

Reversible Inactivation of Monkey Superior Colliculus. I. Curvature of Saccadic Trajectory

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Aizawa, Hiroshi and Robert H. Wurtz. Reversible inactivation of monkey superior colliculus. I. Curvature of saccadic trajectory. *J. Neurophysiol.* 79: 2082–2096, 1998. The neurons in the intermediate layers of the monkey superior colliculus (SC) that discharge before saccadic eye movements can be divided into at least two types, burst and buildup neurons, and the differences in their characteristics are compatible with different functional contributions of the two cell types. It has been suggested that a spread of activity across the population of the buildup neurons during saccade generation may contribute to the control of saccadic eye movements. The influence of any such spread should be on both the horizontal and vertical components of the saccade because the map of the movement fields on the SC is a two-dimensional one; it should affect the trajectory of saccade. The present experiments used muscimol injections to inactivate areas within the SC to determine the functional contribution of such a spread of activity on the trajectory of the saccades. The analysis concentrated on saccades made to areas of the visual field that should be affected primarily by alteration of buildup neuron activity. Muscimol injections produced saccades with altered trajectories; they became consistently curved after the injection, and successive saccades to the same targets had similar curvatures. The curved saccades showed changes in their direction and speed at the very beginning of the saccade, and for those saccades that reached the target, the direction of the saccade was altered near the end to compensate for the initially incorrect direction. Postinjection saccades had lower peak speeds, longer durations, and longer latencies for initiation. The changes in saccadic trajectories resulting from muscimol injections, along with the previous observations on changes in speed of saccades with such injections, indicate that the SC is involved in influencing the eye position during the saccade as well as at the end of the saccade. The changes in trajectory when injections were made more rostral in the SC than the most active burst neurons also are consistent with a contribution of the buildup neurons to the control of the eye trajectory. The results do not, however, support the hypothesis that the buildup neurons in the SC act as a spatial integrator.

INTRODUCTION

Saccades are the rapid eye movements used to redirect gaze. Visually guided saccades require that information, represented on spatial maps in the visual system, be transformed into temporally modulated activity in the oculomotor system. One of the key sites in the brain involved in this visual-motor transformation is the superior colliculus (SC). Neurons in the intermediate layers of the SC discharge before saccades, and stimulation of the SC evokes saccades (see review by Sparks and Hartwich-Young 1989). These saccade-related neurons recently have been divided into two general categories: burst neurons and buildup neurons (Munoz and Wurtz 1995a). Burst neurons have a brief visual response and then a sharp increase in activity just before the onset of saccades

of given amplitude and direction and are also referred to as saccade-related burst neurons (Sparks 1978). Buildup neurons frequently also have a burst of activity just before saccades but in addition have a buildup of activity before saccade onset. The feature used to distinguish between burst and buildup neurons is the continuing activity in the interval between the initial visual response and the onset of the saccade in buildup neurons, and the lack of that activity in burst neurons. The buildup neurons share this increase in activity before the saccade with the long-lead saccade-related neurons (Mohler and Wurtz 1976), the quasivisual cells (Mays and Sparks 1980), and the prelude bursters (Glimcher and Sparks 1992).

Each burst or buildup neuron has a movement field: the area of the visual field associated with an increase in the discharge rate before saccades to that part of the visual field (Wurtz and Goldberg 1972). The movement fields of individual cells form an orderly two-dimensional map within the intermediate layers of the SC in register with the visual fields in the superficial layers (Cynader and Berman 1972; Mohler and Wurtz 1976; Wurtz and Goldberg 1972). The shape of the movement fields of the burst and buildup neurons is frequently different. Burst neurons increase their discharge rate before saccades of a given optimal direction and amplitude. Before saccades of substantially larger or smaller amplitudes, they show no change in activity so that these movement fields are well circumscribed and have been referred to as closed movement fields (Munoz and Wurtz 1995a). Most buildup neurons, on the other hand, discharge before any saccade in a given direction that is larger than a given amplitude, and these movement fields have been referred to as open-ended (Munoz and Wurtz 1995a). Within these open-ended movement fields, the timing of the discharge with respect to the saccade changes systematically; for saccades with larger and larger amplitudes beyond the optimal for the particular buildup neuron, the discharge occurs later and later during saccade generation. This progressively later activity for neurons more rostral within the SC led to the suggestion that the activity in these buildup neurons represents a spread of activity across the SC from caudal to rostral during the course of a saccade (Munoz and Wurtz 1995b). This spread of activity in the monkey SC shares with the moving hill of activity in the cat, described earlier by Munoz et al. (1991), the characteristic that neurons more rostral in the SC than those initially active become active later in the course of the saccade.

The differences in the activity between the burst and buildup neurons led to the suggestion that they play different roles in the generation of saccades (Munoz and Wurtz

1995b; Optican 1994). The burst neurons were taken as providing the desired change in eye position that would be carried out by the impending saccade, as had been proposed previously (see review by Sparks and Mays 1990), but a different role was proposed for the spread of activity among the buildup neurons. In both the cat (Lefèvre and Galiana 1992; Munoz et al. 1991) and the monkey (Munoz and Wurtz 1995b; Optican 1994), the hypothesis was that the moving hill or the spread of activity conveys information about the movement of the eye during the saccade. A specific hypothesis of the role of this spread of activity in the monkey was advanced by Optican (1995), who suggested that the spread of activity might fulfill the requirements of the resettable integrator that is a necessary component in the feedback control models of saccade generation. In the present experiments we have attempted to test the predictions of this specific model and of the more general hypotheses that the spread of activity influences the movement of the eye during the saccade.

The specific predictions of the SC as a resettable integrator can best be specified using the simplified outline of the model shown in Fig. 1A. This model (Optican 1994, 1995) is a modification of the feedback control model originally proposed by Robinson (1975) and incorporates a resettable integrator in the feedback pathway (Jürgens et al. 1981). The SC provides two outputs. The burst cells provide the desired direction and amplitude of the saccade (the ΔE in Fig. 1A). Thus the population of burst cells active before the saccade indicate the amplitude and direction of the impending saccade. The buildup cells convey information about how far the saccade has progressed (the $\Delta E'$ signal in Fig. 1A); the spread of activity in the buildup cells across the two-dimensional map of the SC acts as a spatial integrator that fills the role of the resettable integrator. The spread across the buildup layer is driven by the velocity command generated in the brain stem; as the activity spreads toward the rostral pole, the distribution of activity changes and the $\Delta E'$ increases. When the output of the buildup layer ($\Delta E'$) matches that of the burst neurons (ΔE) at a summing junction outside the SC, the motor error (e_m in Fig. 1A) goes to zero, and the saccade ends. A more general view of the function of the spread of activity across the buildup neurons is that the entire trajectory of the saccade is influenced by this spread of activity and, that is, by the distribution of activity across the buildup layer.

A critical test of the functional contribution of such a spread of activity among the buildup neurons would be to alter this activity and measure any resulting changes in saccades. The model predicts that when the spread is disrupted the output of the buildup layer ($\Delta E'$) should be affected. In particular, when the injection is rostral within the SC, the center of activity in the buildup layer should be pushed caudally, resulting in hypermetric saccades. Such an alteration of the SC pattern of activation ought to change not

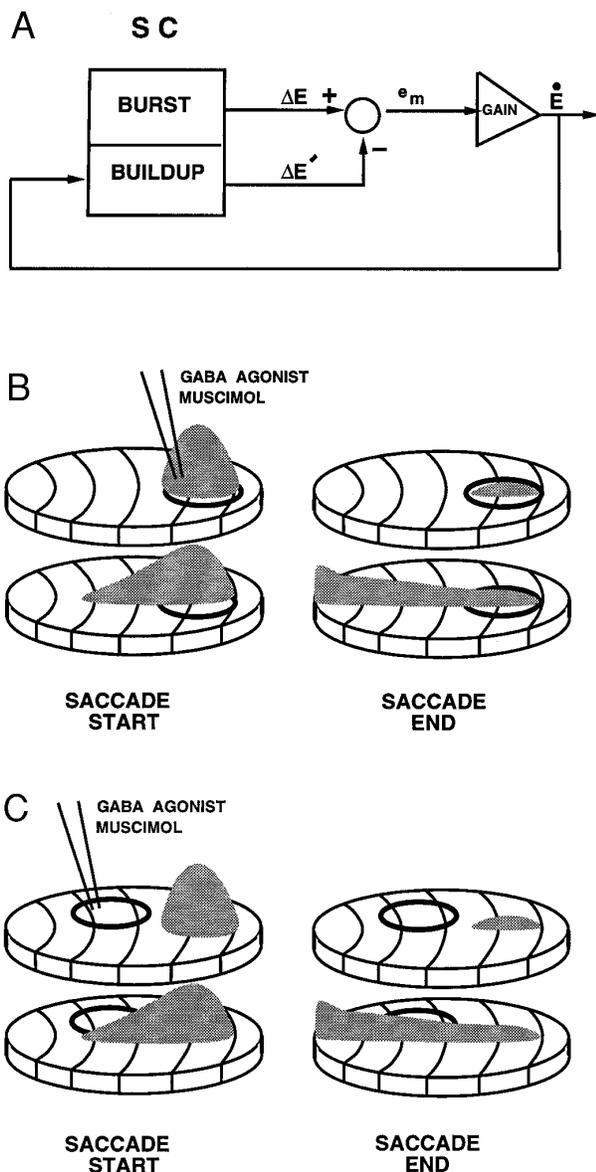


FIG. 1. Logic of the muscimol injections within the superior colliculus (SC) as a test of the function of the spread of activity among the buildup neurons during saccade generation. A: the feedback control model for saccade generation advanced by Optican (1995). Of the 2 outputs from the SC, the burst neurons provide the desired change in eye position (ΔE) and the buildup neurons provide the current extent to which the eye position has changed during the saccade ($\Delta E'$). When these 2-dimensional values are equal there is no longer a motor error (e_m), the eye velocity signal goes to zero, and the eye stops moving. The eye velocity signal also is fed back to the buildup neurons and is envisioned as the necessary input for producing the spread of activity in these neurons. Reducing the activity of the buildup neurons should reduce $\Delta E'$, which should lead to saccades that overshoot the target. B and C: effect of muscimol injections into different regions of the SC map. The schematic drawing shows the map for the burst and buildup neurons on separate layers because these neurons tended to be recorded at different depths within the SC. The activity in the population of neurons is indicated for a sample saccade of $\sim 40^\circ$ in amplitude by the mound of activity in each layer; the size of the mounds are derived from the experimental observations of Munoz and Wurtz (1995b). The activity in the 2 layers is shown schematically at about the start of the saccade (left) and at about the end of the saccade (right). In B, the muscimol injection is placed caudal on the SC map and should affect both burst and buildup neurons. In C, the muscimol injection is placed so that it maximally affects neurons rostral to the area of the SC where the burst and buildup neurons are initially active related to the impending saccade. Any spread of activity should cross the SC area maximally affected by the muscimol injection. Whereas the optimal experiment would inactivate only buildup neurons, the muscimol inactivations alter activity in both the burst and the buildup neurons. The rostral and caudal injections may also be accompanied by a diffusion of muscimol that would be beyond that shown schematically.

only the horizontal and vertical position at the end of the saccade, but it should change the relative horizontal and vertical contributions to the saccadic trajectory: the curve traced out by plotting the vertical component of the movement against its horizontal component.

Figure 1, *B* and *C*, illustrates the logic of our experiment. The burst and buildup neurons are represented schematically by the separate layers on the map of the SC because these cells were found at slightly different depths within the SC (Munoz and Wurtz 1995a). The map extends from the rostral end on the left representing small saccades to the caudal end representing large saccades, with saccadic directions having upward or downward components being more medial or lateral within the layers. The shaded mounds of activity represent the populations of active neurons at the start of the saccade (Fig. 1, *B* and *C*, *left*) and near the end of the saccade (Fig. 1, *B* and *C*, *right*). The activity of the burst neurons simply rises and falls at one location; the activity of the buildup neurons shows a rostral spread of activity. We used injections of a γ -aminobutyric acid (GABA) agonist (muscimol) to reversibly reduce the activity of the SC neurons. Muscimol should act at the endogenous GABA_A receptors on neurons near the injection site within the SC, should inhibit the activity of these neurons, and should reduce the contribution of the affected neurons to saccade generation. Injection of muscimol into the SC would inhibit both burst and buildup neurons (as well as overlying visual cells) in that area. Saccades to points in the visual field represented by burst and buildup cells inactivated by the muscimol should be disrupted (Fig. 1*B*), as has been shown by previous experiments using either muscimol or lidocaine (Hikosaka and Wurtz 1985, 1986; Lee et al. 1988; Schiller et al. 1987; Sparks et al. 1990). In contrast, if the injection is made rostral to the location of the active burst neurons (Fig. 1*C*), the injection should

inactivate the burst cells that are not as active with the large saccades and should inactivate the buildup neurons that are active because of the spread of activity. In this case, the injection should reduce the $\Delta E'$ signal more than the ΔE signal, and the eye should *overshoot* the target. The altered activity of the buildup neurons should also affect the trajectories of saccades. The separation of the inactivations is unlikely to be as discrete as shown schematically in Fig. 1, *B* and *C*, but the figure emphasizes the *relative* effect of the two injections on the burst and buildup neurons.

Following muscimol injections into the SC, we find no overshooting of the saccades as we would expect from the integrator model of the SC buildup neurons. Instead, many saccades reach the target, and those that do not usually undershoot the target rather than overshoot it. We do, however, find that such injections alter the trajectory of saccades and that these alterations begin with changes in the initial direction and speed of the saccades. We conclude that these changes in trajectory are consistent with an influence of buildup neuron activity on eye position during the saccades, but that they do not support the hypothesis that the buildup neurons fulfill the role of a spatial integrator. The following paper (Quaia et al. 1998) analyzes the pattern of these changes for saccades made to targets throughout the visual field and considers alternative interpretations of these changes for evaluating the role of the SC in saccade generation.

A preliminary report of the experiments in this report has been published previously (Aizawa and Wurtz 1994).

METHODS

Physiological and behavioral procedures

We studied the SC control of saccadic eye movements in two rhesus monkeys (*Macaca mulatta*) that weighed between 5 and

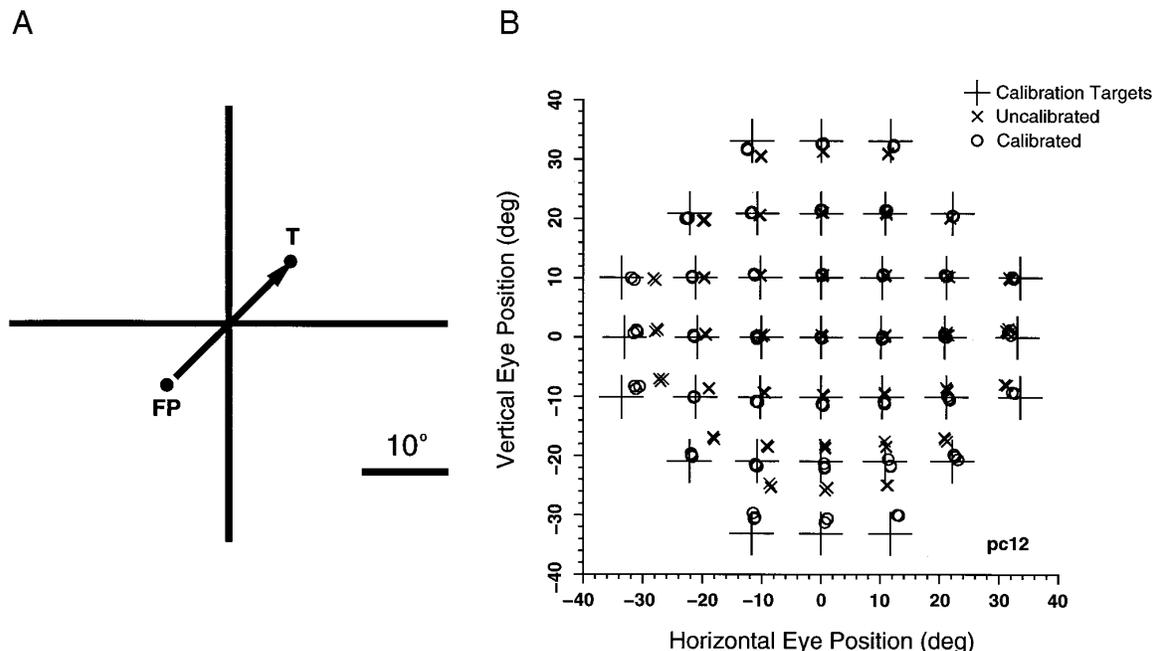


FIG. 2. Methods used for positioning saccades across the center of the visual field (*A*), and calibration of the saccadic recording system (*B*). *A*: saccades were made across the center of the field so as to maximize the linearity of the recording system. The fixation point (FP) was placed so that the saccade passed across the center of the screen to reach the target (T). *B*: comparison of measurement of saccades before and after use of the calibration procedure. See METHODS for details.

TABLE 1. *Muscimol injections with significant decreases (2 SD reduction) in saccade velocity*

Experiment		Saccade		Injection		
Number	File	Amplitude, deg	Direction, deg	Concentration, $\mu\text{g}/\mu\text{l}$	Volume, μl	Dose, μg
1	<i>pd02</i>	5	R&U, 60	2	0.45	0.9
2	<i>pd16</i>	15	L&U, 55	5	0.8	4.0
3	<i>ak12</i>	11	R&U, 45	2	0.6	1.2
4	<i>ak14</i>	11	R&U, 45	2	0.6	1.2
5	<i>pc18</i>	6	R&U, 40	2	0.3	0.6
6	<i>pd05</i>	6	R&U, 40	5	0.3	1.5
7	<i>pd06</i>	6	R&U, 40	5	0.6	3.0
8	<i>pb03</i>	14	R&U, 40	5	0.8	4.0
9	<i>ak07</i>	11	L&U, 35	1	0.5	0.5
10	<i>ak08</i>	11	L&U, 35	2	0.5	1.0
11	<i>ak09</i>	11	L&U, 35	2	0.4	0.8
12	<i>ak20</i>	11	L&U, 35	2	0.5	1.0
13	<i>ak21</i>	11	L&U, 35	2	0.5	1.0
14	<i>ak22</i>	11	L&U, 35	2	0.75	1.5
15	<i>ak34</i>	11	L&U, 35	2	0.55	1.1
16	<i>ak16</i>	22	L&U, 35	2	0.5	1.0
17	<i>pe12</i>	5	L, 0	5	0.7	3.5
18	<i>pe23</i>	10	L&D, 10	5	0.6	3.0
19	<i>pe17</i>	10	L&D, 15	5	0.4	2.0
20	<i>pe21</i>	10	L&D, 15	5	0.6	3.0
21	<i>pe22</i>	15	L&D, 30	5	0.6	3.0
22	<i>pe19</i>	8	L&D, 45	5	0.7	3.5
23	<i>pc10</i>	8	R&D, 50	5	0.8	4.0
24	<i>pc12</i>	8	R&D, 50	5	0.8	4.0
25	<i>pc13</i>	8	R&D, 50	5	0.8	4.0
26	<i>pd03</i>	8	R&D, 50	2	0.3	0.6
27	<i>pd04</i>	8	R&D, 50	5	0.3	1.5
28	<i>pe15</i>	5	L&D, 60	5	0.6	3.0
<i>Caudal SC injections</i>						
29	<i>pb05</i>	36	R&U, 80	5	0.8	4.0
30	<i>pb18</i>	36	R&U, 80	5	1.4	7.0
31	<i>ak27</i>	44	R&D, 15	2	0.5	1.0
32	<i>ak28</i>	44	R&D, 15	2	1.0	2.0
33	<i>ak29</i>	44	R&D, 15	5	0.6	3.0
34	<i>ak32</i>	44	R&D, 15	5	0.5	2.5
<i>Rostral SC injections</i>						
35	<i>pc05</i>	<1	R&U, 80	5	0.7	3.5
36	<i>pc07</i>	4	R&U, 35	5	0.8	4.0
37	<i>pc08</i>	3	R&U, 20	5	1.5	7.5
38	<i>pc09</i>	3	R&U, 20	5	1.0	5.0

The saccadic amplitude and direction were determined by the center of the movement fields of the multiple cell activity of the wire extending out the tip of the injection syringe and by the end point of the saccade evoked by stimulation through the same wire. These 2 measures were in agreement except in *experiments 35–38*. In these 4 cases, there were discrepancies between the preferred saccade judged by multiple cell recording and electrical stimulation, and we list the amplitude and direction of the saccades evoked by electrical stimulation. SC, superior colliculus; R, rightward; U, upward; L, leftward; D, downward.

12 kg. The monkeys (2 males, identification letters *A* and *P*) were prepared using the same procedures recently described (Munoz and Wurtz 1993a). Eye movements were recorded using the magnetic search coil technique (Fuchs and Robinson 1966; Judge et al. 1980). Single or multiple cell recordings from the SC were made through an implanted recording cylinder angled 38° posterior of vertical; the center was directed at the midline 15-mm above and 1-mm posterior to the interaural line. 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.

During the experiments, monkeys were seated in a primate chair with the head restrained for the duration of the experiment (3–6 h). The monkey had an unobstructed view of 70 × 70° ($\pm 35^\circ$ from center in any direction) of a tangent screen positioned 57 cm

in front of it. Each behavioral trial lasted ~2–3 s and was preceded by an initial 2- to 3-s period in which the screen was diffusely illuminated (1.0 cd/m²) and the monkey was not required to fixate. At the start of each behavioral trial, the background light was extinguished, and the task was performed in total darkness except for the presence of the back-projected target spots produced by projecting the image of red light emitting diodes (LEDs; 0.3 cd/m²). This light/dark cycle prevented the monkey from becoming dark adapted. The first target spot, referred to as the fixation point, came on 250 ms after the monkey was in the dark. The monkey had to look at the fixation point and maintain fixation for 1.0–1.5 s before making a saccade to a new target that appeared in the peripheral visual field at the same time that the fixation point was turned off.

To use the linear range of the eye coil system for all larger

saccades, we shifted the location of the fixation point on each trial so that the saccade was made across the central region of the field. For example, for a 20° saccade upward and to the right shown in Fig. 2A, we moved the fixation point (FP) to the left 10° and down 10° so that to reach the target (T) the monkey made the saccade in the center of the screen. We did this shift of fixation point position for all saccades 5° in amplitude or larger.

During the periods of fixation before the saccade, the monkey was required to keep its eye within a computer-controlled window of ± 1 to $\pm 5^\circ$ for both horizontal and vertical eye positions to obtain the liquid reward. For the saccade targets, the smallest window ($\pm 1^\circ$) was used for small distances from the center of the screen ($< 5^\circ$), and the largest window was used for the largest target eccentricities ($> 40^\circ$). After the injections, the window size was sometimes increased if the monkey was unable to do the task. If the monkey's eyes left this window, the trial was aborted and the monkey received no reward on that trial. The monkey was allowed up to 500 ms to initiate the saccade after receiving the final signal to go and an additional 500 ms to enter the computer-controlled window around the target. If both of these conditions were not met, then the trial was aborted and no reward was delivered.

A monkey would typically perform between 1,500 and 3,000 trials in a 3- to 6-h experimental period as it worked to satiation for water rewards. It was then returned to its home cage. Records were kept of the weight and health status of the monkeys, and supplemental fruit and water were provided as needed. The monkeys were under the care of the institute veterinarian.

We used a visually guided saccade task to measure the monkey's ability to make accurate saccades to a series of targets in the visual fields. We used a grid of targets that varied in amplitude (2, 5, 10, 20, 30, 40, and 50°) and in direction (by 15° steps, 0, 15, 30, 45°, etc). In some cases, we concentrated this sampling of saccades for directions that were of particular interest depending on the location of the planned injection while other areas of the visual field were sampled at 30° direction intervals. Targets were placed in the visual field both ipsilateral and contralateral to the side of the SC with the planned injection.

Muscimol injection procedures

Before the muscimol injection, we used tungsten microelectrodes to identify saccade-related cells within the SC and to locate their movement fields. We used this information to select the points within the collicular map of saccades at which to make injections, and then positioned guide tubes ~ 4 mm above these points. We then determined the movement fields of the burst/buildup cells

in a given guide tube and the depth at which these cells were encountered.

On the day before the injection, the monkey's saccades to the grid of targets were recorded with four to six saccades to each target presented in random order. On the day of the injection, a 30-gauge syringe needle with a microwire extending from the tip (Crist et al. 1988) was lowered into the SC to the same depth at which saccade-related neurons had been recorded previously using a microelectrode, and this depth was verified by recording the activity of single and multiple cells and stimulating through the microwire. We then pressure injected muscimol into the SC at the rate of $0.2 \mu\text{l}/30 \text{ s}$, and waited ≥ 15 min before withdrawing the syringe. We took the time at the end of the injection as the zero time for following the effect on saccades. We began systematically recording the monkey's saccades to the same targets tested before the injection after the muscimol effect became evident as indicated by changes in the saccades to the center of the visual field affected by the injection. We then recorded the saccades to the same targets after one or more days following the injection to verify recovery. All results represent comparisons of the monkey's behavior in the period after the injection with its behavior before the injection or after recovery. Such comparisons take into account any damage that might occur as a result of previous injections.

Table 1 lists the injections that produced saccadic deficits. The saccade amplitudes and directions shown were determined by the center of the movement fields of the multiple cell activity recorded by the wire extending out the tip of the injection syringe and by the endpoint of the saccade evoked by stimulation through that wire (biphasic negative/positive 0.5-ms pulses at 500 Hz for 100 or 200 ms at a current that produced a saccade of regular amplitude and at a latency of ~ 20 ms). These two measures were in agreement except for the four cases listed in the caption of Table 1. The table also lists the amount of muscimol used in each case. There is considerable variability between the quantitative effect at different injection sites that may be due to such unmeasured factors as the amount of fluid actually injected, any flow up along the side of the injection needle, and the amount of spread of muscimol within the SC for that particular injection. The table shows the injections made, but the most accurate measure of the injection is the extent of the behavioral changes. There was also some variation in the location of the SC reached through a guide tube in the same grid location that may be due to the different paths taken by the exploring microelectrode and the injection needle because the guide tube stopped ~ 4 mm above the SC.

For those injections near the rostral pole of the SC, we avoided injections into the fixation zone. In previous studies (Munoz and Wurtz 1993b), injections into the fixation region were done when neurons at the site showed reduced discharge during large saccades,

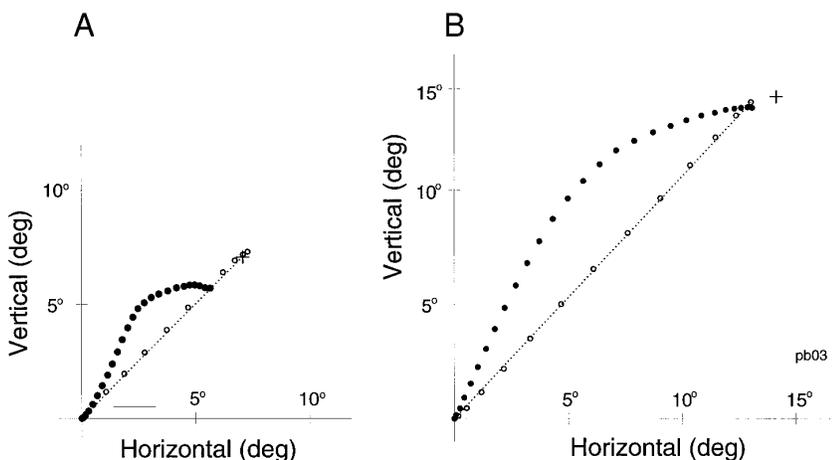


FIG. 3. Salient changes in saccades following SC muscimol injections. Trajectory of saccades 45 min after a muscimol injection (\bullet) compared with normal saccades (\circ) to the same visual targets ($+$). Eye position was sampled and is shown every 2 ms; \circ , preinjection; \bullet , postinjection. In this and all subsequent plots the amplitudes indicated on the axes are in polar coordinates. A: a saccade to the area affected by the muscimol injection. Saccades after the injection were hypometric. B: a saccade to the visual field adjacent to that most affected by the injection remains normometric after the injection. Trajectories of both the altered amplitude and the normometric saccades were curved convex upward. In both cases the direction was altered at the very beginning of the saccade, and the speed was reduced. Injection pb03 (see Table 1).

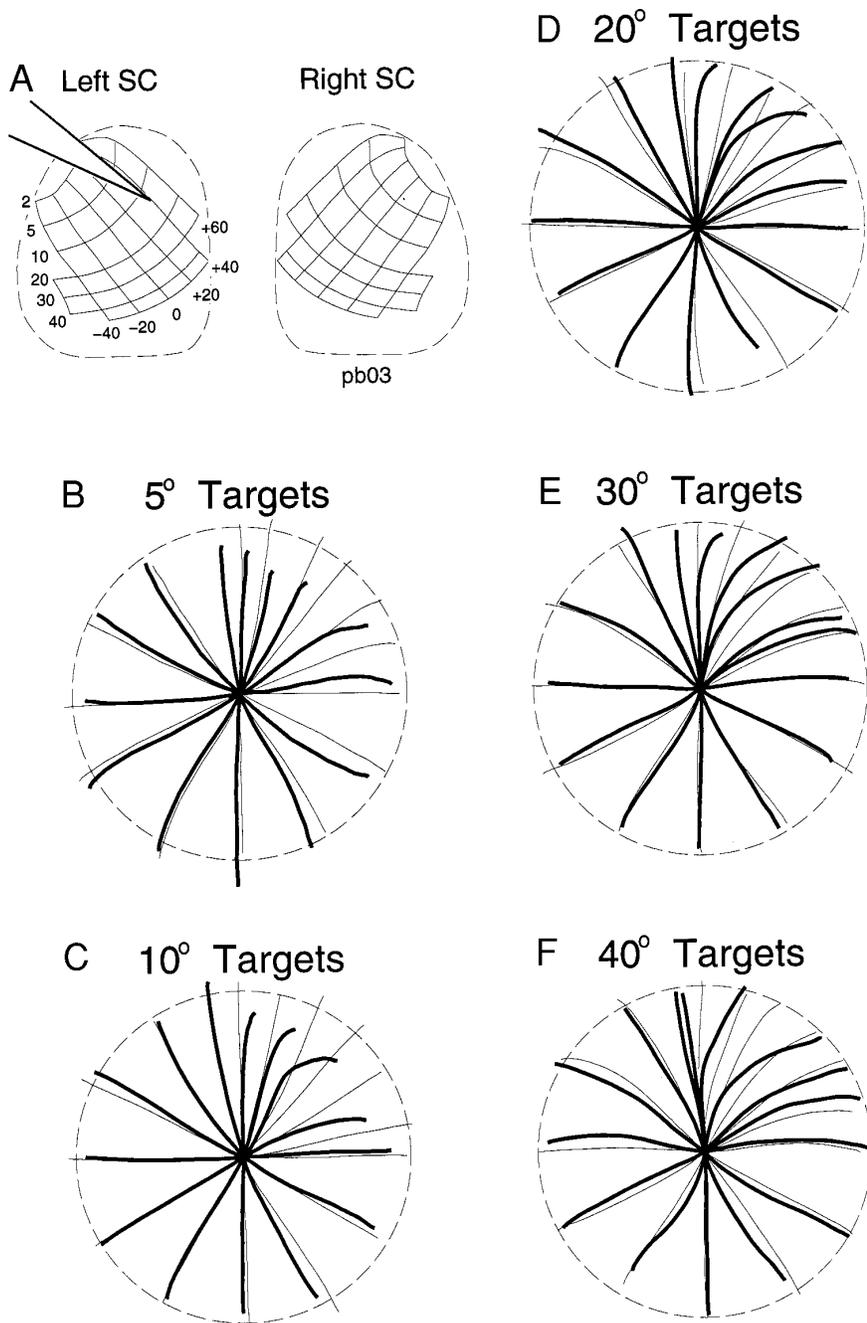


FIG. 4. Curvature of saccades to targets in the region of the visual field affected by the injection of muscimol. A: the site of the muscimol injection (*injection pb03*, same injection as in Fig. 3) is shown on the drawing of the motor map of the SC (after Robinson 1972). B–F: trajectories recorded before (thin lines) and after (22–51 min, thick lines) the injection. Saccades were to visual targets in 15 directions at eccentricities of 5° (B), 10° (C), 20° (D), 30° (E), and 40° (F). Circles indicate the stated target distance in each section. The pre- and postmuscimol comparison is made between 1st saccades without correctives because these subsequent corrective saccades could be made using the visual information derived from regions of the field close to the fovea that were not altered by this injection. The postmuscimol saccades shown are all the 4th saccade to each target made after the injection; if no saccade was made on the 4th trial, none is shown. The preinjection saccades shown are also the 4th ones in that set of premuscimol trials. This injection affected saccades to the top right quadrant, and these saccades were curved convex upward.

stimulation inhibited the onset of saccades, but the stimulation did not generate small saccades. We followed these rules to *avoid* injections into fixation neurons. We think that the spread of muscimol into the adjacent fixation neurons was minimal because we did not see any shortened latency for saccades to the ipsilateral visual field (Munoz and Wurtz 1993b) as would be expected if the fixation neurons were altered (see Fig. 9B, for example).

Calibration and data analysis

Eye position was recorded with a resolution of 0.1°, and the horizontal and vertical eye position signals were each digitized at 0.5 or 1.0 kHz. After the experiment, saccades were identified and marked using a previously described computer program that identified the onset and termination of each saccade using a tem-

plate matching method (Waitzman et al. 1991). The saccade recognition was reviewed by the experimenter. Velocity measures were derived from the stored position information.

We used a calibration procedure that corrects for the nonlinearity of the magnetic search coil method and compensated for less than ideal positioning of the search coil on the eye. The calibration corrections were applied to all points for both pre- and postmuscimol data. We used an eight-parameter model of the eye coil system to make these corrections. The relationship between the actual eye position (θ , ϕ) and the measured eye position (e_h , e_v) was

$$e_v = g_v * \sin(\phi + \phi_0) + b_v \tag{1}$$

$$e_h = g_h * \sin(\theta + \theta_0) * \cos(\phi + \phi_0) + b_h \tag{2}$$

where b_h and b_v are the offsets for the horizontal and vertical

components; θ_0 and ϕ_0 are the tilt of the coil on the eye, θ_0 for the yaw and ϕ_0 for the pitch; g_h and g_v are the gains for the horizontal and vertical coils.

The corrections made for the nonlinearity of the magnetic search coil method (Fuchs and Robinson 1966) were the sine-nonlinearity [$\sin(\phi + \phi_0)$ in Eq. 1 and $\sin(\theta + \theta_0)$ in Eq. 2] and the horizontal-vertical coupling [$\cos(\phi + \phi_0)$ in Eq. 2]. The coil gains can be different for positive (p) and negative (n) directions for each horizontal and vertical component. The model therefore has four gains for each, i.e., g_{hp} , g_{hn} , g_{vp} , g_{vn} : g_{hp} when $e_h - b_h \geq 0$; g_{hn} when $e_h - b_h < 0$; g_{vp} when $e_v - b_v \geq 0$; g_{vn} when $e_v - b_v < 0$. Placement of the coil on the eye with its center off from the real center of the eye can produce an asymmetric gain, and this was compensated by the introduction of the coil tilt terms, θ_0 and ϕ_0 . It should be noted that the use of θ_0 and ϕ_0 is only a mathematical way of dealing with the asymmetric gains and may not be equal to the real tilt of the eye coils.

To obtain values for the eight parameters used for calibration of the experimental data, we collected data for a separate calibration file. For this file, the monkey fixated 3–5 times at each of 30–40 target points on a grid (Fig. 2B) that were presented in random order. Before obtaining the eight parameters from this file, the samples were checked for errors by the experimenter, although we found little variance among samples for the same target. The eight parameters (g_{hp} , g_{hn} , g_{vp} , g_{vn} , b_h , b_v , θ_0 , and ϕ_0) were then determined using a least-squares fit between known target locations and measured eye positions at all points tested. We collected this calibration file in almost every session before the injections were made, and the data from the experiments were therefore calibrated using the parameters obtained in the same session. Figure 2B shows a sample of the effect of the calibration for a grid of points for three fixations uncalibrated (x) and after calibration (o).

Control procedures

As Hikosaka and Wurtz (1985) reported, muscimol injection into SC can produce both an ipsilateral upward shift of the field scanned by saccades and later a largely horizontal nystagmus, which in severe cases can make it difficult for the monkey to maintain fixation. In our experiments, a significant shift of the field scanned by the monkey was observed in 12 of 38 sessions, and nystagmus was observed in 7 sessions. When these changes took place, they began 40–80 min after the injection. The lower frequency of nystagmus in these experiments than in the previous ones (Hikosaka and Wurtz 1985) may be due to smaller amounts of muscimol used in the present experiments. Because we measured the amplitude and direction of the saccade from the point of fixation, any systematic error in the monkey's ability to maintain fixation would change the retinal position of the target, and we therefore ended data sampling when we noticed either fixation difficulty or nystagmus.

To check whether these factors might be influencing the measurements collected earlier in the experiments, we ran several tests in every session to verify that fixation was not altered. The monkeys were run on a fixation task using the array of fixation points throughout the field (Fig. 2B). In addition, we blinked off the fixation targets to see whether there was any slow drift or nystagmus during the blink period. We also collected spontaneous eye movement in dim light and in total darkness to detect any shift in the scanned visual field. Both because we systematically checked for the presence of these factors and because we stopped sampling as these problems developed, we think that problems with fixation were excluded from the data.

As already noted, for all saccades 5° or larger we shifted the fixation point to an eccentric position so that the saccades were made across the center of the screen. This had the advantage of measuring the saccade within the linear range of the eye coil but

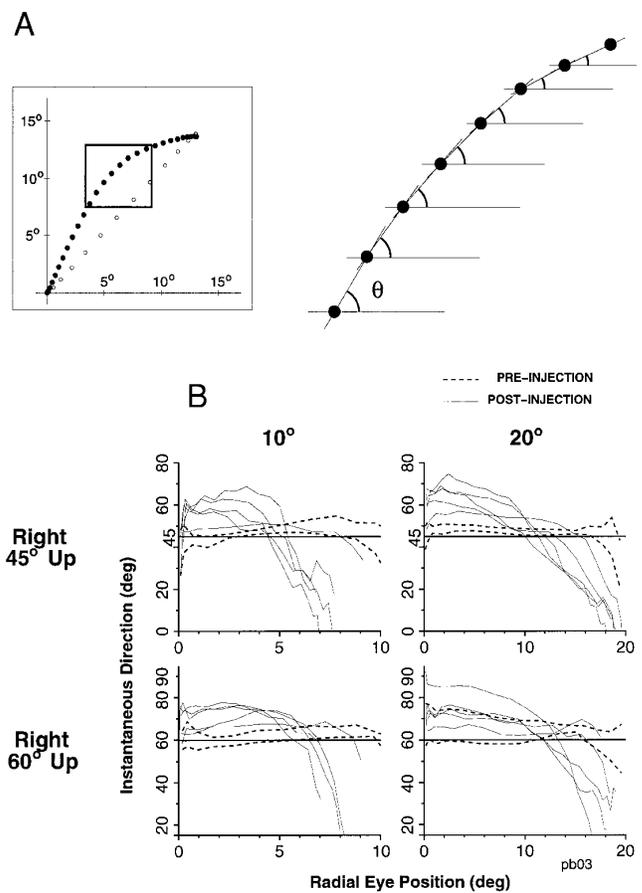


FIG. 5. Consistency of the curvature of saccades to the same targets as shown by the instantaneous direction of saccades before and after the injection. Same injection as in Fig. 3. A: calculation of instantaneous direction. In the schematic drawing for 8 points in the postmuscimol saccade (those in the box in the inset), direction is represented by the angle between the tangent to the saccade and the horizontal (0°) each time the eye position was sampled during the saccade. Instantaneous direction at time t is as follows: Direction (deg) = $\text{atan}\{[\text{Ev}(t+1) - \text{Ev}(t)]/[\text{Eh}(t+1) - \text{Eh}(t)]\}$, where $\text{Eh}(t)$, $\text{Ev}(t)$, $\text{Eh}(t+1)$, $\text{Ev}(t+1)$ are horizontal and vertical eye positions at time t and $(t+1)$. B: instantaneous directions for pre- and postmuscimol saccades. Graphs in the left column show saccades of 10° amplitude that were both curved and hypometric, and graphs in the right column show saccades of 20° amplitude that were curved but still had nearly the same amplitude after the injection as before. On each graph, the ordinate shows instantaneous direction, and the abscissa shows radial eye position from the beginning of the saccade on the left to the end of the saccade on the right. The horizontal line shows the straight line direction to the target, the thin lines the individual postinjection saccades, and the dashed lines \pm SD around the mean for preinjection saccades. The variance after the injection is larger due in part to the continually changing effect of the injection over time, and we therefore show the individual traces for the postmuscimol saccades in this and subsequent figures. These plots show the consistency in the curvature of the saccades both before and after the muscimol injections. They also show that the deviation in saccadic direction at the beginning of saccades was consistent in both hypometric (10°) and normometric (20°) saccades. The 2 traces showing little effect of the muscimol in the 10° saccades were the 1st recorded after the injection and may not yet show the effect of the injection that becomes evident later.

the disadvantages of allowing the monkey to know the direction of the saccade before the fixation point went off and of introducing a change of eye position into the experiment. In addition, we allowed a gap of 15 ms between the time the fixation point went off and the target came on to allow time for the scanner mirror to move to the new target. To verify that these procedures did not

introduce problems, we tested the effect of the shift of the fixation location in two injection experiments by comparing 20° saccades from the center and from the eccentric fixation points in the ipsilateral visual field. We saw no indication that the shift in the fixation yielded any different results from the trials for which no position or anticipation effect was present. In addition we compared the saccades made from a fixation point in the center of the screen (produced by a fixed LED and therefore not requiring any delay for mirror movement) with and without the 15-ms delay. We found no systematic differences.

RESULTS

Saccades after muscimol injections

We made 38 successful injections of muscimol into the SC of 2 monkeys. The largest effects on the saccades were highly consistent across injections and are illustrated by the results of an injection in the middle of the rostral to caudal extent of the SC shown in Fig. 3. Before the injection, the saccades to the targets were nearly straight and accurate (○ in Fig. 3 shows eye position at 2-ms intervals). After the injection, many saccades made to the area affected by the muscimol injections failed to reach the target (Fig. 3A, ●); they were hypometric compared with the premuscimol saccades. They were also curved, in this case, convex upward. In contrast, saccades made to adjacent regions in the visual field had amplitudes comparable with those before the injection (Fig. 3B, ●). These sac-

cades, however, also had curved trajectories, again convex upward. The curved saccades, both those that were hypometric and those that were normometric, had two further consistent and salient characteristics: there was an error in the direction of the saccades that was evident from the very start of the saccade, and the saccades were slower (as indicated by the shorter distances between successive eye positions). The changes in the accuracy and speed of the saccades have been observed previously for saccades made to the areas of the field maximally affected by the reversible inactivation (Hikosaka and Wurtz 1985, 1986; Lee et al. 1988; Schiller et al. 1987; Sparks et al. 1990). In this report we will concentrate on the characteristics of the saccades that were as accurate after the injection as before (Fig. 3B as opposed to Fig. 3A) because we can analyze the change in the trajectory without the added complications of saccadic inaccuracy.

We made injections in different regions within the SC to fully explore the alteration in the trajectory of the saccades. Table 1 lists the injections and their location within the SC as indicated by the optimal saccadic amplitude and direction of neurons at the site of the injection and/or the amplitude and direction of the saccades evoked by stimulation at the site. The major difference between the results of these injections depended on the location of the injection within the SC: the medial to lateral and the rostral to caudal location of the injection in the SC.

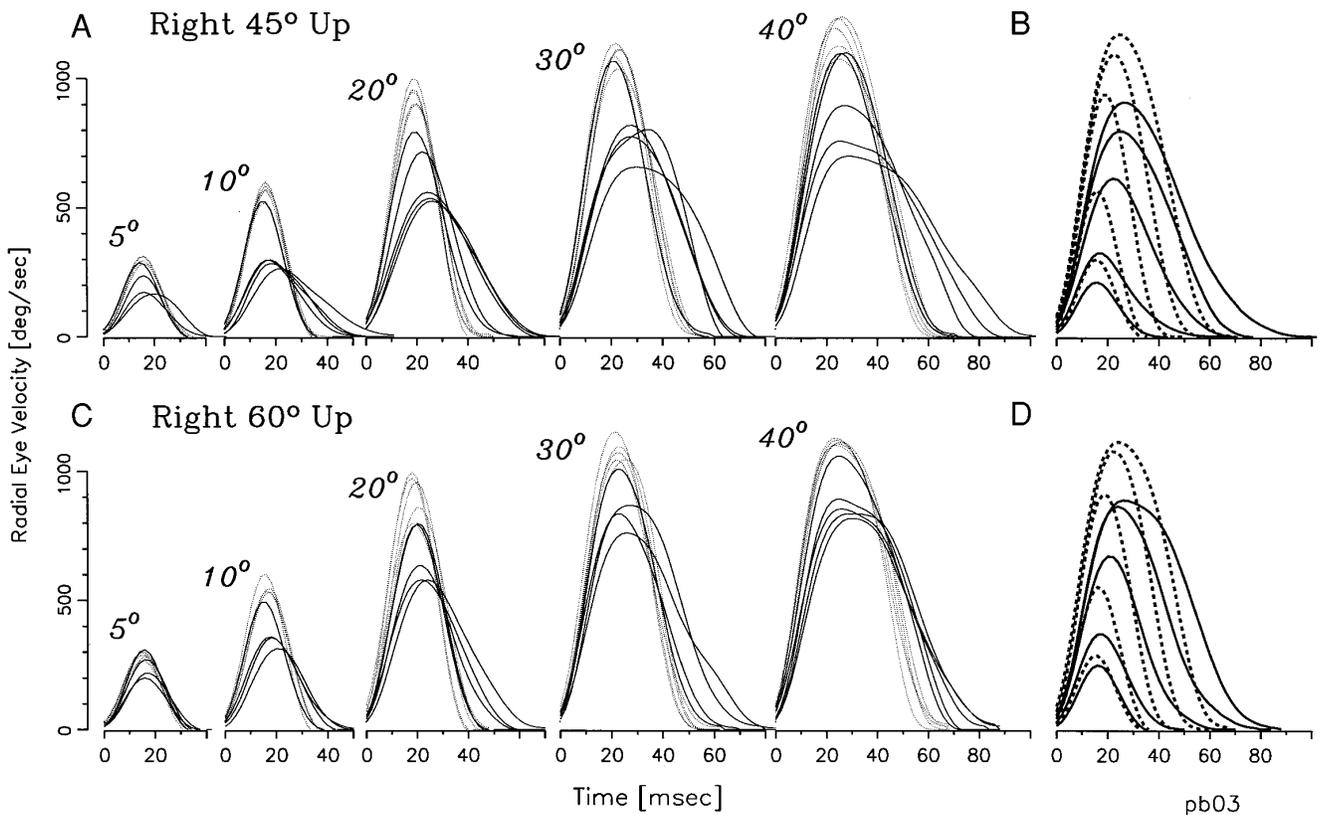


FIG. 6. Change in velocity early in the curved saccades. Same injection as in Fig. 3 and includes the saccade directions and amplitudes shown in Fig. 5B. Dotted lines are for individual preinjection saccades, and the solid lines are for the individual postinjection saccades. In A and C, saccades are to targets between 5 and 40° eccentricity at 45 and 60° right and up. Means for these saccades are shown in B and D with dashed lines for preinjection and solid lines for postmuscimol saccades. The radial velocity decreases early in the postmuscimol saccades.

Alteration of saccade trajectory by mid-SC injections

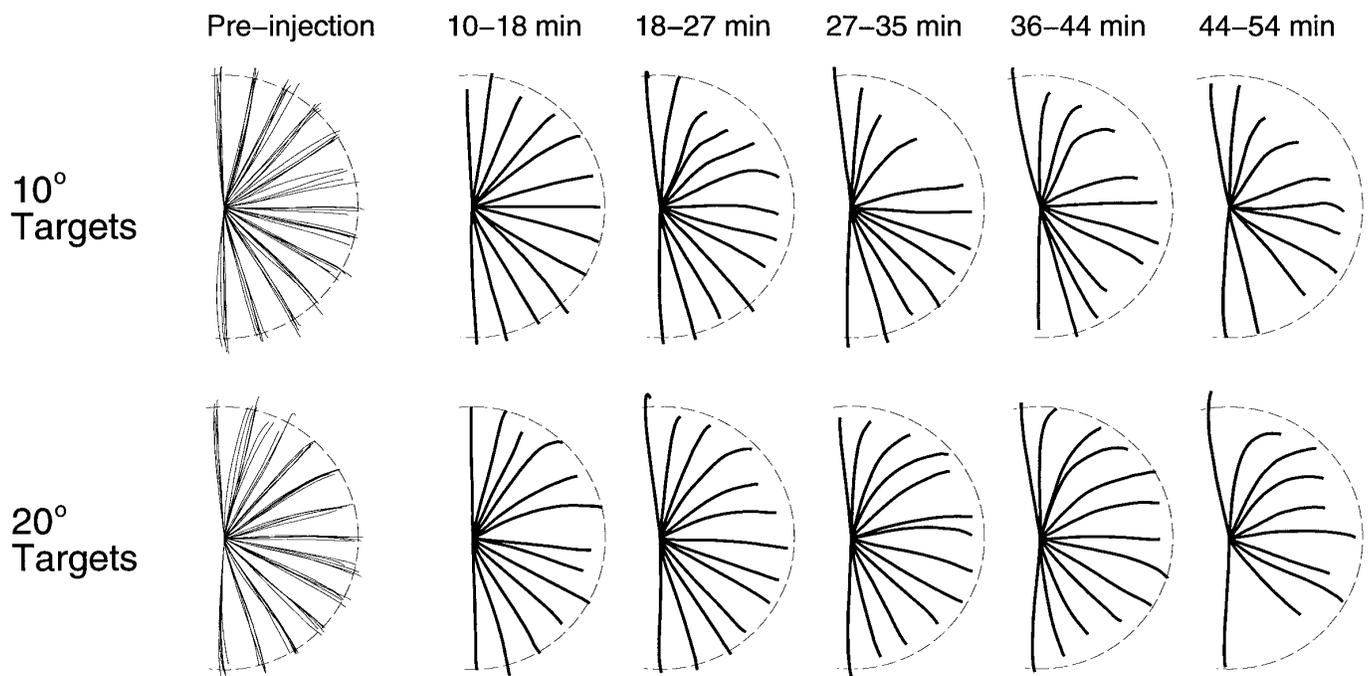
Figure 4 shows the extent and type of trajectory changes after a muscimol injection at the location in the SC shown in Fig. 4A (same injection as in Fig. 3). The muscimol injection was centered at a point in the left SC where activity of burst and buildup neurons was maximal for 40° right upward saccades of ~14° amplitude. Each plot in Fig. 4 shows saccades to targets in different directions for a given amplitude indicated by the circle (5–40°, Fig. 4, B–F).

The saccades before the injection (thin lines in Fig. 4, B and C) came close to the target, but after the injection (thick lines) the saccades to the targets in the visual field related to the injection (right upward) did not reach their target. This is particularly noticeable for saccades to the 10° amplitude targets on the top right (Fig. 4C) and for those to the 5° targets (Fig. 4B). For the larger 20 and 30° saccades (Fig. 4, D and E), the saccades tended to come to the same location as the preinjection saccades. The endpoints of those saccades modified by the injection (Fig. 4, B and C) were consistently hypometric; they were rarely hypermetric even for those saccades that went beyond that area (Fig. 4D). This was a consistent observation in the other muscimol injections as well, a point we will consider in more detail in the next paper (Quaia et al. 1998).

Before the injection, the sample saccades shown to each of these targets had relatively straight trajectories. After the injection, the trajectories were curved rather than straight. For example, for the saccades to the 45° angle and 20° eccentric target (Fig. 4D), the normal trajectory was almost straight along the +45° direction line throughout the saccade. In contrast, the postmuscimol saccade began in a more up-

ward direction instead of +45° direction. When the eye came to the midpoint of the saccade, the direction started changing to become less upward and more horizontally directed at the termination of the saccade. Note that this curvature is largely limited to the saccades to the top right visual field (that contralateral to the SC injected) but is present in saccades that have altered amplitudes as well as some that do not. For very large saccades (40°; Fig. 4F) the curvature in the top right quadrant was still evident, although several saccades were inaccurate. Note that the saccades near the vertical meridian in this injection were also altered; saccades to the target straight up from the fixation point were deflected into the ipsilateral visual field following the injection.

The striking characteristic of the saccades shown in Figs. 3 and 4 is not only that some saccades are curved even though they still get to the target, but that they started out in the wrong direction at the very beginning of the saccade. This change in direction is highly consistent not only for saccades to different targets as shown in Fig. 4 but also for successive saccades to the same target as shown in Fig. 5. Figure 5A shows the calculation of a measure of the instantaneous direction during the course of a saccade. Figure 5B compares the pre- and postmuscimol saccades made 45 and 60° up and to the right with the change in direction plotted against the radial eye position. The standard deviation for the preinjection saccades (Fig. 5B, dashed lines) is narrow enough to show that these saccades were consistent before the injection. The horizontal line indicates the direction straight to the target. The thin lines are individual postinjection saccades, and the variability is largely due to the change in the effect of muscimol over time after the injec-



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FIG. 7. Time course of the change in saccade trajectory after a muscimol injection. Same injection as in Fig. 3, but showing only the contralaterally directed saccades for targets at 10 and 20° eccentricity. Records were taken in random order during the 8 min of each sample period shown across the *top* of the figure and during the preinjection period on the *right*.

tion. To avoid taking means and SDs of nonstationary processes, we will show only the individual traces of the postinjection saccades. The traces show the consistency of the deflection of the saccades to the targets and that the direction change occurs very early in the saccade. For example, for the 10° amplitude saccades in Fig. 5C, the instantaneous direction of most of the postmuscimol saccades is too close to the vertical at the start of the saccade, but then this initial error in direction is compensated for later in the saccade by a direction less than the 45° direction. The compensation is not sufficient for the eye to reach the same position as it did before the injection. This later compensation, however, is enough for the 20° saccade to reach about the same position it did before the injection. In all of the cases we observed, the curvature of the saccades was highly consistent from trial to trial, and in those cases in which the curvature was changed, the change occurred early in the saccadic trajectory.

The speed of the saccades also changed consistently early in the saccades as shown in Fig. 6, which shows the change in radial eye velocity over time during saccades before (dotted lines) and after (solid lines) the injection for the same saccadic directions as in Fig. 5B. The speed was clearly slowed for all saccades and most clearly for saccades of 10°

amplitude and greater. The salient point, however, is that the saccades were slowed early in the trajectory as indicated by the divergence of the pre- and postinjection curves early on the graph. This was true for the saccades to the visual field area where saccades were hypometric as well as those that were normometric.

As we have indicated, there is some variability in the trajectories of the postinjection saccades shown in Figs. 5 and 6 that is due in part to the change of the effect of the muscimol injection over time. Figure 7 illustrates the time course of the effect for the same injection but for just two saccadic amplitudes and for just those saccades to the contralateral visual field. Samples were taken across the entire grid of points in random order and this took ~8 min depending on how assiduously the monkey performed the task. For the 10° saccades into the affected area on the top right, the saccades were substantially inaccurate by 18–27 min and became progressively more inaccurate to the same location and over a larger part of the field by the time the 44- to 54-min time period was reached. Similarly, for the saccades that reached the targets but whose trajectory was altered, such as those to the 20° targets, the effect was clearly evident in the 18- to 27-min period, was clearest at 36–44 min, and

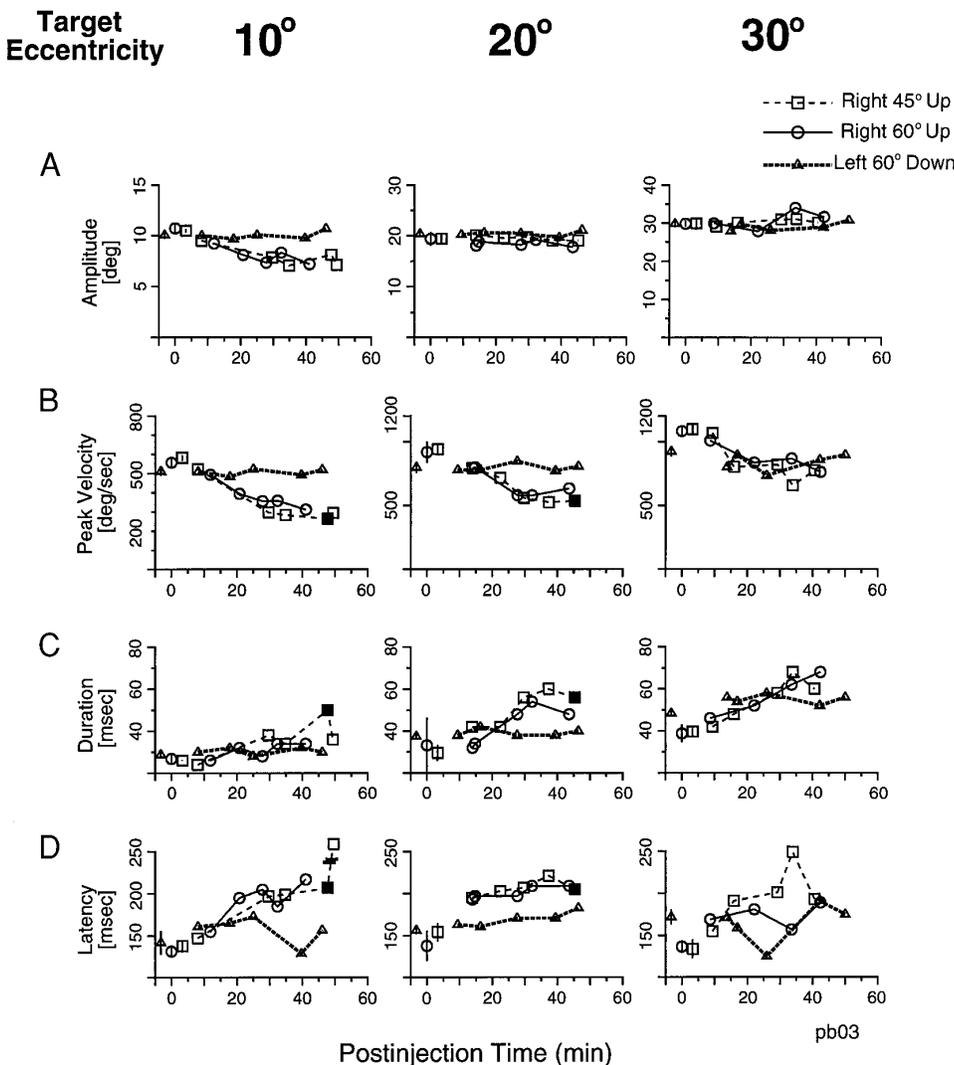


FIG. 8. Quantification of the decrease in amplitude and peak velocity, and the increase in duration and latency for saccades with curved trajectories. Same injection as in Fig. 3. *A*: radial amplitude of the saccades pre- and postmuscimol for comparison with other parameters. The ordinate shows radial amplitude of each saccade, and the abscissa is the time when each saccade was made after muscimol was injected. The vertical lines on the premuscimol values for each target indicate SE. The filled square for the 5th saccade in the 10 and 20° graph indicates the data for the saccades shown in Fig. 3. *B*: Peak radial velocity of the saccades. Peak velocity is slower not only for hypometric, but also for curved normometric saccades. *C*: duration of saccades. *D*: latency of saccade onset after visual target presentation. Longer latency was observed not only with hypometric saccades, but also with curved normometric saccades.

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then saccades began to show some errors in reaching the targets at the 44- to 54-min period. Even for these 20° saccades that became inaccurate with the further spread of muscimol, there was a consistency in the difference in accuracy over the three sets of samples over the 18- to 44-min periods. Saccades of 10° made to the visual field close to the area related to the injection became hypometric, whereas 20° saccades to the visual field were only slightly displaced but the trajectories were altered. For presentation of the trajectory changes, we have picked the postinjection time period when the saccades had the maximum trajectory change but still reached the targets, and this time varied somewhat from injection to injection.

Figure 8 quantifies the change in several parameters of the saccades over time. The saccadic directions for accurate but curved saccades (20 and 30° column for Right 45° Up, Right 60° Up) and hypometric curved saccades (10° column for Right 45° Up, Right 60° Up), are indicated on each graph. The peak velocity and saccade duration changed whether the saccade was accurate or not as is evident from the previous

illustration of the saccades. In addition the latencies of the saccades were also increased. The longer latencies were equally evident for the 10, 20, and 30° saccades.

In summary, muscimol injections produced saccades to one part of the visual field whose trajectories were curved whether the saccades remained accurate or not. The curvature started at the beginning of the saccades as did a slowing of the velocities of the saccades that led to longer durations. Saccades also had longer latencies.

Injection into caudal and rostral SC

Activity among the buildup neurons was observed to spread rostrally but not caudally (Munoz and Wurtz 1995b), and this observation suggests that an injection in the caudal SC should have a different effect from the injections in the middle of the SC considered so far. The large amplitude saccades, made to the area of the field affected by a caudal injection, should have their direction and amplitude altered, but smaller saccades should not show any modification be-

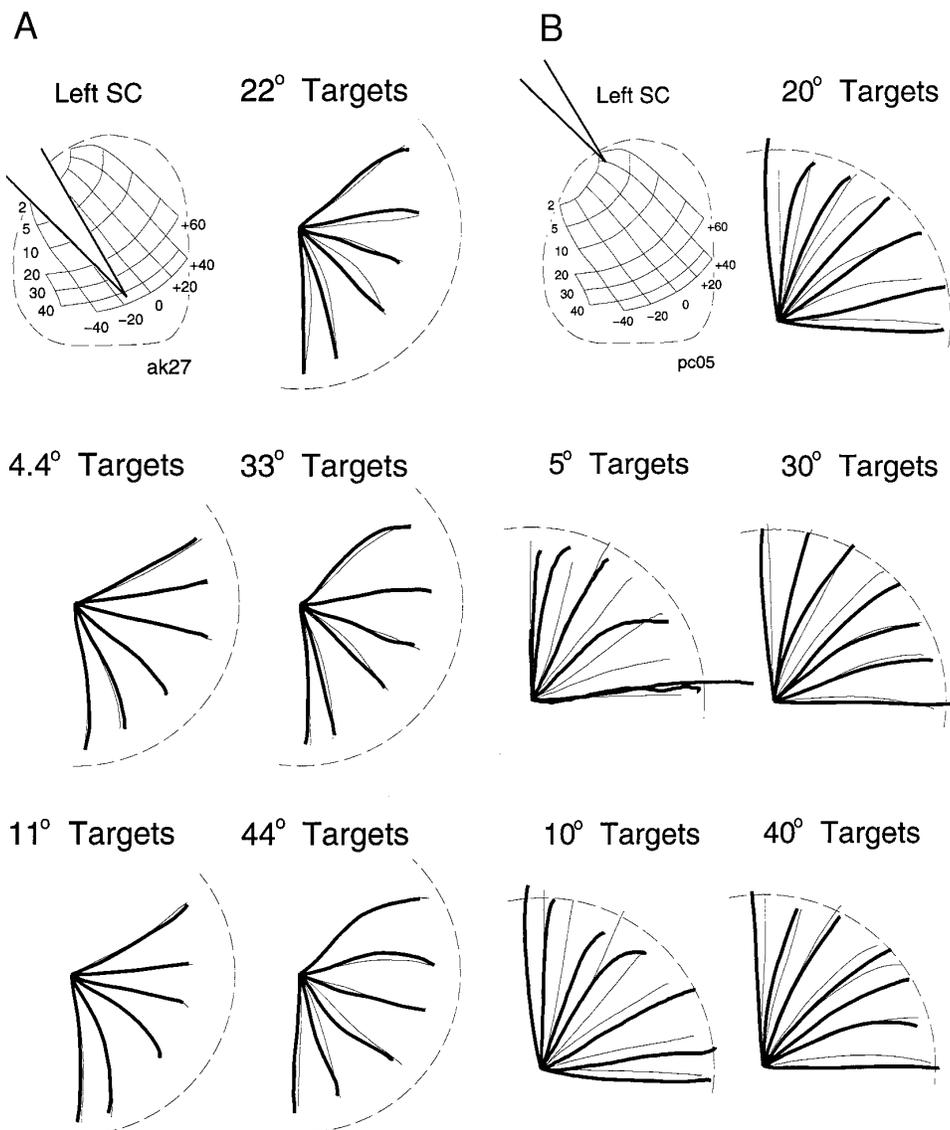


FIG. 9. Comparison of saccade trajectories made in the caudal (A) and the rostral (B) SC. Same format as in Fig. 4. A: example of an injection into the caudal SC related to large saccades that left smaller saccades unaltered. Postmuscimol saccades were taken 36–49 min after the injection. B: example of an injection in the more rostral SC related to small saccades that did not alter the trajectory for very large saccades. Saccades were made 45–60 min after the injection (thick lines).

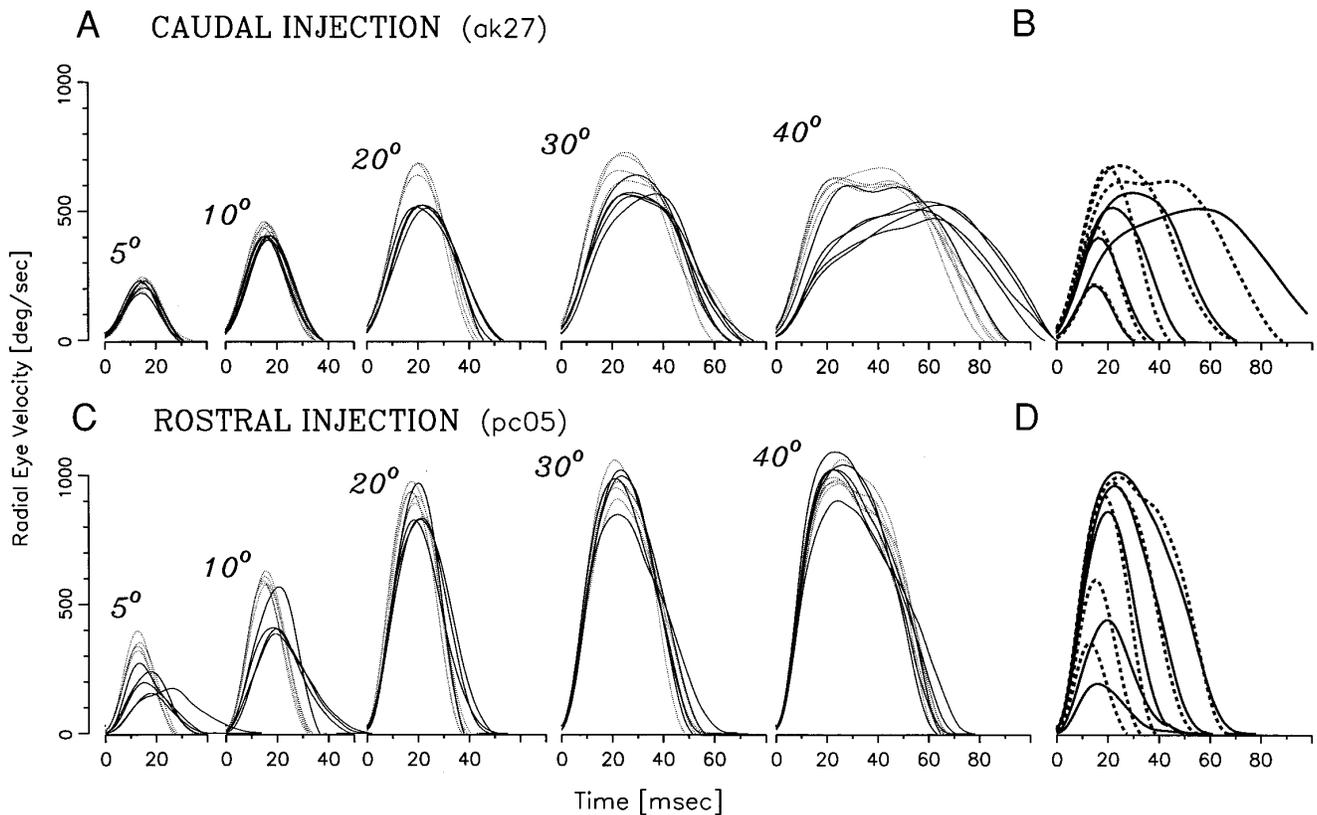


FIG. 10. Change in radial velocity during individual saccades for saccades following injections into the caudal (A and B) and rostral (C and D) SC shown in Fig. 9. For simplicity in A, the amplitudes shown in Fig. 9A are rounded off (e.g., 11 to 10°). Same organization as in Fig. 6.

cause the more rostral spread of activity should be unaltered by the caudal injection. Figure 9A shows the change in saccades after an injection in the caudal SC representing saccades 44° in amplitude directed ~15° down. After the injection, saccades to this area are altered as indicated by the convex upward and downward deflections of the post-muscimol saccades (44° saccades in Fig. 9A) and the clear changes in eye velocity for these same large saccades (44° saccades in Fig. 10A). Note that, for the saccades directly toward the affected area in Fig. 9A, the saccades are not deflected. Small saccades appear to be minimally affected as indicated by the 4.4° saccades in Fig. 9A and the velocity traces for these saccades in Fig. 10A. Thus, although the effect of the injection at the caudal site is not large, there is no indication of an alteration of the small saccades related to the SC rostral to the site of the injection.

By the spreading activity hypothesis, injections in the rostral SC should alter all saccades associated with activity originating caudal to the injection site in addition to affecting the amplitude and direction of small saccades related to the site of the injection. Figure 9B shows the effects of an injection into the rostral SC among neurons that discharged before saccades of ~1° in amplitude. This injection produced mildly hypometric saccades to targets of 5 and 10° eccentricity in the top right quadrant as well as curved trajectories to these targets (Fig. 9B). The velocity of these saccades was also altered (Fig. 10C). Saccades to adjacent targets and somewhat larger saccades to the same quadrant were normo-

metric but were curved (Fig. 9B). This curvature is clearer in the samples of radial velocity in Fig. 10C. The largest saccades were minimally affected.

DISCUSSION

Comparison with previous SC inactivation studies

Previous inactivation experiments on the SC with the GABA agonist muscimol have shown that saccades made to targets in the region of the visual field most closely related to the inactivated site in the SC (comparable to the injections shown schematically in Fig. 1B) do not reach the target; they show altered amplitude and direction (Hikosaka and Wurtz 1985). We have verified these observations along with the observations that the speed of the saccades is reduced and the latency for initiation is increased. We also found that the trajectories of these saccades were altered, which is evident from illustrations in previous experiments but was not systematically investigated (Hikosaka and Wurtz 1985, 1986).

The central goal of our current experiments, however, was to look at the trajectory of the saccades that were *not* directed to regions of the visual field most closely related to the injection site within the SC (comparable to that in Fig. 1C). For such saccades, we found that many reached the visual targets just as they did before the injection but with trajectories that were altered from nearly straight before the injection

to curved after the injection. The curvature was highly consistent so that saccades to one part of the field had the same direction of curvature and successive saccades to the same target had similar curvatures. The change in the trajectories began as soon as the saccades began; the initial directions were not toward the target as they had been before the injection. The saccades reached the target only because there was a compensation later in the saccades for this early misdirection, and they curved around to reach the targets. The speed of the saccades also was slowed after the injection, and this slowing also occurred at the onset of the saccade. In addition to these changes in the initial speed and direction of the saccades, the peak speed was reduced, the duration was lengthened, and the latency for initiation was increased. These changes in trajectory add to the previous observations on changes in speed (Hikosaka and Wurtz 1985, 1986; Lee et al. 1988; Schiller et al. 1987; Sparks et al. 1990), which indicate that the SC influences eye position during saccades as well as at the end of saccades.

Logic and limitations of the present experiments

The interpretation of these experiments is dependent on the extent to which the burst and buildup neurons are differentially affected by the muscimol injections at different locations in the SC. The experiments are based on three assumptions derived from observations made in previous experiments. First, we assumed the following characteristics of the burst neurons: the neurons active before a saccade have a peak of activity for an optimal amplitude saccade and a gradient of reduced activity for saccades away from that optimum (Sparks and Hartwich-Young 1989); the mound of activity rises and falls at one point on the SC map (Munoz and Wurtz 1995b); roughly one-fourth of the burst neurons in the SC are active for each saccade, and the fraction of the population of SC cells remains roughly the same for saccades of different sizes (Munoz and Wurtz 1995b). The second assumption was that the area of the visual field where the saccades did not reach the target was related to the inactivated region of the SC where the burst and buildup neurons were maximally activated; previous experiments with muscimol (Hikosaka and Wurtz 1985, 1986) have shown that, as the injection was placed among burst neurons in different regions of the SC, saccades to corresponding parts of the visual field were maximally affected. The third assumption was that, while the buildup neurons showed their largest activity at the same site on the SC map as the burst neurons, many of them were also active for all saccades larger than that optimum (Munoz and Wurtz 1995b). This means that all neurons rostral to the initially active buildup neurons would be active: the spread of activity described in the INTRODUCTION.

Injection of muscimol does not produce a pinpoint effect in the SC, but rather an alteration within a region, and there is almost certainly spread of the muscimol with time. What are the consequences of this experimental reality on the logic of the present experiments? As expected from previous experiments, when we made injections into one area of the SC, such as that related to large saccades (Fig. 1B), we saw the errors in the amplitude of the saccades to targets in the part of the visual field related to the injection site. We inter-

pret this as due to the inactivation of the SC neurons at the site of the injection, and these neurons would include both burst and buildup neurons. When the injection site was moved more rostral in the SC (Fig. 1C), we found that the larger saccades reached the target but that they still had curved trajectories. Reaching the target is consistent with the previous observations for saccades to points remote from those most affected by the muscimol injection (Hikosaka and Wurtz 1985), but it does not explain the persistence of the curved trajectory of the larger saccades. We think that this curvature could result from the inactivation of the buildup neurons through which the rostral spread of activity would pass with all larger saccades. In contrast, the burst neurons would be only minimally active for the larger saccades, and thus a further inactivation by the muscimol should not produce any striking effect. If the muscimol were to spread from the region of small to large saccades, we would expect that such spread should alter the amplitude of the larger saccades as it does the amplitude of the small saccades. The internal confirmation within our observations is that the amplitude of the larger saccades are close to normal, which they should not be if the burst neurons were altered. Thus it seems that a reasonable interpretation is that it is the inactivation of the buildup neurons at the site of the injection that alters the saccadic trajectory.

There are several limitations to our experiments and their interpretation that should be made explicit. We have referred to only two classes of neurons in the SC, the burst neurons and buildup neurons. The burst neurons may be a relatively homogeneous population of neurons, although a subcategory of visually guided neurons has been identified (Mohler and Wurtz 1976). The buildup neurons are probably more heterogeneous because they show more variation in their activity and in their movement fields (Munoz and Wurtz 1995b). In addition, there may be other neuron types that are altered by the injections that we are not aware of so that our reference to the inactivation of buildup neurons could be restated as inactivation of nonburst neurons, but we think this would be as awkward to state as it is logically correct. We also did not make injections that significantly affected the neurons referred to as fixation neurons in the rostral SC (Munoz and Wurtz 1993a,b), which might represent a rostral extension of the buildup neurons, because inactivation of these neurons by muscimol leads to breaks in fixation and the generation of extraneous saccades.

One consistent problem in the present experiments was to produce localized injections within the SC map but at the same time to affect enough of the map so as to alter any spread of saccade-related activity. We made a number of small injections in which we saw little detectable change in saccades, so we tended to use larger injections than in experiments aimed at perturbing the amplitude and direction of the saccades to small regions of the visual field (Lee et al. 1988; Sparks et al. 1990) but smaller than many of those in the original experiments on the SC that produced nystagmus (Hikosaka and Wurtz 1985). Because we settled on injection sizes that were just adequate for consistently altering saccadic trajectory, the relatively large size of the injections we used is significant in itself, and our experiments may indicate that the spread is quite broad over large regions of the SC. We are presumably seeing the consequence of

trying to alter a behavior controlled by a population of neurons; unless a sufficient number of neurons are altered, changes in saccades are not detectable.

SC as the neural integrator

The experimental results do not offer support for the proposal that the SC is the neuronal substrate of a saccadic integrator (Fig. 1A). The spread of activity in the SC buildup neurons (Munoz and Wurtz 1995b) or the moving hill of activity observed in the cat by Munoz et al. (1991) have been proposed as a mechanism to perform the spatial integration of a velocity feedback signal needed during saccade generation (Droulez and Berthoz 1988, 1991; Lefèvre and Galiana 1992; Optican 1994, 1995; Wurtz and Optican 1994). Placing this integrator in the SC raises expectations about the postinjection saccades that are not confirmed. First and foremost is the expectation that if the neural integrator were disrupted, the saccades would overshoot the target. For example, in Fig. 1A, if the output of the buildup layer ($\Delta E'$) were reduced (as would be the case with the injection in Fig. 1C), the motor error should reach zero later, the eye should keep moving longer, and the saccade should be *hypermetric*. We rarely observed hypermetric saccades after the muscimol injections; saccades were normometric or hypometric. There is of course the possibility that the saccades would be hypermetric if allowed to go to completion, but that they are truncated for some reason, such as the omnipause neurons in the pons coming on earlier and ending the saccade earlier, as is discussed in the following paper (Quaia et al. 1998). But even if this were true, it would not explain the consistent observation that the saccadic trajectory changes in the middle of the saccade and that change in direction brings the saccade onto the target. If the buildup neurons are acting as the neural integrator and they are altered, what information is available to bring the eye on the target? Taken together, these observations argue against considering the SC as the site of a feedback integrator.

Injection results and the spread of activity

The idea that the buildup neurons might contribute to the control of eye position during saccades arose from the single cell recording experiments that concluded that there was a rostral spread of activity within the buildup neurons during a saccade (Munoz and Wurtz 1995b). As outlined in Fig. 1, B and C, the spread across the two-dimensional SC map should alter both the horizontal and vertical components of the saccade and therefore should alter the saccadic trajectory. Our finding of a consistent curvature of the saccades after the muscimol injections into the SC is consistent with this hypothesis. Furthermore this provides the first direct experimental evidence that the SC rostral to the most active zone does contribute to the saccade generation; the single cell studies can only provide a correlation of neuron activity and behavior.

The consistent modification of the *initial* velocity of saccades by the muscimol injections was at first surprising. Because the spread of activity is not complete until the end of the saccade (Munoz and Wurtz 1995b), an intuitive expectation is that larger saccades with initial activity in the

caudal SC would be modified late in their trajectory as the spread of activity reached an injection area more rostral in the SC. However, although the spread of activity is not complete until near the end of the saccade, the spread has certainly begun and includes the rostral buildup neurons before the onset of the saccade (see saccade onset graphs in Figs. 3–5 in Munoz and Wurtz 1995b) so that by the time that the eye starts to move, the buildup neurons are already active over a larger area of the SC than are the burst neurons. Altering the activity of the more rostral buildup neurons by a rostral muscimol injection therefore could contribute to the saccade from its onset, and the change in initial velocity might logically be a result of the change in the activity of the buildup neurons. The change in initial velocity could also result from a modification of the output of the entire population of buildup neurons, as has been suggested by Gandhi et al. (1994).

The muscimol injections that provided the least compelling indication of the spread of activity were those most rostral in the SC (Figs. 9B and 10C) because the effect on the largest saccades was minimal. This might indicate that it is the fraction of the buildup neurons affected by an injection in addition to the location within the SC that is critical. For example, in the case of an injection in the middle SC, possibly 50% of the buildup neurons rostral in the SC to the area initially active with large saccades might be altered, but a more rostral injection might alter only 10% of the buildup neurons active with the large saccade. The smaller effect of the rostral lesions on large saccades might reflect the fraction of the active SC that is inactivated.

Consideration of the possible mechanisms underlying these observations is dependent on the pattern of changes in initial speed and direction for saccades to targets throughout the visual field, and we will consider such maps in the following paper (Quaia et al. 1998).

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