Direction and speed tuning to visual motion in cortical areas MT and MSTd during smooth pursuit eye movements

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Inaba N, Miura K, Kawano K. Direction and speed tuning to visual motion in cortical areas MT and MSTd during smooth pursuit eye movements. J Neurophysiol 105: 1531–1545, 2011. First published January 27, 2011; doi:10.1152/jn.00511.2010.—When tracking a moving target in the natural world with pursuit eye movement, our visual system must compensate for the self-induced retinal slip of the visual features in the background to enable us to perceive their actual motion. We previously reported that the speed of the background stimulus in space is represented by dorsal medial superior temporal (MSTd) neurons in the monkey cortex, which compensate for retinal image motion resulting from eye movements when the direction of the pursuit and background motion are parallel to the preferred direction of each neuron. To further characterize the compensation observed in the MSTd responses to the background motion, we recorded single unit activities in cortical areas middle temporal (MT) and MSTd, and we selected neurons responsive to a large-field visual stimulus. We studied their responses to the large-field stimulus in the background while monkeys pursued a moving target and while fixated a stationary target. We investigated whether compensation for retinal image motion of the background depended on the speed of pursuit. We also asked whether the directional selectivity of each neuron in relation to the external world remained the same even during pursuit and whether compensation for retinal image motion occurred irrespective of the direction of the pursuit. We found that the majority of the MSTd neurons responded to the visual motion in space by compensating for the image motion on the retina resulting from the pursuit regardless of pursuit speed and direction, whereas most of the MT neurons responded in relation to the genuine retinal image motion.

In the natural world, objects in the visual scene move against a rich background of visual features. Even when our eyes are in motion, we perceive a stable world in spite of the motion of the images on the retina caused by the eye movements. The middle temporal (MT) and the dorsal part of the medial superior temporal (MSTd) areas of macaque monkeys are reported to be rich in motion-sensitive neurons and closely linked to the perception of visual motion (Britten et al. 1992; Celebrini and Newsome 1994; Duffy and Wurtz 1991; Graziano et al. 1994; Maunsell and Van Essen 1983; Newsome et al. 1988; Saito et al. 1986; Sakata et al. 1983; Sakata et al. 1985; Williams et al. 2003). We (Inaba and Kawano 2010; Inaba et al. 2007) previously reported neuronal correlates in area MSTd that reconstruct a stable visual world, in spite of the motion of images on the retina resulting from eye movements. We studied the responses of MSTd and MT neurons to a visual background that moved briefly at various speeds during smooth pursuit and stationary fixation and found that most MSTd neurons were more sensitive to the actual motion of the background in space than to its motion on the retina, whereas most MT neurons showed the reverse tendency. Thus MSTd neurons were much more likely than MT neurons to distinguish between external and self-generated motion of the background during pursuit eye movements. These findings suggested that MSTd neurons respond to visual motion in the external world while compensating for retinal image motion by utilizing information about eye movements. In fact, it has been reported that some MST neurons encode extra-retinal information related to the movements of the eyes (Ilg and Thier 2003; Newsome et al. 1988; Sakata et al. 1983).

In our previous studies (Inaba and Kawano 2010; Inaba et al. 2007), the pursuit target always moved at 20°/s in the direction parallel to the preferred direction of each neuron; therefore, it was not possible to investigate the detailed characteristics of the compensation. To better understand the compensation observed in MSTd neurons during smooth pursuit, we investigated the effects of pursuit eye movements on the neuronal responses to a briefly presented moving visual background. In the present study, we focused on two questions: 1) regarding tracking speed, we asked whether retinal image motion is compensated for irrespective of the speed of the pursuit eye movements; and 2) regarding the direction of tracking, we asked whether retinal image motion is compensated for irrespective of the direction of the pursuit eye movements.

To address the above issues, we carried out the following experiments on MT/MSTd neurons responsive to large-field visual motion. In the first set of the experiments, monkeys either fixated on a stationary target or pursued a target moving at one of three different speeds in the neuron’s preferred or antipreferred direction, while the background image moved in the direction parallel to the pursuit direction at various speeds. We found that the activity of the majority of MSTd neurons depended on the stimulus speed on the screen irrespective of pursuit eye movements, whereas most of the MT neurons depended on the speed on the retina. In the second set of experiments, the monkeys either fixated on a stationary target or pursued a target moving in one of four directions (preferred, antipreferred, and perpendicular to the preferred direction), while the background image moved in one of eight directions (horizontal, vertical, and diagonal). We found similar direction-tuning profiles of most MT neurons during pursuit and fixation when the background motions on the retina were identical, whereas the direction-tuning profiles of a larger population of the MSTd neurons during pursuit were similar to that during fixation when the background motions on the screen were identical. The results show that area MSTd in-
volves neurons that are sensitive to the absolute motion of the background in space, regardless of pursuit speed and direction. These results suggest that the MT neurons code for the direction and speed of the retinal image motion, whereas the majority of the MSTd neurons compensate, at least in part, for the self-induced retinal image motion regardless of the direction and speed of pursuit and code for the direction and speed of the image motion in space.

MATERIALS AND METHODS

The procedures used in the present study were similar to those previously described (Inaba and Kawano 2010; Inaba et al. 2007; Kawano et al. 1994). All experimental protocols were approved by the Animal Care and Use Committee of Kyoto University.

Animal preparation. Two male rhesus monkeys (monkeys S and K; Macaca mulatta) weighing 7 and 9 kg were used in this study; they were also used in our previous studies (Inaba and Kawano 2010; Inaba et al. 2007). Before surgery, all animals were trained to track a small target spot, and anatomical images were obtained using MRI scans (Signa Horizon). Surgeries were performed while the animals were under general anesthesia with pentobarbital sodium. Under sterile conditions, scleral search coils for measuring eye position were chronically implanted (Judge et al. 1980), and a head holder and recording chambers were embedded in a dental acrylic cap that covered the top of the skull. The recording chambers were stereotaxically placed to allow for a dorsal approach to the parietal cortex in the vertical orientation (stereotaxic coordinates: AP: –2 to –4 mm; ML: ± 16 to 18 mm).

Recording technique and histology. Initial mapping penetrations of the cortex in the dorsal part of the superior temporal sulcus (STS) were made with hand-made glass-coated tungsten electrodes; MRI scans were used to confirm the location of the STS. Within the STS, neurons were identified as either MSTd or MT neurons according to previously published reports of their location relative to the STS and their receptive field characteristics (Gattass and Gross 1981; Komatsu and Wurtz 1988a). Single units were recorded with tungsten microelectrodes (Microprobe, FHC, or Nano Biosensors). Vertical microelectrode penetrations were made via transdural guide tubes inserted under general anesthesia with pentobarbital sodium. Under sterile conditions, scleral search coils for measuring eye position were chronically implanted (Judge et al. 1980), and a head holder and recording chambers were embedded in a dental acrylic cap that covered the top of the skull. The recording chambers were stereotaxically placed to allow for a dorsal approach to the parietal cortex in the vertical orientation (stereotaxic coordinates: AP: –2 to –4 mm; ML: ± 16 to 18 mm).

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Behavioral paradigms and visual stimuli. The animal was seated in a primate chair in a dark room with its head fixed by a head holder. The animal faced a translucent tangent screen subtending 80° × 80° at the viewing distance of 40 cm. Since our principle interest was to further characterize the properties of the neurons that discharge in relation to background motion, we searched neurons by presenting a moving large-field random-dot pattern and selected neurons responsive to it. After isolating a single unit, we observed its responses to motion of the large-field random-dot pattern (80° × 80°) while the animal fixated a stationary target at the center of the screen. To determine the neuron’s preferred direction of motion for the random-dot pattern, the stimulus was moved at a constant velocity (20–80°/s) in eight directions spaced at 45° intervals (horizontal, vertical, and diagonal). If the neuron responded to motion of the large-field random-dot pattern with directional preference, we performed the experiments on the neuron.

After the preferred direction was determined for each neuron, the monkey was required either to pursue a target spot moving at a constant speed or to fixate on a stationary target spot. The target was a red spot that was back-projected onto the screen by a light-emitting diode projector and moved by a set of mirror-galvanometers. In the present study, we used a random-dot pattern (80° × 80°) as the large background image (see Fig. 1). The random-dot pattern consisted of white dots (1° in diameter; luminance = 5.0 cd/m²) on the black background (luminance = 0.06 cd/m²). The background image was back-projected onto the screen by a slide projector and moved by another set of mirror-galvanometers. The galvanometers controlling image motion could be moved independently of the pursuit target.

We observed the neuronal responses in areas MSTd and MT to motion of the background image while the animal fixated the stationary target spot or pursued the moving target spot. At the start of each trial, the stationary target appeared on the dark screen (see Fig. 1). The animal had to position and keep its eyes on the target, which either remained stationary (fixation paradigm; Fig. 1A, left) or moved at a constant speed (pursuit paradigm; Fig. 1A, right, and Fig. 1B). For the pursuit paradigm, step-ramp target motions were used (Rashbass 1961): after the animal positioned its eyes on the target, located in an eccentric position, the target made a 0.5–2° step away from the center of the screen and then traversed back to the center via a ramp motion. The direction and size of the step were selected according to the speed of the target ramp to minimize the likelihood of catch-up saccades. When the target reached the center 500 ms after the onset of the target ramp motion, the background image was suddenly turned on for 200 ms and either remained stationary or moved at a constant speed. An electromechanical shutter in the light path was used to turn the background stimulus on and off. The total duration of each target ramp motion was 1,000 ms. The target spot was then turned off, indicating the end of the trial. At the end of the trial, the animal received a fluid drop as a reward for keeping its eyes within 2.5° of the target spot throughout the trial.

In this study, we present the results of two sets of experiments. In the first set of the studies (pursuit-speed experiment), we observed neuronal responses to visual motion of the random-dot pattern (–40 to +60°/s) while the animal fixated on a stationary target or pursued the moving target spot. Positive/negative values of speed indicate motion in the preferred/antipreferred direction. In this situation, the monkey fixated on or pursued the target moving at 5, 10, or 20°/s in the preferred or antipreferred direction when the visual image was either stationary or moved in the same or opposite direction as the pursuit target (Fig. 1A). The background image contained a trajectory (1°-wide black band) for the pursuit target to facilitate the monkey’s tracking performance. We rotated the background image with respect to the direction of the pursuit target trajectory path (see Inaba and Kawano 2010).

In the second set of the studies (pursuit-direction experiment), we recorded neuronal responses in areas MT and MSTd to the motion of random-dot pattern to test whether the direction tuning relative to the external world is preserved during fixation and pursuit. The random-dot pattern was moved in eight directions, separated by 45°, from the center of the background image at 20°/s on the screen or on the retina, while the monkey performed pursuit or fixation (Fig. 1B). The pursuit target was moved at 20°/s in four directions (preferred direction, preferred direction + 90°, antipreferred direction, and antipreferred direction + 90°). In the pursuit-direction experiment, the background image did not contain a black trajectory for the target spot.

For measuring and mapping the visual receptive field, we displayed a target (0.3°) and a random-dot pattern (1° × 1° to 10° × 10°), created by MATLAB PsychoToolbox (Pelli 1997), on the screen using a mirrored reflection digital light processing projector (WT6000, NEC) in place of the slide/light-emitting diode projectors and the galvanometer system. Visual receptive-field mapping was conducted while the animal looked at the central fixation target as the random-dot pattern moved at a constant velocity (20–80°/s) in the preferred direction.
Data collection and analysis. Stimulus presentation and data collection were controlled by a personal computer using the REX system (Hays et al. 1982). Eye movements were measured with the electromagnetic search-coil technique (Fuchs and Robinson 1966). Voltage signals encoding the horizontal and vertical components of the eye position were low-pass filtered with RC circuitry (170 Hz, 3 dB) and digitized to a resolution of 12 bits at a 1-kHz sampling rate. All data were stored and transferred to a personal computer for analysis using an interactive computer program based on MATLAB (Mathworks, Natick, MA). Eye-position data were smoothed with a digital low-pass filter (33 points, 30 Hz, 3 dB), and eye velocity was obtained by two-point backward difference of the eye-position data to detect saccades using velocity criteria (> target velocity ± 25°/s). A time-amplitude window discriminator was used to identify spikes with a time resolution of 1 ms. Spike-density histograms were calculated by convolving the spike trains with a Gaussian curve (σ = 10 ms) (Richmond et al. 1987). Latencies of neuronal responses were estimated by using the spike density profile to determine the response window. Briefly, we first determined the mean spike density and SD over the 200-ms time period before the onset of background motion (baseline activity) and then estimated latency by finding the earliest time at which the spike density profile exceeded the baseline activity by 3 SDs. The latency estimates were obtained from the neuronal responses to the background motions in the neuron’s preferred direction both on the screen and on the retina. The range of latency estimates (25–75% quantiles) was 37–60 ms (median: 45 ms) for the MT neurons and 53–83 ms (median: 65 ms) for the MSTd neurons. Because our primary target was the neurons in area MSTd, neuronal responses to the motion of the background stimulus were measured as the average spike density from 50 to 250 ms after the onset of the background stimulus presentation (i.e., from 550 to 750 ms after the onset of the target ramp motion). Note that shifting the temporal interval by 10 ms earlier caused less change to the results. Thus the 200-ms interval was sufficiently long to obtain robust measurements for the neuronal responses to background motion. For all analyses, at least three repetitions of each stimulus condition (7.9 ± 3.5 trials; means ± SD) were required for each neuron. We exposed the animal to stimulus conditions in a pseudorandomized order. The speed of the background stimulus on the retina was computed by subtracting the mean eye speed from the background speed during the presentation of
the background image (i.e., over the period from 500 to 700 ms after the onset of the pursuit target motion).

In the pursuit-speed experiment, we first examined the “motion” to which a neuron is sensitive. A neuron could respond to either “motion on the screen” or “motion on the retina.” Otherwise, a neuron could show an intermediate characteristic between these two extremes. To determine the response characteristic for each neuron, we examined the neuron’s performance for discriminating the direction of the background motion. If a neuron is more sensitive to the “motion on the screen,” then the neuron should be able to discriminate the direction of stimulus motion on the screen with better performance, compared with motion on the retina. The MT/MSTd neurons that we studied in this study responded to background motion with direction selectivity. Therefore, in the presence of two classes of motions (motion in the neuron’s preferred direction and motion in the antipreferred direction), individual neurons were able to discriminate two classes of motions by their responses. In other words, they were able to classify stimulus motion into these two classes by their firing rate; i.e., a larger firing rate suggests motion in the preferred direction. Thus the neuron’s firing rate obtained from each trial can be regarded as a numeric value representing the degree to which an instance is a member of the “motion in the preferred direction.” The receiver operating characteristics (ROC) analysis applied to the neural responses allows us to measure the performance of this classification by each neuron. First, two ROC curves were obtained: one as a classifier for motion on the screen and another as a classifier for motion on the retina. Then, the area under the ROC curve (AUC), a common measure for classifier performance (Fawcett 2006), was calculated for each ROC curve to quantify the neuron’s performance. Comparing the performance as a classifier for motion on the screen with that for motion on the retina can thus clarify the motion to which the neuron is sensitive. The neuronal responses obtained from individual trials when the background motion was 20°/s or less during smooth pursuit at 5, 10, and 20°/s in both directions were used in this analysis.

In the pursuit-speed experiment, to quantify the relationship between the neuronal responses and the speed of the random-dot pattern, we calculated the response shifts of speed tuning curves of each neuron using “double-sigmoid function analysis” (Inaba and Kawano 2010). We fitted the function to calculate the speed tuning curves of each neuron as described by the following formula:

\[
R(s) = a_1 + (a_2 - a_1) \frac{1}{1 + \exp^{-b_1(s - \omega)}} - \frac{1}{1 + \exp^{-b_2(s - \omega)}} \]  

(1)

Parameters \(a_1\) and \(a_2\) correspond to the baseline and peak firing rate of the neuron, respectively, in response to the background motion. The speed of the background image motion is denoted by \(s\). The slopes of the rising and falling gradients of the speed tuning curves correspond to \(b_1\) and \(b_2\), respectively. Parameter \(\omega\) determines the shift in the speed tuning response. The fitting was performed by using self-written scripts in addition to available packages in MATLAB (function “finnsearch”).

In the pursuit-direction experiment, we fitted a von Mises function involving three free-parameters (\(a\), \(b\), and \(\theta_0\)), modified from well-known von Mises distribution (circular normal distribution),

\[
y(\theta) = a \cdot e^{k \cos(\theta - \theta_0)}, 
\]

(2)
to characterize the neuron’s direction-tuning profile for each of the behavioral conditions. This function is a periodic and the optimal direction is represented by \(\theta_0\). Amplitude of response modulation (\(A\)), defined by the difference between the maximum and minimum values of the functions, is given by:

\[
A = a(e^{b} - e^{-b}). 
\]

(3)
The width at half-maximum (tuning width, \(\sigma\)) is given by:

\[
\sigma = \text{ArcCos}\left(\frac{\log((e^{b} + e^{-b})/2)}{b}\right) \]  

(4)

which gives a measure of sharpness of the tuning. The values of \(\theta_0\), \(A\), and \(\sigma\) were used to quantify the similarity between the direction-tuning profiles during fixation and during pursuit.

To distinguish between the two types of direction-dependence properties (motion on the screen or on the retina), we adopted partial correlation analyses that had been used in previous studies (Gizzi et al. 1990; Movshon and Newsome 1996). We computed the partial correlations for the conditions of the same retinal image motion (\(R_{ret}\)) and for the conditions of the same background motion on the screen (\(R_{scr}\)) by the following formula:

\[
R_{ret} = \frac{r_{ret} - r_{scr}r_{ret,scr}}{\sqrt{(1 - r_{ret}^2)(1 - r_{ret,scr}^2)}} 
\]

(5)

\[
R_{scr} = \frac{r_{scr} - r_{ret}r_{ret,scr}}{\sqrt{(1 - r_{scr}^2)(1 - r_{ret,scr}^2)}} 
\]

(6)

where \(r_{ret}\) and \(r_{scr}\) represent the correlations between the direction-selective responses under the fixation and pursuit conditions when the background motion is the same on the retina and on the screen, respectively, and \(r_{ret,scr}\) is the correlation between the direction-selective responses during pursuit under the condition of the same background motion on the retina and those under the condition of the same background motion on the screen.

RESULTS

We recorded neuronal activity in the STS in four hemispheres of two awake, behaving monkeys, and we examined the activities of neurons that discharged in response to motion of a large-field visual image. All of these neurons responded in a directionally selective manner to the motion; their average firing rates in the preferred directions were greater than or equal to 1.5 times of those in the antipreferred directions. We identified 135 direction-selective neurons in the MSTd area (43 from monkey S and 92 from monkey K) and 88 in the MT area (38 from monkey S and 50 from monkey K) physiologically, based on the receptive field properties of the recorded neurons and their locations relative to the STS (Gattass and Gross 1981; Komatsu and Wurtz 1988a).

Pursuit-speed experiment. In our previous studies, we reported that the majority of the MSTd neurons responded to the background motion on the screen, whereas most MT neurons responded to motion on the retina (Inaba et al. 2007). To confirm these results from a different point of view, we applied the ROC analysis in the present study, to determine the motion to which a neuron is more sensitive, i.e., “motion on the screen” or “motion on the retina” (see MATERIALS AND METHODS for details).

Figure 2, A and B, shows neural responses of an MSTd neuron obtained from individual trials plotted as a function of background speed on the screen (A) and as a function of background speed on the retina (B). Although it is not necessarily clear whether the responses were determined by motion on the screen or on the retina because of trial-by-trial variability of neural responses, the neuron’s direction selectivity appears to be clearer when the responses are plotted against background speed on the screen than on the retina. Thus this neuron may be able to classify stimulus motion “on the screen” better than “on the retina”, into “motion in the preferred direction” or “motion in the antipreferred direction” based on

\[
\sigma = \text{ArcCos}\left(\frac{\log((e^{b} + e^{-b})/2)}{b}\right) \]  

(4)
its firing rate. Figure 2C shows the ROC curves as classifiers for motion on the screen (red) and for motion on the retina (blue). The ROC curve associated with motion on the screen (red line) lies in a more northwest region compared with the ROC curve associated with motion on the retina (blue line); AUC was 0.99 as a classifier for motion on the screen and 0.78 as a classifier for motion on the retina. These results indicate that this neuron has better performance as a classifier for motion on the screen and is thus more sensitive to motion on the screen.

Figure 2, D and E, shows the neural responses of an MT neuron. In contrast to the MSTd neuron shown in Fig. 2, A–C, the data plots show clear direction selectivity for background motion on the retina than on the screen, which is confirmed by the ROC curves (Fig. 2F). The ROC curve as a classifier for motion on the retina (blue line) lies in a more northwest region than that for motion on the screen (red line); AUC was 0.99 as a classifier for motion on the retina and 0.87 as a classifier for motion on the screen. These results indicate that the MT neuron has a better performance as a classifier for motion on the retina and is thus more sensitive to motion on the retina.

The ROC analysis was conducted for 66 MSTd neurons (13 from monkey S and 53 from monkey K) and 38 MT neurons (12 from monkey S and 26 from monkey K). Figure 3 compares the performance as a classifier for motion on the screen with that for motion on the retina. This scatter plot demonstrates a clear difference between neurons in the MT area (filled circles) and those in the MSTd area (open circles). The data points for most MT neurons lie above the unity line, indicating that these neurons worked better as classifiers for motion on the retina. On the other hand, the majority of the MSTd neurons worked better as classifiers for motion on the screen, although the data points were distributed rather widely. These findings are consistent with our previous observations that the majority of the MSTd neurons that responded to large-field visual motion was more sensitive to motion of the background motion on the screen.
screen, while most neurons in the MT area were more sensitive to motion on the retina (Inaba and Kawano 2010, Inaba et al. 2007).

We then examined whether the neurons in both areas were able to shift their speed tuning curves to compensate for the retinal image motion brought about by changes in pursuit speeds (5, 10, and 20°/s) in both the preferred and antipreferred directions. Figure 4A shows a mean response of the MSTd neuron shown in Fig. 2, A–C, to brief motion of a background stimulus moving in its preferred direction (leftward) at 20°/s on the screen while the animal fixated on a stationary target. The moving background stimulus was visible only for 200 ms (from 500 to 700 ms; shaded area). The neuron increased its firing rate with a latency of ~50 ms in response to the background motion. The same background motion (on the screen) resulted in a similar pattern of neuronal activity even when the monkey pursued a target moving in the preferred direction at 20°/s (Fig. 4B). Notice that the motion of the background stimulus on the retina was almost zero under this condition (see Fig. 4B, bottom). The responses to the 20°/s background motion on the screen when the monkey pursued the target at two different speeds (10 and 5°/s) in the preferred direction are shown in Fig. 4, C and D, respectively. The magnitude of the neuron’s response was very similar across all four tracking conditions (fixation and pursuits at three different speeds), while the motion of the background image on the retina was different (Fig. 4, bottom).

Figure 5A shows the dependence of the mean firing rate on the background speed in each of the seven tracking conditions (fixation and pursuits at 5, 10, and 20°/s in the preferred and antipreferred directions) for the same neuron. The mean firing rate of the neuron over the time interval from 50 to 250 ms after the background stimulus onset was plotted as a function of the speed of the background motion on the screen when the monkey fixated on the stationary spot or pursued the target moving at six different speeds. The neuronal responses under the seven tracking conditions were very similar based on the screen coordinates; the neuron responded more vigorously as the stimulus speed increased in the preferred direction, while the responses were almost unchanged as the stimulus speed increased in the antipreferred direction.

To examine the amount of compensation for retinal image motion during pursuit, the shifts of the speed tuning curves for the six pursuit conditions relative to the fixation condition were...
obtained by using double-sigmoid function analysis (see MATERIALS AND METHODS). The relative shifts of this MSTd neuron for the six pursuit conditions with the target moving at 5°/s (red) in the preferred direction and at 5°/s (green) in the antipreferred direction, or remained stationary at the center of the screen (black). Neuronal responses to the background motion at various speeds on the screen (A and C) and on the retina (B and D), respectively. Note that in B and D, some data points were outside the display range. Positive and negative values indicate the speeds of the visual motion of background stimulus in the preferred and antipreferred directions, respectively.

Figure 5B shows the same data in Fig. 5A but now plotted as a function of the speed of the background on the retina. Pursuit eye movements in the preferred or antipreferred direction caused the speed tuning curve to shift along the axis representing the stimulus speed on the retina. The relative shifts for the six pursuit conditions with the target moving at −20, −10, −5, 5, 10, and 20°/s were 6.2, 4.3, 3.5, 0.09, 0.92, and 4.5°/s, respectively.

Figure 5B shows the same data in Fig. 5A but now plotted as a function of the speed of the background on the retina. Pursuit eye movements in the preferred or antipreferred direction caused the speed tuning curve to shift along the axis representing the stimulus speed on the retina. The relative shifts for the six pursuit conditions with the target moving at −20, −10, −5, 5, 10, and 20°/s were 6.2, 4.3, 3.5, 0.09, 0.92, and 4.5°/s, respectively (Fig. 5B). The responses of this MSTd neuron were closely correlated with the background motion on the screen (Fig. 5A), rather than the motion on the retina (Fig. 5B).

The same analysis revealed that the responsiveness of the MT neuron shown in Fig. 2, D–F, to the image motions defined by the screen and retinal coordinates was opposite to that of the MSTd neuron. The responses of the MT neuron were more dependent on the retinal speed of the background stimulus. This is evident from plots showing the dependence of the mean firing rate on the speed of the background on the screen (Fig. 5C) and on the speed of the background’s retinal image (Fig. 5D) in each of the seven tracking conditions for the MT neuron. The differences between the seven plots in Fig. 5D are obviously much smaller than between those in Fig. 5C, which is the inverse of the situation described for the MSTd neuron in Fig. 5, A and B. The relative shifts in the speed tuning curves of the MT neuron shown in Fig. 5, C and D, were −19.8, −9.8, −6.9, 4.6, 8.5, and 17.9°/s based on the screen coordinates, whereas based on the retinal coordinates, they were −0.03, 0.6, −1.5, 0.02, −0.8, and −1.3°/s, respectively. Note that as shown in Fig. 5, the speed tuning of most MSTd neurons showed a sigmoidal dependence on the speed of the background motion, whereas most MT neurons showed band-pass properties, as pointed out in our previous report (Inaba and Kawano 2010).

The same analysis conducted for 66 MSTd neurons and 38 MT neurons revealed a systematic difference between the responses of the MSTd and MT neurons to the background motion defined by the screen and retinal coordinates. The results are summarized as frequency histograms for the MSTd neurons (Fig. 6, A and B) and MT neurons (Fig. 6, C and D). Thus the majority of MSTd neurons responded in relation to the motion on the screen rather than on the retina, whereas most MT neurons were sensitive to retinal image motion rather than the motion on the screen.

As shown in Fig. 6, E and F, the relative shifts in the speed tuning curves differed depending on the preferred or antipreferred direction of the pursuit. To quantify the compensation as a function of pursuit speed, we computed regression lines separately for the data during pursuit in the preferred and
antipreferred directions. If the rate of compensation was 100% of that required for accurate encoding of background motion on the screen, the slope and y-intercept of the regression line based on the screen coordinates (Fig. 6E) should be zero, whereas those based on the retinal coordinates (Fig. 6F) should be −1 and zero, respectively (gray solid lines). Alternatively, if there was no compensation (0%), the slope and y-intercept based on the screen coordinates should be +1 and zero (gray broken lines), respectively, whereas those based on the retinal coordinates should be zero. The slopes of the regression lines for the MSTd neurons based on the screen coordinates during pursuit in the antipreferred and preferred directions (\(R^2 = 0.92\) and 0.98) were 0.1 and 0.4, respectively (Fig. 6E, solid lines), whereas based on the retinal coordinates (\(R^2 = 0.99\) and 0.97) they were −0.9 and −0.5, respectively (Fig. 6F, solid lines). The y-intercepts during pursuit in the antipreferred and preferred directions based on the screen coordinates were 4.3 and 1.2, respectively, whereas those based on the retinal coordinates were 3.9 and 0.4, respectively. Note that the 95% confident intervals of all the y-intercepts involved zero (i.e., not significant). These results suggest that the rate of compensation during pursuit in the preferred direction was ~50–60% of that required for accurate encoding of the background motion on the screen, while the compensation during pursuit in the antipreferred direction was relatively accurate. This anisotropic dependence on pursuit direction was not explicit in the relative response shifts of the MT neurons. The slopes of the regression lines for the MT neurons during pursuit in the antipreferred and preferred directions based on the screen coordinates (\(R^2 = 0.99\) and 0.99) were 0.8 and 1.0, respectively (Fig. 6E, dashed lines), whereas they (\(R^2 = 0.90\) and 0.98) were −0.1 and 0.02, respectively, based on retinal coordinates (Fig. 6F, dashed lines). The y-intercepts during pursuit in the antipreferred and preferred directions based on the screen coordinates were 0.4 and 0.1, respectively, whereas they were 0.9 and 0.1, respectively, based on retinal coordinates. Note that the 95% confident intervals of these y-intercepts all involved zero (i.e., not significant).

Pursuit-direction experiment. The results from previous studies (Chukoskie and Movshon 2009; Inaba and Kawano 2010; Inaba et al. 2007) and those described above were restricted to situations in which the target and background image were moved along the axis of the preferred direction of each neuron. The second set of experiments was designed to clarify whether the compensation is achieved even when the directions of pursuit and background are out of the axis.

For the example shown in Fig. 7, we selected the direction and speed of the background motion on the screen to be the same (20°/s) during fixation (Fig. 7A, left, black arrows) and during pursuit in the preferred direction (left, red arrows). In this case, the direction and speed of the retinal image motion during pursuit (right, red arrows) were different from those during fixation (black arrows). Figure 7B illustrates the direction-tuning profiles of the responses of the MSTd neuron, which is the same neuron shown in Fig. 5. A and B, to laminar motion of the background image at 20°/s on the screen while the animal was fixating on a target that was either stationary (black line) or moving leftward at 20°/s (red line). This neuron showed similar dependence on stimulus motion in the eight different directions on the screen, despite the fact that the motion of the background images on the retina was clearly different (Fig. 7A, right).

Similar results were obtained from the same neuron during pursuits in the three other directions, i.e., downward, rightward, and upward (see Fig. 8A, shown by cyan, blue, and green lines, respectively). To quantify the similarity between the direction-tuning profile during fixation and during pursuit, the von Mises function was fitted to the data of the direction-tuning profile for each of the behavioral conditions (see MATERIALS AND METHODS for details). The differences in the optimal direction between fixation and pursuit conditions, \(\theta_{\text{diff}} = \theta_{\text{pursuit}} - \theta_{\text{fixation}}\), were −8.87, −3.16, −0.12, and −1.13° for leftward (red), downward (cyan), rightward (blue), and upward pursuit (green), respectively, while normalized differences in amplitude, defined as \(A_{\text{diff}} = (A_{\text{pursuit}} - A_{\text{fixation}})/A_{\text{fixation}}\), were −0.17, −0.21, −0.05, and −0.11, respectively, and normalized differences in tuning width, \(\sigma_{\text{diff}} = (\sigma_{\text{pursuit}} - \sigma_{\text{fixation}})/\sigma_{\text{fixation}}\), were 0.06, 0.05, −0.03, and −0.01, respectively.

In an additional experiment, we arranged for the retinal motion of the background stimulus to be roughly the same (8 directions of laminar motion at 20°/s on the retina) during fixation and pursuits at 20°/s in four different directions. The direction-tuning profiles for the visual motion on the retina are shown in Fig. 8B for the same neuron as in Fig. 8A. Note that the same direction-tuning curve during fixation is shown in Fig. 8. A and B (black line). It is clear that the activation associated with the brief background motion showed substantial differences during fixation and pursuits, in particular, in response amplitude and tuning width. The normalized differences in amplitude between fixation and pursuits (\(A_{\text{diff}}\)) were −0.18, −0.41, −0.71, and −0.19 for leftward (red), downward (cyan), rightward (blue), and upward pursuit (green), respectively. The normalized difference in tuning width (\(\sigma_{\text{diff}}\)) were 0.17, −0.03, −0.06, and −0.09, respectively. During the leftward pursuit (red), the background stimuli (moving at 20°/s on the retina) all moved on the screen with directions of <90° deviate from the neuron’s preferred direction. On the other hand, interestingly, during the rightward pursuit (blue), the background stimuli moved on the screen with directions of >90° away from the neurons’ preferred direction (cf. Fig. 7A, right).

To further examine the similarity between the fixation and pursuit conditions, we analyzed the correlation between the direction-tuning curves for background motion under the fixation and pursuit conditions. Partial correlations were adopted to remove the effects of correlations between conditions involving the same motion on the screen and on the retina. For the neuron shown in Figs. 7 and 8, A and B, the partial correlation coefficients for the condition of the same motion on the screen (\(R_{\text{scr}}\)), and for the condition of the same retinal motion (\(R_{\text{ret}}\)) were 0.85 and −0.37, respectively, for the leftward pursuit (red lines in Fig. 8, A and B, respectively). For downward, rightward, and upward pursuit, the values of \(R_{\text{scr}}\) were 0.75, 0.91, and 0.99, respectively, and the values of \(R_{\text{ret}}\) were 0.75, 0.33, and 0.84, respectively. Thus the dependence on stimulus direction of the MSTd neuron correlated better to motion on the screen than on the retina.

In contrast to the MSTd responses, the responses of MT neurons were more dependent on the retinal motion of the background image. Figure 8C shows the direction-tuning profiles for the visual stimuli that moved at 20°/s on the screen of
Fig. 6. Frequency histograms of the relative response shifts of MSTd and MT neurons. A and B: distributions of the relative response shifts of neurons in area MSTd for pursuits on the basis of the stimulus speed on the screen (A) and on the retina (B), respectively. C and D: distributions of the relative response shifts of neurons in area MT for pursuits on the basis of the stimulus speed on the screen (C) and on the retina (D), respectively. Pursuit target was moved at 5°/s (orange), 10°/s (magenta), and 20°/s (red) in the preferred direction, or at 5°/s (cyan), 10°/s (blue), and 20°/s (green) in the antipreferred direction. E and F: relative response shifts of neurons in areas MSTd (filled circles and solid lines) and MT (open circles and dashed lines) plotted against the pursuit speeds on the basis of the stimulus speed on the screen (E) and on the retina (F), respectively. Gray solid and broken lines represent no compensation and 100% compensation, respectively.
an MT neuron. Substantial differences during fixation and pursuits were found. On the other hand, the direction-tuning profiles for the visual stimuli moved at 20°/s on the retina were similar independent of the behavioral conditions (Fig. 8D). The partial correlation coefficients were also calculated. For rightward, upward, leftward, and downward pursuits the values of $R_{scr}$ were 0.63, 0.44, 0.50, and 0.61 respectively, and the values of $R_{ret}$ were 0.98, 0.98, 0.99, and 0.99, respectively. It is clear that the directional selectivity of the MT neuron showed much stronger dependence on the retinal image motion.

Figure 9 summarizes the influences of pursuit on the direction-tuning profiles characterized by the von Mises functions (Eq. 2). In the majority of the MSTd neurons, the direction-tuning profiles for visual motion on the screen during each of pursuit conditions agreed well with that during fixation (Fig. 9, A, C, and E), although the response amplitude (A) during pursuit in the preferred direction tended to be slightly smaller than that during fixation (red line in Fig. 9C). On the other hand, the pursuit eye movements had more impact on the direction-tuning profiles for visual motion on the retina (Fig. 9, B, D, and F). Although the optimal direction ($\theta_{opt}$) during pursuit tended to be unchanged (Fig. 9B), the response amplitude (A) was influenced, in particular, by pursuit in the anti-preferred direction of the neurons (Fig. 9D, blue line). The tuning width ($\sigma$) also tended to be narrower or wider depending on the pursuit direction (Fig. 9F). In contrast, in the majority of the MT neurons, the direction-tuning profiles for visual motion on the retina tended to be similar regardless of the behavioral conditions (Fig. 9, H, J, and L), whereas the direction-tuning profiles for visual motion on the screen...
during pursuit (Fig. 9, G, I, and K) depended on pursuit direction.

To further distinguish between the two types of direction-dependence properties (motion on the screen or on the retina) of the MSTd and MT neuronal activation, the values of the partial correlation coefficients for motion on the screen and retina ($R_{\text{sr}}$ and $R_{\text{ret}}$) were plotted against one another (Fig. 10). The class boundaries of the distribution of the partial correlations separate the neurons into three cell types: “retinal-motion tuned” cells that are more sensitive to motion on the retina, “spatial-motion tuned” cells that are more sensitive to motion on the screen, and intermediate or “unclassified” cells. We adopted a criterion probability of 0.1 to define these regions. In Fig. 10A, we plotted the data from the MSTd neurons (open circles) during pursuit in the preferred direction. Approximately 16.4% of MSTd neurons (10/61) were classified as spatial-motion tuned and 19.7% as retinal-motion tuned (12/61), whereas 63.9% were unclassified (39/61). For the other three pursuit conditions with a target moving in the preferred direction + 90°, the antiprefered direction, and the antiprefered direction + 90°, respectively (Fig. 10, A-D). Most neurons in MT (greater than ~60%) exhibited significant direction-tuning properties for visual motion on the retina rather than on the screen, whereas MSTd neurons were more broadly correlated with direction and speed of visual motion either on the screen or on the retina.

DISCUSSION

We recently reported that when presented with a moving large-field random-dot pattern as a background stimulus, the majority of the neurons in the MSTd area were more sensitive to the actual motion of the background in the external world than to its motion on the retina during pursuit eye movements, whereas most MT neurons were sensitive to the retinal image motion (Inaba and Kawano 2010; Inaba et al. 2007). The observation was consistent with the idea that the neurons in area MSTd reconstruct a stable world by compensating for the retinal slip of the background resulting from the pursuit eye movements. However, it was not clear whether this compensation in area MSTd occurred regardless of pursuit speed and direction, because, in the previous studies, the speed of the pursuit target was always 20°/s and both the target and background image were moved in parallel to the preferred direction of each neuron.

In the present study, pursuit-speed experiments were designed to examine whether neurons in areas MSTd and MT that respond to large-field visual motion are able to compensate for retinal image motion of the background irrespective of pursuit speeds. We first examined the motion to which individual neurons are more sensitive, “motion on the screen” or “motion on the retina” by using a novel methodology. The ROC analysis was applied to the neural responses obtained from
individual trials during pursuit at different speeds for each neuron. We then measured the performance of each neuron in its classification of the stimulus motions into motion in the preferred direction or in the antiprefered direction. Comparison between performance as a classifier for motion on the screen and a classifier for motion on the retina (Fig. 3) revealed that most MT neurons worked better as classifiers for motion on the retina, whereas the majority of the MSTd neurons worked better as classifiers for motion on the screen. These findings support the argument that the majority of the MSTd neurons responsive to large-field visual motion were more sensitive to motion on the screen, while most neurons in the MT area were more sensitive to motion on the retina. The present findings also suggest that there are neurons in area MSTd that compensate for retinal image motion irrespective of pursuit speeds.

We then examined whether the neurons in both areas were able to shift their speed tuning curves to compensate for the retinal image motion brought about by changes in pursuit speeds (5, 10, and 20°/s) in both the preferred and antiprefered directions. It was found that the majority of MSTd neurons shifted their speed tuning curves to compensate for self-induced retinal image motion when the speed of the pursuit target was 20°/s, as previously reported (Inaba and Kawano 2010; Inaba et al. 2007). This characteristic was also seen when it was 10 or 5°/s. Thus the MSTd population showed an approximately linear decrease in the compensatory shift as a function of pursuit speed (Fig. 6E, solid lines). These results suggest that the speed tuning responses of the MSTd neurons to the external world are preserved irrespective of pursuit speed. Chukoskie and Movshon (2009) reported that only a minority of MST neurons showed this type of response property. This discrepancy might be due to a significant difference in visual stimuli used in these studies; i.e., we used large-field visual stimuli (80 × 80°) and studied response characteristics of the neurons responsive to the stimuli, whereas Chukoskie and Movshon used stimuli restricted to the hot-spot of the neurons’ receptive field. We also found a striking difference between MSTd and MT neurons. Most MT neurons did not show compensation for self-induced retinal image motion at any pursuit speeds, suggesting that the MT neurons are sensitive to genuine retinal image motion. This finding is consistent with that from the ROC analysis in the present study and with previous findings (Chukoskie and Movshon 2009; Erickson and Thier 1991; Inaba and Kawano 2010; Inaba et al. 2007).

In the pursuit-direction experiments, we tested whether either MT or MSTd neurons modify their direction tuning for background motion as a function of the retinal image motion induced by the pursuit. In the experiments, we again found that most MT neurons were much more sensitive to genuine retinal image motion. The direction-tuning profiles for visual motion on the retina were similar irrespective of the behavioral conditions of the monkeys (see Figs. 8–10). The results from the analyses of partial correlation coefficients showed that the majority of the MT neurons were classified as retinal-motion tuned cells and few as spatial-motion tuned cells. These findings support the conclusion that the MT neurons code for visual motion on the retina.

On the other hand, a relatively small population of the MSTd neurons showed the response patterns that were related to visual motion on the retina. The analyses of partial correlation coefficients revealed that 5–20% of the MSTd neurons could be regarded as retinal-motion tuned cells. Thus the majority of the MSTd neurons were influenced more or less by smooth pursuit to compensate for self-induced retinal image motion as follows. First, as shown in Fig. 8A, there were neurons in area

![Fig. 9. Effects of pursuit on direction-tuning profiles of the MSTd (A–F) and MT (G–L) neurons.](http://jn.physiology.org/)

**Fig. 9.** Effects of pursuit on direction-tuning profiles of the MSTd (A–F) and MT (G–L) neurons. Distributions for the differences in direction-tuning profiles on the basis of the stimulus motion on the screen (A, C, E, G, I, and K) and on the retina (B, D, F, H, J, and L) are shown at the left and right, respectively. Distributions for difference in optimal direction ($\theta_{\text{opt}}$) in degrees (A, B, G, and H), normalized differences in amplitude ($A_{\text{diff}}$) (C, D, I, and J), and normalized differences in tuning width ($\sigma_{\text{diff}}$) (E, F, K, and L) are shown. Colors indicate pursuit direction as in Fig. 8.

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MSTd whose responses were determined almost completely by visual motion on the screen. Second, for the majority of the MSTd neurons, the direction-tuning profiles for motion on the screen were similar between fixation and each of the pursuit conditions as shown in Fig. 9. Third, for the MSTd neurons, direction-tuning profiles for visual motion on the retina during pursuit in the antipreferred direction (see blue lines in Figs. 8B and 9D) showed that the response amplitude was significantly small, as if suppressed uniformly, which is consistent with the previous finding by Chukoskie and Movshon (2009). Note that, under this situation, all test stimuli moved “on the screen” with directions /H1102290° away from the neurons’ preferred direction (cf. Fig. 7A, right). Finally, the analyses of the partial correlation revealed that 16 – 43% of neurons in area MSTd can be classified as spatial-motion tuned cells (that are sensitive to motion on the screen), indicating that area MSTd involves neurons that codes for visual motion in space during pursuit eye movements in different directions. However, we should also note that many MSTd neurons were still remained unclassified based on the results from partial correlation analyses. The data points of the MSTd neurons distributed over the entire upper-right region. This continuum from one extreme to another may suggest important characteristics of the population of the MSTd neurons. A similar continuum is also seen for the results of the ROC analysis in Fig. 3. These results suggest that the compensations for self-induced retinal image motion are often imperfect and highly dependent on individual neurons in the MSTd, which might be related to illusory percept during smooth pursuit (see below).

The compensatory effects in the MSTd neurons might depend on the direction of smooth pursuit. The analyses of the partial correlation revealed that, among the conditions with four different pursuit directions, the neuronal responses were most significantly compensated for the self-induced retinal image motion when the monkeys were tracking the target moving in the antipreferred direction (43%). This property is consistent with the observation in the pursuit-speed experiment and in our previous studies (Inaba and Kawano 2010; Inaba et al. 2007) that the shift of the speed tuning response during pursuit in the preferred direction was smaller than that during pursuit in the antipreferred direction (see Fig. 6, E and F). Such an anisotropic dependence on the pursuit direction could be due to characteristics of either the available visual inputs (e.g., direction and speed tuning) or insufficient extra-retinal information or both. Further experiments are needed to clarify this issue.

Apparently, our visual system is capable of compensating for the effects of pursuit eye movements on the self-induced retinal slips. However, illusions such as the Filehne illusion (Filehne 1922; Mack and Herman 1973), the Aubert-Fleischl phenomenon (1887; Aubert 1886; Duffy and Wurtz 1991; Fleischl 1882), and the Duncker illusion (Duncker 1929; Zivotofsky et al. 1995; Zivotofsky et al. 2005) demonstrate that this compensation is not always perfect. Consistent with these studies, the MSTd neurons in the present study showed partial
but not perfect compensation for the self-induced retinal slip motion.

In area MSTd, there are neurons sensitive to some types of motion other than laminar motion we used here, such as expansion, contraction, and rotation of large-field visual stimuli (Duffy and Wurtz 1991; Graziano et al. 1994; Orban et al. 1992; Saito et al. 1986). It has been reported that some of the MST neurons are tuned for the retinal position of the focus of expansion (the heading of the observer) or the center of rotation and contraction and that they modify their tuning to partially compensate for the retinal position shift caused by pursuit (Bradley et al. 1996; Maciokas and Britten 2010; Shenoy et al. 2002). Shenoy et al. (2002) found that, regardless of pursuit speed, the MSTd representation compensates on average for ~55% of the focus of expansion displacement. Considering that the expansion stimuli consisted of image components moving in different directions, our observation of insufficient compensation in the pursuit-direction experiment might point to a similar underlying mechanism.

Both MT and MST contain neurons that discharge during smooth pursuit of a small target in the dark, called visual-tracking neurons or pursuit cells (Komatsu and Wurtz 1988b; Sakata et al. 1983). In the present study, we found that some MT and MSTd neurons exhibited pursuit-related responses when the animal pursued a target moving against a dark background before the presentation of the background image (see Fig. 7B). As reported in our previous reports (Inaba and Kawano 2010; Inaba et al. 2007), such pursuit-related modulations were relatively weak compared with the responses to large-field visual motion. The lack of strong modulation during pursuit could be due to our screening method using a moving large-field random-dot pattern. To understand what sort of pursuit-related signals were presented. This allowed us to examine whether extra-retinal signals were used for the compensation at each pursuit direction and speed. We found that most of the MT neurons were more sensitive to retinal image motion of the background. On the other hand, in area MSTd, there were significant numbers of neurons that were more sensitive to the actual motion of the background in space than to its motion on the retina regardless of pursuit speed and direction. We conclude that there are a good number of neurons in area MSTd that integrate retinal and extra-retinal information required for perceiving motion of the visual background in space during smooth pursuit eye movements.

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DISCLOSURES

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

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