Neuronal Responses Related to Smooth Pursuit Eye Movements in the Periarcuate Cortical Area of Monkeys

MASAKI TANAKA AND KIKURO FUKUSHIMA

Department of Physiology, Hokkaido University School of Medicine, Sapporo 060, Japan

Tanaka, Masaki and Kikuro Fukushima. Neuronal responses related to smooth pursuit eye movements in the periarcuate cortical area of monkeys. J. Neurophysiol. 80: 28–47, 1998. To examine how the periarcuate area is involved in the control of smooth pursuit eye movements, we recorded 177 single neurons while monkeys pursued a moving target in the dark. The majority (52%, 92/177) of task-related neurons responded to pursuit but had little or no response to saccades. Histological reconstructions showed that these neurons were located mainly in the posterior bank of the arcuate sulcus near the sulcal spur. Twenty-seven percent (48/177) changed their activity at the onset of saccades. Of these, 36 (75%) showed presaccadic burst activity with strong preference for contraversive saccades. Eighteen (10%, 18/177) were classified as eye-position-related neurons, and 11% (19/177) were related to other aspects of the stimuli or response. Among the 92 neurons that responded to pursuit, 85 (92%) were strongly directional with uniformly distributed preferred directions. Further analyses were performed in these directionally sensitive pursuit-related neurons. For 59 neurons that showed distinct changes in activity around the initiation of pursuit, the median latency from target motion was 96 ms and that preceding pursuit was −12 ms, indicating that these neurons can influence the initiation of pursuit. We tested some neurons by briefly extinguishing the tracking target (n = 39) or controlling its movement with the eye position signal (n = 24). The distribution of the change in pursuit-related activity was similar to previous data for the dorsomedial part of the medial superior temporal neurons (Newsome et al. 1988), indicating that pursuit-related neurons in the periarcuate area also carry extraretinal signals. For 22 neurons, we examined the responses when the animals reversed pursuit direction to distinguish the effects of eye acceleration in the preferred direction from oppositely directed eye velocity. Almost all neurons discharged before eye velocity reached zero, however, only nine neurons discharged before the eyes were accelerated in the preferred direction. The delay in neuronal responses relative to the onset of eye acceleration in these trials might be caused by suppression from oppositely directed pursuit velocity. The results suggest that the periarcuate neurons do not participate in the earliest stage of eye acceleration during the change in pursuit direction, although most of them may participate in the early stages of pursuit initiation in the ordinary step-ramp pursuit trials. Some neurons changed their activity when the animals fixed a stationary target, and this activity could be distinguished easily from the strong pursuit-related responses. Our results suggest that the periarcuate pursuit area carries extraretinal signals and affects the premotor circuitry for smooth pursuit.

INTRODUCTION

When a small moving object appears in the visual field, primates can stabilize the object’s image on the fovea with saccadic and smooth pursuit eye movements. Although evidences for the involvement of frontal cortex in the control of saccades can be found in earlier reports (e.g., Bizzi 1968; Bruce and Goldberg 1985; Bruce et al. 1985; Robinson and Fuchs 1969), the role of the frontal cortex in guiding smooth pursuit eye movement is relatively recent. Within this decade, a number of behavioral observations in patients and monkeys with cortical damage have revealed that the frontal eye fields (FEF) are involved in smooth pursuit. Lesion in the FEF of both humans and monkeys results in a reduction of pursuit gain that is predominantly ipsilateral (in patients: Morrow 1996; Morrow and Sharpe 1990; in monkeys: Keating 1991, 1993; Lynch 1987; MacAvoy et al. 1991). In addition, electrical microstimulation applied to the posterior part of the monkey arcuate sulcus evokes continuous slow eye movements directed mainly ipsilaterally (Bruce et al. 1985; Gottlieb et al. 1993, 1994; Keller and Heinen 1991; MacAvoy et al. 1991; Tian and Lynch 1996a). More recently, unit recording studies from behaving monkeys have shown that the fundus and the posterior bank of the arcuate sulcus contain cells the activity of which is related to smooth pursuit eye movement and is strongly directional (Gottlieb et al. 1994; MacAvoy et al. 1991). These studies showed that more than half of the neurons discharge before the onset of smooth pursuit and that the activity of many increases in proportion to pursuit velocity. They also showed a correlation between the directional preference of the recorded cells and the direction of slow eye movements elicited by electrical microstimulation at that site.

Despite these valuable findings, several questions remain regarding the activity of these neurons. First, the contribution of the visual input to the activity during the maintenance of pursuit has not been examined and compared with that in other pursuit pathways (Heinen 1995; Kawano et al. 1994; Mustari et al. 1988; Newsome et al. 1988; Sakata et al. 1983). Second, the neuronal responses to the change in pursuit direction have not been studied, and such data may provide information to understand the role of these cells. For example, a number of behavioral studies in monkeys have suggested that there is a pursuit “switch” that gates or multiplies the visuomotor transmission for pursuit in one direction (Goldreich and Lisberger 1992; Grasse and Lisberger 1992; Schwartz and Lisberger 1994). Examination of the neuronal activity during change in pursuit direction may provide useful information on whether or not pursuit-related neurons in the periarcuate area can serve such a function. Third, the effect of eye position on the activity of the pursuit-related neurons has not been compared with the activity of eye-position-related neurons that also are modu-
lated during smooth pursuit (Bizzi 1968). Finally, as described previously for saccade-related burst neurons (Bruce and Goldberg 1985; Schall 1991b) and fixation-related neurons (Suzuki and Azuma 1977; Hanes et al. 1998) in the periaqueductal area, a possible dependence of the activity during fixation on the task condition should be examined because previous studies have shown that some saccade-related burst neurons have preparatory activity for saccades in the preferred direction (Bruce and Goldberg 1985; Schall 1991b) and that some neurons discharge when the animal fixates a stationary target that serves a cue for manual movement (Suzuki and Azuma 1977).

To resolve these issues, we investigated the neuronal activity in the periaqueductal cortical area of alert monkeys that pursued a small moving target in the dark. We first analyzed the response properties of pursuit-related neurons and compared them with those reported previously (Gottlieb et al. 1994). Then visual components of pursuit-related activity were tested by using a technique described in the extrastriate visual cortices (Kawano et al. 1994; Newsome et al. 1988).

We also examined neuronal responses during change in the pursuit direction toward the preferred direction and the modulation of the activity during fixation before and after pursuit. Preliminary results have appeared in abstract forms (Tanaka and Fukushima 1996, 1997a).

METHODS

Animal preparation

Two male adult Japanese monkeys (Macaca fuscata, weighing 12 and 9 kg) were used in these experiments. Initially, the monkeys were trained to leave their home cages and sit in a primate chair voluntarily. The procedures described below were evaluated and approved by the Animal Care and Use Committee of the Hokkaido University School of Medicine.

Animals were sedated with ketamine hydrochloride (Ketaral, 25 mg im) and anesthetized with pentobarbital sodium (Nembutal, 25 mg/kg ip). Atropine (1 mg) was administered subcutaneously. Under aseptic conditions, animals were intubated, and a mixture of 70% nitrous oxide and 30% oxygen was used to augment anesthesia. Electrocardiogram and expired CO₂ were monitored during the surgery. Supplemental anesthesia using 0.5–3.0% halothane was administered as necessary.

A pair of head holders was mounted on the skull, and a coil of wire was implanted under the conjunctiva of one eye to record eye movements (Fuchs and Robinson 1966). The head holders and a connector for the eye coil were bonded rigidly to the skull with tiny screws and dental acrylic. Analgesics and antibiotics were administered postsurgically. After behavioral training for several months, a recording chamber was implanted using the same surgical procedures.

Visual stimulus and behavioral training

The monkeys sat in a primate chair facing a translucent, tangent screen located 55 cm from their eyes. During experiments, their heads were restrained firmly by the head holders, and eye position was recorded continuously by the scleral search coil method (Fuchs and Robinson 1966). The visual target was a rear projected red laser spot (0.2° diam), the position of which was controlled by a pair of mirror galvanometers. The mirror positions and all other stimulus events were controlled by a computer that also was used for off-line data analysis (see further text). Experiments were carried out in the dark except for the target spot. To avoid any visible streak, the laser diode that produced the target spot was extinguished for 20 ms while the target jumped. The pulse signal to extinguish the target also was recorded, and the time of the pulse offset was measured as the onset of the target motion (Tanaka and Fukushima 1997b).

Initially the animals were trained to fixate a stationary target. An electrical window was set around target position, and the monkeys were rewarded by drops of sugar water when eye position was within the window for 0.5–2 s. The size of the window was decreased gradually, and the target was moved. During recording sessions, we usually rewarded the animals when the eye remained within a 2–3° window for 1–2 s.

The tasks presented here were a visually guided saccade task and pursuit tasks. In the visually guided saccade task, the monkey first fixated a stationary target at the center of the screen. After 1–2 s, the target jumped to a new position 5–20° away from the center of the screen, and the monkey made a saccade to the visible target. The amplitude of target jumps was determined on each block of trials (we usually used either 10 or 15° steps), and the direction was selected randomly from a set of two to five directions for each trial.

In the pursuit task, the target was moved in a step-ramp fashion (Rashbass 1961). The trials began with the appearance of a target at the center of the screen. After a random fixation period (1–1.5 s), the target jumped in one direction and moved smoothly in the opposite direction. The magnitude of a target step and the speed of target motion were varied for each block of trials. The direction of the target motion was one of eight directions spaced radially at 45° intervals, and it was selected on each trial from a set of two to five different directions either randomly or sequentially. When we searched for pursuit-related neurons, the target stepped 3° and moved back at 20°/s for 880 ms in the direction selected sequentially either from a set of four obliques or from a set of four meridians. The duration of the target motion was prolonged up to 1,600 ms for the trials with larger steps. After an excursion, the target suddenly stopped and remained stationary for an additional 880–1,500 ms. Intertrial intervals varied from 200 to 2,000 ms, usually 500 ms. Several variants of the pursuit task also were used.

BLINK AND STABILIZATION. To quantify the contribution of visual inputs to the activity during pursuit, the target was extinguished briefly (blink) or controlled by the eye position signal (stabilized) while the animals pursued a moving target (Heinen 1995; Kawano et al. 1994; Newsome et al. 1988). These conditions were interleaved in 30–80% of the trials in which the target moved in the preferred direction at 20°/s. In the blink trials, the target was extinguished 230–580 ms after the target motion onset for 100–200 ms. In the stabilized trials, the galvanometers were driven by the eye position signal for 200–400 ms after the target had moved for 230–580 ms. The duration and onset of these periods were constant through a block of trials. When the target image was stabilized on the retina, the target jumped slightly (<1°) to a predetermined foveal location. These small target steps could not be eliminated because we stabilized the target images simply using the eye position signal.

DOUBLE-RAMP TASK. For some neurons, responses to the change in pursuit direction were examined. To do this, the target moved in a step-ramp-step-ramp fashion along the preferred direction. The target first appeared 10° eccentrically. After a random fixation interval (1,000–1,500 ms), the target stepped 2° further peripherally and moved back (10°/s) toward the screen center for 1,000 ms. Then the target stepped 4° in the same direction and moved in the opposite direction (i.e., toward the original fixation point) for an additional 1,500 ms (10°/s). Two directions of target motion along the same axis were presented alternatively.
but not saccade trials, it is very likely that the population of the

Saccade 48 (27) (1994). Subsequent analyses were performed on Macintosh com-

Pursuit 92 (52)

recorded, single neurons were isolated using a time-amplitude ing ) , preferred direction (f

d

f

V

7

7

m

vertical eye position signals were differentiatedIpsilateral 21103

Excited Horizontal and vertical eye position signals were differentiatedIpsilateral 21103

Contralateral 21103

Vertical 21103

Omnidirectional 21103

Suppressed 21103

Saccade 48 (27)

Presaccade

Ipsilateral 336

Contralateral 81119

Vertical 718

Omnidirectional 213

Post sac cade 606

Suppressed 336

Eye position

Ipsilateral 18 (10)

Contralateral 527

Vertical 303

Omnidirectional 202

Fixation 8210 (6)

Target offset 134 (2)

Others 325 (5)

Total 11859177

Percentages are in parentheses.

TABLE 1. Summary of all task-related neurons

<table>
<thead>
<tr>
<th>Neuron Type</th>
<th>Monkey</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pursuit</td>
<td></td>
<td>92 (52)</td>
</tr>
<tr>
<td>Excited</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ipsilateral</td>
<td>21</td>
<td>31</td>
</tr>
<tr>
<td>Contralateral</td>
<td>23</td>
<td>37</td>
</tr>
<tr>
<td>Vertical</td>
<td>14</td>
<td>3</td>
</tr>
<tr>
<td>Omnidirectional</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Suppressed</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Saccade</td>
<td>48</td>
<td>(27)</td>
</tr>
<tr>
<td>Presaccade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ipsilateral</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Contralateral</td>
<td>8</td>
<td>19</td>
</tr>
<tr>
<td>Vertical</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Omnidirectional</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Post sac cade</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Suppressed</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Eye position</td>
<td></td>
<td>18 (10)</td>
</tr>
<tr>
<td>Ipsilateral</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Contralateral</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Vertical</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Omnidirectional</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Fixation</td>
<td>8</td>
<td>10 (6)</td>
</tr>
<tr>
<td>Target offset</td>
<td>1</td>
<td>4 (2)</td>
</tr>
<tr>
<td>Others</td>
<td>3</td>
<td>5 (5)</td>
</tr>
<tr>
<td>Total</td>
<td>118</td>
<td>59</td>
</tr>
<tr>
<td></td>
<td></td>
<td>177</td>
</tr>
</tbody>
</table>

STEP-STOP TASK. In the step-ramp task described earlier, the monkeys often predicted the termination of target motion and decreased pursuit velocity before the target stopped. Therefore we examined responses to the termination of pursuit using trials in which the target stopped after a short tracking interval. In these trials, the target appeared at the center of the screen and stepped 3° and moved oppositely at 20°/s. After 480 ms, the target stepped forward (3°) and stopped. Then the target remained stationary for 1,000–1,500 ms. In some blocks, 20–50% control trials were interleaved in which the target neither stepped nor stopped after it began to move.

Recording procedure

After training in the various oculomotor tasks, which lasted for several months, a recording cylinder (19–20 mm diam) was mounted over a hole trephined in the skull under aseptic condition. Glass-insulated elgiloy electrodes (0.8–2 MΩ at 1 kHz with 10–20 μm tips) were introduced transdurally in the stereotaxic plane through the recording cylinder that was centered at A25–27 and L14–15. This approach enabled us to easily reconstruct the penetrations but made it difficult to penetrate cortical areas more lateral than L19. The electrodes were lowered by a hydraulic microdrive (Narishige, MO-10) while the animals performed the pursuit tasks. Because we searched for neurons during step-ramp pursuit trials but not saccade trials, it is very likely that the population of the task-related neurons in this study was biased toward the neurons that modulated during pursuit.

When neuronal activity related to oculomotor behavior was recorded, single neurons were isolated using a time-amplitude window discriminator. The pulse signals produced by the discriminator were fed into a frequency to voltage converter, and the corresponding voltage was monitored on-line along with eye position and stimulus signals using two storage oscilloscopes (Iwatsu, DMS-6430). We also used an audiometer to search for task-related neurons and to define the preferred direction of these neurons on-line. Neuronal activity and all other events were stored on analog tapes for off-line analysis as described in the following section.

Data acquisition and analysis

Horizontal and vertical eye position signals were differentiated by analog circuits (DC-50 Hz, −12 dB/oct) and then filtered (DC-30 Hz, −6 dB/oct) to obtain eye velocity. All stimulus events, eye movements, and neuronal activity were digitized off-line at either 500 or 1,000 Hz with software developed by Fuchs et al. (1994). Subsequent analyses were performed on Macintosh computers using homemade and commercial programs.

For the activity related to the step-ramp pursuit task, saccades were eliminated manually from the eye velocity traces, and data were aligned with the onset of target motion. Data were averaged for each target direction and only data containing ≥10 correct trials were used for quantitative analysis. To quantify the neuronal activity in the step-ramp pursuit task, average responses for the following three task intervals were measured: 300-ms period before the onset of target motion (baseline), the 600-ms interval beginning from 50 ms after the onset of target motion (response period), and a 300-ms period beginning from 300 ms after the target stopped (2nd fixation period). During the third period, monkeys fixated a stationary target at an eccentric location. Using these sets of data, two indices were calculated. For the estimation of directional preference, a directionality index (DI) (Baker et al. 1981; Colby et al. 1993) was computed by the following equation

\[ DI = 1 - \frac{(R_{opp} - B_{opp})}{(R_{pref} - B_{pref})} \]

where \( R_{opp} \) indicates the average activity during the response period when the monkey pursued in the direction opposite to the preferred direction and \( B_{opp} \) is the baseline activity in the same trials. The \( R_{pref} \) and \( B_{pref} \) are the average responses calculated from pursuit trials in the preferred direction. If the neurons have strong directional preference, the DI is near 1. When the activity is suppressed by oppositely directed pursuit, the value is >1. We also adopted a modulation index (MI) to quantify the modulation in activity during two fixation intervals before and after pursuit. The equation was

\[ MI = \frac{(\text{second fixation} - B_{pref})}{(R_{pref} - B_{pref})} \]

where the difference of activity between two fixation periods was divided by the response to smooth pursuit. This equation was calculated only from trials in which the monkey pursued in the preferred direction. When the activity is determined only by eye position, the MI is >1. If the activity is modulated significantly by smooth pursuit, the value is near 0. When the activity before pursuit is greater than that after pursuit, MI becomes negative value.

For some cells where ≥10 responses to pursuit in eight different directions were recorded, the extent of the directional tuning was examined by fitting a Gaussian curve (Colby et al. 1993; Gottlieb et al. 1994) with the equation

\[ f(x) = \text{resting} + A \exp\left\{-0.5(x - d)^2/\sigma^2\right\} \]

Where \( f(x) \) was the average response to pursuit in the eight directions, and the other four parameters, the resting rate (resting), preferred direction (d), maximum modulation at thepreferred direction (A), and the tuning index (σ), were calculated by the Marquardt method (Colby et al. 1993; Gottlieb et al. 1994). Note that the resting rate fit by this equation is not the same as the value measured from the experimental data (baseline). As described in RESULTS, the tuning curves were presented
FIG. 1. Examples of neuronal responses in the step-ramp pursuit paradigm. A and B: pursuit-related neurons. C: eye-position–related neuron. HE, horizontal eye position; HE, horizontal eye velocity; VE, vertical eye position; VE, vertical eye velocity. First and 2nd triangles of each trial indicate the appearance of a target and the onset of target motion, respectively. Horizontal bar indicates 1 s. Vertical calibration indicates 20° for eye position and 30°/s for eye velocity. Activity of all these cells in multiple trials will appear in subsequent figures (Figs. 10A, 12, and 14).

with the mean of the baseline activity calculated from trials for the eight directions. To compare the tuning width to the values previously reported, the full-width at half-maximum (FWHM) of the activity also was calculated by following formula (Gottlieb et al. 1994)

\[
\text{FWHM} = \sigma \sqrt{2 \ln 2}
\]

To quantify any possible visual component of pursuit-related responses, the activity after the onset of target blink and stabilization was measured during the period beginning from 60 ms after blink or stabilization onset and lasting for the same interval as the target manipulation. These average responses were subtracted from the baseline activity and were compared with
FIG. 2. Example of a typical pursuit-related neuron. A: responses to vertical smooth pursuit eye movements. Data are aligned with the onset of target motion (time 0). Traces show vertical target (VT) and eye position (VE), average vertical eye velocity (VEg), and neuronal activity (raster and histogram). Target and eye position traces are shown with slight offset. Target stepped 3° and moved in the opposite direction at 20°/s. B: responses to vertical pursuit when the target stepped 15° and moved at 20°/s. Average eye velocity are the mean of ≥10 pursuit responses, and the traces are interrupted by the occurrences of saccades. Note that this neuron discharged at the onset of upward slow eye movement and continued firing during downward saccades elicited by the large target step (B, left). C: responses in visually guided saccade trials. Data are aligned with the onset of saccades. Target stepped 15° vertically.

the modulation of activity during the corresponding task interval in control trials (Kawano et al. 1994; Newsome et al. 1988).

For activity related to saccades, data were aligned with saccade onset. No quantitative analysis for saccade-related activity was performed in this study.

**Histology**

Several recording sites were marked by iron deposits produced by positive current (10–15 μA for 60–100 s) through the electrodes. After recording was completed, animals were anesthetized deeply with pentobarbital sodium (>50 mg/kg ip) and
physiological saline followed by 3.5% formalin containing 2% ferrocyanide. The brains were blocked and equili-
brated with 30–40% sucrose. Coronal sections were cut on a freezing microtome (MICROM, HM440E) at 60 and 50 μm for

FiG. 3. Responses to pursuit in 8 directions. This neuron was recorded in the right hemisphere and responded to pursuit in the right-up direction. Activity for 600-ms intervals indicated by black bars below the rasters are plotted (middle). Broken line in the polar plot indicates the average activity before the target motion onset.

FiG. 4. Distribution of preferred directions of all directionally sensitive pursuit-related neurons.

FiG. 5. Distribution of the directional indices (DIs) of directionally sensitive pursuit-related neurons. Indices were calculated from the step-ramp pursuit trials in both the preferred and the opposite directions.
sites were reconstructed based on the marking sites, histologically identified electrode tracks and the stereotaxic coordinates of the penetrations.

**RESULTS**

All 177 task-related neurons recorded in this study are summarized in Table 1. Of these, 158 (89%) neurons fell into three major groups. The majority (52%, 92/177) responded to smooth pursuit eye movements but had no or only a slight response to saccades. The second group (27%, 48/177) changed their activity around the onset of saccades. Most (75%, 36/48) of them discharged before the onset of saccades and many showed a strong preference for contraversive saccades. Eighteen (10%) neurons were classified as eye-position-related neurons. Although these neurons also discharged during pursuit, we could distinguish them from pursuit-related neurons, which were activated consistently during pursuit regardless of eye position (see further text). Because our interest was pursuit-related neuronal activity, we searched for neurons during step-ramp pursuit trials in which saccade occurrences were minimized. Such a task condition may have resulted in a bias toward pursuit-related neurons.

Among 92 pursuit-related neurons, 85 (92%) responded to pursuit with strong directional preferences. Subsequent analyses focused on these 85 directionally sensitive pursuit-related neurons. Of the remaining seven pursuit-related neurons, three showed only a decrease in activity during pursuit (Table 1, suppressed), and four responded equally to pursuit for all eight directions (Table 1, omnidirectional).
Responses to step-ramp pursuit tasks and pursuit-related neurons

Figure 1 shows three examples of task-related neuronal activity observed in the step-ramp pursuit trials (Rashbass 1961). Figure 1, A and B, shows examples of pursuit-related neurons, and Fig. 1C shows an eye-position-related neuron. For each single trial, the onset of the fixation point and the onset of target motion were denoted by successive triangles on the eye position trace (HE or VE). For the neuron shown in Fig. 1A, the activity increased when the monkey performed leftward smooth pursuit (left) and stopped before eye movement was terminated. This neuron also showed transient activity at the end of rightward smooth pursuit (right). For the neuron shown in Fig. 1B, the activity increased when the eyes moved smoothly downward (left) and was suppressed when the eyes moved upward (right). This neuron also showed an increasing activity during the

![Figure 7](image-url)
FIG. 8. Responses of a pursuit-related neuron in the blink and stabilized trials. In the blink trials, the target briefly (150 ms) extinguished. In the stabilized trials, the target was controlled by eye position signals for 300 ms. Vertical dashed lines indicate the onset and the offset of the blink or stabilized interval, respectively. Note that the activity changed but continued during those periods.

Fixation period before the target moved in either direction. Figure 1C shows an example of eye-position–related activity. This neuron also responded to downward smooth pursuit (left) and was suppressed by upward smooth pursuit (right). However, this neuron continued firing vigorously even after downward slow eye movement was terminated (left). Responses in multiple trials of these neurons will appear in subsequent figures (Figs. 1A, 12, and 14).

Figure 2 illustrates the activity of a typical pursuit-related neuron in other oculomotor tasks. This neuron responded to upward smooth pursuit in the step-ramp trials. The data in step-ramp trials are aligned with the onset of target motion (Fig. 2, A and B), and those in saccade trials are aligned with the onset of saccades (Fig. 2C). Even when the step amplitudes were increased from 3° (Fig. 2A) to 15° (Fig. 2B), the responses consistently began at the onset of upward slow eye movements regardless of occurrence of downward saccades elicited by a large target step (Fig. 2B, left). No change in activity was observed when the monkey generated saccades to a stationary target at 15° up or down (Fig. 2C).

Directional Preference. Figure 3 shows the activity of a typical directionally sensitive pursuit-related neuron in eight pursuit directions. Each panel shows average horizontal and vertical eye velocity and rasters of neuronal responses for several trials in each direction. The polar plot indicates the average neuronal activity that was calculated for the 600-ms response interval indicated by black bars below the rasters (beginning from 50 ms after target motion onset, see Methods). The dotted circle at the origin indicates baseline activity, calculated from the 300-ms interval before target motion onset (see Methods). This neuron preferred right-up pursuit and was suppressed during pursuit in the opposite direction. The distribution of preferred directions of all 85 directionally sensitive pursuit-related neurons recorded in this study is summarized in Fig. 4. The number of neurons were plotted for the eight directions relative to the recording sites. Our sample was distributed nearly evenly for all directions with slight bias toward the contralateral side (37 contralateral, 31 ipsilateral) and no bias for vertical (27 upward, 28 downward).

The strength of directional preference was estimated by the directionality index (DI) calculated from the average responses of ≈10 trials for both the preferred and the opposite directions (Baker et al. 1983; Colby et al. 1993) (see Methods). The DI near 1 indicates strong directional, near 0 indicates no directional preference and >1 shows that the activity is suppressed by pursuit in the nonpreferred direction. For the neuron in Fig. 3, the DI was calculated from both the right-up and the left-down pursuit trials, and the value was 1.08. The distribution of the DIs for 72 directionally sensitive pursuit-related neurons is shown in Fig. 5. Of these neurons, 89% (64/72) were strongly directional (DI > 0.7) and 40% (29/72) were suppressed during oppositely directed pursuit (DI > 1.1). The average (±SD) of the indices was 1.13 ± 0.44 and median was 1.04.

To quantify the sharpness of directional tuning, we constructed a tuning curve by fitting the average (≈10 trials) responses for eight directions with a Gaussian function (see Methods). For the neuron in Fig. 3, the curve was centered at 22.5° and the σ of the Gaussian function was 44.7°, corresponding to the FWHM of 105.3°. Examples of
measurements. The data were aligned with the onset of target motion, and the latencies of the neurons were 110 ms (left) and 68 ms (right), whereas the latency of pursuit were 121 ms (left) and 111 ms (right), respectively. The latencies were measured for 59 neurons that showed a clear change in activity at the initiation of pursuit, and the distribution of latencies are summarized in Fig. 7B. The median latency relative to the onset of target motion was 96 ms (range from 62 to 255 ms; 105.6 ± 34.1 ms). When the latencies relative to the onset of pursuit were calculated, the median was −12 ms (range from −86 to 156 ms; −6.9 ± 37.0 ms). Seventy-five percent (44/59) of these neurons discharged before the onset of pursuit. Of these, 77% (34/44) preceded by >10 ms and 50% (22/44) by >20 ms.

**Extraretinal component of pursuit-related activity**

To determine whether the pursuit-related activity includes responses to the motion of target images during pursuit (i.e., retinal slip), the target was briefly extinguished (blink trials) or controlled by the eye position signal (stabilized trials) when the monkeys pursued a moving target spot in the dark. Figure 8 compares the responses in ordinary step-ramp trials (Control) to the responses in the blink and stabilized trials. This neuron showed reduced activity when the target was extinguished (blink) and when the target image was stabilized on the retina (stabilized) but clearly continued firing. In this example, the discharge at 60 ms after the onset of blink and stabilization were 78 and 70% of the value for the same periods in the control trials. We examined responses in the blink trials for 39 neurons and in the stabilized trials for 24 neurons. The ratio of the responses during target blink and stabilization to the responses without them was calculated for each neuron (see METHODS). According to the ratios, individual neurons were categorized into five groups (Fig. 9, top) to compare the data from the medial superior temporal (MST) area reported previously (Fig. 9, bottom) (Kawano et al. 1994; Newsome et al. 1988). The distribution of the change in activity was similar to that for the neurons in the dorsomedial part of the MST (MSTd) reported by Newsome, Wurtz, and Karmos (1988). The mean in the blink trials was 0.86 and that in the stabilized trials was 1.01, respectively. Of these neurons, 72% (28/39) in the blink trials and 54% (13/24) in the stabilized trials showed changes in activity within 30% of the control values.

**Response to velocity step**

A previous study suggested that “pursuit cells” in the FEF provide an eye acceleration signal related to pursuit initiation and maintenance (Gottlieb et al. 1994). To further examine this possibility, we tested whether pericruciate pursuit-related neurons respond to eye velocity changes (i.e., acceleration) when the animal pursued in the direction opposite to the preferred direction. Figure 10 shows the activity of three pursuit-related neurons that we examined this possibility, we tested whether pericruciate pursuit-related neurons respond to eye velocity changes (i.e., acceleration) when the animal pursued in the direction opposite to the preferred direction. The neuron in Fig. 10A (same neuron as Fig. 1A) discharged preceding leftward pursuit (20°/s) in ordinary step-ramp pursuit trials (left). In the double-ramp trials (middle), the monkey first pursued rightward (10°/s) and then reversed the pursuit direction to leftward (10°/s). The
A step-ramp  double-ramp  step-stop

B step-ramp  double-ramp  step-stop

C step-ramp  double-ramp  step-stop

Time after target motion onset (ms)
activity changed immediately before the eyes were accelerated leftward (vertical line). In the step-stop trials (right), this neuron discharged when the monkey terminated pursuit in the opposite direction (rightward, 20°/s). The activity of this neuron was consistently related to the change in eye velocity (i.e., acceleration) toward the preferred direction. The cells in Fig. 10, B and C, discharged slightly before the onset of pursuit in the step-ramp trials (left), however, in the double-ramp trials (middle), the changes in activity were delayed and were preceded by the onset of eye acceleration toward the preferred direction. In the step-stop trials (right), the activity of these neurons was either delayed (Fig. 10B) or absent (Fig. 10C).

Response latencies for 22 pursuit-related neurons that showed a clear change in activity during double-ramp trials are summarized in Fig. 11. The latencies were calculated relative to the onset of eye acceleration toward their preferred direction (Fig. 11A) and relative to the target motion onset (Fig. 11B). Negative values in Fig. 11A indicate that the cells discharged before the eyes were accelerated in the preferred direction. Of these 22 neurons, 20 also were tested in the step-stop trials; however, only the data of 9 neurons that showed a clear change in activity are plotted. For the other 11 neurons, the responses to the termination of pursuit were either absent or too sluggish to determine the onset of the activity. In Fig. 11, data from the neurons in Fig. 10 are dots connected by thick lines. For these trials, the eyes were accelerated in the preferred direction at 112 ms (111.7 ± 8.0 ms, n = 22), 123 ms (122.5 ± 11.5 ms, n = 22), and 100 ms (100.1 ± 11.6, n = 9) after target motion onset in the step-ramp, double-ramp, and step-stop trials, respectively. In the double-ramp trials, average eye velocity reached zero at 108 ms (107.6 ± 18.2 ms, n = 22) after the eyes were accelerated toward the preferred direction. Most neurons discharged before the onset of pursuit in the step-ramp trials; however, the onset of the activity was delayed for many neurons in the double-ramp trials. About one-half (13/22) of the neurons discharged at or after eye acceleration toward the preferred direction (Fig. 11A) in the double-ramp trials, indicating that these neurons cannot participate in the earliest stage of eye acceleration during the change in the pursuit direction, though these can participate in the early stages of pursuit initiation in the usual step-ramp trials.

Activity before and after pursuit

The neuron shown in Fig. 8 responded strongly to pursuit in the right-down direction, and it continued firing even after the monkey terminated pursuit. Some pursuit-related neurons showed weak responses after the monkey terminated pursuit and fixated a stationary target at an eccentric location. However, this type of neuron is different from eye-position–related neurons described previously (Bizzi 1968; Segraves 1992) in several ways. First, the activity of pursuit-related neurons during pursuit was much greater than that during fixation. Second, pursuit-related neurons discharged at the initiation of pursuit even when the target was moved after large steps as shown in Fig. 2B. Finally, pursuit-related neu-
FIG. 12. Example of an eye-position–related neuron, same as in Fig. 1C. A: responses when the target stepped 3° and moved vertically at 20°/s. B: target stepped 15° and moved at 20°/s. C: target stepped 15°. Histograms are constructed from the activity in the trials toward the preferred direction (downward).

rons discharge vigorously at the initiation of pursuit, whereas eye-position–related neurons gradually increased their activity in the step-ramp pursuit trials. An example of eye-position–related neuron is shown in Fig. 12 (same neuron as Fig. 1C), for comparison with the activity of a pursuit-related neuron (cf. Fig. 2). This neuron discharged during downward pursuit, and the activity was suppressed by upward pursuit (Fig. 12A). However, the onset of the activity was delayed when a large step was introduced (Fig. 12B). The activity was consistently related to eye position in the visually guided saccade task as well (Fig. 12C).

To quantify the modulation of activity during fixation before and after pursuit, we calculated the MIs for 76 pursuit-related neurons and 12 eye-position–related neurons. The MI compares the activity of two fixation intervals divided by the response to pursuit (see METHODS). The MI of a pursuit-related neuron with no modulation after pursuit is 0, whereas that of an eye-position–related neuron with no pursuit-related responses is >1. When the activity before the onset of target motion was greater than that after pursuit, the MI is a negative value. The distribution of the MIs indicates that these two neuron types can be clearly distinguished from each other, even though many pursuit-related neurons modulate their activity during fixation before and after pursuit.

As in Fig. 13, some pursuit-related neurons showed negative MIs, indicating that the activity before target motion onset was greater than that after pursuit. Among 76 pursuit-related neurons, 20% (15/76) had MIs less than −0.2, indicating that modulation in activity before pursuit is >20% of pursuit-related response. One example of such neurons is shown in Fig. 14 (same neuron as Fig. 1B). The MI of this neuron was calculated from downward pursuit trials and the value was 0.52. In Fig. 14A, data from upward (top) and downward pursuit trials (bottom) were aligned with the fixation point onset (left) and the target motion onset (right). The activity gradually increased toward the onset of target motion and was suppressed by upward pursuit (top) or was strongly enhanced by downward pursuit (bottom). The DI of this neuron was 1.81. Because previous studies indicated the tonic activity of some saccade-related burst neurons in the FEF reflects the anticipation of a saccade in their preferred direction (Bruce and Goldberg 1985; Schall 1991b), we examined whether the buildup activity changes when the direction of target motion was randomized fully so that the monkey could not predict the subsequent pursuit direction. Figure 14B shows the responses in two blocks of trials. In
one block, the target moved in one direction selected randomly from a set of four oblique directions. In another block, the direction of target motion was selected randomly from the other four directions (i.e., up, down, right, left). The activity before target motion onset did not change and the activity was still selective for downward pursuit. Because the monkey could not have anticipated only downward target motion in these randomized blocks of trials, the buildup activity does not seem to be activity related to preparation for downward pursuit. Instead, the activity seems to be related to anticipation of target motion in any direction.

We recorded 10 neurons that showed only the buildup activity before the target motion onset. One example of such neurons is shown in Fig. 15. This neuron showed the buildup activity in the step-ramp pursuit task (Fig. 15A) as well as in the visually guided saccade task (Fig. 15B). In both tasks, the activity was suppressed once the target had moved. The activity of this neuron also was examined when the target was briefly (200 ms) extinguished immediately before the target motion onset (gap trials). Figure 15, C and D, show the responses in four task conditions that were randomly interleaved in one block of trials. The target moved randomly either right or leftward and a temporal ‘‘gap’’ (200 ms) was introduced in one-half of the trials. Figure 15C shows the responses in nongap trials, and Fig. 15D shows those in the gap trials. The buildup activity was truncated during the gap interval.

Localization of task-related neurons

The recording sites of task-related neurons are shown in Fig. 16. For both monkeys, pursuit-related neurons were recorded from penetrations through the posterior portion of the arcuate sulcus. Histological reconstructions showed that these neurons were located mainly in the posterior bank of the arcuate sulcus near the arcuate spur (Stanton et al. 1993), extending to the depth of the anterior bank. These areas seem adjacent to the ‘‘general region of the FEF’’ (Burman and Bruce 1997) and correspond to the caudal edge of the sites at which low currents (≤50 µA) evoke contraversive saccades (Bruce and Goldberg 1985). Figure 16 also shows that the saccade-related burst neurons often were found in the posterior bank of the arcuate sulcus and even around the arcuate spur (right).

DISCUSSION

Recently, lesion and electrical microstimulation studies have shown that the posterior part of the arcuate sulcus is involved in the smooth pursuit system (Keating 1991, 1993; Lynch 1987; MacAvoy et al. 1991; Tian and Lynch 1996a; see Keller and Heinen 1992 for review). Single-unit recording studies in the fundus and the posterior bank of the arcuate sulcus have suggested that these cortical areas provide signals to initiate and maintain smooth pursuit eye movement (Gottlieb et al. 1994; MacAvoy et al. 1990). Our results have shown that most pursuit-related neurons carry extraretinal signals and many discharge during change in pursuit direction. We also have shown that some pursuit-related neurons change their activity when the animals fixate a stationary target before and after the target motion.

Pursuit-related response and comparison with the previous study

We found pursuit-related neurons in the posterior part of the arcuate sulcus near the arcuate spur in two Japanese monkeys. These neurons often were intermingled with saccade-related burst neurons. Anatomic localization of these neurons is similar to that of the pursuit cells reported in rhesus monkeys (Gottlieb et al. 1994; MacAvoy et al. 1991) and is somewhat caudal to the site where electrical microstimulation evokes slow eye movements in Cebus monkeys (Tian and Lynch 1996a).

Most pursuit-related neurons had strong directional preferences, and many (40%) were suppressed during pursuit in the nonpreferred direction. The directional preferences of these neurons were broadly tuned. When the extent of the directional tuning was examined, the full-width at half-maximum of the responses ranged from 95.9° to 210.8° with median 153° (n = 17, 148.5 ± 39.4°), whereas that of the pursuit cells reported previously was 105° (n = 80) (Gottlieb et al. 1994). Because our sample was much smaller than that of the previous study, the differences may not be significant. We also have shown that most (75%) pursuit-related neurons discharge before the initiation of pursuit, and the median latency for the neurons is −12 ms (n = 59, −6.9 ± 37.0 ms), comparable with previous observations (−19 ms, n = 69) (Gottlieb et al. 1994).

These results show that pursuit-related neurons in this study have properties similar to the pursuit cells of previous studies (Gottlieb et al. 1994; MacAvoy et al. 1991), so we will use the term ‘‘frontal pursuit area’’ (FPA) (Keating et al. 1996; Schwartz and Lisberger 1994) for the sites where we recorded pursuit-related neurons.

Extraretinal component during maintenance of pursuit

Previous studies in the cortical MT and MST areas quantified the visual components of the pursuit-related activity (Kawano et al. 1994; Newsome et al. 1988) and showed that the visual properties of the pursuit-related activity recorded in the MSTd were different from those in the lateral portion of the MST (MSTl) and the foveal representative middle temporal area (MTf) (Newsome et al. 1988). When a moving target was extinguished briefly or stabilized on the retina so that the image motion was reduced greatly during the maintenance of smooth pursuit, many pursuit-related neurons in the MSTd continued firing, whereas those in the MSTl and MTf decreased (but did not cease entirely) their activity. They therefore concluded that the MSTd neurons receive extraretinal inputs related to smooth pursuit eye movements and suggested that the MST forms an internal positive feedback circuit in the pursuit system that provides signals for the maintenance of pursuit (Newsome et al. 1988). Using similar techniques, we have examined the contribution of visual inputs to pursuit-related activity recorded from the FPA and compared our data with those from the MST. When a moving target was briefly extinguished, 72% of pursuit-related neurons changed their activity, but the change was within 30% of control values. Only a small change in activity was observed for many neurons when the target image was stabilized on the retina. The distribution
of changes in activity was similar to that of the MSTd (Fig. 9), indicating that pursuit-related neurons in the FPA also carry extraretinal signals during maintenance of pursuit.

Although electrical microstimulation applied to the MSTI and MTf alters ongoing pursuit, that applied to the MSTd does not (Komatsu and Wurtz 1989). Lesions in the MSTI produce directional pursuit deficits, but those in the MSTd do not (Dürsteler and Wurtz 1988). Because MST pursuit cells that receive extraretinal signals were recorded frequently in the MSTd, these observations suggest that the extraretinal signals in the MSTd may not be used for the performance of pursuit maintenance, or alternatively, the signals are further processed in other cortical areas before they affect the premotor pursuit circuits. For the FPA, the eyes are accelerated by electrical microstimulation both during fixation (Gottlieb et al. 1993) and during pursuit (Tanaka, unpublished observations). Lesions in the FPA greatly reduce the gain of ipsiversive smooth pursuit (Keating 1991; Lynch 1987; MacAvoy et al. 1991). These results indicate that the signals in the FPA can directly affect the premotor pursuit circuits. Considering the significant anatomic connections from the extraretinal visual cortices and the posterior parietal cortices to the pericruciate areas, it is likely that the extraretinal signals in these higher visual cortices influence the activity of the premotor pursuit circuits via the FPA.

Response to velocity step

Previous study has shown that FPA provides an eye acceleration signal related to pursuit initiation (Gottlieb et al. 1994). At the same time, some FPA neurons showed eye velocity sensitivity during maintenance of pursuit (Gottlieb et al. 1994). In this study, we have examined the neuronal activity at the initiation of pursuit, during change in pursuit direction, and at the termination of pursuit, using the step-ramp, double-ramp, and step-stop paradigms, respectively. These paradigms enabled us to examine neuronal responses related to eye acceleration with different eye velocities. If pursuit-related neurons send eye acceleration signals to generate slow eye movements toward their preferred direction, the activity always would precede the change in eye velocity (i.e., acceleration). Some neurons consistently discharged before the eyes were accelerated in their preferred direction in all these paradigms. However, in the double-ramp paradigm, the onset of the activity was delayed relative to eye acceleration for many neurons, and about half neurons discharged at or slightly after eye acceleration even though these neurons discharged before pursuit initiated in the ordinary step-ramp paradigms (Fig. 11). These results indicate that these pursuit-related neurons cannot participate in the earliest stages of eye acceleration during change in pursuit direction (but can influence the early stages of initial eye acceleration in the usual step-ramp trials). When the responses to the termination of pursuit in the nonpreferred direction were examined, many neurons showed no or slight change in activity.

The variety of responses in the double-ramp and the step-stop trials suggest that pursuit-related neurons code a mixture of eye velocity and eye acceleration signals with variable weights and thresholds. If so, the activity related to eye acceleration in these trials might be inhibited by the signal related to oppositely directed eye velocity, and the onset of the activity might be delayed. Indeed, for many pursuit-related neurons, the activity was suppressed by pursuit in the nonpreferred direction (Fig. 5). Previous study showing that some FPA neurons have sensitivity to pursuit velocity also may support this possibility (Gottlieb et al. 1994). Such a summation of eye movement signals has been reported in the cerebellum (in the ventral paraflocculus) (Shidara et al. 1993).

Activity modulation during fixation

The activity of pursuit-related neurons was modulated not only by visuomotor parameters but also by the task requirements. Some pursuit-related neurons showed a buildup of activity when the animals fixated a stationary target before the target moved. Some studies of saccade-related burst neurons recorded from the FEF showed context-dependent activity that was thought to be related to the preparation for subsequent saccades (Bruce and Goldberg 1985; Schall 1991b). Such preparatory activity also was reported for cells in the supplementary eye fields (Schall 1991a), in the lateral intraparietal area (Andersen et al. 1990), and in the superior colliculus (Glimcher and Sparks 1992). Because we provided neither information for the subsequent pursuit direction nor a delay period between the information and the onset of target motion in this study, we could not examine possible activity related to the preparation of pursuit in the preferred direction. Instead, we examined the neuronal activity when the direction of subsequent target motion was fully randomized and showed that the buildup of activity still was observed. Therefore the buildup activity observed in this study does not seem to reflect the preparation for pursuit in the preferred direction. The activity was observed equally in pursuit-related neurons for all directions. This may be the...
FIG. 14. Example of a pursuit-related neuron that showed a buildup activity, same neuron as in Fig. 1B. A: responses in the vertical pursuit trials. Data are aligned with the appearance of fixation point (left) and the onset of target motion (right). This neuron discharged before the target motion. Activity ceased at the initiation of upward pursuit (top) or increased during downward pursuit (bottom). Fixation periods of these trials were 1.5–2 s. B: responses to pursuit in 8 directions. Data for vertical pursuit are the same as in A. Data were obtained from 2 blocks of trials; in 1 block, the target moved in 1 of the 4 oblique directions in random order. In the other block, the direction of target was selected randomly from other 4 directions (i.e., right, left, up, down). Note that the buildup activity during fixation is equal to all directions. Directional tuning of this neuron is constructed by measuring the average activity for 600-ms period beginning from 50 ms after target motion onset (middle). Vertical calibration of each histograms represents 100 spikes/s.

reason why the increasing activity did not result in the slow eye movements, although electrical microstimulation applied to the FPA can initiate slow eye movements when the animals fixate a stationary target (Gottlieb et al. 1993; Keller and Heinen 1992; MacAvoy et al. 1990). The buildup of activity seems to reflect either the anticipation of subsequent eye movements regardless of their direction or visual attention directed toward the fixated target that will provide a cue for required eye movements. Similar activity has been reported in periaqueductal neurons that discharge when the animals fixate a target that serves as a cue for manual movement (Suzuki and Azuma 1977).

Recently it has been shown that the activity of fixation cells in the rostral pole of the superior colliculus has directional preference during smooth pursuit, suggesting that these cells encode motor errors for both pursuit and saccades (Krauzlis et al. 1997). Some pursuit-related neurons in the FPA also discharge when the animals actively fixate a stationary target before it moves, and they have a directional preference during pursuit. The FPA pursuit-related neurons showed no or only slight change in activity at the onset of saccades, at least within the range we tested (5–20°), and most of them discharged before the target moved into the visual field of the preferred pursuit direction (cf. Figs. 2B and 7B). However, further experiments concentrating on smaller target steps may reveal other aspects of the pursuit-related signals in the FPA.

Possible role of the FPA in the smooth pursuit system

A number of behavioral studies have suggested that there is a “switch” in the pursuit system that modulates the strength of sensory-motor transmission for pursuit (Grasse and Lisberger 1992). Lisberger and his colleagues have probed the state of the pursuit system by introducing a perturbation of target motion and shown that the eye movement
FIG. 15. Example of a neuron that showed only a buildup activity before the onset of target motion. A: responses in the horizontal step-ramp pursuit trials (20°/s). B: responses in the horizontal saccade trials. C and D: responses in the horizontal pursuit trials (30°/s). Target was briefly (200 ms) extinguished before it moved (D, vertical arrow). In all panels, data are aligned with the onset of fixation point (left) and the onset of target motion (right). See the text for details.

responses are largest when the perturbation is applied along the axis of ongoing smooth pursuit (Schwartz and Lisberger 1994). They concluded that the visuomotor transmission for pursuit is multiplied during smooth pursuit eye movement (Goldreich and Lisberger 1992; Kahlon and Lisberger 1996; Schwartz and Lisberger 1994). Such a gain control of the pursuit system also is suggested by the observations that electrical microstimulation applied to the extrastriate visual cortex (Komatsu and Wurtz 1989) and to the dorsolateral pontine nucleus (May et al. 1985) produces short-latency alterations in slow eye velocity when the animals perform smooth pursuit but not when the animals fixate a stationary
target. Grasse and Lisberger (1992) have provided further evidence for the existence of such a function by examining eye movements of an aberrant monkey that could hardly generate upward smooth pursuit but could accelerate his eyes normally when upward target motion was introduced during downward pursuit. They examined eye movement responses of the monkey to the directional change in target motion using tasks similar to our double-ramp tasks (see Fig. 8 of Grasse and Lisberger 1992). For the aberrant monkey, the initial upward eye acceleration was normal, but eye velocity decreased as soon as it reached zero. These authors concluded that the monkey had a deficit in the upward pursuit switch (Grasse and Lisberger 1992). Because one-half of our FPA neurons do not participate in the earliest stage of eye acceleration during change in pursuit direction in the double-ramp tasks, dysfunction in the FPA might be a possible cause of the abnormality of eye movement responses observed in the aberrant monkey reported previously.

It is known that chronic damage in the FPA reduces the gain of pursuit but does not abolish it (Keating 1991, 1993). Recent lesion studies have shown that the FPA is essential for the generation of high gain smooth pursuit but not for the generation of slow eye movements elicited by a moving texture (Keating et al. 1996). These results suggest that the FPA may contribute to the variable gain of visuomotor transmission for pursuit and that the FPA may be located in another pursuit pathway besides the direct extrastriate-ponto–cerebellar pathway (Keller and Heinen 1991; Yamada et al. 1996), which also contributes to the slow eye movements elicited by a moving large texture (e.g., Kawano et al. 1994). The variable gain element for pursuit seems either independent of the slow eye movement system triggered by a moving large texture (Grasse and Lisberger 1992; Keating et al. 1996) or, alternatively, to play only a minor role in controlling the gain of the slow eye movements when the direct visuomotor pathway receives strong inputs from a moving large texture (Grasse and Lisberger 1992).

In this study, we have shown that pursuit-related neurons in the FPA carry extraretinal signals, comparable with those in MSTd. Because latencies vary from cell-to-cell in the double-ramp and the step-stop trials, we have suggested that pursuit-related activity may reflect a sum of eye movement parameters. Such eye movement signals may emerge from either subcortical premotor circuitry and/or the other cortical areas including the intraparietal areas, area 7a and the MST. All these cortical areas have reciprocal connections with the arcuate areas (Stanton et al. 1995; Tian and Lynch 1996b) and contain cells that encode eye position and pursuit signals (Andersen et al. 1990; Bremmer et al. 1997; Duhamel et al. 1997; Squatrito and Maioli 1997). In addition, the posterior parietal areas display signals related to visual attention or intention of subsequent behavior as well (for reviews, see Andersen 1996; Goldberg 1996).

Although many FPA neurons cannot participate in the earliest stage of eye acceleration during change in pursuit direction, the finding that almost all FPA neurons discharge before eye velocity in the preferred direction in both the double-ramp and the step-ramp trials indicates that the FPA can act as a variable gain element in the early stages of pursuit in the preferred direction. Such FPA neurons are eminently suited to play a role in gain control because they discharge during pursuit and are carrying signals independent of retinal slip. It is likely that the FPA receives eye movement signals that consist of eye acceleration, eye velocity, and even eye position, which are relayed to the premotor circuits so that the pursuit system generates high gain slow eye movements. Such a circuit also might be activated by slow eye movements elicited by moving large textures, but the gain control mechanism may be masked by the prominent input to the direct visuomotor pathway.

A recent study from our laboratory showed that the periar- cuate areas also receive vestibular inputs and that many pur- suit-related neurons seem to encode gaze velocity in space (Fukushima et al. 1997), similar to the gaze velocity Pur-
kinje cells in the floccular complex of cerebellum (Lisberger and Fuchs 1978; Miles et al. 1980; Stone and Lisberger 1990). These properties of FPA neurons will be documented in future reports.

We thank Dr. C.R.S. Kaneko for valuable comments on the manuscript, Dr. S. Kurkin for computer programs, Dr. Y. Suzuki for surgical procedures, Y. Kobayashi for histological assistance, and M. Yasuda for the animal care.

This work was supported by the Core Research for Evolutional Science and Technology of Japan Science and Technology Corporation, Grants in future reports. ments elicited by microstimulation in the primate frontal eye field. Nature 69: 786–799, 1993.


SARATA, H., SHIBUTANI, H., and KAWANO, K. Functional Properties of


