Visual Tracking Neurons in Primate Area MST Are Activated by Smooth-Pursuit Eye Movements of an “Imaginary” Target

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Ilg, Uwe J. and Peter Thier. Visual tracking neurons in primate area MST are activated by smooth-pursuit eye movements of an “imaginary” target. J Neurophysiol 90: 1489–1502, 2003. First published May 7, 2003; 10.1152/jn.00272.2003. Because smooth-pursuit eye movements (SPEM) can be executed only in the presence of a moving target, it has been difficult to attribute the neuronal activity observed during the execution of these eye movements to either sensory processing or to motor preparation or execution. Previously, we showed that rhesus monkeys can be trained to perform SPEM directed toward an “imaginary” target defined by visual cues confined to the periphery of the visual field. The pursuit of an “imaginary” target provides the opportunity to elicit SPEM without stimulating visual receptive fields confined to the center of the visual field. Here, we report that a subset of neurons [85 “imaginary” visual tracking (iVT)-neurons] in area MST of 3 rhesus monkeys were identically activated during pursuit of a conventional, foveal dot target and the “imaginary” target. Because iVT-neurons did not respond to the presentation of a moving “imaginary” target during fixation of a stationary dot, we are able to exclude that responses to pursuit of the “imaginary” target are artifacts of stimulation of the visual field periphery. Neurons recorded from the representation of the central parts of the visual field in neighboring area MT, usually vigorously discharging during pursuit of foveal targets, with no case responded to pursuit of the “imaginary” target. This dissociation between MT and MST neurons supports the view that pursuit responses of MT neurons are the result of target image motion, whereas those of iVT-neurons in area MST reflect an eye movement-related signal that is nonretinal in origin. iVT-neurons fell into two groups, depending on the properties of the eye movement–related signal. Whereas most of them (71%) encoded eye velocity, a minority showed responses determined by eye position, irrespective of whether eye position was changed by smooth pursuit or by saccades. Only the former group exhibited responses that led the eye movement, which is a prerequisite for a causal role in the generation of SPEM.

INTRODUCTION

The execution of smooth-pursuit eye movements (SPEM) is tightly linked to the presence of a target moving in front of a background; this is the reason that SPEM have been successfully used as a biological probe in studies of visual motion processing (for review see Ilg 1997). On the other hand, this close linkage makes it very difficult to clarify whether the neuronal activity observed during the execution of SPEM is related to signals other than visual motion. SPEM-related single-unit activity has among others been demonstrated amply in various parts of the occipitoparietal cortex (Bremmer et al. 1997a,b; Erickson and Dow 1989; Erickson et al. 1989; Hyvärinen and Poranen 1974; Kawano et al. 1984; Komatsu and Wurtz 1988a,b; Mountcastle et al. 1975; Newsome et al. 1988; Robinson et al. 1978; Sakata et al. 1983; Thier and Erickson 1992). To define the contribution of these neurons to the generation of SPEM, a major concern has been to distinguish visual and nonvisual components of the pursuit-related responses.

A first step to this end was the elimination of any visible background whose pursuit-induced retinal image motion might have evoked visual responses during the execution of SPEM. Sakata and colleagues could indeed show that many neurons in the occipitoparietal cortex, referred to as “true pursuit cells” (Sakata et al. 1983) or “visual-tracking (VT) neurons” (Kawano et al. 1984), remained activated by SPEM even in the absence of a visual background. The next step in the attempt to support the existence of nonvisual pursuit-related activity was to eliminate retinal motion of the target during maintained SPEM. Two different approaches were used: The first one consisted in briefly (150 to 200 ms) turning the pursuit target off (Kawano et al. 1994; Newsome et al. 1988; Sakata et al. 1983; Thier and Erickson 1992), whereas the second one applied stabilization of the target image on the retina by electronic means (Newsome et al. 1988).

Using these techniques, the following results were obtained: Neurons in the middle temporal area MT displayed pursuit-related activity that declined as soon as the retinal image motion was removed, reflecting a purely visual nature of the responses (Newsome et al. 1988). In contrast, neurons in the medial superior temporal area MST did not change their activity in response to removal of the retinal image motion, indicative of a nonretinal eye movement–related signal contributing to the discharge (Newsome et al. 1988; Thier and Erickson 1992). In view of these results, biologically oriented models of SPEM usually assign area MT the role of a decoder of retinal image motion, while placing area MST further upstream in the processing for smooth-pursuit eye movements (Dicker and Thier 1999). For instance, the nonretinal signal related to the eye movement available in area MST has been suggested to underlie the ability of observers to maintain smooth-pursuit eye movements in the absence of target image motion (Robinson et al. 1986).

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However, this interpretation of the role of areas MT and MST is not fully conclusive for two reasons. First of all, the persistence of responses in area MST during removal of target image motion may simply be a consequence of some visual storage mechanism allowing MST neurons to bridge short periods without image motion. Second, turning the target off or stabilizing the target electronically on the retina not only affects image motion but also leads to a drop in eye velocity (Becker and Fuchs 1985; Kawano et al. 1994). Hence, one might argue that VT-neurons in area MST show maintained responses in the absence of target image motion because of visual storage, rather than exploiting nonretinal information on the eye movement. On the other hand, area MT neurons might actually use nonretinal information on the eye movement, but immediately react to changes in eye velocity induced by target image removal because of very sensitive speed tuning. To resolve the ambiguities of the interpretation of pursuit-related activity recorded from neurons in areas MT and MST, a target would be needed, not activating the processors of visual motion in the central parts of the visual field, while still being able to induce and to maintain high-gain SPEM. These are the features of "imaginary" targets based on peripheral cues as introduced by Wyatt and colleagues (1994). We recently reported that monkeys can also be trained to pursue such "imaginary" targets with high-gain SPEM (Ilg and Thier 1999) and presented evidence supporting the view that pursuit evoked by these "imaginary" targets is different from pursuit of isolated peripheral elements. In the present work, we have exploited "imaginary" targets to readdress the existence of eye movement-related signals in the visual areas of the superior temporal sulcus.

METHODS

Major parts of the methods used in this study, especially the visual stimulation and the eye movement recordings and their analysis, were described previously in a preparatory study reporting the eye movements elicited by "imaginary" targets in monkeys (Ilg and Thier 1999). We therefore restrict the description of methods to those aspects not covered in the earlier report.

Chronic recordings from awake and trained rhesus monkeys

Two female and one male rhesus monkeys were used in the present study. Using surgical procedures described in detail elsewhere (Ilg and Thier 1996), they were implanted with a head holder, a recording chamber, and a subconjunctival search coil. All animal procedures were carried out in accordance with the guidelines set forth by the National Institutes of Health and German law and were approved by the local ethics committee. The center of each recording chamber was aimed at the lateral parts of area MST (lateral 19, posterior 3.5, and dorsal 16 mm) tilted 30° posterior in the parasagittal plane. Single-unit activity was recorded using glass-isolated tungsten electrodes. The microelectrode signal was preamplified, low-pass filtered at 10 kHz, and fed into an action potential detector, based on either a conventional window discriminator (first 2 monkeys) or a template-matching spike detector (3rd monkey; MSD Alpha Omega). The occurrence of spikes was sampled with a temporal precision of 250 μs. Horizontal and vertical eye positions were sampled at 12 bits with 1 kHz per channel.

After the termination of the recording period, the monkeys were killed and their brains were cut parasagittally into 40-μm sections. The sections were stained for cell bodies (Nissl) or myelin (Gallyas), the latter to delineate the borders of area MT in the posterior wall of the superior temporal sulcus (STS). The reconstruction of recording sites was based on relating micro-drive readings to the locations of multiple small injections of fluorescent tracers made at various locations within the region of the STS explored.

Experimental paradigms and classification of responses

Most of the paradigms required the absence of visible background structures to avoid inadvertent visual stimulation. This is why the monkeys were tested in complete darkness without any background cues perceived by human observers. Furthermore, to prevent dark adaptation of the monkey, two bright LEDs were switched on each time, when at the end of an individual trial a juice reward was delivered.

While the microelectrode approached areas MT and MST, the monkeys tracked a single dot moving on a circle (period 3 s, radius 10°) at constant angular velocity to activate pursuit-related neurons, independent of their individual direction preferences and to pinpoint the preferred direction (Thier and Erickson 1992). Once pursuit-related activity was encountered and the preferred direction determined, the following tests were carried out.

Pursuit of an "imaginary" target

The first test required SPEM of a target moving in a step-ramp manner. After fixation of the target presented straight-ahead for a variable duration (500–1,000 ms), the target stepped centrifugally (step size varied from 0 to 10°) and subsequently moved into the opposite direction at a constant speed of 10°/s. The step-ramp trajectories were carried out along the preferred–nonpreferred axis of a given neuron, as determined by responses to circular pursuit. Pursuit direction on this axis was chosen at random with on average 50% of all trials carried out in the preferred direction of the neuron. The target was either a foveal cue, the intersection of two diagonal lines (real target, see Fig. 1A) within a rectangular square (20 × 20°), or, alternatively, the void center of the same structure ("imaginary" target), obtained by blanking the central 12 × 12° region of the figure, including the intersection (see Fig. 1B).

As indicated in Fig. 1, the dimensions of the gaze control windows (±5° horizontally, ±2.5° vertically) were smaller than the blanked area in case of the "imaginary" target. Trials were aborted if the deviation of gaze from the target exceeded the tolerance window. The two target types were presented randomly interleaved. To reveal whether pursuit direction and/or the choice of target type had an influence on the discharge of a neuron, we calculated the mean single-trial response for an 1,800-ms period starting 200 ms after target onset and extending to the end of trial and subjected the resulting responses to a 2-factorial ANOVA; significance level P < 0.05 with the two factors target type ("imaginary" vs. real) and pursuit direction (preferred vs. nonpreferred).

Gap paradigm. As explained in the introduction, one of the approaches used in previous work to demonstrate nonretinal responses has been to turn off the pursuit target for several 100-ms periods (gap paradigm). In our version of this gap paradigm, we asked the monkeys to pursue a red dot target (diameter 30 min of arc) moving in the same manner as specified for the "imaginary" target. During maintained pursuit, the dot target was turned off for 200 ms unpredictably on half of the trials. The analysis involved the measurement of the mean neuronal discharge within a 200-ms interval starting 100 ms after the disappearance of the target as well as the measurement of mean eye velocity in this period. The resulting measures were compared with the mean discharge and mean eye velocity in the identical period of time in trials with the target being on. Wilcoxon rank sum tests (P < 0.05) were run to reveal whether the neuronal discharges or eye velocities were different.

Passive visual stimulation. To rule out that responses evoked by pursuit of the "imaginary" target were visual responses to movements of the target retinal image, stimulating the peripheral parts of the visual field, we moved the "imaginary" figure passively while the
monkeys kept fixation of a stationary dot stimulus (Fig. 1C). In addition to the standard “imaginary” figure with a void center of $12 \times 12^\circ$, we also used variants with smaller void centers (8 and $4^\circ$) and in addition the real figure. The figures were moved back and forth for 1,000 ms each at $10^\circ$/s along the preferred–nonpreferred axis of a neuron. The response was characterized by the mean discharge rate during the 1,000-ms time interval when the stimulus moved in the preferred direction.

To assess whether visual responses were likely to contribute to the pursuit-related responses obtained, we compared the responses to pursuit of the real target, the “imaginary” target, and the corresponding passively moving “imaginary” figure by subjecting the response measures to a one-factorial ANOVA ($P < 0.05$) with subsequent post hoc comparisons based on Scheffé tests to localize the conditions giving rise to significantly different responses. In addition to stimulating neurons passively with different variants of the “hourglass” figure, we used standard stimuli (bars and random-dot kinemato-grams) to assess receptive field boundaries and the preferences for retinal movement direction and speed.

VESTIBULAR STIMULATION. Vestibular testing was confined to rotations about the yaw axis, using a motorized turn table, which allowed rotation of the monkey en blocus sinusoidally (standard parameters $10^\circ$ amplitude, 3-s period). Rotation was carried out either in complete darkness or, alternatively, with a small fixation spot moving with the head, thereby suppressing the vestibuloocular reflex (VOR).

RESULTS

We recorded the activity of 438 neurons located in the STS of 3 rhesus monkeys while the animals performed SPEM elicited by a real or an “imaginary” target. The postmortem reconstruction of the recording sites revealed that 82 of them could be attributed to area MT and 356 neurons to area MST.

Neurons in area MT responded frequently to pursuit of a real target, especially if the receptive field included the fovea. Figure 2 shows the response of a typical example in which the reconstruction of the recording site revealed a location within area MT. This neuron had a receptive field size of $2 \times 2^\circ$ including the fovea and was activated by pursuit of a real target to the right. The response in this case (and all other neurons from area MT) was attributed to movement of the target image within the borders of the receptive field. This is indicated by the fact that this and all other MT neurons were not activated by pursuit of the “imaginary” target, restricting retinal image motion to the visual field periphery far away from the receptive field. Note that the response to pursuit of the real target moving in the neuron’s preferred direction showed strong fluctuations. These fluctuations were attributed to oscillations in eye velocity around target velocity as described earlier (e.g., Goldreich et al. 1992; Lisberger and Movshon 1999). If the eye speed exceeded target speed, the direction of retinal image motion was inverted and the neuron was silent. Conversely, whenever

FIG. 1. Sketch of experimental paradigms and stimuli used. A: monkey was asked to track movement of intersection of two diagonal lines (real target) defining “hourglass”–like figure, which had overall size of $20 \times 20^\circ$. B: monkey tracked movement of invisible center of same structure (“imaginary” target), obtained by blanking central $12 \times 12^\circ$ region of figure, including intersection of “hourglass.” Size of void region was $12 \times 12^\circ$. Dimension of eye position control window in A and B, delineated in sketches by four angles, was $10 \times 5^\circ$. C: control experiment in which monkey fixated stationary dot while “imaginary” figure was moved across visual field (eye position control window $5 \times 5^\circ$).
the eye speed was smaller than the target speed, the residual retinal image motion of the target was directed in the preferred direction and the neuron was activated. Comparable observations could be made for all other neurons from area MT, suggesting that pursuit responses in this area are solely determined by retinal image motion.

Figure 3 shows the response of a typical MST neuron that, unlike the example from area MT, was characterized by identical responses to pursuit of a real and an "imaginary" target. It may be noted that the pursuit-related responses of this neuron had a rather long latency, lagging the onset of target movement by 200 ms and the onset of eye movement by 100 ms. As indicated by results of 2-factorial ANOVA (significant effects of target type \( P < 0.0001 \), direction \( P < 0.0001 \), and significant interaction between both factors \( P = 0.04 \)), this neuron preferred pursuit of real target in its preferred direction.

Figure 3 shows the response of a typical MST neuron that, unlike the example from area MT, was characterized by identical responses to pursuit of a real and an "imaginary" target. It may be noted that the pursuit-related responses of this neuron had a rather long latency, lagging the onset of target movement by 200 ms and the onset of eye movement by 100 ms. As the more systematic analysis of neuronal latencies at the end of the RESULTS section will show, such long latencies were more an exception than the rule. The 2-factorial ANOVA with the two factors direction of target movement and target type (real vs. "imaginary" target) revealed a highly significant influence of the direction of target movement \( P < 0.0001 \) and no significant effect of target type \( P = 0.28 \) or interaction of the two factors on the neuronal response \( P = 0.45 \). We performed the same statistical analysis on all 438 neurons activated by pursuit; 178 (40\%) of them showed a significant effect of the direction of the target or eye movement \( P < 0.05 \) and a nonsignificant effect of target type or interaction of both factors \( P > 0.05 \).

The neurons constituting this group were without exception located in area MST. On the other hand, out of the remaining 260 neurons that did not meet these statistical criteria, 82 were located in area MT.

The receptive fields of area MST neurons are comparatively large and the boundaries probably never sharp. It is thus reasonable to argue that the responses to the "imaginary" target were a consequence of the peripherally located target constituents, encountering some residual receptive field sensitivity in...
these peripheral parts of the visual field. If this were indeed the case, one would expect visual responses to a moving "imaginary" target during fixation of a stationary target as well (passive visual stimulation). We assessed the sensitivity to passive visual stimulation in 178 neurons, all located in area MST.

We evoked responses to passive visual stimulation with four "hourglass" stimuli, differing in the size of the central void area as depicted in Fig. 3C. Note that this neuron gave the same strong response to pursuit of the real and the "imaginary" targets. The "imaginary" target with a 12° center, which caused a strong response when used as a pursuit target, was completely ineffective when used as the passive visual stimulus. On the other hand, decreasing the size of the void area of the passive visual stimulus resulted in an increase of the response. The preferred direction of the visual response was identical to the preferred direction of the pursuit-related response. When we applied a one-factorial ANOVA to compare the responses evoked by tracking of the real target, tracking of the "imaginary" target, and the visual response evoked by passive visual
stimulation of the same figure, there was a highly significant ($P < 0.0001$) effect of stimulus type. Post hoc tests (Scheffé) showed that the effect of stimulus type was attributed to significant differences between the visual response (to the “imaginary” target) compared with the pursuit activity evoked by the real ($P = 0.0017$) or the “imaginary” target ($P = 0.0001$). On the other hand, the responses evoked by pursuit of the real and the “imaginary” targets were the same ($P = 1.0$). This result clearly indicates that in this particular MST neuron, the pursuit-related activity evoked by tracking of the “imaginary” target did not result from a sensitivity to retinal image motion in the peripheral visual field.

On the other hand, in a substantial number of neurons (93 out of 178 tested), most of them with large receptive fields as revealed by testing with manually controlled stimuli, the responses evoked by pursuit of the “imaginary” target were most probably a consequence of stimulation of peripheral parts of the receptive field, as indicated by similar responses to passive visual stimulation with the standard “imaginary” target pattern. An example is shown in Fig. 4.

In this neuron, there was no significant difference between the response to tracking of a real and an “imaginary” target, respectively (2-factorial ANOVA, nonsignificant effect of factor target type: $P = 0.233$). Only the direction of pursuit affected the response significantly (factor direction: $P < 0.0001$). The visual origin of the response evoked by tracking of the “imaginary” target in this neuron was undoubtedly demonstrated by the clear response to the moving “imaginary” target during passive visual stimulation. The statistical analysis (ANOVA) did not reveal any significant differences in the

![Image](image-url)
discharge rates during pursuit of the real and “imaginary” targets and during passive visual stimulation (ANOVA *P* = 0.295).

In 85 neurons (48% out of 178), the activity evoked by tracking of the real and the “imaginary” targets, respectively, was not statistically different, while at the same time, passive visual stimulation with the “imaginary” target pattern was ineffective. We will refer to these 85 neurons as “imaginary” VT-neurons (iVT-neurons). The reconstruction of the recordings sites revealed that all iVT-neurons were located within the fundus or the anterior wall of the STS, or, in other words, outside of area MT and inside of area MST. The breakdown of the number of neurons recorded from both areas is shown in Table 1.

To demonstrate that iVT-neurons are indeed equally sensitive to tracking of the real and the “imaginary” targets, we plotted the pursuit-related responses elicited by both types of target (Fig. 5). The linear regression fitted to this plot was highly significant (*P* < 0.0001) and the slope did not deviate significantly from unity (*P* = 0.128).

Previous work has shown that many VT-neurons recorded from area MST show a persistence of their pursuit-related activity during temporal removal of the pursuit target. When we applied this test to iVT-neurons, the response of 69 out of 85 (=81%) iVT-neurons was not affected significantly (Wilcoxon test, *P* > 0.05; see Methods) by the target disappearance. Figure 6 shows the responses of a typical iVT-neuron (A, same neuron as in Fig. 3) as well as that of a purely visual neuron (B, same neuron as in Fig. 4) that failed to be classified as an iVT-neuron based on its sensitivity to peripheral visual cues. The iVT-neuron (Fig. 6A) maintained its activity (*P* = 0.645, Wilcoxon test), whereas the visual neuron showed a clear drop of its discharge (*P* = 0.009, Wilcoxon test) as a consequence of the removal of the visual input (Fig. 6B). Conversely, 270/353 (=70%) of the non-iVT-neurons tested were affected significantly by removal of the pursuit target [i.e., they exhibited a significant change in their discharge rate (*P* < 0.05) as a consequence of SPEM target removal]. However, as pointed out in the introduction, the eye movements were not identical in the condition with or without a target. The eye velocity decreased significantly (*P* = 0.003 in Fig. 6A, *P* = 0.019 in Fig. 6B; Wilcoxon test) as soon as the target was removed.

**Distribution of preferred directions of iVT-neurons**

Figure 7 shows the distribution of the preferred directions of all the iVT-neurons recorded from area MST. The preferred direction was the one out of the four (up, down, left, and right) directions tested in which the pursuit-related activity was maximal. As can be seen, there was a strong and statistically significant (test of binomial distribution, *P* < 0.0001) bias for ipsiversive smooth pursuit.

As shown by previous work on MST and already exemplified in Fig. 3, iVT-neurons also responded to visual motion during fixation of a stationary target. Out of the 85 iVT-neurons, 72 showed a clear directionally selective visual response. Only the remaining 13 neurons (15%) did not show a visual response; at least, we were not able to elicit a response with our visual stimuli. The majority of the visually responsive neurons (64 out of 85, 75%) displayed identical preferred directions for the visual response and the pursuit-related response. Only 8 iVT-neurons (10%) had a visual preferred direction opposite to the preferred direction for SPEM.

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**TABLE 1. Breakdown of total numbers of recorded neurons**

<table>
<thead>
<tr>
<th></th>
<th>Area MT</th>
<th>Area MST</th>
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<tr>
<td>Identical responses during pursuit of real and “imaginary” target</td>
<td>82</td>
<td>356</td>
</tr>
<tr>
<td>Significantly different responses during pursuit of real and “imaginary” target</td>
<td>82</td>
<td>178</td>
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<tr>
<td>Identical responses during pursuit of real and “imaginary” target</td>
<td>82</td>
<td>178</td>
</tr>
<tr>
<td>Significantly different responses during pursuit of real and “imaginary” target</td>
<td>198</td>
<td>93</td>
</tr>
<tr>
<td>Insensitive to peripheral visual stimulation</td>
<td>85</td>
<td>93</td>
</tr>
<tr>
<td>Sensitive to peripheral visual stimulation</td>
<td>60</td>
<td>25</td>
</tr>
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**FIG. 5. Scatter plot of mean discharge rate evoked by tracking of “imaginary” target as function of mean discharge rate evoked by real target. Discharge rate was determined during 1,800-ms steady-state pursuit as explained in Methods.** Plot considers 85 neurons classified as iVT-neurons. Regression is highly significant (r = 0.97, *P* < 0.0001) and slope (1.02) is not significantly different from unity (*P* = 0.128).
Vestibular sensitivity of iVT-neurons

In an earlier publication dealing with area MST (Thier and Erickson 1992) it was reported that VT-neurons in this area responded to suppression of the VOR. To make it possible to compare the properties of the iVT-neurons as assessed in the present study with those reported in the aforementioned publication, we tested 13 out of 85 iVT-neurons during suppression of the horizontal VOR. Because of technical limitations, vestibular stimulation was confined to the yaw axis. Ten neurons showed a significant modulation of their discharge rate during suppression of the horizontal VOR ($P < 0.05$, t-test). Most of these neurons (8 of 10) had the same horizontal preferences for pursuit, passive visual stimulation and suppression of the VOR. Figure 8 shows an exemplary neuron whose location is shown in D. This neuron was activated by SPEM to the left, independent of the target’s being real (A) or “imaginary” (B). Passive visual stimulation with a random-dot kinematogram was most effective to the left as well (C) and finally, during suppression of VOR, this neuron responded to head and target movement to the left (E).

The responsiveness of iVT-neurons to suppression of the VOR strongly suggests that these neurons were recorded from a very similar area as the VT-neurons described earlier (Thier and Erickson 1992).

Sensitivity to eye position

So far, we showed that 85 iVT-neurons recorded from area MST responded similarly to SPEM of a real and an “imaginary” target, although in the latter case there was no visual stimulus inside the neurons’ receptive field. However, we did not specify yet whether the observed pursuit-related activity reflected eye position or eye velocity. Many of the iVT-neurons, like the one shown in Fig. 3, displayed more or less constant elevations of their discharge rates for pursuit in their respective preferred directions, suggesting a preference for velocity. Others, like the one depicted in Fig. 9, showed a different pattern, more suggestive of position sensitivity. This iVT-neuron showed a monotonic increase in firing rate during pursuit of both the real and the “imaginary” target. In this example, the change in eye position from pursuit onset to the end of the trial was $24^\circ$.

Linear regression analysis of the discharge rate of this neuron as a function of time or eye position, respectively (shown...
in Fig. 9A), resulted in a significant \( P < 0.0001 \) slope of 60 spikes/s or 5 spikes s\(^{-1}\) deg \(^{-1}\), respectively.

Out of the 85 iVT-neurons, the responses of 25 neurons (29\%) showed eye position sensitivity as revealed by statistically significant nonzero slopes of the regression lines. We will refer to these 25 neurons as iVT\(_{\text{pos}}\)-neurons as opposed to those 60 iVT\(_{\text{vel}}\)-neurons lacking this eye position sensitivity. The reconstruction of the recording sites revealed no clustering or separation of the iVT\(_{\text{pos}}\)-neurons and the iVT\(_{\text{vel}}\)-neurons.

The eye position influence of the pursuit-related activity of iVT\(_{\text{pos}}\)-neurons could reflect a basic sensitivity to eye position irrespective of the kind of eye movement carried out or, alternatively, to eye position during SPEM. To distinguish between these two possibilities, we determined the discharge rates at 10 different orbital positions during fixation of a stationary target. As illustrated in Fig. 10, which depicts the same neuron as shown in Fig. 9, the discharge rate clearly changed with eye position, even in the absence of SPEM.

To determine the sensitivity to eye position in this task, we calculated the mean discharge rate for a period of 500 ms after the movement to a new orbital position. We plotted these means as a function of the \( x\) and \( y \) components of eye position.

Two dimensional-regression analysis of this plot revealed a slope of 5.4 spikes s\(^{-1}\) deg \(^{-1}\) along the horizontal eye position axis for the neuron preferring horizontal pursuit shown in Fig. 10. The sensitivity for horizontal eye position during smooth pursuit had been 5.0 spikes s\(^{-1}\) deg \(^{-1}\) (i.e., it was very similar to the eye position sensitivity during stationary fixation).

The same comparison was carried out for 8 other iVT\(_{\text{pos}}\)-neurons, all of them preferring horizontal SPEM. Figure 11 plots the sensitivity of the horizontal eye position during stationary fixation as a function of horizontal eye position sensitivity during execution of pursuit. Both sensitivities were quite similar, although the regression analysis failed to reveal significance (rank correlation \( P = 0.15 \)).

**Latency**

An important question is whether the pursuit-related activity precedes the start of the eye movement or, alternatively, follows eye movement onset. Obviously, only in the first case, the pursuit-related activity could be causally involved in the generation of SPEM. To determine the latency of the pursuit eye movement as well as of the neuronal activity, we measured for a period of 500 ms ending immediately before target movement onset the baseline eye velocity as well as the mean discharge rate and determined when eye velocity and discharge rate, respectively, first exceeded thresholds given by these means + 1 SD. Figure 12 gives the latencies of the eye movements as well as the latencies of the neuronal responses for both types of targets in the preferred direction of target movement, separately for iVT\(_{\text{vel}}\)-neurons \((n = 60)\) and iVT\(_{\text{pos}}\)-neurons \((n = 25)\).

Figure 12 shows that the latencies of iVT\(_{\text{vel}}\)-neurons were on average shorter than eye movement latencies, whereas the latencies of iVT\(_{\text{pos}}\)-neurons exceeded those of the eyes. This relationship held for pursuit of the real and the “imaginary” target. We tested whether the differences suggested by Fig. 12 were statistically significant by running a 2-factorial ANOVA with the factors eye or discharge rate latency and target type. This analysis revealed different results for the iVT\(_{\text{vel}}\) and iVT\(_{\text{pos}}\)-neurons. For iVT\(_{\text{vel}}\)-neurons, the factor target type had no significant influence on the latencies \((P = 0.176)\), whereas the discharge latency was significantly shorter than the eye movement latency \((P < 0.0001)\). Also the interactions of both factors was not significant \((P = 0.6179)\). In contrast, for the values of the iVT\(_{\text{pos}}\)-neurons, neither the factor target type \((P = 0.314)\) nor the factor eye or discharge latency \((P = 0.482)\) nor the interaction of both factors \((P = 0.8591)\) was significant.

**DISCUSSION**

We used visual targets consisting of peripheral cues only, sparing the 12° of the central visual field to evoke high-gain smooth-pursuit eye movements (SPEM). Single units were recorded from areas MT and MST of the STS and their respective responses to such an “imaginary” target compared with those evoked by conventional dot-pursuit targets, stimulating the central parts of the visual field. Neurons recorded from area MT, activated by smooth pursuit of foveal targets, failed to respond to the “imaginary” target, reflecting the insensitivity of the comparatively small central receptive fields of these neurons to the peripheral cues defining the “imaginary” target. On the other hand, a substantial fraction of neurons recorded from the lateral part of area MST, dubbed iVT-neurons, did not respond differently during SPEM of a real and the “imaginary” target, respectively. The possibility that the responses to the latter target were simply a consequence of the visual cues defining the “imaginary” target, activating visual receptive fields putatively extending far into the periphery, could be excluded by reproducing the retinal image motion prevailing during SPEM by moving the “imaginary” target passively in the absence of eye movements. The iVT-neurons that discharged vigorously during pursuit of the “imaginary” target were not (or much less) activated by the passive visual stimulation. These observations indicate that the pursuit-related activity exhibited by these neurons reflects a nonretinal signal related to the ongoing SPEM.

The preferred directions of the iVT-neurons displayed a very clear bias for directions toward the recording site (ipsiversive). Earlier publications on VT neurons recorded from area MST either reported no bias at all (Komatsu et al. 1994; Newsome et al. 1988) or only a slight ipsiversive bias (Thier and Erickson 1992). Although we do not have an explanation for the differences in distributions of preferred pursuit directions reported, a clear ipsiversive bias would be in accordance with both the ipsiversive pursuit deficit observed after MST lesions (Dürsteler and Wurtz 1988) and the predominantly ipsiversive effect of intracortical microstimulation in area MST on smooth pursuit (Komatsu and Wurtz 1989).

As outlined in the Introduction, a similar conclusion had previously been based on the observation that a subset of neurons in area MST, the VT-neurons, showed maintained pursuit-related activity when, during SPEM of a dot target moving in front of a dark background, the target is turned off for several 100-ms periods (Kawano et al. 1994; Newsome et al. 1988; Thier and Erickson 1992). Actually, iVT-neurons show the same insensitivity to such a transient disappearance of the dot target in this gap paradigm. This suggests that the two groups of neurons might actually be identical. The demonstration of a pursuit-related activation in the absence of any
relevant visual stimulus falling into the receptive field indicates that most probably the gap activity also reflects nonretinal information on the eye movement, rather than a persisting response to retinal image motion. The assumption of an identity of iVT-neurons studied by us and the VT-neurons as described by previous work receives further support from the fact that both groups of neurons are sensitive not only to a nonretinal signal on the eye movement but also to retinal image motion and to head movements. Visual responses originate from retinal image motion inside receptive fields comparatively small for MST standards, emphasizing the central part of the visual field, whereas responses to rotatory head movements can be evoked, if the vestibuloocular reflex is suppressed by fixation of a head-stationary target. All these responses are directional and, moreover, the preferred directions for retinal image motion and eye and head movements seem to coincide (VT-neurons: Newsome et al. 1988; Thier and Erickson 1992; iVT-neurons, this study).

However, the present study of iVT-neurons also revealed one clear deviation from the established picture of VT-neurons in area MST with respect to the kinematic variable reflected by the nonretinal pursuit-related signal. Although previous work has suggested that VT-neurons encode an eye velocity–related signal with saturation of the response at rather low speeds (<20°/s; Komatsu and Wurtz 1988b), only two thirds of our sample of iVT-neurons, the iVT_{vel}-neurons, corresponded to this scheme. On the other hand, one third of our neurons exhibited sensitivity to eye position, rather than eye velocity. Moreover, responses to eye position were not confined to changes in eye position during SPEM. At least a small group of these iVT_{pos}-neurons (n = 9), in which the discharge for various static eye positions could be measured, showed the

FIG. 9. iVT-neuron recorded from area MT exhibiting position sensitivity during pursuit of real (A) and “imaginary” (B) target, moving in preferred (leftward, top row of raster, spike density function shown in black) and nonpreferred (rightward, bottom row of raster, spike density function shown in gray) direction. Conventions as in Fig. 3. C: reconstruction of recording site of this neuron (lateral 16 mm; conventions as in Fig. 2).

FIG. 8. Typical iVT-neuron recorded from area MST. A and B: responses to pursuit of real (A) and “imaginary” (B) target, respectively. Convention as in Fig. 2. C: directional tuning of visual responses, evoked by moving random-dot kinematogram during stationary fixation. D: reconstruction of recording site of neuron (lateral 14 mm). E: discharge of this neuron during suppression of horizontal vestibuloocular reflex (VOR). Sinusoidal trace reflects chair and head position. Occurrence of spikes is indicated by ticks and histogram is plot of instantaneous discharge rate averaged over bins of 100 ms.
same sensitivity to eye position as during SPEM. On the other hand, we did not observe an eye position–dependent modulation of eye velocity–related responses as described by Bremmer and colleagues for smooth pursuit–related responses in both areas MST (Bremmer et al. 1997a) and LIP (Bremmer et al. 1997b). Responses reflecting static eye position have been reported by Squatrito and Maioli (1996, 1997) in area MST. It seems conceivable that the iVT$_{pos}$-neurons observed by us correspond those described by Squatrito and Maioli, although in their studies no attempts were made to exclude a role of eye position–dependent visual stimulation or to test for head movement–related responses. Actually, eye position–related responses were reported by the early work on posterior parietal cortex, before well-defined
The difference in latency characterizing the two groups of iVT-neurons has clear implications for attempts to identify the specific nature of the nonretinal eye movement–related signal. The leading discharge onset of the iVT_vel-neurons precludes any form of sensory feedback as the basis of the early discharge. On the other hand, a number of observations rule out any form of sensory feedback as the basis of the early discharge. In view of these properties, it seems more plausible to assume that these neurons offer a rather crude efference copy of the eye movement. Alternatively, one might argue that the discharge reflects inferred movement of an object of interest, rather than the eye movement. In the case of the gap paradigm, this object would be the small spot, most probably perceived as moving continuously behind an invisible occluder, when temporarily turned off. In the case of the “imaginary” target, the object perceived as moving would be the “hourglass” that, irrespective of its void center, may have a certain quality of completeness. This is suggested by the fact that this figure and probably any other visual stimulus based on peripheral cues sufficient to define a complete figure including invisible central components is able to evoke high-gain SPEM (Ilg and Thier 1999).

If these neurons encoded the percept of object movement, continuous in time and space, they should of course also respond to the movement of objects, temporarily occluded, in the absence of eye movements. We did not test whether this is so in the case of iVT-neurons and are not aware of any pertinent reports on identified VT-neurons. However, Assad and Maunsell (1995) described directionally selective neurons in the STS, able to bridge the temporary disappearance of visual stimuli in the absence of eye movements. Actually, the idea that iVT-neurons encode inferred object motion is not at odds with the idea that their discharge might reflect an efference copy signal. The reason is that an efference copy signal, or some other nonretinal signal describing the eye movement, is needed to maintain the percept of target motion, when during steady-state pursuit very little retinal movement of the target image is left. The idea that iVT-neurons encode efference copy signals rather than oculomotor commands would also be able to explain onset latencies of neuronal discharges lagging eye movement onset. An efference copy signal might as well account for the eye position–related activity of iVT_pos-neurons.

Pursuit of an “Imaginary” Target Activates VT-Neurons

FIG. 11. Sensitivity for horizontal eye position during fixation of stationary target plotted as function of sensitivity for horizontal eye position during smooth-pursuit eye movement (SPEM) of dot target for iVTPos-neurons. Data point marked by circle represents neuron shown in Figs. 9 and 10. Rank correlation analysis of relationship between the two variables resulted in correlation coefficient of 0.516 \( (p = 0.15) \).

FIG. 12. Latencies (means + SD) of neuronal and eye movement responses elicited by real and “imaginary” targets, respectively. Numerical values of mean latency in milliseconds given in addition above each bar. A: latencies for iVTVel-neurons. B: latencies for iVTPos-neurons. Results of statistical analysis given in text.
On the other hand, the fact that the eye position signal usually lags the eye movement onset adds sensory feedback to the list of possible sources to be considered. In any case, the source of these signals remains elusive.

Current models of SPEM assume that cortical structures contribute to smooth pursuit by selecting the relevant object and by extracting its velocity and possibly higher derivatives of its position (Lisberger et al. 1987). Although velocity encoding iVT vel-neurons can be easily assigned a distinct role in pursuit models, which assume that pursuit generation is based on a representation of target velocity in a nonretinal frame of reference (Dicke and Thier 1999), the existence of eye position-encoding neurons in the same structure is not assumed by any of biologically oriented pursuit models we are aware of. Rather, these models have in common that they hold that signals related to eye position are generated at later, subcortical stages, relatively close to the motor periphery. Probably, these models could be modified to accommodate an unexpected biological finding: the existence of eye position information in cortical area MST.

On the other hand, we should also consider the possibility that these neurons, despite their proximity to the iVT vel-neurons may not be involved in pursuit generation at all but might be needed to contribute to generating eye movements to stationary objects. Finally, rather than subserving eye movements, eye position information may be necessary to facilitate visual functions beyond eye movement, benefiting from eye position information. One speculative possibility is that iVT pos-neurons might contribute to the monkey’s ability to infer the position of visual objects, hidden by occluding structures, a view obviously analogous to the “inferred motion” interpretation of iVT vel-neurons. Experimental lesions of MST cause deficits in SPEM (Dürsteler and Wurtz 1988), a fact that in the past has pushed the oculomotor interpretation of MST VT-neurons. However, consideration of their diversity and complexity suggests that they may actually be the basis of much more general representations, tapped by both perceptual and visuomotor systems.

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