Discharge Characteristics of Pursuit Neurons in MST During Vergence Eye Movements

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INTRODUCTION

With the development of a high acuity fovea that covers, at most, only a few degrees of the visual field, it became necessary for frontal-eyed primates to precisely coordinate binocular eye movements to aim the foveae of both eyes at objects of interest. For small objects moving slowly and smoothly in space close to the observer, 2 eye movement systems are used: smooth pursuit and vergence eye movements (see review by Leigh and Zee 1999). The smooth pursuit system rotates both eyes in the same directions (i.e., conjugately) to track target movement in the fronto-parallel plane (frontal pursuit), whereas the vergence system rotates the eyes in opposite directions (i.e., disconjugately) to track targets moving toward or away from the observer (vergence-tracking). Both eye movement systems have the common function of maintaining target images near the foveae to ensure high-quality processing of visual signals associated with the moving target. Because targets could move in any directions in three-dimensional (3D) space, frontal pursuit and vergence signals must be combined to track objects moving in 3D (see Fukushima 2003 for review).

It is well known that the medial superior temporal (MST) visual areas are essential for initiation and maintenance of frontal pursuit and contain all the signal components needed to reconstruct target motion in space including retinal image-slip velocity of a target and eye velocity (see review by Andersen 1997; also Bremer et al. 1997, 1999; Dicke and Thier 1999; Dursteler and Wurtz 1988; Dursteler et al. 1987; Komatsu and Wurtz 1988a,b; Kawano et al. 1984; Newsome et al. 1988; Sakata et al. 1983; Thier and Erickson 1992). Sakata et al. (1983) provided the first description of MST neurons related to vergence-tracking of a small light-emitting diode (LED) target moving in depth. However, they reported that depth-tracking neurons showed little, if any, change during frontal pursuit and that the discharge characteristics of vergence-related neurons were not fully described in this pioneering study (also Sakata et al. 1980). Later studies tested MST neurons mostly in response to motion of large fields of dots (Inoue et al. 1998; Takemura et al. 2000, 2001, 2002). Therefore, basic yet important questions still remain unanswered on how MST neurons respond during vergence-tracking of a small spot that requires precise coordination of binocular eye movements (motor-fusion) to create sensory-fusion required for stereoscopic vision and disparity vergence (see review by Leigh and Zee 1999). Recent studies have shown that the majority of pursuit neurons in the caudal parts of the frontal eye fields (FEF) particularly in the fundus of the arcuate sulcus discharge not only for frontal pursuit but also for vergence eye movements (Fukushima et al. 2002a). Because FEF is known to have reciprocal connections with the middle temporal (MT) and MST (Stanton et al. 1988, 1993, 1995; Tian and Lynch 1996a,b; Tusa and Ungerleider 1988), it is possible that pursuit-in-3D signals come from MST. To understand how pursuit-in-3D signals are generated in the caudal FEF, it is important to examine discharge characteristics of pursuit-related neurons in MST during vergence-tracking using motion of a small spot. First, we asked whether pursuit-in-3D signals are already present in MST and examined the percentage of pursuit neurons in MST that discharge for both frontal pursuit and
vergence-tracking. Second, to determine how MST is involved in vergence-tracking for a fused target image, we examined discharge characteristics of MST neurons during vergence-tracking induced by a small spot. Third, to determine whether MST neurons carry visual information about spot motion in depth (i.e., disparity and/or disparity-velocity), we examined visual responses of MST pursuit neurons to a small virtual target spot moving in depth while the monkeys fixated another stationary spot. Finally, to determine whether MST pursuit neurons could be involved in initiation of vergence tracking induced by a small spot, we examined latencies of neuronal responses with respect to onset of vergence eye movements. Some of the results have been presented in preliminary form (Fukushima et al. 2003).

METHODS

General procedures

Two Japanese male monkeys (Macaca fuscata, H, K, 3.9–4.5 kg) were used in this study. Our specific protocols were approved by the Animal Care and Use Committee of Hokkaido University School of Medicine. We have already published detailed descriptions of our surgical procedures elsewhere (e.g., Fukushima et al. 2004), and thus only a brief account is provided here. Before surgery, each monkey was sedated with ketamine hydrochloride [5 mg/kg, intramuscularly (im)], and then anesthetized with pentobarbital sodium [25 mg/kg, intraperitoneally (ip)] and additional anesthesia (0.5–1.0% halothane mixed with 50% nitrous oxide and 50% oxygen) was administered as necessary. Under aseptic conditions, 2 head holders were affixed to the skull to allow stabilization during recording experiments. A scleral search coil was implanted underneath the conjunctiva of each eye to record vertical and horizontal components of eye movements for both eyes (Fuchs and Robinson 1966; Judge et al. 1980). Analgesics (pentazocine, 0.2 mg/kg) and antibiotics (penicillin G sodium, 20,000 U) were administered postsurgically to reduce discomfort and guard against infection.

Training procedures

Each monkey was seated in a primate chair in darkness with the head restrained in the horizontal stereotaxic plane, facing a 22-in. computer display (Mitsubishi, RDF 221S) placed 65 cm away from the eyes. The interocular distance of the monkeys in this study varied between 20 and 21 mm. Visual objects (target spot, visual pattern; see below) were presented inside a 30 × 20° portion of the visual field. Visual stimuli were generated as 2 alternating images viewed by left or right eyes through polarization shutter glasses that were switched at 120-Hz rate (Fig. 1A). This setup allowed us to reproduce target motion in virtual 3D space. A red spot of 0.5° angular size at the screen distance of 65 cm was used as the main target in all experiments. To elicit vergence-tracking, a stereo virtual target was moved either in the midsagittal plane sinusoidally (Fig. 1A) or in ramp/step trajectories (see below). Throughout the text, “sinusoidal vergence target movement” refers to sinusoidal oscillation of the vergence target angle. Our setup allowed us to induce pure vergence eye movements or frontal pursuit in both humans and monkeys (Fig. 1, B–D; also Kurkin et al. 2003). In this study, a virtual spot was moved between 10 and 65 cm from the eyes and that movement required vergence eye movements of 10°. Object motion in the fronto-parallel plane was generated at a predefined virtual distance from the monkey, mostly at the screen distance. The monkeys were rewarded for pursuing the moving target. Eye position signals were calibrated for each eye separately by requiring the animal to fixate the stationary target or pursue a slowly moving one at 0.2 Hz. Target position signals (at 120 Hz) were derived from digital-to-analog outputs and were displayed on a monitor screen for comparison with other signals.

The monkeys were trained and rewarded for performing in 2 tasks: 1) pursuit of a target moving in the frontal plane or in depth; 2) fixation of a stationary target spot while a 2nd spot or visual pattern (see below) appeared and moved in various directions. After the animals were trained in these task conditions, a recording chamber was stereotaxically implanted (center aimed at posterior 5 mm and lateral 15 mm) on the skull to allow single-unit recording in MT/MST (e.g., Komatsu and Wurtz 1988a; Newsome et al. 1988).

Recording procedures and behavioral paradigms

For our search stimulus, the target moved sinusoidally along oblique trajectories that were generated by combinations of frontal motion and motion in depth at 0.5 Hz (Fig. 1A). Once responsive single neurons were encountered as judged visually and on the audio monitor, neuronal responses were tested during frontal pursuit in 8 cardinal directions separated by 45° (vertical, horizontal, and oblique directions) and during vergence-tracking in the midsagittal plane from 65- to 10-cm depth at 0.5 Hz. To confirm whether neuronal responses were related to vergence eye movements and not associated with motion of a single eye (Zhou and King 1998), vergence-tracking was tested while the target moved in depth aligned on either the left or the right eye (Fig. 1, E and F). To examine velocity sensitivity during vergence eye movements, the monkey tracked the target spot moving in depth with a variety of frequencies (0.1–2.0 Hz).

To examine whether MST pursuit neurons maintain discharge modulation during vergence-tracking without the presence of a vergence target image on the retina (cf. Newsome et al. 1988), the target was extinguished (blanked) for 400 ms at fixed position in a circle at 0.5 Hz (±10°) during sinusoidal tracking in the preferred direction. The monkeys were required to continue their pursuit in the absence of a target.

To examine latencies of vergence-related neuronal responses we used steps or ramps of target motion in depth. For vergence step testing, the spot moved from far (65 cm) to near (10 cm) and back with random intertrial intervals between 1 and 3.5 s. The monkeys were required to make rapid convergence and divergence eye movements to acquire the target. The vergence target was also moved in a ramp fashion over the same distance (10–65 cm) at 10–20/s for some neurons.

To examine visual responses to target motion in depth, monkeys fixated a 0.5° stationary target spot (first spot) while a second spot (test spot, 0.6°) moved sinusoidally in depth from 65 to 10 cm in the midsagittal plane (see Fig. 1A). The first spot was presented 0.5° above the moving test spot at 40 cm in front of the eyes. The test spot was moved at different frequencies (0.5–2.0 Hz) to examine velocity sensitivity of the visual response while the monkeys fixated the stationary spot. The first spot was occasionally extinguished while the test spot was presented continuously and the monkeys were then required to track the test spot. This procedure was used to reward the...
MST NEURONAL ACTIVITY DURING VERGENCE-TRACKING

A mid-sagittal plane
Vergence tracking

frontal pursuit

monitor
screen

LCD
shuttered
glasses

left eye
right eye

B Horizontal pursuit

Target
LHE
LHE

C Vertical pursuit

Target
LVE
LVE

D Midsagittal vergence tracking

Target
LHE
RHE
LHE-RHE

E Left eye aligned

Target
LHE
RHE
LHE-RHE

F Right eye aligned

Target
LHE
RHE
LHE-RHE

G Fixation with a random dot pattern (5° x 5°) moving horizontally

Pattern vel

up 10°

left ipsi

down

right 10°

contra

right 40°/s

left

up 10°

down

right 40°/s

left

H.c71

J Neurophysiol • VOL 93 • MAY 2005 • www.jn.org
monkeys for pursuing the test spot so that this stimulus would not become behaviorally meaningless and so that they would, presumably, attend to it, similar to previous studies (Fukushima et al. 2000, 2002b). For some neurons, the test spot was stepped between 65 and 10 cm with a variable intertrial interval (1–3 s). The test spot also moved in the frontal plane in the above 8 cardinal directions to examine visual motion response.

To confirm that discharges of our neurons are consistent with the known discharge characteristics of MST pursuit neurons (e.g., Komatsu and Wurtz 1988a), visual responses were also tested by using a visual pattern that consisted of 36 randomly distributed squares; the size of each square ranged between 0.5 and 1.5° and the pattern covered 20 × 20° of visual angle. The pattern was presented at the plane of the screen and was moved sinusoidally in various directions in the frontal plane at 0.5 Hz while the monkeys were required to fixate the 0.5° stationary spot as in the task with the moving second spot task. A smaller pattern (5 × 5°) was presented at different positions (vertical, horizontal, or diagonal directions at 10° eccentric from the central fixation point) to examine visual receptive fields while the monkeys fixated the central fixation spot.

Data analysis

The data were analyzed off-line as previously described (Fukushima et al. 2000, 2002a,b). Cell discharge was discriminated with a dual time–amplitude-window discriminator and digitized together with eye position, chair position, and target position signals at 500 Hz using a 16-bit A/D board. Eye position signals were differentiated by analog circuits (DC-100 Hz, −12 dB/octave) to obtain eye velocity. Stimulus position signals for sinusoidal task conditions were also differentiated by software to obtain velocity. Vergence eye movements were calculated as the difference between the horizontal components of the left and right eyes. The traces were displayed and saccades were removed from eye velocity traces using our interactive computer program (Fukushima et al. 2000). We did not manipulate spike data for purposes of analysis in this study. All traces were aligned with stimulus velocity for 10–30 cycles, to allow construction of raster and histograms of neuronal responses. To quantify responses, each cycle was divided into 64 equal time bins. A sine function was fitted to averaged velocities and cycle histograms of cell discharge, exclusive of the bins with zero spikes, by means of a least-squares error algorithm. Responses that had a harmonic distortion (HD) of more than 50% or a signal-to-noise ratio (S/N) of < 1.0 were discarded: S/N was defined as the amplitude of the fundamental frequency component divided by the amplitudes of the 3rd through 8th harmonic, and HD as the amplitude of the 2nd harmonic divided by that of the fundamental (Wilson et al. 1984). The phase shift of the peak of the fitted function relative to upward or rightward stimulus velocity was calculated as a difference in degrees. Sensitivity (re: stimulus velocity) was calculated as the peak amplitude of the fundamental component fitted to the cycle histogram divided by the peak amplitude of the fitted stimulus velocity (i.e., target velocity for frontal and depth tracking, velocity of test spot or pattern motion for visual responses). For those neurons that satisfied HD and S/N criteria, sensitivity (re: stimulus velocity) ≥0.10 spikes/s/° was taken as significant modulation (Fukushima et al. 2000, 2002a,b).

For responses with diagonal stimulus directions during frontal pursuit, radial stimulus velocity was first calculated as a square root of the sum of the squares of the vertical and horizontal components, and sensitivity (re: stimulus velocity) was calculated by dividing the amplitude of discharge modulation by radial stimulus velocity. The phase shift of cell response with diagonal preferred direction was calculated relative to the rightward component of eye or stimulus velocity. Eye velocity during frontal pursuit and vergence eye velocity during vergence-tracking were calculated similarly after deleting saccades. Sensitivity (re: eye velocity) of neuronal responses was also calculated by dividing peak discharge modulation by peak eye velocity during frontal pursuit. Sensitivity (re: vergence eye velocity) of neuron responses during vergence-tracking was calculated similarly by dividing peak discharge modulation by peak vergence eye velocity.

Vergence eye velocity sensitivity of neuronal response during tracking at different frequencies was calculated by plotting the amplitude of discharge modulation of each neuron against the peak amplitude of vergence eye velocity and by fitting those points with a linear regression.

To analyze visual responses to a 2nd spot motion or pattern movement in depth, all traces were aligned with the 2nd spot or on the pattern cycles. Traces that contained saccades or slow eye movement were removed because they were indicative of the monkeys’ failure to fixate the stationary spot, and only those traces with eye position changes of < 1° during each cycle were selected and analyzed as previously described (Fukushima et al. 2000, 2002b).

To examine latencies of eye and cell responses to vergence target steps, over 20 trials were aligned with onset of target motion to obtain mean responses. Traces in which saccades appeared within about 200 ms of the target onset were omitted. SDs of the mean responses were calculated for the 200-ms interval immediately before target motion onset, and these values were used as the control. Onset of vergence eye movements in response to target steps was determined as the time at which mean vergence eye velocity deviated ±2SD of the control value (Akao et al. 2004). Similarly, onset of the cell’s responses to target steps was determined as the time at which the mean discharge rate exceeded 2SD of the control value. Latencies of discharge modulation of individual neurons relative to onset of eye movements were calculated by subtraction.

Histological procedures

Near the conclusion of recordings in monkey K, the sites of pursuit neuron activity recordings were marked by passing current (10–15 μA for 60–100 s; 800–1,200 μC) through the tip of a tungsten electrode with an iron-plated tip. After recording was completed, this monkey was deeply anesthetized by pentobarbital sodium (50 mg/kg, ip). After histological fixation, coronal sections were cut at 100-μm thickness on a freezing microtome. These sections were then stained using the Nissl method to determine the locations of single-neuron recording. One monkey is still a subject in ongoing studies.

Results

Consistent with previous studies (e.g., Komatsu and Wurtz 1988a), in this study we recorded many neurons in the temporoparietal area that exhibited a variety of responses during target tracking, ranging from only visual responses to only pursuit-related discharges. Because our main objective of this study was to examine vergence-related discharge characteristics, we selected neurons that responded during pursuit for target motion in 3D (i.e., along the 8 cardinal directions separated by 45° and/or in depth; see Methods). We did not include visual-only neurons in this study. Because our recording tracks for such pursuit-related neurons were found primarily in MST (see below), we call them MST pursuit neurons in this study.

Classification of MST pursuit neurons during pursuit-in-3D

We recorded a total of 242 neurons whose activity was modulated during sinusoidal pursuit of a target moving in 3D virtual space (see Methods) in 2 monkeys (123 from monkey H, 119 from monkey K). Of these, 219 neurons were tested during both frontal pursuit and vergence-tracking (115 from monkey H, 104 from monkey K). We classified these pursuit-
responding neurons as belonging to one of 3 groups on the basis of whether they responded to frontal pursuit alone, vergence alone, or frontal pursuit and vergence (Table 1). Although there was a slight difference in the percentage of neurons classified in each group in the 2 monkeys [Table 1(a)–(c)], the majority of neurons responded only during frontal pursuit in both monkeys (mean for the 2 = 61.1%). In some cases, neurons that exhibited robust discharge modulation during frontal pursuit also exhibited weak discharge modulation during mid sagittal vergence-tracking. However, careful examination of neuronal response during one-eye–aligned tracking conditions (see METHODS) revealed that such modulation was not attributed to true vergence-related activity.

Representative discharges are illustrated in Fig. 1, B–F for a neuron that responded during horizontal but not during vertical pursuit (Fig. 1, B and C). During mid sagittal vergence-tracking this neuron exhibited weak modulation during divergence velocity (Fig. 1D). If this modulation were related to true vergence-tracking, it should have been modulated during the divergence phase in conditions where motion of the target was aligned with one eye (see METHODS). When the spot moved along the left-eye–aligned plane, this neuron increased discharge during divergence velocity (Fig. 1E). However, when the spot moved along the right-eye–aligned plane, neuronal response increased activity during convergence velocity (Fig. 1F). This oppositely directed response pattern in left- and right-eye–aligned conditions cannot be explained by vergence-tracking alone. Rather, these oppositely directed neuronal response patterns occurred when either the right or left eye moved toward rightward, suggesting that the modulations were related to the rightward component of frontal pursuit (Fig. 1B). Minimum discharge modulation during mid sagittal vergence-tracking is consistent with this interpretation (Fig. 1D).

Discharge characteristics of these frontal pursuit neurons are consistent with the known discharge characteristics of MST pursuit neurons in the following 2 points: the relatively large size of visual receptive fields (Komatsu and Wurtz 1988a) and maintenance of discharge modulation during pursuit while the target was briefly turned off (i.e., blanking) (Newsome et al. 1988). An example of the former is illustrated in Fig. 1G. During fixation of a stationary spot, this frontal pursuit only neuron also responded to visual pattern movement with the visual preferred direction opposite to the frontal pursuit preferred direction (Fig. 1, G vs. B, leftward vs. rightward preferred directions, respectively). The visual receptive field of this neuron was larger than 10°, including the fovea (Fig. 1G), consistent with the known characteristics of MST neurons (e.g., Komatsu and Wurtz 1988b). The maintenance of discharge modulation during pursuit with target blanking is also consistent with MST neurons (see below).

Representative responses of frontal pursuit + vergence and vergence-only neurons [Table 1(b) and (c)] are illustrated in Fig. 2 during vergence-tracking. This vergence-only neuron (Fig. 2, A–D) discharged during convergence velocity (Fig. 2A) but modulation during frontal pursuit was not well correlated with pursuit eye movements (Fig. 2D), whereas the frontal pursuit + vergence neuron (Fig. 2, E–H) discharged during divergence velocity (Fig. 2E) with clear modulation during frontal pursuit along an oblique direction (Fig. 2H). During one-eye–aligned tracking conditions (Fig. 2, B–C and F–G), both neurons exhibited discharge modulation consistent with their discharges during mid sagittal vergence-tracking. For example, the neuron shown in Fig. 2A discharged during convergence velocity in both right-eye–aligned and left-eye–aligned tracking (Fig. 2, B and C), whereas the neuron shown in Fig. 2E exhibited discharge modulation during divergence velocity during both right-eye–aligned and left-eye–aligned tracking (Fig. 2, F and G). Thus, these responses are clearly different from the response of a frontal pursuit only neuron in the same conditions as illustrated in Fig. 1, E and F, and were indeed related specifically to vergence-tracking. We tested discharge modulation during one-eye–aligned tracking for 25 pursuit neurons and confirmed that they indeed responded to vergence eye movements. Thus, MST contains pursuit neurons that discharge only for vergence-tracking (mean for the 2 monkeys = 18.3%; Table 1). MST also contains a similar percentage of pursuit neurons that responded to both frontal pursuit and vergence-tracking [mean for the 2 monkeys = 20.5%; Table 1(b) and (c)].

Table 1. Classification of MST pursuit neurons during pursuit-in-3D in two monkeys and comparison of percentages of pursuit neurons that discharge for frontal and/or depth pursuit in MST, FEF, and SEF

<table>
<thead>
<tr>
<th>Tracking in 3D</th>
<th>Monkey H</th>
<th>Monkey K</th>
<th>Total</th>
<th>FEF1</th>
<th>FEF2</th>
<th>SEF1</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Frontal pursuit only</td>
<td>62 (53.9%)</td>
<td>72 (69.2%)</td>
<td>134 (61.1%)</td>
<td>30 (25%)</td>
<td>35 (20.7%)</td>
<td>35 (62%)</td>
</tr>
<tr>
<td>(b) Vergence only</td>
<td>26 (22.6%)</td>
<td>14 (13.5%)</td>
<td>40 (18.3%)</td>
<td>12 (9%)</td>
<td>28 (16.6%)</td>
<td>6 (11%)</td>
</tr>
<tr>
<td>(c) Frontal pursuit + vergence</td>
<td>27 (23.5%)</td>
<td>18 (17.3%)</td>
<td>45 (20.5%)</td>
<td>80 (66%)</td>
<td>106 (62.7%)</td>
<td>15 (27%)</td>
</tr>
<tr>
<td>(d) Total</td>
<td>115</td>
<td>104</td>
<td>219</td>
<td>122</td>
<td>169</td>
<td>56</td>
</tr>
</tbody>
</table>

A total of 219 MST pursuit neurons were examined in monkeys H and K during both frontal pursuit and vergence-tracking. Pursuit-related MST neurons were classified into 3 groups according to whether they responded to frontal pursuit only (a), vergence only (b), or both (c). Data for FEF1, FEF2, and SEF1 pursuit neurons are taken from Fukushima et al. (2002a), Akao et al. (2005), and Fukushima et al. (2004), respectively. Because the search task conditions were different in the first 2 studies, the data are summarized separately. In Fukushima et al. (2002a), a horizontal screen was used to present a vergence target, whereas a stereo-target was used in Akao et al. (2005) similar to the present study.

Comparison of velocity sensitivity during vergence-tracking and frontal pursuit

During vergence-tracking, MST pursuit neurons exhibited response phases near vergence target/eye velocity (Fig. 2). To examine their discharges in more detail, Fig. 3A plots sensitivity (re: vergence target velocity) against response phase for vergence-only neurons (open circles) and frontal pursuit + vergence neurons (dots) during tracking at 0.5 Hz. Distributions of the 2 groups of neurons are similar. For comparison, Fig. 3B plots distributions between sensitivity and phase (re: frontal target velocity) during frontal pursuit for frontal pursuit + vergence and some frontal pursuit only neurons (dots).
FIG. 2. Representative discharges of vergence-only neuron (A–D) and frontal pursuit + vergence neuron (E–H). Discharge during midsagittal vergence-tracking (A, E), right-eye–aligned (B, F) and left-eye–aligned (C, G) vergence-tracking, and frontal pursuit (D, H). LE in H indicates magnitudes of left vectorial eye velocity. For other abbreviations, see Fig. 1.
Although they are distributed widely, many were distributed with their phases near velocity (i.e., $\approx 0$ and $\pm 180^\circ$). Figure 3C compares sensitivity (re: target velocity) during vergence-tracking and frontal pursuit for vergence-only neurons (open circles) and frontal pursuit + vergence neurons (dots). Sensitivities (re: vergence target velocity) for the 2 groups of neurons are similar with mean values ($\pm$SD) of 1.19 ($\pm$0.97) and 1.07 ($\pm$0.50) spikes/s$^2$/s, respectively. Sensitivity (re: frontal target velocity) of frontal pursuit neurons (mean $\pm$SD, 1.45 $\pm$ 0.21 spikes/s$^2$/s) is also similar to sensitivity (re: vergence target velocity) of all vergence-responding neurons (mean $\pm$SD, 1.14 $\pm$ 0.11 spikes/s$^2$/s).

Vergence eye velocity sensitivity during sinusoidal vergence-tracking

To further examine velocity sensitivity of MST pursuit neurons during vergence-tracking, we compared discharge modulation of each neuron to sinusoidal vergence target motion at different frequencies with a constant amplitude ($\pm 10^\circ$). Frontal pursuit + vergence neurons and vergence-only neurons behaved similarly. Most of these neurons had increased amplitude of discharge modulation at higher frequencies. Representative discharges are illustrated in Fig. 4, A and B during vergence-tracking at frequencies from 0.3 to 1.0 Hz for a frontal pursuit + vergence neuron (A) and vergence-only neuron (B). Amplitudes of discharge modulation of both neurons increased as the target frequency increased (Fig. 4). The response phase of both neurons lagged as the tracking frequency increased. At 1 Hz, a distortion in phase was obvious in vergence eye velocity (Fig. 4B), and discharge modulation of this neuron also showed a distortion.

Figure 5, A and B, plots responses of the 2 groups of neurons (filled and open symbols for frontal pursuit + vergence and vergence-only neurons, respectively) during sinusoidal vergence target motion at different frequencies. Phase values (re: vergence target velocity) were widely distributed, but many were found near 0 or 180$^\circ$ (lead) at 0.3–0.5 Hz, corresponding to convergence velocity or divergence velocity, respectively, then lagged at higher frequencies (Fig. 5A). Although sensitivity (re: vergence target velocity) decreased at higher target frequencies, for many neurons the decrement was minimal (Fig. 5B).

Amplitudes of discharge modulation of many neurons increased as the target frequency increased (Fig. 5C). To compare the tracking performance over this same frequency range, Fig. 5, D–F, plots simultaneously recorded vergence eye movements. At frequencies $<0.5$ Hz, vergence eye velocities of our monkeys exhibited minimal phase lags (re: target velocity) with mean gains about 0.9 (Fig. 5, D and E). At higher frequencies, however, gains gradually dropped and phase lags increased. At $\geq 1.2$ Hz, gain sharply dropped with further phase lags. Vergence eye velocities increased up to 1.0–1.2 Hz, then sharply dropped (Fig. 5F).

To further compare neuronal and eye movement responses, we normalized phase-shift and sensitivity data for each neuron. For this, we first calculated differences in phase shifts of individual neurons at frequencies $>0.7$ Hz relative to the value of each neuron at 0.5 Hz because phase shifts were mostly constant at 0.3 and 0.5 Hz and because virtually all neurons
were tested at 0.5 Hz. Mean (±SD) differences were then calculated for each frequency. The results are plotted in Fig. 5, G–I for neuronal responses and vergence eye movements. The results indicate similar dynamics of MST neuronal responses and vergence eye movements during tracking of a vergence target.

To examine velocity sensitivity of individual neurons during vergence-tracking, we plotted amplitude of discharge modulation against vergence eye velocity for each neuron during vergence target motion up to 1 Hz because vergence eye velocities of these monkeys sharply decreased >1 Hz (Fig. 5F). Figure 6 summarizes the results for those neurons for which more than 3 different target frequencies were tested (n = 21, 12 frontal pursuit + vergence neurons, 9 vergence-only neurons). Frontal pursuit + vergence and vergence-only neurons are shown by filled and open symbols, respectively. Linear regression analysis indicated that about half (11/21 = 52%, Fig. 6, A and B) showed a linear relationship between amplitude of discharge modulation and peak vergence eye velocity. The mean slope and correlation coefficient were 0.92 (range 0.3–1.81) spikes/s/°/s and 0.95, respectively. Some neurons (5/21 = 24%) also increased amplitude of discharge modulation at higher vergence eye velocities, although the correlation was weak (Fig. 6C). In a minority of neurons tested (5/21 = 24%) regression analysis showed no significant correlation between amplitude of discharge modulation and vergence eye velocity (Fig. 6D), suggesting that their responses may reflect vergence eye position. These results indicate that the activity of MST pursuit neurons codes vergence eye velocity and position.

![Midsagittal vergence tracking](image)

**FIG. 4.** Discharges of MST frontal pursuit + vergence (A) and vergence-only (B) neurons at different frequencies of target motion in depth. Abbreviations as in Fig. 1.

**FIG. 5.** Comparison of responses of MST pursuit neurons and vergence eye movements. A–C: response phase (A), sensitivity (B, re-vergence target velocity), and amplitude of discharge modulation (C) are plotted against vergence target frequency with different keys for each neuron. Responses of each neuron are connected by lines. D–F: phase (D), gain (E), and eye velocity (F) of simultaneously recorded vergence eye movements are plotted against vergence target frequency. G: compares phase differences of responses of individual neurons and vergence eye movements at frequencies >0.7 Hz relative to the values at 0.5 Hz. Means ± SD are plotted at 0.7, 1.0, 1.2, 1.5, and 2.0 Hz by different keys as indicated. H and I: similar plots for differences in sensitivity of individual neurons (H) and gain of vergence eye movements (I) at frequencies >0.7 Hz relative to the values at 0.5 Hz. −, indicates decrease.
Maintenance of vergence-related discharge modulation

It has been shown that MST pursuit neurons maintain discharge modulation during brief blanking of a tracking target (Ilg et al. 2004; Newsome et al. 1988; Sakata et al. 1983). We examined whether vergence responses of MST pursuit neurons also exhibited similar discharge characteristics by briefly (400 ms) blanking the tracking target. Target blanking during vergence-tracking was tested for 13 (10 vergence-only and 3 frontal pursuit/vergence) neurons. Representative discharges are shown in Fig. 7, A and B for a vergence-only neuron. The vergence target was extinguished during convergence-tracking (Fig. 7A). During the blank period, neuronal modulation continued. Figure 7B compares discharge modulation and associated vergence eye velocity with and without target blanking (thick and thin lines, respectively). During blanking, vergence eye velocity clearly decreased, but this neuron maintained discharge similar to the modulation without blanking.

To quantify blanking effects, we calculated mean discharge rates during the last 200 ms of the blanking period and mean rates for an equivalent portion of the tracking cycle without blanking for each neuron. By dividing the former by the latter, we calculated a ratio for each neuron. The results are plotted in Fig. 8A for the 13 neurons tested. The majority showed only a slight decrease during blanking with the mean for 13 neurons of 0.90 (±0.45SD, open square, Fig. 8A). Although the number of frontal pursuit + vergence neurons (open circles) was small, their distribution seems similar to that of vergence-only neurons (dots) (Fig. 8A).

To compare neuronal responses with vergence eye movements further, Fig. 8B plots the changes in vergence eye velocity during target blanking during the same time intervals calculated for neuronal activity. During blanking vergence eye velocity decreased with the mean of 0.54 of the control values (Fig. 8B). Figure 8C compares the change in response of each neuron and simultaneously recorded vergence eye velocity by connecting the 2 by straight lines. Decrease in vergence eye velocity was not correlated with decrease in neuronal activity, indicating dissociation between the discharge of most MST pursuit neurons and vergence eye velocity in the blanking target condition (see DISCUSSION).

For comparison, target blanking was also tested for 14 frontal pursuit only neurons during frontal pursuit. The ratios (re: control value without blanking) were similarly calculated and are plotted for each neuron in Fig. 8D. Consistent with the previous report (Newsome et al. 1988), frontal pursuit only neurons maintained discharge modulation during target blanking. The mean normalized ratio was 0.98 (±0.19SD).

**FIG. 6.** Vergence eye velocity sensitivity of MST frontal pursuit + vergence and vergence-only neurons. A–D: amplitudes of discharge modulation are plotted against peak vergence eye velocity for each neuron. A and B: linear regressions are drawn for their responses.
We also blanked the target for 800 ms in 3 frontal pursuit + vergence neurons before the target changed the direction so that the monkey was required to continue vergence-tracking by changing its direction. As illustrated in Fig. 7, C and D, all 3 neurons discharged appropriately during blanking associated with convergence eye movements without the tracking target. At the reappearance of the tracking target, these neurons exhibited responses associated with increased vergence eye velocity (Fig. 7, arrows). These results suggest that, like frontal pursuit, MST pursuit neurons maintain vergence-related discharge modulation without a retinal image of the tracking target (see DISCUSSION).

Visual responses of MST pursuit neurons to spot motion in depth: comparison with vergence-tracking responses

It is well known that MST neurons respond to motion of a visual pattern (see review by Andersen 1997; Bremmer et al. 1997, 1999; Dicke and Thier 1999; Dursteler et al. 1988; Dursteler and Wurtz 1987; Kawano et al. 1984; Komatsu and Wurtz 1988a,b; Newsome et al. 1988; Sakata et al. 1983; Thier and Erickson 1992). To examine whether MST pursuit neurons carry visual information about motion in depth of a small spot and how neuronal responses for vergence-tracking of the spot and visual responses in depth are related to each other, we examined visual responses to a spot (0.6° diameter) moving sinusoidally in depth while the monkeys fixated a stationary spot (see METHODS). A total of 35 neurons were examined that responded during vergence-tracking. These include 23 neurons that responded only during vergence-tracking and 12 neurons that responded to both frontal pursuit and vergence-tracking. About one third of these neurons (12/35 = 34%; 7 of the 23 and 5 of the 12) showed visual responses to spot motion in depth. Tested neurons include 10 of the 14 neurons for which blanking of a vergence target was examined, and 2 of the 10 responded to spot motion in depth.

An example is illustrated in Fig. 9, A–C for a vergence-only neuron. This neuron discharged with the peak modulation near divergence velocity (A) and it also exhibited a visual response when the 2nd spot moved toward the monkey during fixation of a stationary target. Modulation was relatively strong at half that seen during vergence-tracking (Fig. 9, A vs. B). Because the monkey fixated the stationary spot well (relatively stable eye position) during this testing, modulation was most likely attributable to visual motion in depth (Fig. 9, B and C). In all neurons we tested, peak vergence eye velocity at 0.5–0.7 Hz ranged from 15 to 20°/s, whereas residual, peak vergence eye velocity induced by 2nd spot motion at the same frequencies during fixation of the 1st stationary spot was <0.2°/s. Because amplitudes of discharge modulation to 2nd spot motion were typically half of the amplitudes during vergence-tracking, the modulation of neuron activity to 2nd spot motion cannot reflect residual vergence eye movements.
To compare sensitivity of visual- and vergence-related responses for individual MST neurons, sensitivity of visual responses to the velocity of 2nd spot is plotted in Fig. 9D against sensitivity (re-vergence target velocity) during vergence-tracking for vergence-only neurons (open circles) and frontal pursuit + vergence neurons (dots). E: plots phases (re-velocity of 2nd spot motion in depth) of visual responses during fixation against phase (re-vergence target velocity) during vergence-tracking for visual responding neurons. Neurons marked with asterisk discharged before vergence eye movements induced by step target motion in depth as summarized in Fig. 11E. Thin lines in D and E indicate slope 1.

To further compare preferred directions for visual responses and vergence-tracking preferred directions of individual neurons, response phases relative to the 2nd spot velocity in depth during fixation were plotted against phase values of vergence target velocity, respectively, at 0.5 Hz. Phase values are widely distributed, but about half (7/12) showed similar phase values (i.e., they were scattered near the dashed line or near 180° in top left, Fig. 9E). This suggests that they had similar preferred directions for vergence-tracking responses and visual target motion responses; for example, neurons that exhibited convergence velocity during vergence-tracking responded when the vergence target moved toward the monkey. Some of the remaining half showed opposite phase values (points near the top straight line, Fig. 9E). Discharge modulation of the neuron shown in Fig. 9, A and B is an example of such opposite responses.

Visual responses of MST pursuit neurons to spot motion in depth: velocity sensitivity

To further examine visual response characteristics of MST pursuit neurons, Fig. 10, A and B, plots visual responses to 2nd spot motion of 10 neurons that were tested at different frequencies. Responses of each neuron are connected by lines. Phase values at 0.5 Hz are widely distributed, but many are found near 0° (peak velocity of 2nd spot motion in depth).
toward the monkeys), and at higher frequencies response phases lagged. Sensitivity (re: 2nd spot velocity) decreased at higher frequencies (Fig. 10B). For these neurons we calculated relative phase difference (re: values at 0.5 Hz) of each neuron and plotted mean (± SD) phase differences in Fig. 10C at frequencies >0.7 Hz. This was to compare visual responses with vergence eye movement related responses at higher frequencies (Fig. 5G). Mean phase lags progressively increased as the target frequency increased. Differences in sensitivity (re: 2nd spot velocity) were calculated similarly relative to the value at 0.5 Hz for each neuron. Sensitivity decreased at higher frequencies (Fig. 10D). These phase/gain characteristics are quite similar to those during vergence-tracking (Figs. 10, C and D vs. 5, G and H).

Figure 10, E and F, plots amplitude of discharge modulation against velocity of 2nd spot moving in depth; discharge modulation of 6 neurons increased as velocity of the 2nd spot increased up to 27°/s (Fig. 10E). Fitting a linear regression for those points for each neuron resulted in regression coefficients ranging from 0.15 to 0.97 spikes/s°/s, suggesting that these neurons carry velocity information of 2nd spot motion in depth. In the remaining neurons (4/10), regression coefficients were flat without a significant correlation between amplitude of modulation and velocity of the 2nd spot (Fig. 10F).

The visual responses of these neurons are specific to spot motion in depth because the majority of responding neurons (9/12, Fig. 9E) did not respond to spot motion and/or pattern motion in frontal plane tested for 8 cardinal directions (see METHODS). This indicates that spot motion in depth responses of our neurons were not attributed to retinal slip in the frontal plane, but rather they were induced by disparity and/or disparity velocity (see DISCUSSION). Only 3 neurons (2 frontal pur-
suit + vergence and one vergence-only) exhibited a visual response to frontal pattern motion. Preferred directions to frontal pattern motion of frontal pursuit + vergence neurons were the same for one neuron and the opposite for the other. The remaining vergence-only neuron exhibited an oblique-preferred direction to frontal pattern motion.

**Latency of discharge modulation of MST pursuit neurons to step target motion in depth**

To determine whether MST pursuit neurons could be involved in initiation of vergence-tracking induced by a small step, we tested latencies of their discharges during vergence-tracking induced by step and/or ramp target motion in depth for a total of 38 MST pursuit neurons (see METHODS). MST contains some pursuit neurons that discharge before vergence eye movements. Representative discharges are illustrated in Fig. 11, A–C. The neuron shown in Fig. 11, A and B discharged before vergence eye movements induced by step (Fig. 11A) and ramp (Fig. 11B) target motion in depth. Latencies between the 2 tracking task conditions were compared for 8 neurons, and they were similar as seen in Fig. 11, A and B.

Because one third of MST neurons tested exhibited visual responses to sinusoidal spot motion in depth (Fig. 9), the initial discharge to step target motion may reflect a visual response. To dissociate visual responses from vergence-tracking responses and to compare discharge modulation during each, we examined discharge modulation of 10 neurons during the 2 task conditions: one during vergence-tracking and the other during fixation of a stationary target while a 2nd spot stepped for the identical distances in depth, thus applying only disparity stimuli without eye movement. An example is illustrated in Fig. 11, C and D for a divergence neuron (Fig. 11C) whose responses are aligned with the onset of vergence target step (Fig. 11D). As illustrated in Fig. 11D, 5 of the 10 neurons tested exhibited a visual response. However, their visual modulation was much weaker in all neurons tested (compare Fig. 11, C vs. D), suggesting that initial discharge modulation induced by step target motion in depth during vergence-tracking cannot be explained by the visual response alone.

Figure 11E summarizes latency distributions of the 38 neurons (22 vergence-only and 16 frontal pursuit + vergence) with respect to the onset of vergence eye movements. Some of both groups of neurons (14/38) discharged before the onset of vergence eye movements. Eleven neurons (11/38 = 29%) discharged more than 20 ms before the onset of vergence eye movements. Neurons that discharged before vergence eye movements are indicated by * in Fig. 9, D and E. These neurons exhibited similar preferred directions for vergence-tracking response and visual target motion response (see above). All other neurons in Fig. 9E discharged after vergence eye movements. Figure 11F plots latencies with respect to vergence target onset for the same neurons shown in Fig. 11E. Latencies are distributed widely, but the earliest latencies were typically 70–100 ms after onset of target motion in depth.

**Recording location**

Figure 12 depicts representative recording tracks in one monkey (K). Neurons that exhibited discharge modulation during tracking of a target were found in the areas shown by thick lines. Most of these tracks passed through the rostral bank of the superior temporal sulcus, consistent with the location of MST (Fig. 12). Vergence-only neurons (open circles) and frontal pursuit + vergence neurons (dots) were intermingled and were found widely in MST. Visual-only neurons were often found near the bottom of each track. The other monkey (H) is still being used for other experiments.

**DISCUSSION**

The present study examined discharge characteristics of MST pursuit neurons during vergence eye movements induced by motion a small spot in depth between 10 and 65 cm from the eyes. Motion of the vergence target was positioned to elicit either symmetric or asymmetric vergence responses so that we could distinguish frontal pursuit from true vergence-related responses. Similarly, during fixation a separate visual stimulus was moved in depth to distinguish disparity-dependent visual responses from vergence responses per se. Our results not only confirm the pioneering studies of Sakata and colleagues (1980, 1983) but also extend them by demonstrating that, in addition to the well-known role of MST in frontal pursuit, some MST neurons have properties appropriate for playing a role in disparity vergence eye movements. Furthermore, the present results indicate that, although MST contains neurons that are modulated during both frontal pursuit and vergence-tracking, the populations of MST and FEF pursuit neurons have markedly different discharge properties.

**Disparity sensitivity in macaque cortex**

Our studies relied on production of vergence eye movements based on small-field stimuli that activated disparity-sensitive neurons. Early quantitative studies of disparity sensitivity in monkey V1 and V2 identified different classes of neurons including ones that were tuned for “near,” “zero,” and “far” disparities (Poggio and Fisher 1977; Poggio et al. 1988). Disparity-sensitive neurons have been reported at many levels of cerebral cortex including V1, V2, V3, V4, MT, MST, lateral intraparietal area (LIP), ventral intraparietal (VIP), and FEF (see reviews by Cumming and DeAngelis 2001; Tsao et al. 2003).

DeAngelis and Newcombe (1999) demonstrated patches of disparity-sensitive neurons in MT. A visual target moving from far to near would activate a population of neurons in a disparity domain, creating a motion in depth signal that could be delivered to MST. Unfortunately, we do not know how disparity domains in MT are connected to neurons in MST. Disparity-velocity–sensitive neurons in MT and MST could provide initial error signals for guiding vergence eye movements in a manner comparable to that observed for frontal pursuit.

**Disparity and vergence sensitivity in MST and other cortical areas**

The pioneering studies of Sakata and colleagues (1980, 1983) discovered neurons in posterior parietal cortex (including MST) that were modulated in relation to the depth of fixation or vergence-tracking per se. For example, they reported that 11 of 70 visual tracking neurons had responses related to depth pursuit using a small spot. This percentage (11/70 = 16%) is similar to the percentage of vergence-only
neurons in the present study (Table 1). Later studies used large-field visual stimuli to identify disparity-sensitive neurons in area MST (Roy et al. 1992). These investigators found neurons in MST that were responsive mostly to either near or far disparity. By including conditions where the depth of fixation was varied, these investigators concluded that neurons in MST signaled depth of an object relative to the fixation plane. They did not include vergence testing of disparity-sensitive neurons. Complimentary studies using large-field disparity stimuli were recently conducted in MST by Kawano...
and colleagues (Takemura et al. 2001). Their studies elicited a short-latency disparity-vergence response (<60 ms) by delivering steps of disparity in a large-field, random-dot stimulus. However, because short-latency disparity-vergence only examined the open-loop part of vergence before any opportunity for visual feedback and volitional vergence effort could affect the response, it is not clear to what extent MST neurons might reside on the sensory or motor side of the vergence response.

In contrast to studies on short-latency reflex vergence, our studies specifically address both open-loop and closed-loop components of disparity-vergence. In our studies, we used small targets that were limited in spatial size (<1°) so they activated only foveal and parafoveal regions of each retina. We found that a significant proportion (>20%) of MST pursuit neurons were modulated during vergence, some in relation to vergence alone (18%) and others with disparity and vergence sensitivity (21%). MST pursuit neurons exhibited phase and sensitivity changes that paralleled changes in actual vergence eye movements (Figs. 4 and 5, G–I). In fact, at least half of our population of vergence-related MST neurons had high correlations between unit firing rate and vergence-velocity (Fig. 6, A and B), suggesting that some MST neurons could play a role in vergence production. Similarly, using steps of disparity, we found that 29% of vergence-related MST neurons had response onsets that lead vergence onset, allowing MST to play a role in vergence initiation and maintenance.

Our use of target blanking during closed-loop vergence indicates that some MST neurons are sensitive to vergence-position and not simply visually sensitive. Similarly, using a fixation condition to control vergence position and testing with a probe stimulus moving in depth, we have been able to show that vergence-sensitive MST neurons are not always driven by visual motion in depth. Production of accurate vergence eye movements requires both disparity-position and disparity-velocity information. We found that about one third of MST pursuit neurons tested were sensitive to disparity-position and disparity-velocity produced by motion in depth of a 2nd foveal/parafoveal target during fixation (Figs. 9 and 10).

The source of vergence-related activity in MST is unknown. It could be generated de novo in MST or be a result of reciprocal connections with FEF (Stanton et al. 1988, 1993, 1995; Tian and Lynch 1996a,b; Tusa and Ungerleider 1988), or perhaps ascending inputs from subcortical areas including deep cerebellar nuclei that could furnish ascending projections (see below). Gamlin and Yoon (2000) performed the first studies demonstrating vergence- and accommodation-sensitive neurons in macaque FEF. They demonstrated that FEF neurons were responsive to disparity steps that elicited vergence eye movements. Their visual stimulus delivery system permitted separate monitoring of vergence and accommodation. In our studies we did not independently measure accommodative state, so it is possible that some MST neurons with vergence-related responses also were sensitive to accommodation. Because MST and FEF have strong reciprocal connectivity (Stanton et al. 1988, 1993, 1995; Tian and Lynch 1996a,b; Tusa and Ungerleider 1988), it may be instructive to compare vergence-related response properties in the 2 areas. Similarities in vergence eye velocity sensitivity were observed in both areas during vergence-tracking (Fig. 6, A and B) (Akao et al. 2005; Gamlin and Yoon 2000). Pursuit neurons in both areas maintained discharge modulation during blanking of a tracking target moving in depth (Figs. 7 and 8) (Fukushima et al. 2002a; Sakata et al. 1983). It has been suggested that MST forms an internal positive feedback circuit for frontal pursuit that provides signals for the maintenance of pursuit (Newsome et al. 1988). It is possible that similar positive feedback circuits exist for vergence-tracking that could involve both FEF and MST, thus enabling those neurons to maintain discharge during target blanking.

However, clear differences were also observed in discharge characteristics between FEF and MST (also Akao et al. 2005). A majority of pursuit neurons in FEF are selectively tuned to pursuit-in-3D with individual neurons being tuned for different vergence trajectories (Fukushima et al. 2002a). Although the present study indicates that MST also contains neurons that discharge for both frontal pursuit and vergence-tracking, the percentage of such neurons in MST is much lower than the percentages of pursuit neurons in FEF (Table 1, 21% = 45/219 vs. 66% = 80/122 for FEF1 or 63% = 106/169 for FEF2, P < 0.0001, χ² test; Akao et al. 2005), suggesting the possibility that pursuit-in-3D signals are generated primarily in FEF. However, frontal pursuit and/or vergence signals are also found in the supplementary eye fields (SEF) (Fukushima et al. 2002a).
MST projections and to have reciprocal connections with FEF (Schlack et al. 2003). SEF is known to receive MST projections and to have reciprocal connections with FEF and project directly to mesencephalic and pontine regions including nucleus reticularis tegmenti pontis (NRTP) (Schall et al. 1993; Shook et al. 1990). The percentage of pursuit neurons in SEF that discharge for both frontal pursuit and vergence-tracking is similar to the percentage in MST (Table 1, 27% = 15/56 vs. 21% = 45/219), and much lower than the percentages in FEF. Although many VIP neurons have disparity sensitivity, it has been reported that VIP neurons discharge after the onset of frontal pursuit with the mean latencies of 160–266 ms (Schlack et al. 2003). This indicates that it is unlikely that VIP neurons are involved in the initiation of pursuit eye movements. These results taken together suggest that synthesis of frontal and depth pursuit signals may be achieved primarily by FEF using MST signals that provide separate frontal and depth pursuit signals.

MST and FEF pursuit neurons exhibited further differences in their responses to spot motion in depth especially in the following 3 points (Akao et al. 2005). First, in contrast to the similar dynamics of MST neuronal responses and vergence eye movements during tracking of a vergence target at frequencies > 0.7 Hz (Fig. 5, G–I), phase shifts (re-target velocity) of the majority of FEF pursuit neurons remained virtually constant up to 1.5 Hz, although there are a group of FEF pursuit neurons that exhibited phase lags similar to eye movement responses. Second, in contrast to the visual responses of some MST pursuit neurons that revealed phase lags as target frequency increased (Fig. 10C), the phase shifts of visual-related responses of the majority of FEF pursuit neurons were also mostly constant (Akao et al. 2005). These differences suggest that responses of MST pursuit neurons are dominated by retinal inputs during vergence-tracking, although their responses can be maintained during blanking, whereas the FEF signals seem to reflect reconstructed target motion in depth, similar to the activity of FEF pursuit neurons during frontal target motion as reported earlier (Fukushima et al. 2002b). It is well known that MST contains all the signal components needed to reconstruct frontal target motion in space including retinal image-slip velocity of a target and eye velocity (e.g., Dicke and Thier 1999). The directional preference of MST pursuit neurons for the eye movement and for frontal visual motion direction is known to be either the same or opposite, and the opposite responses might play a role in creating a motion contrast signal (e.g., Sakata et al. 1983). The present study also showed that some MST pursuit neurons exhibited similar or opposite preferred directions for vergence-tracking responses and visual responses to spot motion in depth. These responses may in part contribute to a similar function for motion contrast in depth.

The third difference is that the percentage of pursuit neurons in FEF that discharged before the onset of vergence eye movements was significantly higher than that in MST in the present study (44/72 = 61% vs. 14/38 = 37%, P < 0.01, $\chi^2$ test; Akao et al. 2005). This difference suggests that FEF plays a larger role in generation of vergence eye movements. Consistent with this interpretation is the similar preferred directions in the majority of FEF pursuit neurons for vergence eye movements and for visual responses to spot motion in depth (Akao et al. 2005). The time compensation observed for delays for visual and/or motor responses to spot motion in depth in FEF pursuit neurons described above may contribute to maintaining target images near the foveae during movement, similar to the activity of FEF pursuit neurons during frontal target motion (Fukushima et al. 2002b). These results suggest a difference in main roles for FEF and MST: an involvement of FEF pursuit neurons primarily in generation of pursuit-in-3D, whereas MST may be involved in earlier stages of processing visual signals for target motion in depth with mostly separate coding for frontal and depth pursuit.

**Pathways for vergence eye movements**

Cortical signals could influence vergence eye movements by several different pathways. First, cortical areas (MST, FEF, SEF) with known vergence-related neurons might project to the pontine centers including the dorsolateral pontine nucleus (DLPN) and NRTP. Some DLPN neurons have been reported to respond during vergence-tracking (Zhang and Gamlin 1997). Similarly, neurons in NRTP have been shown to play a role in vergence eye movements (Gamlin and Clarke 1995). These authors found neurons that responded to changes in vergence with some neurons showing increased response for far viewing and others for near viewing. Microelectrical stimulation near these neurons produced comparable changes in vergence state. DLPN and NRTP selectively target different regions of the cerebellum. DLPN has the strongest projections to the ventral paraflocculus and NRTP to the vermis.

The organization of vergence-related pathways in the cerebellum is only poorly understood (see Leigh and Zee 1999 for review). The ventral paraflocculus projects both to the vestibular nuclei and to the interpositus (IP) and dentate nuclei that could furnish ascending signals (Nagao et al. 1997). Vergence signals are found in the ventral paraflocculus (Miles et al. 1980) and the posterior IP (Zhang and Gamlin 1998). Specifically, Zhang and Gamlin (1998) identified a region of IP that appears to be specialized for supporting far viewing. Similarly, electrical stimulation in IP produces divergence. Vergence signals are also found in the fastigial nuclei (Zhang and Gamlin 1996). Lesions in the dorsal vermis in monkeys induce a convergence bias during monocular fixation in the absence of disparity cues (Takagi et al. 2003), and chemical inactivation of the caudal fastigial nucleus is reported to impair vergence eye movements (Gamlin and Zhang 1996). These observations suggest an involvement of the vermis in the control of vergence eye movements. It should be noticed that all these cerebellar areas contain frontal pursuit neurons, suggesting a possibility that they may carry pursuit-in-3D signals, although this possibility needs to be tested.

To drive ocular motoneurons, pursuit-in-3D signals must be converted into commands to control the conjugate and disconjugate motions of the 2 eyes, and further into monocular commands appropriate to drive the right and left eyes. Signals appropriate for such commands are found in the brain stem (e.g., Mays et al. 1986; Zhou and King 1998; see review by Leigh and Zee 1999).

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