ms of saccade onset is critical for generating saccade curvature.

**Influence of final stimulation frequency on saccade curvature**

Even when the deadtime is optimal for producing curved saccades, a wide range of curvature values is still obtained...
A logical explanation is that the amount of curvature may depend on the frequency of stimulation immediately before saccade onset. Our stimulation train varied in frequency across its duration from 10 to 250 Hz. Depending on when the saccade occurred with respect to the onset of the stimulation, the mean stimulation frequency immediately before the saccade could vary. We quantified “final frequency” as the mean stimulation rate in the final 30 ms before saccade onset. In Fig. 10A, we plot saccade trajectories grouped by final frequency for a representative FEF stimulation site. The saccades clearly show greater curvature in the direction of the FVS as final frequency increases, and in general, stimulation-induced curvature is greater for saccades to the Ipsi location than to the Contra location. In Fig. 10B, for the same site, we plot the curvature of each saccade as a function of final frequency. Again, the greatest amount of curvature is seen at high final frequencies for saccades made to the Ipsi location. For these saccades, the stimulating electrode is located in the same side of the FEF as the representation of the saccade target.

Plots of corrected curvature versus final frequency for Ipsi and Contra target locations across all 22 stimulation sites are shown in the left panels of Fig. 11. As for the example site, the amount of trajectory curvature toward the FVS increases systematically with increasing final frequency. Furthermore, stimulation is more effective in producing saccade curvature when the representation of the target is in the same FEF as the stimulation (Ipsi location) than when they are in opposite sides of the FEF (Contra location). We quantified these effects by calculating Pearson correlation coefficients for corrected curvature and final frequency across the entire data set. Not surprisingly, the correlations were highly significant ($P < 0.001$) for saccades to both target locations, and the Ipsi location showed a larger correlation ($r = 0.375$) than the Contra location ($r = 0.24$). This Ipsi/Contra difference was significant ($P = 0.01$). For comparison, we reanalyzed SC stimulation data from experiments that followed a very similar procedure (McPeek and Keller, 2003), and found that the correlations between corrected curvature and the final frequency of SC stimulation were also highly significant (Ipsi, $r = 0.437$; Contra, $r = 0.383$; $P < 0.001$ for both). Overall, the correlations for the SC were higher than those for the FEF, but this difference was significant only for the Contra location (Ipsi, $P = 0.26$; Contra, $P = 0.01$).

To compare stimulation and recording in the FEF, in the right panels of Fig. 11, we plotted mean saccade curvature as a function of FEF perisaccadic firing rate, across all cells, for the Ipsi and Contra locations. In this analysis, for each trial, we simply obtained the corrected curvature and firing rate over the 50-ms perisaccadic period. Trials were binned according to firing rate, and we plotted the mean corrected curvature of all trials in that bin. While this treatment of the data allows for easy comparison with the stimulation results, it should be noted that it obscures the modulation in activity related to curvature away from the distractor site. Because trials here are sorted by raw firing rate, rather than by curvature, the curved away movements are mixed in with a much larger number of straight movements, thereby masking their effect on FEF activity.

Similar to the stimulation results, we see a systematic increase in curvature with increasing FEF cell activity. As established in the analyses in the previous section, there is also a slightly stronger correlation between FEF cell activity and curvature for the Ipsi location, where the recorded distractor activity is in the same side of the FEF as the target activity, than for the Contra location, where the two are in different hemispheres. Taken together, the stimulation and recording data indicate that there is a greater effect on curvature when...
Saccade curvature and target selection in the FEF and SC

When a saccade target is presented with distractors, a selection process must isolate the target as the saccade goal, while suppressing activity related to the distractors (McPeek and Keller 2002a; Schall and Hanes 1993). Several studies have observed the occurrence of curved saccades in tasks in which a distractor is presented along with a saccadic target (Doyle and Walker 2001; Godijn and Theeuwes 2002; McPeek and Keller 2001; McSorley et al. 2004). Neural recordings in the SC during distractor tasks have found that curved saccades are associated with the presence of two populations of active neurons in the SC: one representing the target and the second representing a distractor (McPeek and Keller 2003; Port and Wurtz 2003). Activity at the distractor site peaks shortly before the movement and is quenched early in its execution, whereas activity at the target site maintains its usual relationship with the movement. These results in the SC suggest that curved saccades arise when a saccade is executed before target selection has been fully resolved. Under this hypothesis, lingering competition between the target and distractor stimuli perturbs the trajectory of the movement (McPeek and Keller 2001, 2003; Theeuwes and Godijn 2004; Van der Stigchel et al. 2006; Walker et al. 2006).

If curved saccades are related to target selection, curvature-related activity should not be confined to the SC, but rather should be seen in other areas involved in target selection. We chose to study the FEF because it has been well established that the FEF plays a central role in target selection (Schall 2002). Furthermore, activity in the FEF normally has little correlation with low-level movement parameters, unlike the SC: activity in many SC neurons is normally well correlated with the peak velocity and onset and offset times of saccades (Sparks 1978; Sparks and Hartwich-Young 1989; Sparks et al. 1990; Waitzman et al. 1991). In contrast, FEF activity is poorly correlated with these parameters (Segraves and Park 1993), suggesting that the FEF is more involved in higher-level aspects of oculomotor function. Thus our finding that FEF activity is correlated with saccade curvature supports the idea that the curvature arises from competition during target selection.

Overall, the results seen here for the FEF are very similar to what we have previously reported for the SC (McPeek and Keller 2003). This suggests that the curvature seen here may involve the whole network of brain areas involved in target selection. Indeed, the SC and FEF are closely interconnected (Leichnetz and Goldberg 1988; Lynch et al. 1994; Segraves and Goldberg 1987; Sommer and Wurtz 2001, 2004), and FEF activity has been shown to have a strong influence on activity in the SC (Schlag-Rey et al. 1992). Thus it is possible that the FEF stimulation effects seen here are caused by orthodromic activation of corresponding sites in the SC (Helmisnki and Segraves 2003). However, it should be noted that, in addition to its direct and indirect projections to the SC, the FEF has independent access to the brain stem (Huerta et al. 1986; Schiller et al. 1980; Segraves 1992), although this pathway normally may not be capable of initiating saccades (Hanes and Wurtz 2001).

Neural mechanisms underlying curved saccades

Suprathreshold stimulation of FEF has long been known to evoke saccades of a given direction and amplitude, determined...
by the site of stimulation (Bruce et al. 1985; Robinson and Fuchs 1969). When two sites are stimulated simultaneously, or when electrical stimulation is combined with a visual target (Schiller and Sandell 1983), averaging saccades are often obtained. These movements are directed to a location that is the weighted average of the locations represented by the two active sites. It seems likely that the curvature seen here results from a similar process, because for curved saccades, we initially see elevated activity at both target and distractor sites. We speculate that the increased activity at the distractor site produces an averaging effect such that the initial direction of the saccade is deviated toward the distractor. The subsequent quenching of this distractor-related activity (either through the resolution of competition in the search paradigm or through cessation of microstimulation) re-establishes the target as the sole saccade goal, and consequently, the saccade trajectory curves around so that the movement ends near the target.

This explanation assumes that the FEF encodes the endpoints of saccades with respect to initial fixation, rather than representing the moment-by-moment vector of movement. If the instantaneous vector of movement were coded, during the final corrective phase of curved saccades, the locus of greatest activity should not be the site which codes the initial target location, but rather a site that codes the remaining motor error between the current eye position and the target. To rigorously test this idea, it would be necessary to record from neurons coding this final direction of movement. Port and Wurtz (2003) explored this issue in the SC using two-electrode recordings, and found that SC activity does not encode the final trajectory of the corrective portion of the movement. We did not perform such recordings, but our data here and in the SC show that the level of activity of neurons coding the location of the target with respect to initial fixation is the same regardless of whether the saccade is straight or curved, lending credence to the idea that the FEF and SC code final target position, rather than directly controlling the trajectory of movement. This idea is also supported by the results of colliding saccade experiments in the FEF (Mushiake et al. 1999; Schlag and Schlag-Rey 1990) and by numerous studies in the SC (Frens and Van Opstal 1997; Goossens and Van Opstal 2000; Keller and Edelman 1994; Keller et al. 1996, 2000; Schlag-Rey et al. 1989; Stanford and Sparks 1994). Under this explanation, FEF and SC activity is related to curvature because it represents a shift in the desired displacement signal, and the trajectory of the movement is determined by downstream brain stem or cerebellar areas. Recent neural models have shown the feasibility of this scheme for producing realistic curved-saccade trajectories (Arai and Keller 2005; Quaia et al. 1999; Walton et al. 2005).

Relationship with behavioral studies of saccade curvature

Recently, there has been a proliferation of studies investigating saccade curvature in various behavioral tasks (Doyle and Walker 2001; Godijn and Theeuwes 2002; Ludwig and Gilchrist 2003; McSorley et al. 2004; Sheliga et al. 1994; Theeuwes et al. 2005; Walker et al. 2006; see Van der Stigchel et al. 2006 for review). Curvature has been taken as a proxy to indicate the state of activity in the oculomotor system when saccades are made in the presence of expected or unexpected distractors with different levels of salience, or when attention has been focused at a given location in the visual field. Many of these studies have speculated that curvature is specifically related to activity in the SC or FEF. Previous recording studies have shown a link between saccade curvature and SC activity (McPeek and Keller 2003; Port and Wurtz 2003). This study establishes that FEF activity is also related to saccade curvature.

Several studies have reported that saccades tend to curve away from a previously attended location (Sheliga et al. 1994, 1995; Tipper et al. 2001; Van der Stigchel and Theeuwes 2005). One explanation for this effect, first articulated by Sheliga et al. (1994), is the “suppression hypothesis,” which posits that attention is associated with increased activity in oculomotor areas and that subsequent inhibition of this attention-related activity before saccade onset results in curvature away from the previously attended location. Consistent with this hypothesis, recent neurophysiological evidence indicates that FEF and SC cells increase their activity when spatial attention is directed into their RFs (Ignashchenkova et al. 2004; Kodaka et al. 1997; Thompson et al. 2005) and that microstimulation of the FEF or SC can shift attention to the location coded by the stimulation site (Cavanaugh and Wurtz 2004; Moore and Armstrong 2003; Moore and Fallab 2001; Müller et al. 2005). This study, along with SC results in earlier studies (McPeek and Keller 2003; Port and Wurtz 2003), provides another piece of evidence consistent with the suppression hypothesis, namely, that modulation of activity in the SC and FEF systematically affects saccade curvature.

Curvature both toward and away from distractors has been reported in other behavioral studies, and it has been hypothesized that curvature toward a distractor occurs when there is residual competition between the target and distractor stimuli, whereas curvature away occurs when the distractor stimulus can be strongly inhibited before saccade initiation (McSorley et al. 2006; Van der Stigchel et al. 2006; Walker et al. 2006). Consistent with this idea, we show here that higher FEF activity at a distractor site causes curvature toward the distractor. Conversely, when FEF activity at a distractor site is suppressed at the time of saccade initiation, we find a tendency for saccades to curve away from the distractor. However, it should be noted that our study differs from the behavioral studies, in that curvature toward or away from one distractor site in our study is always accompanied by curvature in the opposite direction with respect to another distractor site, due to the symmetric configuration of the search array. Nonetheless, the pattern of our results is compatible with the general scheme that has been proposed in these studies.

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