T. J. Turner, S. M. Goldin, *Science* **252,** 443 (1991); I. Bezprozvanny, J. Watras, B. E. Ehrlich, *Nature* **351,** 751 (1991); J. H. Horne and T. Meyer, *Biochemistry* **34,** 12738 (1995).
15. M. D. Stern, *Cell Calcium* **13,** 183 (1992).
16. J. H. Horne and T. Meyer, data not shown.
17. We thank C. Nicchitta, G. Augustine, P. Casey, J. Thissen, and K. Dolinski for helpful discussions, and M. Teruel for setting up the electroporation apparatus and the rapid image capturing system. Synthesis of caged $InsP_3$ was performed in the laboratory of J. Walker (University of Wisconsin, Madison, WI; supported by NIH grant P01-HL-47053). Supported by NIH grants RO1-GM-48113 and GM-51457.

22 October 1996; accepted 28 April 1997

Shared Motor Error for Multiple Eye Movements

R. J. Krauzlis,* M. A. Basso, R. H. Wurtz

Most natural actions are accomplished with a seamless combination of individual movements. Such coordination poses a problem: How does the motor system orchestrate multiple movements to produce a single goal-directed action? The results from current experiments suggest one possible solution. Oculomotor neurons in the superior colliculus of a primate responded to mismatches between eye and target positions, even when the animal made two different types of eye movements. This neuronal activity therefore does not appear to convey a command for a specific type of eye movement but instead encodes an error signal that could be used by multiple movements. The use of shared inputs is one possible strategy for ensuring that different movements share a common goal.

Distinct sensory and motor functions are localized in different regions of the brain. In the visual system, for example, attributes such as form and motion may be processed in largely separate areas (*1*). However, it is not known how the results of such specialized processing are combined to produce a single coherent percept, an issue that is often referred to as the "binding problem" (*2*). A similar question applies to motor systems, because most actions, despite their unitary appearance, are composed of multiple movements, each controlled by different brain regions. For example, when we visually search the contents of a room, we use a combination of saccadic and pursuit eye movements, interspersed with periods of fixation. The individual movements are quite distinct: Saccades are brief high-velocity movements that interrupt fixation and abruptly reorient the eyes toward eccentric visual targets, whereas pursuit is a continuous slow movement that smoothly rotates the eyes to maintain alignment with moving targets. These movements are also mediated by largely distinct neuroanatomical pathways (*3*). The anatomical pathways underlying saccades and fixation include such cortical regions as the lateral intraparietal sulcus and the frontal eye fields and such subcortical regions as the superior colliculus and brainstem reticular formation. In contrast, the pathways underlying pursuit include such cortical regions as the middle temporal area and medial superior temporal sulcus and such subcortical regions as the basilar pons and cerebellum. What enables these different oculomotor subsystems to interact harmoniously, despite this modular design? One possibility is that they overlap at early stages of movement preparation. For example, the visual capture of a single target with different types of eye movements would be facilitated if they shared a mechanism for target selection. Indeed, recent behavioral experiments have suggested that there are common inputs for triggering the onset of saccades and pursuit (*4*). The data from our present study provide evidence for overlap in the underlying neural pathways.

Our experiments focused on the superior colliculus (SC) of primates, a laminated midbrain structure known to be important for the generation of saccadic eye movements (*5*). The superficial layers of the SC contain visually responsive neurons that form a retinotopic map of visual space, whereas the deeper layers contain saccade-related neurons that form a corresponding motor map. In most of this motor map, neurons in the intermediate and deep layers increase their firing rate before, or burst during, saccades of a particular direction and amplitude. However, in the portion of the map corresponding to the fovea, located at the rostral end of the SC, neurons are tonically active during periods of steady fixation and decrease their firing rate for most saccades. Accordingly, these neurons have been referred to as "fixation cells" in the cat (*6*) and monkey (*7*) and are believed to be important for determining when saccades are initiated. We now show that these neurons report mismatches between eye and target positions as do neurons elsewhere in the SC motor map. Furthermore, they are also modulated by the small mismatches that occur during pursuit eye movements. Together, these two results suggest that SC neurons might encode a more general form of motor error rather than commands for specific movements.

We first show that neurons in the rostral

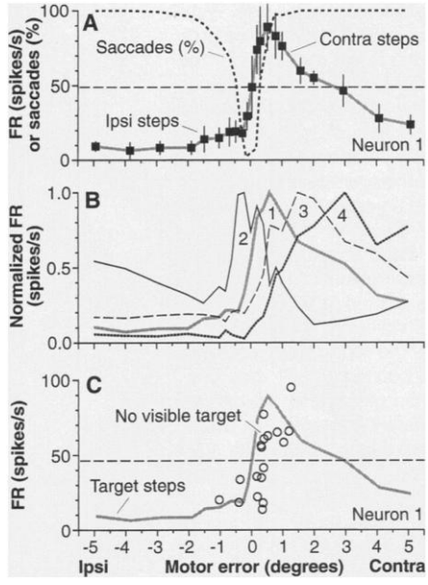

Fig. 1. Tuning of neurons in the rostral SC for small mismatches between eye and target positions. (**A**) Modulation in the firing rate (FR) of neuron 1 recorded after small ipsiversive (ipsi) and contraversive (contra) steps of a target presented on a homogeneous background. Square symbols plot the average firing rate from 12 trials over an interval beginning 100 ms after the step and lasting either 100 ms or until 8 ms before any corrective saccade. Error bars indicate ±1 SD. Dotted line indicates the percentage of trials in which each amplitude of the target step elicited a saccade. Saccades were detected as any eye movement exceeding 5°/s and 800°/s^2; these criteria identified saccades as small as 0.05°. Dashed line indicates the average firing rate with no target steps. (**B**) Modulation of four rostral SC neurons (numbers 1 through 4) after small steps; all were recorded from the right SC of one monkey. The data have been normalized so that the peak of each curve equals 1. (**C**) Firing rate of neuron 1 recorded as the monkey maintained fixation after the visual stimulus was extinguished. Circles indicate the average firing rate during each of 18 saccade-free intervals lasting 73 to 230 ms and are plotted as a function of the average motor error during each interval. Dashed line indicates the average firing rate across all intervals. The superimposed gray curve shows the discharge of the same neuron when the stimulus was still present, as in (A).

Laboratory of Sensorimotor Research, National Eye Institute, National Institutes of Health, Bethesda, MD 20892, USA.

*To whom correspondence should be addressed at Salk Institute, Post Office Box 85800, San Diego, CA 92186, USA.

SC were tuned for small mismatches between eye and target positions during fixation, mismatches that are often referred to as "saccadic motor errors." While we were recording from single neurons in the rostral SC (8), we stepped a stationary and fixated target spot unexpectedly to eccentric locations along the horizontal meridian. Such steps caused changes in the firing rate that began 50 to 70 ms after the target displacement and often resulted in small corrective saccades. The average firing rate measured in the interval after the transient visual response but before the saccade-related activity is shown for one neuron in Fig. 1A (9). As indicated by the solid line, the neuron showed an increase in activity for contralateral steps less than 2° (with a peak at ~0.5°), with reduced activity at all flanking locations (the horizontal dashed line indicates the firing rate with zero motor error). The superimposed dotted line shows the frequency with which each amplitude of target step elicited saccades: The dip around zero indicates that small steps usually did not elicit saccades. This "dead zone" for saccades is noteworthy, because the firing rate of this neuron was strongly modulated by small (0.2° to 0.4°) contraversive and ipsiversive steps, even though these displacements resulted in maintained fixation. However, steps that were just slightly larger (0.5° to 1.0°) produced similar changes in the firing rate but almost always elicited saccades. The firing rate of this neuron was therefore not predictive of whether a saccade would be made, but it was tuned for a particular range of saccadic motor errors.

Other neurons in the rostral SC were likewise tuned for mismatches between eye and target positions, but not necessarily for the same range of step sizes. For example, the graph in Fig. 1B shows tuning curves for four neurons: the same neuron as in Fig. 1A plus three additional neurons. As suggested by these curves, the population of neurons encoded a range of saccadic motor errors around the fovea: The peaks of the tuning curves ranged from 3.2° contralateral to 0.4° ipsilateral (mean, 0.99° contralateral; n = 20), with the majority (75%) located on the contralateral side. Neurons in the rostral SC therefore do not appear to constitute a separate group but form a continuum with saccade-related neurons in the caudal SC, differing only in the range of saccadic motor errors that they represent (7). The apparent functional differences between fixation-related and saccade-related neurons may result not from membership in different oculomotor subsystems but from the contrasting relevance of small and large errors to the two forms of eye movement control.

The modulation in firing rate was not simply a visual response because, as shown in previous studies (7), these neurons continued to fire as the monkey maintained fixation even after the visual stimulus was extinguished. For example, the circles in Fig. 1C plot the average firing rate of neuron 1 during short (73- to 230-ms) saccade-free intervals after the target was extinguished. The average firing rate during these intervals (46 spikes/s, shown by the dashed line in Fig. 1C) was not much different from that observed during fixation of a visible target (49 spikes/s, shown by the dashed line in Fig. 1A). Of the neurons tested (n = 19), most maintained or even increased their firing rate during fixation in the absence of a visual stimulus, compared to the firing rate obtained during fixation of a stationary target (average, 133%; range, 57 to 434%). While we were recording from some neurons, we also found that the changes in the firing rate appeared to be related to the variation in eye position after the target was extinguished. The importance of this correlation is that eye position may be related to the motor error associated with the invisible target. As shown in Fig. 1C (gray curve) for neuron 1, the data obtained in the absence of a visible target (circles) displayed a trend that paralleled the tuning curve determined with small target steps (as in Fig. 1A). This correspondence suggests that the tuning of the neuron may reflect an internal estimate of the target location (10).

We next show that the same neurons in the rostral SC were also modulated by the small mismatches between target and eye positions that occurred during pursuit eye movements. Results from neuron 1 are shown in Fig. 2. Consistent with its activity during zero error (Fig. 1), the firing rate of this neuron was 36 to 52 spikes/s (horizontal dashed lines in Fig. 2, A and B) during the period of steady fixation when the target was stationary. When the target (T) moved at a constant speed toward the ipsilateral side (Fig. 2A), the firing rate decreased approximately 70 to 80 ms after the onset of target motion, around the onset of the pursuit eye movement (E, the superimposed eye position traces from each trial, and $\bar{E}$, the average eye velocity across all trials), as indicated by the vertical line. When the target moved toward the contralateral side (Fig. 2B), the firing rate increased around the onset of pursuit. After the initial changes during the onset of pursuit, the firing rate tended to recover by the end of the trial as the eyes more closely matched the movement of the target (Fig. 2, A and B). As summarized in Table 1, the effects displayed by this neuron were representative of our sample. For ipsiversive pursuit, 71% (22 of 31) showed significant changes in the firing rate during the onset

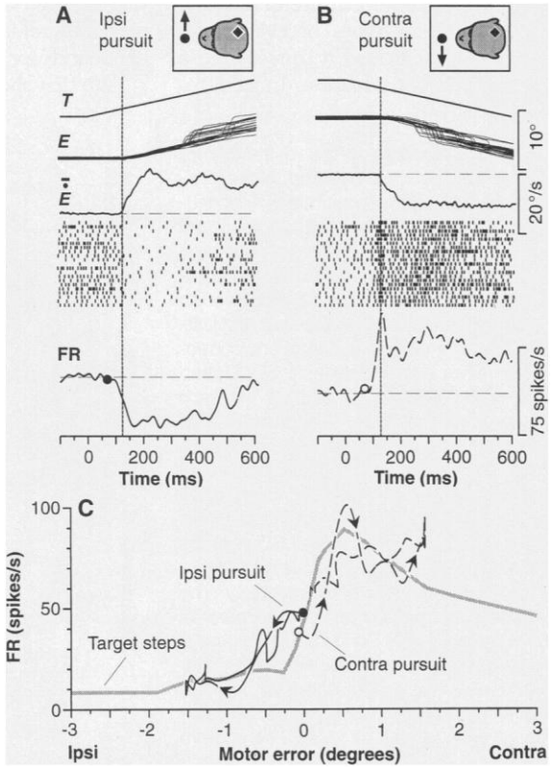

Fig. 2. Response of a neuron in the rostral SC during pursuit eye movements of a ramp target motion. (**A**) and (**B**) Activity of a neuron (1 from Fig. 1) shown during pursuit directed toward the ipsilateral (ipsi) (A) or contralateral (contra) (B) side. Within each panel, the stack of records shows the target position (T), the superimposed eye position traces from each trial (E), the average eye velocity across all trials ($\bar{E}$), a raster display of the neuronal responses, and the average firing rate (FR) shown as a spike density function (using a Gaussian curve with σ = 10 ms). Records are aligned on the onset of target motion (10°/s ramp), which is defined as time zero; vertical lines indicate the onset of pursuit. (**C**) The firing rate of neuron 1 recorded during pursuit as a function of the motor error 70 ms before. Different line types plot the firing rates during ipsiversive (solid line) and contraversive (dashed line) pursuit. Filled and open circles indicate the start of the two curves, corresponding to the firing rate at 70 ms after the onset of target motion. Arrows placed along the curves indicate increasing time. For clarity, arrows are placed only on data from the first half of the trial, when the motor error was increasing. The gray curve is as in Fig. 1C.

of pursuit; all of these changes were decreases. For contraversive pursuit, 74% (23 of 31) showed significant changes in the firing rate: of these, 70% (16 of 23) showed an increase, like the neuron shown in Fig. 2B, whereas 30% (7 of 23) showed a decrease (*11*).

To test whether the changes in the firing rate observed during pursuit were related to the position errors that occurred during tracking, we plotted the same data as a function of motor error rather than as a function of time. We first determined the motor error as a function of time by subtracting eye position from target position. We then plotted the firing rate of the neuron as a function of the motor error one visual latency ago (70 ms) for both directions of pursuit (*12*). The resulting functions are shown by the solid and dashed curves in Fig. 2C. When the target first began to move toward the ipsilateral side (indicated by the filled circles in Fig. 2, A and C), the eyes were stationary; consequently, the firing rate of the neuron dropped as the motor error became progressively more ipsilateral. Once the eyes began to move, the firing rate returned toward its resting rate as the motor error was reduced. Conversely, when the target moved toward the contralateral side (open circles in Fig. 2, B and C), the firing rate increased as the motor error initially increased but later approached its baseline as the contralateral motor error decreased.

Finally, we compared the data obtained during pursuit with the tuning observed with small target steps. As shown in Fig. 2C by the superimposed gray curve (copied from Fig. 1C), the changes in the firing rate observed during pursuit showed a close correspondence to the tuning for the saccadic motor error. We assessed the degree of similarity between the two sets of data by performing a χ^2 test (*13*); the resulting Q score was 0.99, which indicated that there was a 99% probability that the differences between the two sets of data were due to chance. For our sample of 20 neurons tested with both pursuit and steps, the average Q score was 0.819 (range, 0.33 to 0.99), and 11 neurons (55%) had Q scores greater than 0.98. Thus, for the majority of neurons, the firing rate during pursuit eye movements displayed a dependence on motor error that was not different from that observed with small target steps imposed during fixation.

Table 1. Summary of neurons recorded during pursuit eye movements. Changes in firing rate during the onset of pursuit were assessed by comparison of the average firing rates in two intervals: (i) 0 to 100 ms after the onset of target motion (baseline) and (ii) 0 to 100 ms after the onset of eye motion (initiation). Numbers in table indicate the percentage of total neurons (n = 31) showing a significant increase or decrease or no change in firing rate between these two intervals ($P < 0.05$, t test).

	Contraversive pursuit			
	Increase (%)	Decrease (%)	None (%)	Total (%)
Ipsiversive pursuit				
Increase (%)	0	0	0	0
Decrease (%)	32	16	23	71
None (%)	19	6	3	29
Total (%)	52	23	26	100

These results indicate that the firing rate of these neurons in the rostral SC is related to small mismatches between eye position and target position, regardless of whether these errors are associated with a subsequent saccadic or pursuit eye movement or no eye movement. These findings simplify the interpretation of this class of movement-related neurons in the SC, because they argue that there are no fundamental differences between "buildup cells" in the caudal SC and "fixation cells" in the rostral SC; both are tuned for particular, albeit different, amplitudes of motor error. More generally, these findings warrant reconsideration of how these neurons participate in movement preparation. Previous studies have considered the encoding of motor error in the SC to be synonymous with the preparation of a saccade to that location (*5*). Although this may be true in most of the SC, a peculiar aspect of neurons in the rostral SC is that they encode small motor errors that can be either left unresolved or corrected with small saccades or pursuit. Although the modulation in activity that we observed during fixation and pursuit might reflect the planning of saccades that do not get executed, an alternative possibility is that these neurons are not obligatorily linked to a particular motor output but lie upstream from or are part of the sites that determine how and whether to accomplish the movement. At the extreme, our results, together with reports of SC neurons active during head movements (*14*) and even arm movements (*15*), raise the possibility that these neurons encode a more general form of motor error that influences these other movements. The availability of such common error signals could provide a means for maintaining unity across the multiple movements that compose most actions.

REFERENCES AND NOTES

1. S. Zeki, *A Vision of the Brain* (Blackwell Scientific, Oxford, 1993); D. C. Van Essen and J. L. Gallant, *Neuron* **13**, 1 (1994).
2. W. Singer and C. M. Gray, *Annu. Rev. Neurosci.* **18**, 555 (1995).
3. For reviews, see R. J. Leigh and D. S. Zee, Eds., *The Neurology of Eye Movements* (Davis, Philadelphia, PA, 1991).
4. The latency of saccadic and pursuit eye movements is similarly reduced in the "gap paradigm" in both monkeys and humans [R. J. Krauzlis and F. A. Miles, *Vision Res.* **36**, 1973 (1996); *J. Neurophysiol.* **76**, 2822 (1996)]. These data have been interpreted as evidence that there are shared inputs for the initiation of the two types of eye movements. Earlier studies have shown, for example, that lesions of the middle temporal area affect both the speed of pursuit and the amplitude of saccades in response to moving targets [W. T. Newsome, R. H. Wurtz, M. R. Dursteler, A. Mikami, *J. Neurosci.* **5**, 825 (1985); P. H. Schiller and K. Lee, *Visual Neurosci.* **11**, 229 (1994)], but these effects have been interpreted as overlap in sensory processing rather than in movement preparation.
5. D. L. Sparks and L. E. Mays, *Annu. Rev. Neurosci.* **13**, 309 (1990).
6. D. P. Munoz and D. Guitton, *J. Neurophysiol.* **66**, 1624 (1991).
7. D. P. Munoz and R. H. Wurtz, *ibid.* **67**, 1000 (1992); *ibid.* **70**, 559 (1993).
8. We recorded from 31 neurons in the rostral SC of two rhesus monkeys (*Maccaca mulatta*) and obtained similar results in both monkeys, although not all experiments were performed on each cell. The monkeys were trained to look at and follow small (0.3°) spots of light projected onto a featureless background. At the end of individual trials lasting 1 to 2 s, monkeys were given a liquid reinforcement if they maintained their eye position near the target (within 2° for stationary targets and 5° for moving ones). The eye movement and single unit data were acquired with standard methods (*7*). All experimental protocols were approved by the Institutional Animal Care and Use Committee of the National Eye Institute and complied with the Public Health Service Policy on the humane care and use of laboratory animals.
9. The measurement interval started 100 ms after the change in target location and lasted either for 100 ms or until 8 ms before any corrective saccade, whichever came first. This interval was selected to reduce the inclusion of transient activity that was overtly related to the visual stimulus or to subsequent saccadic eye movements. These measurements were therefore taken in a time period that largely excluded the saccade-related activity reported in earlier studies (*7*).
10. Linear regressions were performed on the data from each of 19 neurons; 5 of these showed a significant relation ($P < 0.05$). The absence of a correlation in the remaining neurons may have resulted from the narrow range of eye positions fostered by this experiment and the inability to control the inferred location of the target after it was extinguished.
11. Neurons that decreased their firing rate during contraversive pursuit tended to be tuned for motor errors near zero or slightly ipsilateral (mean, 0.10° ipsilateral; n = 5), whereas neurons that increased their firing rate during contraversive pursuit tended to be tuned for larger contralateral errors (mean, 1.54° contralateral; n = 11).
12. Seventy milliseconds was chosen on the basis of the observed latency of the response to target steps.
13. Each millisecond sample of firing rate recorded during pursuit was assigned to a bin according to motor error; these bins matched the 21 amplitudes of motor error obtained with target steps during fixation (Fig. 1).
14. E. G. Freedman and D. L. Sparks, *Soc. Neurosci. Abstr.* **20**, 142 (1994).
15. W. Werner, *Eur. J. Neurosci.* **5**, 335 (1993).

16. We thank R. Desimone, L. Stone, and our colleagues at the Laboratory of Sensorimotor Research for their comments on an earlier draft of this paper and the Laboratory of Diagnostic Radiology Research for providing magnetic resonance images.

26 December 1996; accepted 29 April 1997