Extraretinal Inputs to Neurons in the Rostral Superior Colliculus of the Monkey During Smooth-Pursuit Eye Movements

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Krauzlis, Richard J. Extraretinal inputs to neurons in the rostral superior colliculus of the monkey during smooth-pursuit eye movements. *J Neurophysiol* 86: 2629–2633, 2001. The intermediate and deep layers of the monkey superior colliculus (SC) are known to be important for the generation of saccadic eye movements. Recent studies have also provided evidence that the rostral SC might be involved in the control of pursuit eye movements. However, because rostral SC neurons respond to visual stimuli used to guide pursuit, it is also possible that the pursuit-related activity is simply a visual response. To test this possibility, we recorded the activity of neurons in the rostral SC as monkeys smoothly pursued a target that was briefly extinguished. We found that almost all rostral SC neurons in our sample maintained their pursuit-related activity during a brief visual blink, which was similar to the maintained activity they also exhibited during blinks imposed during fixation. These results indicate that discharge of rostral SC neurons during pursuit is not simply a visual response, but includes extraretinal signals.

INTRODUCTION

The intermediate and deep layers of the monkey superior colliculus (SC) have long been known to be important for the generation of saccadic eye movements (for reviews see Moschovakis and Highstein 1994; Sparks and Hartwich-Young 1989; Sparks and Mays 1990; Wurtz and Albano 1980). More recently, it has been shown that the rostral SC might also participate in the generation of pursuit eye movements. Neurons in the rostral SC exhibit the same directional preference during pursuit as during saccades: their firing rate increases for eye movements to the contralateral side and decreases for movements to the ipsilateral side (Krauzlis et al. 1997, 2000). These directional preferences during pursuit can be attributed to the tuning of these neurons for contralateral retinal locations around the fovea—a property that can also account for their tonic activity during fixation. Furthermore, altering activity in the rostral SC by microstimulation or chemical injection modifies the metrics of pursuit (Basso et al. 2000), which is consistent with the idea that the SC provides a position error signal that is used by pursuit as well as by saccades. Although these recent results indicate that the rostral SC plays some role in pursuit, interpretation of the single neuron data is complicated by the fact that these neurons also exhibit visual responses to the stimuli used to guide pursuit. Thus the activity recorded during pursuit might be caused by visual inputs to these neurons that are incidentally modified during pursuit and not caused by signals that are instrumental to the control of pursuit. Indeed, some of the earliest studies of the SC made note of pursuit-related activity (Schiller and Koerner 1971; Wurtz and Goldberg 1972) but generally attributed these to visual responses.

During active fixation, many neurons in the intermediate and deep layers of the rostral SC exhibit tonic activity. By showing that these neurons continued to fire when the visual stimulus was briefly turned off during fixation, Munoz and Wurtz (1993) demonstrated that this fixation-related activity was not simply a visual response. We have now employed a similar test to determine whether the modulation of rostral SC neurons during pursuit is similarly caused by extraretinal input. We report that almost all SC neurons in our sample maintained their discharge during a brief visual blink imposed during maintained pursuit and that the small changes in discharge that do occur tend to be in the same direction as those caused by blinks imposed during fixation. These results show that the discharge of rostral SC neurons during pursuit is not caused by retinal input alone but includes extraretinal signals possibly related to the generation of pursuit.

METHODS

We recorded the activity of single neurons in the rostral SC of two rhesus monkeys (*Macaca mulatta*) weighing 9–12 kg. All experimental protocols were approved by the Institute Animal Care and Use Committee and complied with Public Health Service policy on the humane care and use of laboratory animals. The monkeys were under the care of the Institute veterinarian and were prepared for single-neuron recording using methods that were described previously (Krauzlis et al. 2000). Briefly, under isoflurane anesthesia and aseptic conditions, we implanted a search coil around each eye, using the technique of Judge et al. (1980), and attached a head holder and recording chamber with dental acrylic and titanium screws. During experiments, monkeys sat in a primate chair and faced a video monitor that was used to present visual stimuli under computer control (Vision Research Graphics). Extracellular potentials were recorded from neurons in the intermediate and deep layers of the SC (1.0–3.5 mm below the collicular surface) while monkeys tracked a visual stimulus (a bar 0.2° wide and 0.4° high) in exchange for liquid reinforcement. The placement of the recording tracks was guided by structural magnetic resonance images obtained for both monkeys; histology is not yet available because both monkeys are currently involved in related

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studies. After using visually guided saccades to initially map the response fields, we tested neurons with a pursuit blink paradigm (described in the next paragraph), a fixation blink paradigm (Munoz and Wurtz 1993), and memory-guided saccades (Hikosaka and Wurtz 1983) in separate blocks of trials. Based on the activity during visually guided saccades, we tested neurons using memory-guided saccades with target locations at either 3–5° contralateral (for neurons that exhibited increases during small contraversive saccades) or at 10° ipsilateral (for neurons that did not show such an increase). We selected neurons for study ($n = 71$; $n = 48$ and 23 for *monkeys W* and *A*, respectively) that had the same functional properties as those described previously for rostral buildup neurons (Krauzlis et al. 2000). The majority of these neurons ($n = 59$) met the criteria for fixation cells (Munoz and Wurtz 1993): they maintained a firing rate of at least 10 spikes/s during blinks imposed during fixation. The remainder of our sample ($n = 12$) did not satisfy the definition of fixation cells but did exhibit an increase in activity up to 100 ms before the onset of small (~3–5°) contraversive saccades. As described previously (Krauzlis et al. 2000), both types of neurons appear to compose a single functional class that encodes foveal and parafoveal position errors; we refer to them as rostral buildup neurons. Rostral buildup neurons were typically, although not always, found below rostral burst neurons. Spikes from these neurons were isolated and converted to timing pulses with standard electronics (Bak Electronics) and a template algorithm (Alpha Omega Engineering). Collection of spike and eye movement data and the timing of visual stimuli were under the control of a PC running Tempo software (Reflective Computing).

In the pursuit blink paradigm, monkeys performed the tracking task illustrated in Fig. 1*A*, *top*. The target was initially stationary and located at an eccentricity of 12° and then moved at a constant velocity of 15°/s along the horizontal meridian. At the onset of target motion, we displaced the target ~1.5° in the opposite direction to eliminate the need for corrective saccades (Rashbass 1961). As the target crossed the vertical meridian (0°, dotted line), we blinked the target off for 200 ms (shaded bar). The monkey was rewarded for maintaining eye position within 4° of the target position during maintained pursuit. All neurons were tested with a target motion of 15°/s along the horizontal meridian; most neurons were tested both with contraversive and ipsiversive pursuit (Table 1). In addition, all neurons were tested with the fixation blink task described previously (Munoz and Wurtz 1993). For each rostral SC neuron, we aligned the spike and eye movement data on the onset of the blink and measured the average firing rate during two intervals: *1*) a 100-ms blink interval starting 100 ms after the onset of the blink, to allow for a visual latent period (Fig. 1, boxes labeled "b") and *2*) a 100-ms visible interval starting 100 ms before the onset of the blink (Fig. 1, boxes labeled "v"). Blink and visible measurements were made for both the pursuit and fixation tasks. After sufficient training in the pursuit blink paradigm, monkeys were able to maintain a relatively constant eye speed during the blink interval, as indicated by the sample trace of average eye velocity (Fig. 1*A*). On average, eye velocity during blink intervals was slightly but significantly lower (12.6 and 13.9°/s for *monkeys A* and *W*, respectively) than eye velocity during visible intervals (14.3 and 14.2°/s, respectively). Saccades were detected using a combination of eye velocity and acceleration criteria described previously (Krauzlis and Miles 1996), which allowed saccades as small as 0.2° to be detected. To

TABLE 1. *Numbers of rostral buildup neurons tested in the pursuit blink and fixation blink paradigms*

	Blink < Vis	Blink > Vis	Blink = Vis	Total
Pursuit				
Ipsiversive	3	13	48	64
Contraversive	5	16	48	69
Ipsi and contra	2	6	54	62
Ipsi or contra	6	22	43	71
Fixation	3	20	48	71

A total of 71 neurons were studied during at least one direction of pursuit ("ipsi or contra") and most neurons (62/71) were studied during both directions of pursuit ("ipsi and contra"). All of the neurons tested during pursuit were also tested in the fixation blink paradigm. Neurons were divided into three categories, based upon whether the activity during the blink interval was significantly lower ("blink < vis"), significantly higher ("blink > vis"), or not significantly different ("blink = vis") than the activity during the visible interval (*t*-test or Mann-Whitney rank sum test).

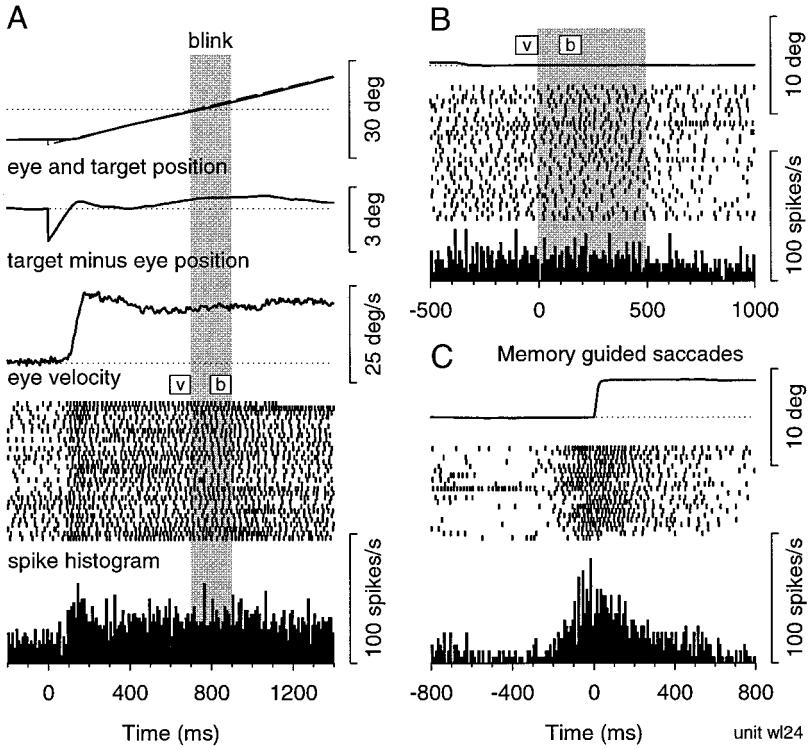

FIG. 1. Activity of a sample rostral superior colliculus (SC) buildup neuron during pursuit, fixation, and saccades when the visual stimulus was removed. *A*: activity during pursuit toward the side contralateral to the recording site. As shown by the raster and spike histogram, the neuron increased its firing rate during pursuit (the target moved at 15°/s) and continued firing when the target stimulus was blinked off for 200 ms (time interval indicated by gray bar). The boxes labeled "v" and "b" indicate the "visible" and "blink" measurement intervals, respectively. Stack of traces shows target and average eye position ($n = 31$ trials), target position − average eye position, and average desaccaded eye velocity (dotted lines indicate 0° and 0°/s). Data are aligned with respect to target motion onset (defined as 0 ms). *B*: activity during fixation. The neuron maintained a constant firing rate during fixation when the target was blinked off for 500 ms (gray bar). Trace above raster and spike histogram indicates average eye position. *C*: activity during memory-guided saccades. The neuron increased its activity when the monkey made a saccade to a remembered stimulus placed 3.5° to the contralateral side. Trace shows average eye position (dotted line indicates 0°). Data are aligned with respect to saccade onset (defined as 0 ms); saccades had latencies of 160–340 ms (mean, 266 ms) with respect to fixation point offset. Bin width for spike histograms is 10 ms.

eliminate any saccade-related modulation from the pursuit and fixation measurements, we excluded all spikes that occurred from 100 ms before to 25 ms after the occurrence of all detected saccades. Statistical significance of differences between measurements was assessed either with a *t*-test or a Mann-Whitney rank sum test, depending on whether or not the data met the criteria for normality and equal variance (SigmaStat).

RESULTS

Most rostral buildup neurons maintained their firing rate during the visual blink applied during either smooth-pursuit eye movements or fixation. Figure 1*A* shows the activity recorded from one sample neuron as the monkey followed a target that was initially stationary and then started to move at a constant speed of 15°/s along the horizontal meridian toward the contralateral (right) side. The neuron had a tonic discharge of ~20 spikes/s during the period of fixation prior to the onset of target motion (defined as time 0) and increased its firing rate to 30–40 spikes/s during pursuit. The increase in activity coincided with changes in position errors (target minus eye position) after the onset of target motion; this increase persisted when the target was blinked off for 200 ms (time interval indicated by gray bar). The same neuron maintained a relatively constant firing rate as the monkey fixated steadily, even when the target was blinked off for 500 ms (Fig. 1*B*), as shown previously for rostral buildup neurons with fixation-related activity (Krauzlis et al. 2000; Munoz and Wurtz 1993). During a memory-guided saccade task (Fig. 1*C*), the neuron exhibited a graded increase in activity that peaked around the onset of the 3.5° contraversive saccade.

We quantified the blink-related changes by comparing the firing rate in a 100-ms blink interval to the firing rate in a 100-ms visible interval. A summary of all of the neurons in the sample ($n = 71$) is provided for pursuit (Fig. 2*A*) and fixation (Fig. 2*B*). Overall, most neurons did not show significant changes in firing rate (open symbols in Fig. 2, *A* and *B*) for stimulus blinks imposed during either pursuit or fixation (Table 1). For those neurons that did exhibit a significant change during the blink (filled symbols), decreases in firing rate were observed in only a small number of neurons during either pursuit (8 data points from 6 neurons) or fixation (3 neurons). To summarize the blink-related changes, we calculated a blink index, which was defined as the average firing rate during the 100-ms blink interval divided by the average firing rate during the 100-ms visible interval. The distributions of these index values for activity during pursuit (Fig. 2*C*; median 1.1) and fixation (Fig. 2*D*; median 1.2) both exhibited peaks near 1.0, as would be expected from the clustering of data points along the unity slope lines in Fig. 2, *A* and *B*. There was no significant difference between the blink index values measured during pursuit and fixation ($P > 0.05$, Mann-Whitney) and neither distribution was significantly different from 1.0 ($P > 0.05$, rank sum test).

The range of blink-induced changes in firing rate is illustrated by the four sample neurons in Fig. 3. The sample included units whose firing rate increased (*top*), remained mostly constant (*middle*), and decreased (*bottom*) during the stimulus blink for pursuit (Fig. 3*A*) and fixation (Fig. 3*B*). However, as evidenced by the similarity between each member

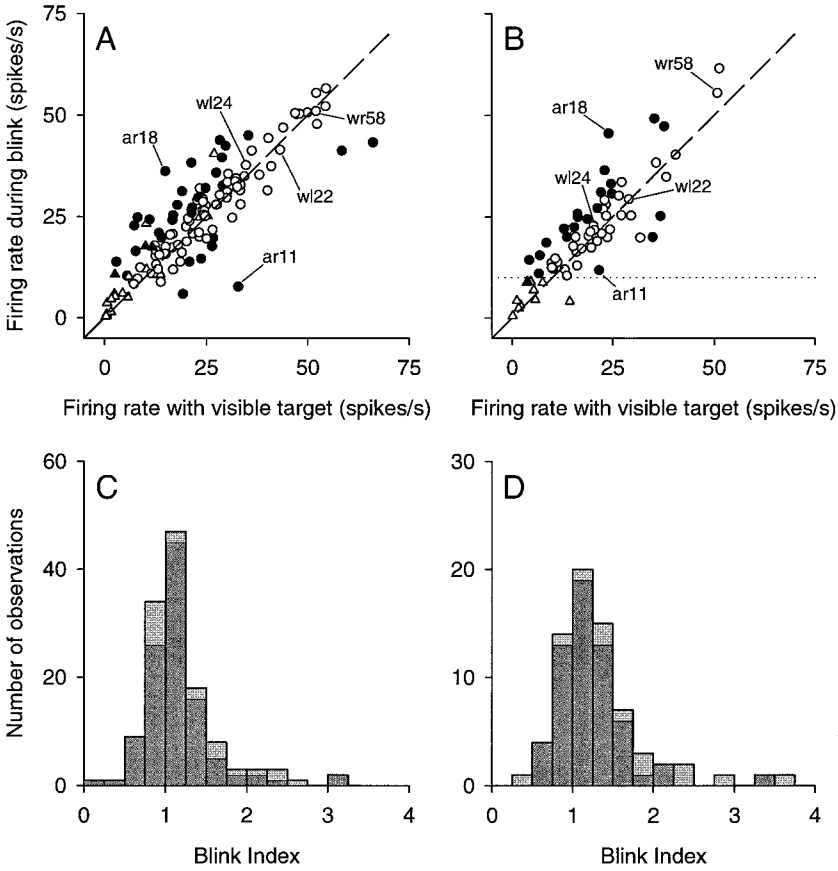

FIG. 2. Summary of rostral buildup neuron activity during stimulus blinks imposed during pursuit and fixation. *A* and *B*: firing rate during the blink interval (a 100-ms interval starting 100 ms after the onset of the blink) is plotted against the firing rate during the visible interval (a 100-ms interval starting 100 ms before the onset of the blink) for pursuit (*A*) and fixation (*B*). Each symbol represents a pair of measurements from a single neuron; filled symbols indicate neurons for which the firing rates in the two intervals were significantly different ($P < 0.05$, *t*-test or Mann-Whitney). Different symbols are used to indicate rostral buildup neurons that also met the criteria for "fixation cells" (circles) and those that did not (triangles). Dashed line indicates unity slope. Labeled lines identify data from neurons whose spike histograms are shown in Figs. 1 and 3. The data are from 71 neurons, most of which were tested both during ipsiversive and contraversive pursuit (see Table 1), producing a total of 133 data points for pursuit (*A*) and 71 data points for fixation (*B*). *C* and *D*: distribution of blink index values measured during pursuit (*C*) and fixation (*D*). The blink index was defined as the average firing rate during the 100-ms blink interval divided by the average firing rate during the 100-ms visible interval. Bars indicate values from neurons that were also fixation cells (dark gray) and those that were not (light gray). The blink index values from ipsiversive pursuit ($n = 64$; median 1.09) and contraversive pursuit ($n = 69$; median 1.08) were combined because the values for the two directions were not significantly different from each other ($P < 0.05$, Mann-Whitney). Three blink index values during pursuit were larger than 4.0 and are not included in the histogram (*C*).

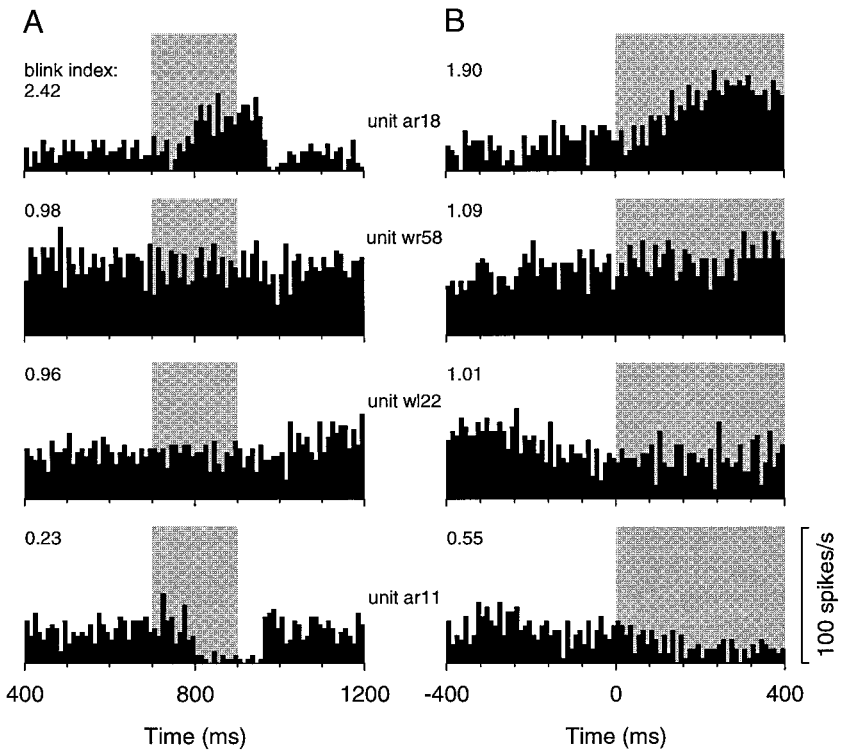

FIG. 3. Range of blink-related changes in firing rate of rostral SC neurons. Each row of plots shows a pair of spike histograms from a single neuron recording during either pursuit (*A*) or fixation (*B*). The target stimulus was blinked off during the time intervals indicated by the gray bar. The numbers listed with each histogram indicate the blink index measured from the data. Bin width for spike histograms is 10 ms.

of paired spike histograms, changes in firing rate associated with stimulus blinks tended to be similar both for pursuit and fixation. We tested the correspondence between blink-related changes during pursuit and fixation by measuring the correlation between the blink index values obtained during pursuit and fixation across the sample of neurons (for pursuit, we took the average of the two blink index values for contraversive and ipsiversive tracking). The blink index values measured for pursuit were modestly but significantly correlated with those measured for fixation ($r = 0.47$, $P < 0.01$, Spearman rank order correlation), which indicated that blink-related changes in firing rate tended to be in the same direction during pursuit and fixation.

To document saccade-related activity, we also examined most of the neurons ($n = 66/71$) during memory-guided saccades. The target location for the memory-guided saccade task was based on the activity during the initial mapping with visually guided saccades. Approximately half of the neurons ($n = 32$, including 24 fixation cells) exhibited increases in activity during small, visually guided saccades to the contralateral side. For these neurons, we observed increases in activity during saccades to remembered stimuli placed at near eccentricities (3–5°) in the contralateral hemifield (Fig. 4, circles). Similar to buildup neurons at more caudal locations in the SC (see Fig. 19*C* in Munoz and Wurtz 1995), the burst activity for these neurons was generally preceded by lesser buildup activity. The remaining neurons ($n = 34$ fixation cells) either increased their activity during visually guided saccades that were too small to test with memory-guided saccades or decreased their activity for all visually guided saccades tested. For these neurons, we observed decreases in activity for remembered stimuli placed 10° in the ipsilateral hemifield (Fig. 4, squares). As shown previously for fixation cells (Munoz and Wurtz 1995), the burst and buildup activities of these neurons were negative for 10° (or larger) saccades. Thus, the neurons we tested with a visual blink during pursuit share the same properties as those previously identified as rostral buildup neurons or fixation cells (Krauzlis et al. 2000; Munoz and Wurtz 1993).

DISCUSSION

We found that the majority of rostral buildup neurons in the monkey SC maintain their firing rate during a brief

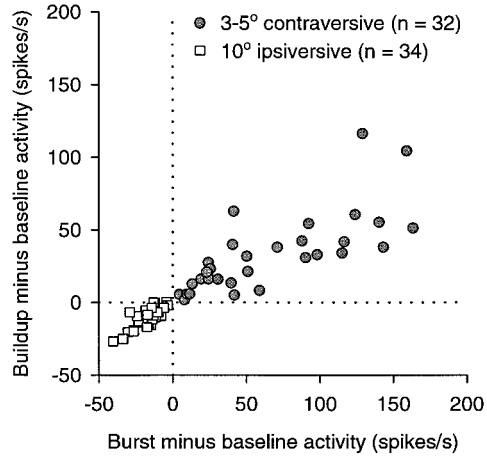

FIG. 4. Activity of rostral buildup neurons during memory-guided saccades. Buildup minus baseline activity is plotted against burst minus baseline activity. Buildup minus baseline activity was defined as the firing rate during the buildup interval (a 75-ms interval starting 100 ms before saccade onset) minus the firing rate during the baseline interval (a 100-ms interval starting 100 ms before fixation point offset). Burst minus baseline activity was defined as the firing rate during the burst interval (spanning 8 ms prior to saccade onset until 8 ms prior to saccade end) minus the firing rate during the baseline interval. Each symbol represents a pair of measurements from a single neuron. Gray circles indicate neurons tested with 3–5° contraversive saccades; open squares indicate neurons tested with 10° ipsiversive saccades.

visual blink imposed during pursuit. Significant decreases in firing rate were observed in only a handful of neurons for blinks imposed during either pursuit (6/71) or fixation (3/71). Furthermore, the changes in firing rate observed for blinks during pursuit were roughly correlated with the changes observed for blinks during fixation. These results indicate that the discharge during pursuit for the majority of buildup neurons in the rostral SC is not caused by visual input alone but includes an extraretinal signal.

These results address an issue similar to that raised previously concerning the pursuit-related activity of neurons in the middle temporal (MT) and medial superior temporal (MST) areas of extrastriate cortex. By briefly turning off the visual stimulus during maintained pursuit, Newsome et al. (1988) found that some neurons in MST continued firing during the visual blink, indicating that they received an extraretinal input, whereas neurons in foveal MT decreased their firing during the visual blink, indicating that their pursuit-related activity was caused by visual input. Similar to the interpretation of the extraretinal signal observed in MST (Newsome et al. 1988), it is possible that the extraretinal signal we observed during pursuit might have been caused by an efference copy of the eye velocity command for pursuit. However, the activity of most rostral SC neurons during pursuit and fixation is better accounted for by tuning for retinotopic positions around the fovea than by sensitivity to eye velocity (Krauzlis et al. 2000). This suggests an alternative interpretation: the extraretinal signal we observed might have been a corollary discharge related to the small position errors that occur during pursuit and fixation. We conclude that, although the exact function and etiology of the activity during pursuit remains unclear, the results rule out the trivial possibility that this activity is simply a visual response. Instead, the results indicate that the signals provided by rostral SC neurons during pursuit and fixation might be based on motor, predictive, or other higher-order signals, as well as on more direct visual inputs.

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