Activity of fixation neurons in the monkey frontal eye field during smooth pursuit eye movements

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Submitted 15 November 2013; accepted in final form 19 April 2014

Izawa Y, Suzuki H. Activity of fixation neurons in the monkey frontal eye field during smooth pursuit eye movements. J Neurophysiol 112: 249–262, 2014. First published April 23, 2014; doi:10.1152/jn.00816.2013.—We recorded the activity of fixation neurons in the frontal eye field (FEF) in trained monkeys and analyzed their activity during smooth pursuit eye movements. Fixation neurons were densely located in the area of the FEF in the caudal part of the arcuate gyrus facing the inferior arcuate sulcus where focal electrical stimulation suppressed the generation of saccades and smooth pursuit in bilateral directions at an intensity lower than the threshold for eliciting electrically evoked saccades. Whereas fixation neurons discharged tonically during fixation, they showed a variety of discharge patterns during smooth pursuit, ranging from a decrease in activity to an increase in activity. Of these, more than two-thirds were found to show a reduction in activity during smooth pursuit in the ipsilateral and bilateral directions. The reduction in activity of fixation neurons began at pursuit initiation and continued during pursuit maintenance. When catch-up saccades during the initiation of pursuit were eliminated by a step-ramp target routine, the reduced activity of fixation neurons remained. The reduction in activity during pursuit was not dependent on the activity during fixation without a target. Based on these results, we discuss the role of the FEF at maintaining fixation in relation to various other brain areas. We suggest that fixation neurons in the FEF contribute to the suppression of smooth pursuit. These results suggest that FEF fixation neurons are part of a more generalized visual fixation system through which suppressive control is exerted on smooth pursuit, as well as saccades.

The frontal eye field (FEF) contains neurons that respond to visual stimuli and neurons that discharge before saccades, and thus the FEF has been postulated to play a role in the generation of saccadic eye movements (Bruce and Goldberg 1985). In addition, the smooth pursuit subregion of the FEF, which is known to be a discrete region near the spur of the arcuate sulcus, contains neurons with activity related to smooth pursuit eye movements (Fukushima et al. 2000; MacAvoy et al. 1991; Ono and Mustari 2009; Tanaka and Lisberger 2002; Tian and Lynch 1996). In addition to this contribution of the FEF to the initiation of eye movements, it has been suggested that this structure contributes to holding the image of a target on the fovea during visual fixation. In the FEF, the suppression of saccades (Azuma et al. 1986; Burman and Bruce 1997; Izawa et al. 2004a, 2004b) and smooth pursuit eye movements has previously been demonstrated by electrical stimulation at an intensity lower than the threshold for eliciting electrically evoked saccades (Esacs) (Izawa et al. 2011). Stimulation of a localized area of the FEF in the caudal part of the arcuate gyrus facing the inferior arcuate sulcus suppressed the generation of both ipsiversive and contraversive saccades and pursuit (area of bilateral suppression; Izawa et al. 2004b, 2011). Within a wide area of the FEF circumscribing the area of bilateral suppression, stimulation suppressed ipsiversive, but not contraversive, saccades and pursuit (area of ipsilateral suppression; Izawa et al. 2004a, 2011). These findings support the idea that the suppressive control of saccades and pursuit may involve a common neuronal assembly in the FEF.

A possible neuronal correlate for the above suppressive control of saccades and smooth pursuit is FEF neurons that discharge during fixation (Bizzi 1968; Suzuki and Azuma 1977). We have previously shown that fixation neurons were concentrated in the area in the FEF where stimulation produced the bilateral suppression of saccades (Izawa et al. 2009). Consistent with the previous report by Suzuki et al. (1979), fixation neurons varied in activity during fixation without a target, from a decrease to an increase in activity relative to that during fixation with a target, suggesting that their activity was not simply visual, but rather was related to active fixation. The discharge of fixation neurons persisted during fixation and usually showed a decrease before the onset of saccades in any direction. Based on these findings, we suggested that the tonic activity of fixation neurons while fixation was maintained may be another expression of the suppressive effects of FEF stimulation. Indeed, fixation neurons in the FEF have been reported to exhibit elevated activity in response to a signal to cancel a planned saccade (Hanes et al. 1998).

To examine the relationship between visual fixation and the suppression of smooth pursuit by FEF stimulation, we recorded the activity of fixation neurons in the FEF during pursuit in trained monkeys. We observed the discharge of a considerable number of fixation neurons in the FEF that showed a decrease in activity during smooth pursuit. These results suggest that the activity of fixation neurons while maintaining fixation may be another expression of the suppressive effects of FEF stimulation.

METHODS

Experiments were performed in two male Japanese monkeys (Macaca fuscata) weighing 7 and 9 kg, respectively. The surgical procedures have been described in previous reports on experiments in which the same monkeys were used (Izawa et al. 2004a, 2004b). All animal experimentation was conducted in accordance with the “Guide for the Care and Use of Laboratory Animals” (Institute of Laboratory Animal Resources, National Research Council, 1996), and the “Guid-
ing Principles for the Care and Use of Animals in the Field of Physiological Sciences (The Physiological Society of Japan, revised in 2001). All surgical and experimental protocols were approved by the Animal Care Committee of Tokyo Medical and Dental University.

**Behavioral training.** During training and experimental sessions, the monkey was seated in a primate chair facing a tangent translucent screen 1.5 x 1.5 m² and 57 cm in front of it. Each monkey was first trained to fixate on a tiny spot of light (0.4° in visual angle, 2 cd/m²) that was generated with a light-emitting diode and back-projected at the center of the screen using a pair of mirrors attached to galvanometers (Suzuki and Azuma 1977; Wurtz 1969). The screen was evenly illuminated at 1.0 cd/m² to eliminate stray light around the spot image on it. The monkey fixated on a center spot and pressed a button with its hand upon the appearance of the spot, which occurred after an intertrial interval of 3–5 s. While the bar was held down, the spot remained illuminated for a variable duration of 1–4 s. The monkey was required to maintain its line of sight within an error window of ±2° around the fixation target. The target was then slightly brightened (0.3 log unit) for 0.5 s. If the monkey released the bar during the short brightening period, it received 0.2 ml of juice as a reward. Otherwise, the trial was terminated without a reward, and a new trial began. Fixation behavior was elicited, since the monkey had to look at the spot to notice its brightening for rapid bar-release. To test the effects of visual stimulation of the fovea on neuronal activity, monkeys were also trained to perform a fixation blink task. In this task, the monkey first fixated on a center spot. After 1 s, the spot disappeared for 400 ms while the monkey had to maintain fixation. The spot then reappeared at the same place. The monkey was rewarded if it steadily fixated throughout the trial, and if it released the bar only during the short brightening period, as in the fixation task.

The monkey was further required to make saccades and then smooth pursuit. For the visually guided saccade (Vsac) task, after a fixation period of 1–1.5 s, the center spot was turned off, and another light spot was turned on elsewhere on the screen as a visual target. The monkey learned to make a saccade to the target, since it had to observe its brightening. If the monkey released the bar during brightening of the target light, it received a reward. The monkey was also trained to make memory-guided saccades (for details, see Izawa et al. 2004a). The memory-guided saccade task was used to examine neuronal activity during saccades without visual targets (Hikosaka and Wurtz 1983). In the smooth pursuit task, the monkey first fixated on the center spot for 1.5 s. After this fixation period, the target moved at a constant velocity. Usually, the velocity and amplitude of target motion were 15°/s and 15°, respectively. At the end of this pursuit period, the target stopped, and the monkey was required to fixate on it for 0.5–1.5 s to receive a reward. To observe early pursuit trajectories without catch-up saccades, the target was also given an initial step (2°) in a direction opposite the velocity of the target (Rashbass 1961).

**Neuronal recordings and experimental procedures.** We used glass-insulated elgiloy microelectrodes (Suzuki and Azuma 1976) with impedances of 0.6–1.2 MΩ at 1 kHz in Ringer solution. The electrode was introduced into the left FEF with a micromanipulator (Narishige, Tokyo, MO-95) attached to an implanted cylinder. Before extracellular recording experiments, we systematically examined the effects of microstimulation in the precurate gyrus at a track interval of 300 μm and depth intervals of 200 or 400 μm (Izawa et al. 2004a, 2004b). Constant-current stimulation trains consisted of 40–60 monopolar cathodal pulses with a 1-ms duration at 5-ms intervals and at ≤80 μA. We determined the thresholds for eliciting Esacs during fixation on the center spot and identified a site as being within the classical FEF when stimulation elicited Esacs at ≤50 μA (Bruce et al. 1985). Stimulation was also applied at the offset of the central fixation point for triggering Vsacs, and the threshold for the suppression of Vsacs was defined in the same way as described before (Izawa et al. 2004a, 2004b).

In extracellular recording experiments, we advanced an electrode while the monkey performed a Vsac task. After isolating a neuron, we analyzed its activity by having the monkey perform a series of tasks. Although we mainly searched for FEF fixation neurons during penetrations, we also identified other classes of FEF neurons using the criteria of Bruce and Goldberg (1985). Neurons with peripheral visual activity but no presaccadic burst activity were classified as visual neurons, neurons with presaccadic burst activity but no peripheral visual activity were classified as movement neurons, and neurons with both peripheral visual and presaccadic burst activity were classified as visuomovement neurons, and their activities were compared with that of fixation neurons. Signals were recorded with an AC-coupled differential amplifier (time constant: 0.5 ms). Discrimination of the action potentials of single neurons from the extracellular recording signal was achieved with a conventional amplitude window discriminator. Several representative recording sites in one monkey were marked with iron deposits by passing currents (electrode positive, 400 μC) through the elgiloy microelectrode (Suzuki and Azuma 1987). At the end of the experiment, the monkeys were deeply anesthetized with pentobarbital sodium and perfused with 6 liters of saline followed by 6 liters of a fixative solution containing 10% formalin. For the monkey with marked recording sites, the fixative solution also contained 2% ferrocyanide. Serial frozen sections of 80 μm were cut coronally from the frontal cortex and stained with thionine. The sections were reconstructed using a camera lucida system. Recording sites were histologically verified to be located in the prearcuate gyrus.

**Experimental control and data acquisition.** The behavioral tasks, presentation of light spots, and data acquisition were controlled by IBM-compatible computers. Eye movements were recorded by a camera measurement system, using the corneal reflection image of infrared light (Iseyo Electric, Tokyo, R-22C-I), with which we could measure horizontal and vertical eye positions with an accuracy of 0.3° and at a sampling rate of 250 Hz. Eye-position signals were calibrated by having the monkey fixate on targets at known eccentricities (10°, 20° and 30°) on the horizontal and vertical meridians and diagonal axes. Horizontal and vertical component signals of eye movements and neuronal activity with respect to behavioral event indicators were stored on computer hard disks and displayed on an oscilloscope. Eye position and neural activity were sampled every 4 ms and 1 ms, respectively. The onset of each saccade was identified in the eye-position traces by a mouse-controlled cursor. Subsequent off-line data analyses were performed using Matlab (MathWorks, Natick, MA) programs. We conducted further analyses here for horizontal eye movements. Mean eye-position signals were obtained by aligning the data with respect to the onset of target motion and calculating the mean within each 4 ms of the data. To obtain eye velocity, the mean eye-position signal was digitally differentiated. Eye velocity was low-pass filtered with a moving average of five data points (−6 dB, 30 Hz). The onset of smooth pursuit was identified as the point in time at which the eye velocity trace crossed the threshold of 3 SDs of the mean of the eye velocity during fixation (300–600 ms before target motion onset). To determine the onset of modulation in the firing rate, we applied the one-sample Kolmogorov-Smirnov test to spike histograms with 10- or 20-ms bin widths aligned with respect to behavioral events (Mano and Yamamoto 1979; Yamauti 1972). We calculated the largest difference between the cumulative distribution curves of sample spike frequencies and spike frequencies during the control period (300 ms for each measurement as described in RESULTS). The modulation, when the firing rate of the neuron increased when the difference exceeded a 0.01 level of significance for a sample of four consecutive bins (one-sided), and the onset time was determined when the increase or decrease in spike frequencies reached a 0.05 level. The one-sample Kolmogorov-Smirnov test was also applied to interspike intervals of spike rasters to confirm measurements made from histograms. Statistical analysis was performed with the Mann-Whitney U-test for single comparisons. A Kruskal-Wallis analysis of variance (ANOVA) was performed for multiple comparisons. Correlations...
between data sets were assessed by measuring the Pearson correlation coefficient.

RESULTS

Identification of fixation neurons in the FEF.

We recorded single units in the FEF and its vicinity in the prearcuate gyrus. To locate the FEF in these monkeys, we first examined depth thresholds for eliciting Esacs and suppressing Vsacs by electrical stimulation in each track (Izawa et al. 2004a, 2004b). The example in Fig. 1A shows the activity of a fixation neuron in the FEF during visual fixation. The activity of this neuron was relatively low and variable during an intertrial interval of 3–5 s while the monkey made saccades spontaneously. When a fixation spot appeared and the monkey foveated it, the neuron increased its firing rate, and the discharge persisted during fixation. The activity of the neuron decreased at the end of fixation. Fixation neurons were identified by their increased firing rate at the start of fixation and the presence of tonic activity during fixation, as described previously (firing rate during steady fixation 0.5–2.5 s after bar-press onset was >2 SDs above the mean firing rate during a 2-s period in the intertrial interval ≥1 s before bar-press onset in the fixation task) (Izawa et al. 2009; Suzuki and Azuma 1977).

Activity of FEF fixation neurons during smooth pursuit. To examine the activity of fixation neurons during smooth pursuit, we recorded their responses to target motion. We recorded from a total of 90 fixation neurons in the FEF during smooth pursuit. We observed different patterns of activity of fixation neurons during smooth pursuit, as summarized in Table 1. We assessed the change in activity of fixation neurons when the mean firing rate during smooth pursuit (100–700 ms after bar-press onset) was 10.220.33.4 on October 28, 2016 http://jn.physiology.org/ Downloaded from

Fig. 1. Identification of a fixation neuron in the frontal eye field (FEF) and its activity during smooth pursuit. **A:** activity of a fixation neuron during visual fixation. Neuronal discharges in successive fixation trials are represented by rasters. The histogram is the result of summing the dots on the raster in 50-ms bins. Horizontal and vertical components of eye position are shown above the raster. The raster and histogram displays are aligned with respect to bar-press onset (vertical dotted line). The 1st to 4th triangles below each raster line mark the appearance of the central fixation point, brightening of the fixation point (cue onset), bar-release (reward onset), and reward offset, respectively. **B and C:** neuronal discharge with a decrease in activity during both ipsiversive (ipsi; B) and contraversive (contra) horizontal smooth pursuit [bilateral suppression (Bsupp) neuron; C]. The velocity and amplitude of target motion were 15°/s and 15°, respectively. The raster and histogram displays are aligned with respect to the onset of target motion (vertical dotted line). The 1st to 4th triangles below each raster line mark the appearance of the central fixation point, bar-press onset, cue onset, and reward onset, respectively. Red lines, average histograms of the population of Bsupp neurons over time for pursuit in this monkey. The calibration in A also applies to B and C. D and E: neuronal discharge in B and C is shown in expanded time scale. **Top:** target position. Each eye velocity profile was obtained from the mean eye position signal. The rapid deflections in eye velocity are associated with catch-up saccades. Horizontal dotted lines, 0°/s. Vertical dotted lines indicate target motion onset. R, right; L, left; U, up; D, down.

Table 1. Classification of fixation neurons due to activity during smooth pursuit

<table>
<thead>
<tr>
<th>Activity Type</th>
<th>Cell Population</th>
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<tbody>
<tr>
<td>Suppressive</td>
<td>35 39</td>
</tr>
<tr>
<td>Bilateral suppression</td>
<td>30 33</td>
</tr>
<tr>
<td>Ipsilateral suppression</td>
<td>5 6</td>
</tr>
<tr>
<td>Contralateral suppression</td>
<td>6 7</td>
</tr>
<tr>
<td>No change</td>
<td>11 12</td>
</tr>
<tr>
<td>Increase</td>
<td>6 7</td>
</tr>
<tr>
<td>Combined</td>
<td>1 1</td>
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<tr>
<td>Eye position</td>
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n, No. of cells.
target motion onset) differed from that during fixation (300–900 ms before target motion onset) by 2 SDs. The same fixation neuron as in Fig. 1A showed a discharge pattern with a bilateral reduction in activity during smooth pursuit. This neuron discharged during fixation and showed a significant decrease in activity during smooth pursuit of a target moving at 15°/s toward the ipsilateral side (Fig. 1B). In addition, the neuron also showed a significant decrease in activity during smooth pursuit of a target moving at 15°/s toward the contralateral side (Fig. 1C). After ipsiversive and contraversive pursuit, the monkey fixated on the target at the new location, and the neuron resumed its firing rate, indicating that the decrease in activity was not related to eye position. The temporal details of eye position, eye velocity, and neuronal discharge with the bilateral reduction in activity during smooth pursuit are shown in Fig. 1, D and E. To further investigate the time course of responses during smooth pursuit, we computed average histograms of the population of fixation neurons with a bilateral reduction in activity during pursuit in this monkey (n = 22; Fig. 1, B and C, red lines). We found that the activity of fixation neurons decreased in concave form during smooth pursuit in both ipsilateral and contralateral directions. Essentially the same discharge pattern with a bilateral reduction in activity during pursuit was also observed for fixation neurons in the other monkey; it tended to start fixation before the onset of the fixation point, and the onset of the increase in activity at the start of fixation relatively fluctuated. Overall, 35 fixation neurons showed this pattern of bilateral suppression (Bsupp neurons, 39%).

Figure 2 shows another discharge pattern of a fixation neuron with a decrease in activity during ipsiversive smooth pursuit, but not contraversive pursuit. This neuron maintained tonic activity during fixation (Fig. 2A) and then showed a decrease in activity during ipsiversive smooth pursuit (Fig. 2, B and D). The neuron resumed its firing rate during refixation after pursuit. This reduction in activity was very similar to that during ipsiversive pursuit observed for the above discharge pattern with a bilateral reduction in activity. However, it did not show a decrease in activity when the monkey performed contraversive smooth pursuit (Fig. 2, C and E). Red lines in Fig. 2, B and C, show average histograms of the population of fixation neurons with an ipsilateral reduction in activity during pursuit in this monkey (n = 15). The activity of fixation neurons decreased in concave form during ipsiversive smooth pursuit, but not contraversive pursuit. Overall, a discharge pattern in which activity was decreased during ipsiversive smooth pursuit and unchanged (n = 25) or increased (n = 5) during contraversive pursuit was observed in 30 fixation neurons [ipsilateral suppression (Isupp) neurons, 33%]. In addition, five fixation neurons showed a decrease in activity during contraversive pursuit but not ipsiversive pursuit [contralateral suppression (Csupp) neurons, 6%]. Therefore, three-fourths of the fixation neurons showed a reduction in activity during smooth pursuit in unilateral or bilateral directions. Among the remaining fixation neurons, 18 did not show a decrease in activity but rather showed maintained or increased activity during both ipsiversive and contraversive smooth pursuit, and 2 showed activity related to eye position. The whole population of fixation neurons is shown quantitatively in Fig. 3, where activity during ipsiversive and contraversive smooth pursuit (15°/s in velocity, 15° in amplitude) is plotted against activity.

Fig. 2. Discharge pattern of a fixation neuron in the FEF with an ipsilateral decrease in activity during smooth pursuit [ipsilateral suppression (Isupp) neuron]. A: activity of a fixation neuron during the fixation task. The triangle below the histogram marks cue onset. B and C: neuronal discharge with a decrease in activity during ipsiversive (B) but not contraversive pursuit (C). The velocity and amplitude of target motion were 15°/s and 15°, respectively. The 1st and 2nd triangles below each histogram mark bar-press onset and cue onset, respectively. Red lines, average histograms of the population of Isupp neurons over time for pursuit in this monkey. D and E: neuronal discharge in B and C is shown in expanded time scale. Each eye velocity profile was obtained from the mean eye position signal. Arrangement is the same as in Fig. 1, except for the rasters.
during fixation. The distributions of fixation neurons in these scatter plots were not discrete but rather formed a continuum.

The example in Fig. 4A shows the discharge pattern of a fixation neuron with maintained activity during both ipsiversive and contraversive smooth pursuit. This neuron increased its firing rate at the start of fixation and discharge persisted throughout the fixation, ipsiversive smooth pursuit, and refixation periods (Fig. 4, A and B, ipsi). Similar tonic discharge was also observed throughout the fixation, contraversive pursuit, and refixation periods (Fig. 4, A and B, contra). We observed this pattern of activity in 11 fixation neurons (12%). In the example in Fig. 4C, a fixation neuron discharged tonically during fixation and showed an increase in activity during both ipsiversive and contraversive smooth pursuit. This pattern of activity was seen in six fixation neurons. As in this example, fixation neurons with increased activity during smooth pursuit tended to increase their firing rate before the onset of target motion (Fig. 4, C and D). In addition, one fixation neuron showed increased activity during ipsiversive smooth pursuit and maintained activity during contraversive pursuit.

Since fixation neurons with suppressed activity during smooth pursuit were most prevalent (see Table 1), we studied the reduction in activity during pursuit in more detail. In the smooth pursuit task, smooth eye movements start with catch-up saccades when a target starts to move at constant velocity and amplitude of target motion were 15°/s and 15°, respectively. B: neuronal discharge in A is shown in expanded time scale. C: a pattern of neuronal discharge with increased activity during both ipsiversive and contraversive pursuit (right). The velocity and amplitude of target motion were 15°/s and 15°, respectively. D: neuronal discharge in C is shown in expanded time scale. Each eye velocity profile in B and D was obtained from the mean eye position signal. Arrangement is the same as in Fig. 2, B–E. The calibrations in A and B also apply to C and D, respectively.
velocity. To investigate the relationship between a decrease in the activity of fixation neurons and catch-up saccades, the target was given an initial step (2°) in a direction opposite the velocity (Fig. 5). An example of the activity of a Bsupp neuron during the smooth pursuit task is shown in Fig. 5A. Eye velocity during pursuit initiation included a transient increase that corresponded to catch-up saccades and was followed by eye velocity during maintained pursuit in both ipsilateral and contralateral directions. During maintained pursuit, eye velocity showed substantial oscillations around the desired velocity (Lisberger et al. 1987). This neuron showed a decrease in activity during both ipsiversive and contraversive smooth pursuit. In the same neuron, we examined activity during pursuit without initial catch-up saccades (Fig. 5B). Catch-up saccades were eliminated using the step-ramp target motion, as was also indicated by the eye velocity traces. This neuron showed a decrease in activity during smooth pursuit bilaterally, despite the absence of catch-up saccades. This result indicated that the reduction in activity of the fixation neuron was related to smooth pursuit per se rather than the initial catch-up saccades. Overall, in 39 fixation neurons that showed a decrease in activity during pursuit unilaterally or bilaterally, we also examined the activity during pursuit without catch-up saccades using the step-ramp stimulus. We confirmed this result by computing average histograms of the population of fixation neurons with a reduction in activity during pursuit with and without catch-up saccades in the ipsilateral (n = 35) and contralateral directions in two monkeys (n = 24) (Fig. 5, A and B, red lines). There was no significant difference in the reduction in activity between ipsiversive smooth pursuit with and without catch-up saccades (Wilcoxon signed-rank test, $P = 0.50, n = 35$). Similarly, there was no significant difference in the reduction in activity between contraversive pursuit with and without catch-up saccades (Wilcoxon signed-rank test, $P = 0.33, n = 24$). On the other hand, in some sustained activity during pursuit, we also observed a transient reduction in activity at the start of smooth pursuit, which was related to initial catch-up saccades (see Fig. 4, C and D).

We assessed the decrease in the activity of fixation neurons associated with smooth pursuit (1-sample Kolmogorov-Smirnov test, $\alpha < 0.05$) compared with the firing rate during steady fixation (300–600 ms before target motion onset). We then measured the latency of the reduction in activity from the onset of smooth pursuit. The eye velocity and firing rate signals have different noise levels; hence the exact time of the latency may have different biases. The example in Fig. 6, A and B, shows the decrease in the activity of a Bsupp neuron during smooth pursuit. The latency of the onset of ipsiversive smooth pursuit from target motion onset was 132 ms, and the latency of the reduction in activity for this neuron from target motion onset was $\sim 120$ ms (Fig. 6A). Therefore, the reduction in activity of the fixation neuron preceded the onset of ipsiversive pursuit by $\sim 12$ ms. Similarly, the latency of the onset of contraversive smooth pursuit from target motion onset was 120 ms, and the latency of the reduction in activity for this neuron from target

Fig. 5. Comparison of the activity of a fixation neuron in smooth pursuit trials with and without catch-up saccades during the initiation of pursuit. A: activity of a Bsupp neuron during pursuit with initial catch-up saccades. The velocity and amplitude of target motion were 15°/s and 15°, respectively. B: neuronal discharge with a decrease in activity during both ipsiversive and contraversive pursuit (15° in amplitude) without initial catch-up saccades. Same neuron as in A. The target was given an initial step (2°) in a direction opposite the velocity (15°/s). Top: target position. Each eye velocity profile was obtained from the mean eye position signal. Horizontal dotted lines, 0°/s. Vertical dotted lines, target motion onset. Red lines, average histograms of the population of fixation neurons with a reduction in activity over time for pursuit with (A) and without catch-up saccades (B) in two monkeys. The calibration in A also applies to B.
motion onset was ~110 ms (Fig. 6B). Therefore, the reduction in activity of the fixation neuron preceded the onset of contraversive pursuit, and the latency was ~10 ms. Although the latencies for this neuron approach the widths of the bins in the underlying histograms, the coarseness of individual measurements is overcome by combining the results across the population of neurons. Overall, the latencies of the reduction in activity from the onset of ipsiversive smooth pursuit had a mean of −19.7 ± 38.3 (SD) ms (n = 35; Fig. 6C). The latencies of the reduction in activity from the onset of contraversive smooth pursuit had a mean of −17.4 ± 37.5 ms (n = 24; Fig. 6D). We did not observe a difference in the latencies of the reduction in activity from the onset of ipsiversive smooth pursuit between Isupp neurons and Bsupp neurons (U-test, P = 0.26). Similarly, there was no significant difference in the latencies of the reduction in activity from the onset of contraversive smooth pursuit between Csupp neurons and Bsupp neurons (U-test, P = 0.64). The preceding time for the reduction in activity of fixation neurons before the onset of smooth pursuit tended to be shorter than that of saccades in both ipsilateral and contralateral directions.

To represent the change in discharge between fixation and smooth pursuit more quantitatively for the full population of fixation neurons, we calculated the ratio of activity during ipsiversive and contraversive pursuit (15°/s in velocity, 15° in amplitude) to activity during fixation (pursuit activity index). Fixation neurons had indexes less than 1 if the activity decreased during smooth pursuit, indexes greater than 1 if the activity increased during pursuit, and indexes of ~1 if the activity did not change. Pursuit activity indexes for fixation neurons with different patterns of activity during smooth pursuit are shown in Table 2. Overall, ipsilateral pursuit activity indexes had a median of 0.56 (interquartile range, 0.51), and contralateral pursuit activity indexes had a median of 0.88 (interquartile range, 0.75) for 90 fixation neurons. To obtain some idea about whether there were differences in the population of fixation neurons (e.g., interneurons), we examined pursuit activity indexes in terms of spontaneous discharge rates of fixation neurons. We found that these pursuit activity indexes for fixation neurons were not clearly related to their spontaneous discharge rates during a 2-s period in the intertrial interval (r = 0.003, P > 0.1 and r = 0.002, P > 0.1 for ipsilateral and contralateral directions, respectively). We also examined pursuit activity indexes in terms of the ratio of activity during fixation (2-s period) to activity during the intertrial interval (2-s period) and found no clear relationship between them (r = −0.15, P > 0.1 and r = −0.16, P > 0.1 for ipsilateral and contralateral directions, respectively). It is possible that the activity of fixation neurons during smooth pursuit was related to discharge patterns during fixation, since pursuit is a continuous movement in contrast to saccades, which are discrete movements. We then examined pursuit activity indexes for fixation neurons in terms of discharge patterns during fixation. During the fixation task, fixation neurons showed some different discharge patterns, as described previously (Izawa et al. 2009): tonic activity at a firing rate that was maintained throughout fixation, tonic activity with a transient increase at the beginning of fixation, tonic activity followed by an increase in activity at the end of the trial, and some combination of these. However, we observed

![Fig. 6. The onset of the reduction in activity of single fixation neurons associated with the onset of smooth pursuit. A and B: decrease in activity during ipsiversive (A) and contraversive pursuit (15° in amplitude) without initial catch-up saccades in response to step-ramp target motion at 15°/s (B). Same neuron is shown as in Fig. 5. Vertical dotted lines, target motion onset. Upward arrows indicate the onset of pursuit. Downward arrows indicate the onset of the reduction in activity of the fixation neuron. C and D: latency histograms of the decrease in the activity of fixation neurons from the onset of ipsiversive (C) and contraversive pursuit (D) (arrows).](http://jn.physiology.org/)
no clear relationship between these discharge patterns during fixation and pursuit activity indexes ($r = -0.04$, $P > 0.1$ and $r = 0.01$, $P > 0.1$ for ipsilateral and contralateral directions, respectively). Therefore, the phasic activity of fixation neurons may not influence smooth pursuit.

We further examined pursuit activity indexes for fixation neurons in terms of their foveal visual responsiveness. To examine foveal visual responsiveness, we examined the activity during the fixation blink task. During steady fixation, the fixation neuron shown in Fig. 1 maintained its activity even when the fixation spot disappeared for 400 ms (Fig. 7A). On the other hand, the neuron shown in Fig. 2 increased its activity during the blink period (Fig. 7B). To represent foveal visual responsiveness, we calculated the ratio of activity during fixation without a target (100–400 ms after the disappearance of the fixation point) to activity during fixation with a target (0–300 ms before the disappearance of the fixation point) for each fixation neuron (blink activity index). Fixation neurons had blink activity indexes less than 1 if their activity was dependent on a visual stimulus. We examined the whole population of fixation neurons, from neurons with foveal visual-related activity to neurons with activity that was related to active fixation. In the scatter plots in Fig. 7, C and D, blink activity indexes are plotted against pursuit activity indexes for 78 fixation neurons. Bsups neurons, Isups neurons, and Csupps neurons are plotted as filled circles, open circles, and open squares, respectively. Neurons with other patterns of activity during pursuit are plotted as gray circles. The distribution of fixation neurons in these scatter plots was not discrete, but rather formed a continuum. We observed that different fixation neurons, which showed a similar pattern of activity during smooth pursuit, exhibited different responses to visual stimulation of the fovea in the fixation blink task, ranging from a decrease in activity to an increase in activity. Fixation neurons with each pattern of activity during pursuit were intermingled at the border, since the change in activity was assessed using the SDs of the firing rate. Blink activity indexes were not significantly different among Bsups neurons, Isups neurons, Csupps neurons, and fixation neurons with no change and an increase in activity during pursuit in bilateral directions (Kruskal-Wallis ANOVA, $P = 0.60$). Therefore, these results indicated that their activity was not simply related to foveal visual stimulation (Suzuki et al. 1979).

Comparison of activity during pursuit and saccades. Although the above fixation neurons showed a reduction in activity unilaterally or bilaterally during smooth pursuit, they

Fig. 7. Activity during smooth pursuit and foveal visual responsiveness of fixation neurons. A: neuronal discharge where tonic activity was maintained during the disappearance of the central fixation point in the fixation blink task. Same neuron is shown as in Fig. 1. B: neuronal discharge with an increase in activity during the disappearance of the fixation point in the fixation blink task. Same neuron is shown as in Fig. 2. The histogram is aligned with respect to the disappearance of the fixation point (vertical dotted line). The horizontal bar below the eye-position traces marks the blink period. The 1st and 2nd triangles below each histogram mark bar-press onset and cue onset, respectively. C and D: blink activity indexes are plotted against ipsilateral (C) and contralateral pursuit activity indexes (D) for fixation neurons ($n = 78$). The marginal histograms are shown on the left and bottom. The histogram of blink activity indexes in C also applies to D. The pursuit activity index was calculated as the ratio of activity during pursuit (100–700 ms after target motion onset) to activity during fixation (300–900 ms before target motion onset). The blink activity index was calculated as the ratio of activity during a 300-ms period before the disappearance of the fixation point to activity during a 300-ms period before the disappearance of the fixation point in the fixation blink task. Filled circles (filled bars), open circles (open bars), and open squares (hatched bars) represent Bsups neurons, Isups neurons, and neurons with a contralateral reduction in activity during pursuit [contralateral suppression (Csupps) neurons], respectively; gray circles (gray bars) represent neurons with other patterns of activity during pursuit (bars, for the marginal histograms).
usually showed a bilateral reduction in activity during saccades. Even among fixation neurons that showed maintained or increased activity during smooth pursuit in bilateral directions, 14 of these 18 neurons showed a bilateral reduction in activity during Vsacs or memory-guided saccades. We then calculated the ratio of activity during 10° Vsacs to activity during fixation (saccade activity index) and compared it with the pursuit activity index. Fixation neurons had indexes less than 1 if the activity decreased during Vsacs, indexes greater than 1 if the activity increased during Vsacs, and indexes of ~1 if the activity did not change. In the scatter plots in Fig. 8, saccade activity indexes are plotted against pursuit activity indexes for 72 fixation neurons. Fixation neurons with a reduction in activity during both smooth pursuit and Vsacs were most prevalent in the ipsilateral direction (Fig. 8A, bottom left quadrant). On the other hand, we observed few fixation neurons with an increase in activity during both smooth pursuit and Vsacs in the top right quadrant of Fig. 8A. In the contralateral direction, a similar distribution was observed where fixation neurons with a reduction in activity during both smooth pursuit and Vsacs were most prevalent (Fig. 8B, bottom left quadrant). To investigate the properties of fixation neurons in the top left quadrant and those in the bottom right quadrant, we examined their blink activity indexes for both ipsilateral and contralateral directions. We found no significant difference in blink activity indexes between fixation neurons with an increase in activity during Vsacs but not smooth pursuit and those with an increase in activity during pursuit but not Vsacs (U-test, P = 0.10).

Relation between FEF fixation neurons and suppression of eye movements. We then examined the effects of stimulation on smooth pursuit at the location of fixation neurons. The example in Fig. 9A shows the activity of a Bsupp neuron during smooth pursuit recorded at the cortical site indicated by an arrow in Fig. 9C. At this site, a stimulus train at an intensity of 15 μA was applied during ipsiversive and contraversive smooth pursuit of a target moving at 15°/s (Fig. 9B). This stimulation produced a decrease in the mean eye velocity during the 100-ms period before the end of stimulation that was >2 SEs of the mean eye velocity in the control (0 μA) for both ipsiversive and contraversive pursuit. Therefore, this result indicated that stimulation suppressed the generation of smooth pursuit in bilateral directions. The effects of stimulation on saccades were also examined at the same site. When stimulation was applied at the onset of the visual target for Vsacs, the generation of ipsiversive and contraversive Vsacs was clearly suppressed at 15 μA. This suppressive effect of stimulation on Vsacs is consistent with the same inverse relationship we demonstrated earlier; fixation neurons reduce their firing during saccades. Figure 9D shows the histological reconstruction of the location of the recording and stimulation site in a frontal plane of the FEF. The site at which the fixation neuron was recorded and also where stimulation suppressed the generation of smooth pursuit as well as saccades in bilateral directions was located in the caudal part of the arcuate gyrus facing the inferior arcuate sulcus. These observations were consistent with our previous findings in that the suppression of smooth pursuit and saccades in bilateral directions was induced by stimulation of the area where fixation neurons were densely located (Izawa et al. 2009, 2011).

To further examine whether FEF fixation neurons contribute to the suppressive effects of stimulation at their locations on smooth pursuit, we mapped the FEF area that was associated with the suppressive effect of stimulation on pursuit and compared it with the distribution of fixation neurons. Figure 10 shows the histological reconstruction of the stimulation and recording tracks in representative frontal planes of the FEF. Open circles show the location of stimulation sites where the suppression of Vsacs occurred bilaterally at thresholds of ≤40 μA when we examined the effects of stimulation at each track at depth intervals of 400 μm. At sites where stimulation induced strong suppression of Vsacs in bilateral directions, we also examined the suppressive effects of stimulation on smooth pursuit (Izawa et al. 2011). We found that pursuit as well as saccades were suppressed bilaterally at thresholds of ≤40 μA at the stimulation sites shown by filled circles. Arrowheads indicate the location of Bsupp neurons (filled), Isupp and Csupp neurons (open), and neurons with other patterns of activity during smooth pursuit (gray). Overall, the distributions of fixation neurons and suppression sites for smooth pursuit and saccades in bilateral directions overlapped considerably in the FEF.

![Fig. 8. Comparison of the activity of fixation neurons during smooth pursuit and visually guided saccades (Vsacs). Saccade activity indexes are plotted against pursuit activity indexes for ipsilateral (A) and contralateral directions (B). The marginal histograms are shown on the left and bottom. The saccade activity index was calculated as the ratio of activity during 10° Vsacs (20-ms period) to activity during fixation (300–600 ms before Vsac onset). The pursuit activity index was calculated as in Fig. 7. Fixation neurons are represented as in Fig. 7. C and D.](http://jn.physiology.org/doi/10.1152/jn.00816.2013)
This study analyzed the activity of fixation neurons in the FEF with respect to visual fixation and smooth pursuit performance. Of the fixation neurons we recorded, about one-third showed a significant reduction in activity during smooth pursuit in bilateral directions (Bsupp neurons). Another one-third showed a reduction in activity during pursuit only in the ipsilateral direction (Isupp neurons). The remaining one-third showed various patterns of activity during pursuit: some showed a reduction in activity during pursuit only in the contralateral direction (Csupp neurons), and others showed no change or an increase in activity during both ipsiversive and contraversive pursuit. The fixation neurons were densely located in the area of the FEF in the caudal part of the arcuate gyrus facing the inferior arcuate sulcus.

In the previous study, electrical stimulation of a localized area of the FEF suppressed the generation of smooth pursuit in bilateral directions. In contrast, within a wide area of the FEF
circumscribing the area of bilateral suppression, stimulation suppressed the generation of ipsiversive, but not contraversive, pursuit (Izawa et al. 2011). The area of bilateral suppression showed good overlap with the area where the fixation neurons were concentrated. Thus the activity of fixation neurons may correspond to suppression by the area of bilateral suppression in the FEF observed in stimulation experiments. Indeed, the size of firing reduction in fixation neurons was correlated with the duration of smooth pursuit but not with eye position, indicating that the reduction was related to pursuit. The activity of the fixation neuron population during smooth pursuit may reflect the organization of fixation neurons in the FEF. It is possible that we recorded fixation neurons at various levels in fixation signal processing. In the hierarchical organization of neural connections, Isupp and Csupp neurons may converge to Bsupp neurons, which were the most common type (39%). Consistent with this idea, Isupp neurons, Csupp neurons, and Bsupp neurons showed similar reduction ratios in pursuit activity indexes. The distributions of Isupp neurons and Bsupp neurons did not clearly correspond, respectively, to the FEF areas for generating ipsilateral and bilateral suppression of pursuit by focal stimulation. This may suggest that the effects of stimulation represent some final functional path of the area rather than the activity of individual neurons. Stimulation within a wide area of the FEF circumscribing the area of bilateral suppression may activate some portion of fixation neurons through cortical connections and result in the ipsilateral suppression of pursuit. Thus the organization of fixation neurons may contribute to the ipsilateral suppression of smooth pursuit as well as the bilateral suppression of pursuit. If signals had been settled at a level prior to the FEF, the activity recorded from fixation neurons should not have varied in the FEF because they should have received similar inputs. Therefore, signals for the control of smooth pursuit may be generated in the FEF where the activity of various levels of fixation neurons is provided. The assembly of fixation neurons in the prefrontal cortex may contribute to the suppressive control of smooth pursuit for maintaining active fixation.

Consistent with the interpretation that signals converge gradually, we observed the degree of input convergence in messages of neurons. Different fixation neurons, which showed a similar pattern of activity during smooth pursuit, exhibited different foveal visual responsiveness in the fixation blink task. Thus visual information may be involved in various levels of fixation neurons in the FEF. Among fixation neurons that maintained activity during smooth pursuit bilaterally, those that showed a decrease in activity during the disappearance of the central fixation point in the fixation blink task were considered to have foveal visual-related activity. These fixation neurons may maintain their discharge while visual stimulation is located near the fovea by enabling smooth pursuit. On the other hand, the reduction in activity during smooth pursuit cannot be attributed to a reduction in the visual input to the fovea resulting from the difference between the eye and target position, since we observed fixation neurons with a reduction in activity during pursuit in one direction but not in the other direction. We also observed a rough tendency that the activity of fixation neurons during smooth pursuit was not clearly influenced by target velocity, indicating that the reduction in activity was not caused by displacements of the target light illuminating the fovea. The reduction in activity of fixation neurons may correspond to the release from the suppression of smooth pursuit during fixation. Therefore, in addition to foveal visual responsiveness, behavioral and attentional factors during fixation and eye movements may also affect the discharge patterns of fixation neurons variously. The increase in activity of fixation neurons during smooth pursuit may reflect a retinal error signal that is the difference between eye and target position or motion. Moreover, the increase in activity of fixation neurons during pursuit may produce the inhibition of fixation signals.

Comparison of fixation neuron activity during pursuit and saccades. In agreement with our previous report (Izawa et al. 2009), fixation neurons usually showed a bilateral reduction in activity during saccades. The reduction in activity may be related to making a saccade but not to disappearance of the fixation point, since fixation neurons varied in activity during disappearance of the fixation point in the fixation blink task. Therefore, the reduction in activity of fixation neurons was observed for both smooth pursuit and saccades. The reduction in activity of fixation neurons occurred with a timing similar to, or slightly before, the onset of smooth pursuit (Fig. 6). The preceding time for the reduction in activity of fixation neurons before the onset of smooth pursuit tended to be shorter than that of saccades (Izawa et al. 2009). This may correspond to the fact that the preceding time for an increase in activity of smooth pursuit neurons before the onset of pursuit was shorter than that of saccade-related movement neurons before the onset of saccades. The duration of the reduction in activity of fixation neurons during smooth pursuit was longer than that during saccades, indicating that the reduction in activity did not correspond to catch-up saccades during the initiation of pursuit. Indeed, the fact that the reduction in activity of fixation neurons persisted during smooth pursuit suggests that their activity can have suppressive effects throughout pursuit. We further confirmed that the reduction in the activity of fixation neurons during smooth pursuit survived the elimination of initial catch-up saccades by step-ramp target motion. When we compared activity during smooth pursuit and Vsacs, fixation neurons with a reduction in activity during both pursuit and Vsacs were most prevalent in both the ipsilateral and contralateral directions (Fig. 8, A and B, bottom left quadrant). However, we also observed fixation neurons that showed different patterns of activity during smooth pursuit relative to that during saccades (Fig. 8, A and B, top left and bottom right quadrants). These populations may reflect another group of fixation neurons or include different functions. The distributions of the fixation neurons with a reduction in activity during smooth pursuit but not saccades and those with a reduction in activity during saccades but not pursuit did not differ clearly in the FEF. The difference in the patterns of activity of fixation neurons during saccades and smooth pursuit may suggest a difference in the control of the two types of eye movements, as was observed in the caudate nucleus (Cui et al. 2003).

While saccadic eye movements occur to rapidly change points of fixation, smooth pursuit eye movements occur to follow slowly moving objects. For the generation of saccades, the FEF sends signals to the superior colliculus (SC) (Segraves and Goldberg 1987; Sommer and Wurtz 2000) and the pons (Segraves 1992), consistent with anatomical projections from the FEF (Komatsu and Suzuki 1985; Künzle and Akert 1977; Stanton et al. 1988). In the horizontal saccadic system, abdu-
cens motoneurons and abducens internuclear neurons terminating on medial rectus motoneurons receive excitatory inputs from the contralateral SC via excitatory burst neurons in the paramedian pontine reticular formation and inhibitory inputs from the ipsilateral SC via inhibitory burst neurons in the paramedian pontomedullary reticular formation (Grantyn and Grantyn 1976; Izawa et al. 1999; Precht et al. 1974). A reciprocal input pattern from the SCS to ocular motoneurons is also revealed in the vertical saccadic system, where trochlear motoneurons receive excitation from the ipsilateral SC via Forel’s field H neurons and inhibition from the contralateral SC via interstitial nucleus of Cajal neurons (Izawa et al. 2007). For the generation of pursuit, ocular motoneurons receive inputs via the vestibular nuclei and nucleus prepositus hypoglossi from the flocculus and paraflocculus of the cerebellum, which receive inputs from the middle temporal area and medial superior temporal area via the pontine nuclei in the traditional pursuit pathway (see reviews: Keller and Heinen 1991; Lisberger et al. 1987). In an alternative pathway, vermal lobules VI and VII receive inputs from the FEF via the pontine nuclei and the nucleus reticularis tegmenti pontis and send pursuit signals to the caudal fastigial nucleus projecting to ocular motoneurons via premotor neurons in the brain stem (Fuchs et al. 1994; Noda et al. 1990). In the pathways for smooth pursuit and saccades, fixation neurons in the FEF may suppress the generation of pursuit and saccades at the premotor level through some different processes, as suggested by the suppressive effects of FEF stimulation on pursuit and saccades (Izawa et al. 2011).

Comparison with other brain structures. The activity of neurons that discharge during fixation in other brain structures has also been examined during smooth pursuit. The discharge of fixation neurons in the posterior parietal cortex has been reported to commonly persist during smooth pursuit independent of the direction of visual tracking (Mountcastle et al. 1975). In the brain stem, omnipause neurons (OPNs) discharge tonically during fixation and stop firing during saccades in all directions (Cohen and Henn 1972; Keller 1974; Luschei and Fuchs 1972; Ohgaki et al. 1987; Strassman et al. 1987). Similar to our present results in FEF fixation neurons, OPNs showed a decrease in activity during smooth pursuit with direction sensitivity different from that during saccades (Missal and Keller 2002). The different patterns of activity, including a bilateral reduction in activity of FEF fixation neurons during smooth pursuit, were reminiscent of those of OPNs. Therefore, fixation neurons in the FEF may provide inputs to OPNs directly or indirectly via the SC (Büttner-Ennever et al. 1999; Gandhi and Keller 1997; Paré and Guitton 1994; Segraves 1992; Segraves and Goldberg 1987; Sommer and Wurtz 2000). Neurons in the rostral SC also discharge tonically during fixation (Munoz and Guitton 1991; Munoz and Wurtz 1993). An ipsilateral decrease in activity of FEF fixation neurons during smooth pursuit was similar to that observed for fixation neurons in the rostral SC by Krauzlis et al. (2000). However, there was a difference in activity during contraversive pursuit between fixation neurons in the FEF and the SC. Whereas fixation neurons in the SC were reported to increase their discharge during contraversive pursuit (Krauzlis et al. 2000), FEF fixation neurons with an ipsilateral decrease in activity during pursuit usually maintained but did not increase their activity during contraversive pursuit in the present study. Therefore, these fixation neurons in the FEF cannot be considered to encode errors between eye and target position which were reported to be encoded by SC fixation neurons. In the FEF, the predominant response of fixation neurons during smooth pursuit was a decrease in activity. These findings suggest that fixation neurons in the FEF, a higher order structure, are involved in the suppression of smooth pursuit. This is also consistent with the idea that the essence of motor control is inhibition. Further analysis of the difference in the patterns of activity of neurons in different brain structures that participate in fixation is needed to understand their individual roles in the fixation system.

The FEF also contains smooth pursuit neurons that show activity associated with smooth pursuit (MacAvoy et al. 1991). It has been reported that smooth pursuit neurons in the perirhinal cortex showed an increase in activity during smooth pursuit in a preferred direction and a decrease in activity during pursuit in the opposite direction (Fukushima et al. 2000; Tanaka and Fukushima 1998). These smooth pursuit neurons did not show activity associated with fixation, although they sometimes showed a buildup of activity before the onset of smooth pursuit. Moreover, in contrast to smooth pursuit neurons which are involved in the control of pursuit velocity, the activity of fixation neurons during smooth pursuit usually did not show a change that varied with target velocity in the range used in small samples. When we examined the suppressive effects of FEF stimulation on smooth pursuit with different velocities, the effects did not clearly depend on the target velocity (Izawa et al. 2011). This finding in stimulation experiments is consistent with the finding in recordings of FEF fixation neurons, although a more systematic examination is needed. Therefore, we could typically differentiate between the activity of fixation neurons and that of smooth pursuit neurons. Thus the populations of fixation neurons and smooth pursuit neurons were distinguished in the FEF. In control of the gain of visual-motor transmission for smooth pursuit, a network model has suggested the contribution of the activity of FEF fixation neurons as well as FEF pursuit neurons and middle temporal area neurons (Lee et al. 2013). The direction-selective reduction in activity of the present fixation neurons during smooth pursuit may be related to the modeling. It would be interesting to examine the possibility of the existence of neurons that have properties in between fixation neurons and smooth pursuit neurons in the FEF in future studies.

Possible functions for FEF fixation neurons. Our results indicated that the activity of FEF fixation neurons during steady fixation was correlated with the suppressive effects of FEF stimulation on smooth pursuit. This is consistent with previous results in stimulation experiments (Izawa et al. 2011). Fixation neurons were densely recorded in the area in which stimulation suppressed the generation of smooth pursuit as well as saccades in bilateral directions. Then the assembly of FEF fixation neurons may be part of a more generalized visual fixation system through which suppressive control is exerted on smooth pursuit as well as saccades.

Concerning the smooth pursuit system, Robinson (1971) and Lisberger et al. (1987) have postulated models in which a copy of the pursuit command encoding eye velocity is fed back positively and, adding to retinal velocity error, reconstructs target velocity. It is possible that the activity of fixation neurons during smooth pursuit may control overshoots of
signals in the smooth pursuit system. The positive feedback of eye velocity in the pursuit system has been proposed to correspond to a corollary discharge (Sperry 1950). Since modulation of fixation neuron activity began at pursuit initiation (the open-loop phase) and continued during pursuit maintenance (the closed-loop phase), the activity of fixation neurons may control overshoots of signals generally in the pursuit system, including a positive feedback pathway. The idea that the activity of fixation neurons may control overshoots of signals may be applicable to the saccadic system, as well as to the pursuit system. The dynamics of responses of fixation neurons during eye movements should be investigated in future studies.

Concerning visual stability, the role of the FEF has been emphasized recently. The pathway from the SC to the FEF via the mediodorsal thalamus was demonstrated to convey a corollary discharge of saccades (see review in Sommer and Wurtz 2008). Mediodorsal thalamic relay neurons, that received input from the SC and projected to the FEF, increased their activity before saccades. Thus the activity of our fixation neurons in the FEF, which increased during fixation and decreased before saccades, may differ from a corollary discharge described by Sommer and Wurtz (2008). Further studies are required to elucidate the relation between the responses of our fixation neurons and corollary discharges.

ACKNOWLEDGMENTS

We thank Y. Shinoda for valuable comments on an earlier draft and M. Takada for his technical expertise.

GRANTS

This research was supported by a Grant-in-Aid for Scientific Research from the Ministry for Education, Science and Culture of Japan and the Naito Foundation to Y. Izawa.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

Author contributions: Y.I. and H.S. conception and design of research; Y.I. performed experiments; Y.I. and H.S. interpreted results of experiments; Y.I. prepared figures; Y.I. drafted manuscript; Y.I. and H.S. interpreted data; Y.I. and H.S. performed experiments; Y.I. analyzed data; Y.I. and H.S. interpreted data; Y.I. and H.S. conceived and designed the experiments; Y.I. and H.S. drafted the manuscript; Y.I. conceived and designed the experiments; Y.I. and H.S. performed the experiments; Y.I. and H.S. analyzed the data; Y.I. and H.S. wrote the paper.

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*S_pel* • doi:10.1152/jn.00816.2013 • www.jn.org