

Activity of Neurons in Monkey Superior Colliculus During Interrupted Saccades

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SUMMARY AND CONCLUSIONS

1. Recent studies of the monkey superior colliculus (SC) have identified several types of cells in the intermediate layers (including burst, buildup, and fixation neurons) and the sequence of changes in their activity during the generation of saccadic eye movements. On the basis of these observations, several hypotheses about the organization of the SC leading to saccade generation have placed the SC in a feedback loop controlling the amplitude and direction of the impending saccade. We tested these hypotheses about the organization of the SC by perturbing the system while recording the activity of neurons within the SC.

2. We applied a brief high-frequency train of electrical stimulation among the fixation cells in the rostral pole of the SC. This momentarily interrupted the saccade in midflight: after the initial eye acceleration, the eye velocity decreased (frequently to 0) and then again accelerated. Despite the break in the saccade, these interrupted saccades were of about the same amplitude as normal saccades. The postinterruption saccades were usually initiated immediately after the termination of stimulation and occurred regardless of whether the saccade target was visible or not. The velocity-amplitude relationship of the preinterruption component of the saccade fell slightly above the main sequence for control saccades of that amplitude, whereas postinterruption saccades fell near the main sequence.

3. Collicular burst neurons are silent during fixation and discharge a robust burst of action potentials for saccades to a restricted region of the visual field that define a closed movement field. During the stimulation-induced saccadic interruption, these burst neurons all showed a pause in their high-frequency discharge. During an interrupted saccade to a visual target, the typical saccade-related burst was broken into two parts: the first part of the burst began before the initial preinterruption saccade; the second burst began before the postinterruption saccade.

4. We quantified three aspects of the resumption of activity of burst neurons following saccade interruption: 1) the total number of spikes in the pre- and postinterruption bursts was very similar to the total number of spikes in the control saccade burst; 2) the increase in total duration of the burst (preinterruption period + interruption + postinterruption period) was highly correlated with the increase in total saccade duration (preinterruption saccade + interruption + postinterruption saccade); and 3) the time course of the postinterruption saccade and the resumed cell discharge both followed the same monotonic trajectory as the control saccade in most cells.

5. The same population of burst neurons was active for both the preinterruption and the postinterruption saccades, provided that the stimulation was brief enough to allow the postinterruption saccade to occur immediately. If the postinterruption saccade was delayed by >100 ms, then burst neurons at a new and more rostral locus related to such smaller saccades became active in association

with the smaller remaining saccade. We interpret this shift in active locations within the SC as a termination of the initial saccadic error command and the triggering of a new one.

6. Buildup neurons usually had two aspects to their discharge: a high-frequency burst for saccades of the optimal amplitude and direction (similar to burst neurons), and a low-frequency discharge for saccades of optimal direction whose amplitudes were equal to or greater than the optimal (different from burst neurons). The stimulation-induced interruption in saccade trajectory differentially affected these two components of buildup neuron discharge. The high-frequency burst component was affected in a manner very similar to the burst neurons. However, the low-frequency component was only transiently affected by the stimulation and resumed immediately after the stimulation, regardless of whether the postinterruption saccade was initiated immediately or delayed beyond 150 ms. These observations indicate that buildup neurons might carry two independent signals: a high-frequency burst component that is similar to that in burst neurons, and a low-frequency discharge related to the rostral spread of activity across the SC.

7. The activity of fixation neurons in the rostral pole contralateral to the site of stimulation, which typically paused for saccades and resumed their tonic discharge at the end of the saccade, showed a more prolonged pause during the interrupted saccades. The time of resumption of fixation cell discharge remained highly correlated with the termination of the postinterruption saccade.

8. We believe that these observations support the hypotheses that place the SC in a feedback loop controlling the amplitude and direction of saccades. In addition, the observations provide further evidence on the role of the SC in saccade generation: the fixation cells in the rostral SC inhibit the activity of the burst and buildup cells in the caudal SC; the burst neurons provide the signal for the total desired change in eye position rather than instantaneous motor error; and the activity of burst cells is held at one locus within the SC for a limited time (100–150 ms) for each saccade and only then can be released to a new site within the SC.

INTRODUCTION

The monkey superior colliculus (SC) is now recognized as critical for the generation of normal saccadic eye movements (Moschovakis and Highstein 1994; Sparks and Hartwich-Young 1989) in large part because of the relation of neuronal discharges in the SC to onset of saccades. Many cells increase their discharge rate before the onset of saccades when those saccades are directed toward a limited region of the visual field, the movement field of the cell (Schiller and Koerner 1971; Sparks 1975; Sparks et al. 1976; Wurtz and Goldberg 1971, 1972). These neurons give a burst of activity just before the saccade, are generally silent

during fixation, and have been referred to as saccade-related burst neurons (Sparks 1978) or simply burst neurons (Munoz and Wurtz 1995a). Most of these neurons have closed movement fields (saccades of the optimal direction whose amplitudes are too great or too small do not evoke discharge) (Moschovakis et al. 1988; Munoz and Wurtz 1995a; Sparks and Mays 1980) and a clipped discharge (the burst of activity ends as the saccade ends) (Waitzman et al. 1991).

Two other groups of neurons have recently been described in the monkey SC: buildup neurons (Munoz and Wurtz 1995a) and fixation neurons (Munoz and Wurtz 1993a). Buildup neurons are distinguished from the burst neurons by having continuous activity between the signal to make a saccade and its onset activity that builds up as the onset of the saccade approaches. These cells usually have open-ended movement fields (all saccades in the optimal direction and equal to or greater than the optimal amplitude are accompanied by an increase in discharge) and tend to have only partially clipped activity. Munoz and Wurtz (1995a) suggested that the buildup neurons were a more heterogeneous group than the burst neurons and might include cells having long-lead activity seen at deeper depths in the SC (Mohler and Wurtz 1976), others with long-lead activity called prelude bursters (Glimcher and Sparks 1992), and the quasivisual cells (Mays and Sparks 1980), although these categories of cells have not been tested under the same experimental conditions. Fixation neurons have been identified in the rostral SC of the cat (Munoz and Guitton 1989, 1991; Munoz et al. 1991a; Peck 1989) and the monkey (Munoz and Wurtz 1993a) that are active during visual fixation and pause with many saccades. Their activity is reciprocally related to that of the saccade-related cells in the more caudal SC.

In outline, the spatiotemporal distribution of activity among the different cell types in the monkey SC recently has been described as follows (Munoz and Wurtz 1995b). Between saccades, the fixation neurons at the rostral pole are active, and the saccade-related cells are largely silent. The first change in activity before a saccade is the gradual increase in the discharge rate of the buildup neurons and the modest reduction in fixation neuron activity. This is followed by a burst of activity preceding the saccade in the burst neurons, and the cessation of activity in the fixation neurons. During the saccade, the spatial distribution of activity in the burst neuron layer remains stationary on the SC motor map as burst activity diminishes (Sparks and Mays 1990; Waitzman et al. 1991). In contrast, in the buildup neuron layer, buildup neurons located progressively more rostrally in the SC begin to discharge during the saccade so that the spatial distribution of activity spreads toward the rostral SC. When this activity reaches the fixation neurons located in the rostral pole of the SC, the saccade ends. Thus two neuronal events within the SC coincide with the termination of the saccade: the termination of the burst discharge of burst neurons and the resumption of fixation neuron discharge.

Several models have emerged that place the SC within a feedback loop controlling saccade accuracy (Arai et al. 1994; Droulez and Berthoz 1991; Lefèvre and Galiana 1992; Munoz and Wurtz 1995b; Munoz et al. 1991a; Optican 1994; van Opstal and Kappen 1993; Waitzman et al. 1988, 1991). These models all vary in their precise architecture and organization of neuronal connections. However, an essential feature of these models is that the SC receives feedback about

ongoing saccades. To test the validity of these new models and evaluate whether the SC does receive feedback, we used electrical stimulation of the fixation neurons at the rostral pole of the SC to interrupt saccades. We find that such stimulation leads to a brief deceleration of saccades after a very short latency (Munoz and Wurtz 1993b). Monkeys compensate for this interruption and ultimately terminate the movement with the eyes close to the target. If the SC does control saccade trajectory, then the brief interruption induced by stimulating one rostral pole of the SC should increase the total duration of the saccade and should delay the time at which burst neurons stop discharging and fixation neurons resume their tonic discharge. On the other hand, if the SC issues a saccadic motor command that cannot be modified after the stimulation-induced interruption of the saccade, then the burst, buildup, and fixation neurons should not modify their discharges when the monkey compensates for the stimulation-induced perturbation. This approach is similar to that of the recent experiments of Keller and Edelman (1994), who interrupted saccades by stimulating the omnipause region of the pons.

We find that after brief electrical stimulation of the rostral pole of one SC during a saccade, activity of burst neurons is interrupted but resumes as the eyes move to the target. The pause in fixation cell discharge is prolonged by the interruption in saccade trajectory. At the termination of the modified saccade, burst neuron discharge ceases and fixation neuron discharge resumes. We believe the changes in activity of these neurons are consistent with the hypotheses that place the SC in a feedback loop controlling saccadic eye movements as well as providing further evidence on the role of SC neurons in saccade generation.

A brief report of some of these experiments has appeared previously (Waitzman et al. 1990).

METHODS

We stimulated and recorded from the SC of four rhesus monkeys (*Macaca mulatta*, identified as monkeys *a*, *c*, *p*, and *q*) that weighed between 5 and 12 kg. The procedures recently described (Munoz and Wurtz 1995a) were used for preparing the monkeys for experiments, and the same monkeys were used for both studies. Eye movements were recorded with the use of the magnetic search coil technique (Fuchs and Robinson 1966; Judge et al. 1980). Electrodes for electrical microstimulation and single-cell recording were directed toward the SC through an implanted recording cylinder angled 38° posterior of vertical; the center was directed at the midline 5 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 experiments the 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° of a tangent screen positioned 86 cm in front of the monkey. Each behavioral trial of ~2–3 s was preceded by an initial 2- to 3-s period of diffuse screen illumination (1.0 cd/m²). This background light was extinguished at the start of each behavioral trial, and the task was performed in total darkness except for the presence of the back-projected target spots produced by red light-emitting diodes (0.3 cd/m²). The light-dark cycle prevented the monkey from dark adapting.

Each task began when the monkey looked at a fixation point that came on 250 ms after the diffuse background illumination was

turned off. The monkey was required to maintain fixation for a random interval (500–1,000 ms) before proceeding with one of the following two saccade tasks. In the visually guided saccade paradigm a new target appeared in the peripheral visual field at the same time that the fixation point was turned off and the monkey had to look at the target. In the memory-guided saccade paradigm, used in three of the four monkeys, the target was flashed for 50–80 ms while the fixation point remained illuminated, and the monkey had to keep looking at the fixation point. After a randomized period of time (400–800 ms), the fixation point was turned off and the monkey had to make a saccade to the remembered location of the target flash. In this memory-guided paradigm, the target was turned off before the saccade began. In both these paradigms, the cue to initiate the saccade was the disappearance of the fixation point, and the monkey was required to maintain fixation until that time.

The monkey was required to maintain fixation within a computer-controlled window of $\pm 1^\circ$ to $\pm 5^\circ$ to obtain a liquid reward. The smallest window ($\pm 1^\circ$) was used for the central fixation point and for small target offsets ($< 10^\circ$), and the largest window was used for the largest target offsets ($> 50^\circ$). If the monkey's eyes left this window, the trial was aborted and the monkey received no reward. The monkey was usually given up to 500 ms to initiate the saccade after receiving the final signal to go (fixation point disappearance) and an additional 500 ms to enter the computer-controlled window around the target (to allow time for any interruption of the saccade due to stimulation). If either the eye in the window or the time constraints were not met, then the trial was aborted. 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, and the monkey was then returned to its home cage. Records were kept of the weight and health status of each monkey and supplemental fruit and water were provided as needed. The monkeys were under the care of the Institute veterinarian.

We studied saccade-related burst neurons, buildup neurons, and fixation neurons with the use of previously described criteria to identify these cells (Munoz and Wurtz 1993a, 1995a). We concentrated on burst neurons; those cells that had a high-frequency discharge just before saccade onset but little activity between the signal to make a saccade and the onset of the saccade. We first determined a target location that elicited the highest discharge rate with saccade initiation during the visually guided saccade task. The amplitude and direction of this target from the fixation point defined the optimal saccade vector of the cell. We then recorded the activity of that cell when the monkey made saccades of that amplitude and direction. We studied only a few buildup neurons; those cells that began to discharge at a low frequency after the signal to make a saccade and whose discharge continued until the onset of the saccade. For the buildup neurons, we also determined the target location that elicited the highest discharge rate of the cell, and then determined the effect of interrupting saccades to both visual and remembered targets. We also studied a few fixation neurons; those cells that discharged tonically when the monkey actively fixated a target of interest and that paused during most saccades.

We stimulated electrically the rostral pole of one SC to interrupt the saccade. Stimulation was at sites adjacent to the location of physiologically identified fixation neurons. Electrical stimulation in this region of the SC prevented the initiation of saccades or interrupted saccades in any direction when presented during the movement (Munoz and Wurtz 1993b). Stimulation was delivered through one of two types of electrodes. We used low-impedance ($< 0.5 \text{ M}\Omega$) tungsten microelectrodes (Frederick Haer) that had been used for recording single-cell activity, and stimulation with these electrodes was monopolar. The other type of stimulating electrodes used was low-impedance ($\sim 100 \text{ k}\Omega$) bipolar concentric electrodes (Kopf, SNE100). Both types of electrodes were lowered through guide tubes into the rostral SC, anchored into the

guide tubes with an epoxy adhesive, and kept in place for 3–7 days. During this time there was only a modest increase in the amount of current required to interrupt a saccade. Stimulation consisted of trains of biphasic pulses (0.3-ms cathodal and anodal pulses) all at 500 Hz with varying intensity and number of stimulus pulses. The intensity of stimulation was usually 20–50 μA and always $< 75 \mu\text{A}$. The number of pulses varied between two and six. The stimulation parameters for the individual experiments are given in RESULTS and the appropriate figure legends.

A major problem in recording the response of the SC neurons was the blocking of the amplifier used for recording single-cell activity in the caudal SC by the stimulation at the relatively nearby site within the rostral SC. In the worst case, we estimated that the amplifier missed action potentials for the duration of the stimulation train and for ~ 1 ms after the end of the train. The best recordings were obtained with the use of the bipolar stimulating electrode positioned in the contralateral rostral SC. In this condition, the stimulus artifacts were small and individual action potentials were discriminated easily during stimulation. Because of the residual concern over lost spikes due to the amplifier blocking, we also searched for cases of spontaneous saccadic interruptions that were not dependent on stimulation (Fig. 7).

In a typical block of trials, visually guided and memory-guided trials were randomly interleaved and electrical stimulation was presented on 50% of these trials. Stimulation was delivered at a predetermined time after disappearance of the fixation point in the visually guided and memory-guided saccade paradigms, which allowed us to stimulate before, during, and after the saccade. The time of stimulation was varied between 150 and 250 ms to coincide with saccadic reaction times of the monkeys. Three outcomes were possible: 1) the initial saccade was over before stimulation occurred; 2) the stimulation interrupted the ongoing saccade; and 3) the stimulation occurred before the start of the initial saccade.

After all the experiments were completed, the monkeys were deeply anesthetized with pentobarbital sodium and perfused through the heart. The brain was fixed with the use of procedures described in Ma et al. (1991). Sections through the sagittal plane were stained with thionin for cells and with the Gallyas stain (Gallyas 1979) for fibers, and examined microscopically to verify that the microelectrode penetrations were through the SC.

To evaluate the relation between cell discharge and specific events (such as the onset or end of an eye movement or train of stimulation), we produced a continuously varying spike density function (MacPherson and Aldridge 1979; Richmond and Optican 1987) aligned on these events. The spike density function for each trial was generated by substituting a Gaussian pulse of fixed width for each spike, and the Gaussians were summed together to produce a continuous function in time. Large values of the spike density function represented a higher probability of spike occurrence, and the peak of the function represents the peak discharge of the cell. The time from peak to $(1/e)$ for each Gaussian pulse was defined as σ , and for all figures and analysis σ had a value of 4 ms, with the exception of Fig. 17 in which σ had a value of 10 ms. Because we were usually interested in showing the relation of cell discharge to individual saccadic interruptions, in all but Fig. 18, the spike densities shown are for individual trials. For Fig. 18 the spike densities shown are mean spike density functions obtained by averaging over a series of trials.

Horizontal and vertical eye positions were digitized at 500 Hz. Saccades were identified and marked during off-line analysis, with the use of a previously described computer program that identified the onset and termination of each saccade with the use of velocity and acceleration threshold criteria (Waitzman et al. 1991). Any saccade recognition failures were corrected by the experimenter after visual inspection of the identifications made by the marking program.

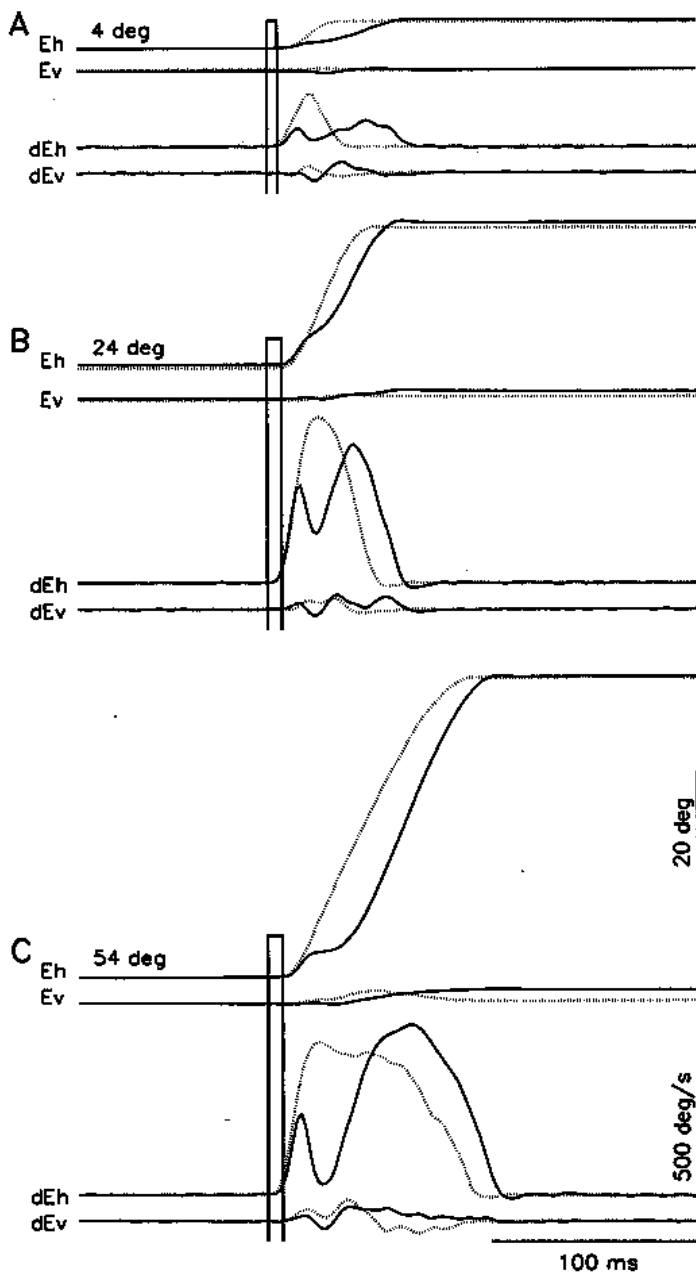


FIG. 1. Stimulation of the rostral right superior colliculus (SC) interrupts saccades. One example of an interrupted saccade (—) and a control saccade (· · ·) for monkey *a* is shown for rightward visually guided saccades to targets 4° (A), 24° (B), and 54° (C) from the fixation point. The 2 vertical lines indicate the time of the electrical stimulation, which consisted of 3 pulses (A) or 4 pulses (B and C) at 500 Hz. Note that despite the interruption the saccades reached the target. Leftward saccades (not shown) were also interrupted. Eh, horizontal eye position; Ev, vertical eye position; dEh, horizontal eye velocity; dEv, vertical eye velocity.

RESULTS

Interruption of saccades by stimulation

Brief high-frequency trains of electrical stimulation of the rostral pole of the SC, adjacent to the location of physiologically identified fixation neurons, interrupted saccades. Figure 1 compares normal saccades on visually guided control trials (· · ·) with saccades altered by electrical stimulation of the right rostral SC (—). In the control condition, the monkey

generated a single saccade to the target, and the velocity profile of this saccade was typical: bell-shaped for 4° and 24° saccades (Fig. 1, A and B) and skewed to the right for the 54° saccade (Fig. 1C). Electrical stimulation delivered to the rostral pole of the SC near the time of saccade initiation led to a brief interruption of the saccade. The effect of the interruption is most notable in the velocity profiles: an immediate deceleration of the saccade. The part of these interrupted saccades initiated before the stimulation-induced interruption we refer to as the preinterruption saccade, whereas the part occurring immediately after stimulation we refer to as the postinterruption saccade.

The amplitude and direction of the ensuing postinterruption saccade was usually sufficient to bring the eyes close to the target, as can be seen in the three individual examples shown in Fig. 1. Figure 2 shows the accuracy of the interrupted saccades in the four monkeys we studied by comparing the saccadic gains for the control and interrupted saccades (preinterruption saccade + postinterruption saccade) for various target positions in both the visually guided and memory-guided paradigms. Notice that the saccades for all the monkeys reached the vicinity of the target despite the interruption induced by electrical stimulation.

The peak velocity versus amplitude relationships of the preinterruption saccades, but not postinterruption saccades, differed from control saccades of the same amplitude. Figure 3 shows the main sequence relationship (amplitude vs. peak velocity) obtained from monkey *a* for control rightward saccades of different amplitudes and during saccades produced by interrupting visually guided saccades of 24° amplitude. Note that the main sequence of the preinterruption saccades (×; solid line) falls somewhat above that for the control saccades (○; dotted line), whereas the postinterruption main sequence (+; dashed line) is close to that for control saccades. The preinterruption saccade had the dynamics of a larger saccade (which it was intended to be), whereas the postinterruption saccade had the dynamics appropriate for its actual amplitude.

Burst neuron activity during saccade interruption

Electrical stimulation of the rostral SC not only led to an interruption of saccades, but it also modified the discharge of burst neurons in the SC. Figure 4 illustrates the discharge of a typical burst neuron during visually guided saccades of optimal amplitude and direction (Fig. 4A), during interruption of these saccades by stimulation (Fig. 4B), and with these two conditions superimposed (Fig. 4C). Figure 4B shows the consistent features of the burst neuron discharge. First, the stimulation not only fractionated the saccade to produce two peaks in the velocity profile, it also fractionated the neuron's saccade-related burst discharge to produce two peaks in the discharge profile. This is most evident from the spike density functions. Second, the number of spikes in the burst (the area under the spike density waveform) remained roughly constant despite the interruption. Third, the increase in time to achieve fixation of the target was matched by a comparable increase in time to the end of the burst. We provide quantitative support for these latter two points below. We consistently observed this interruption and resumption of activity in all of the 22 burst neurons studied in four monkeys.

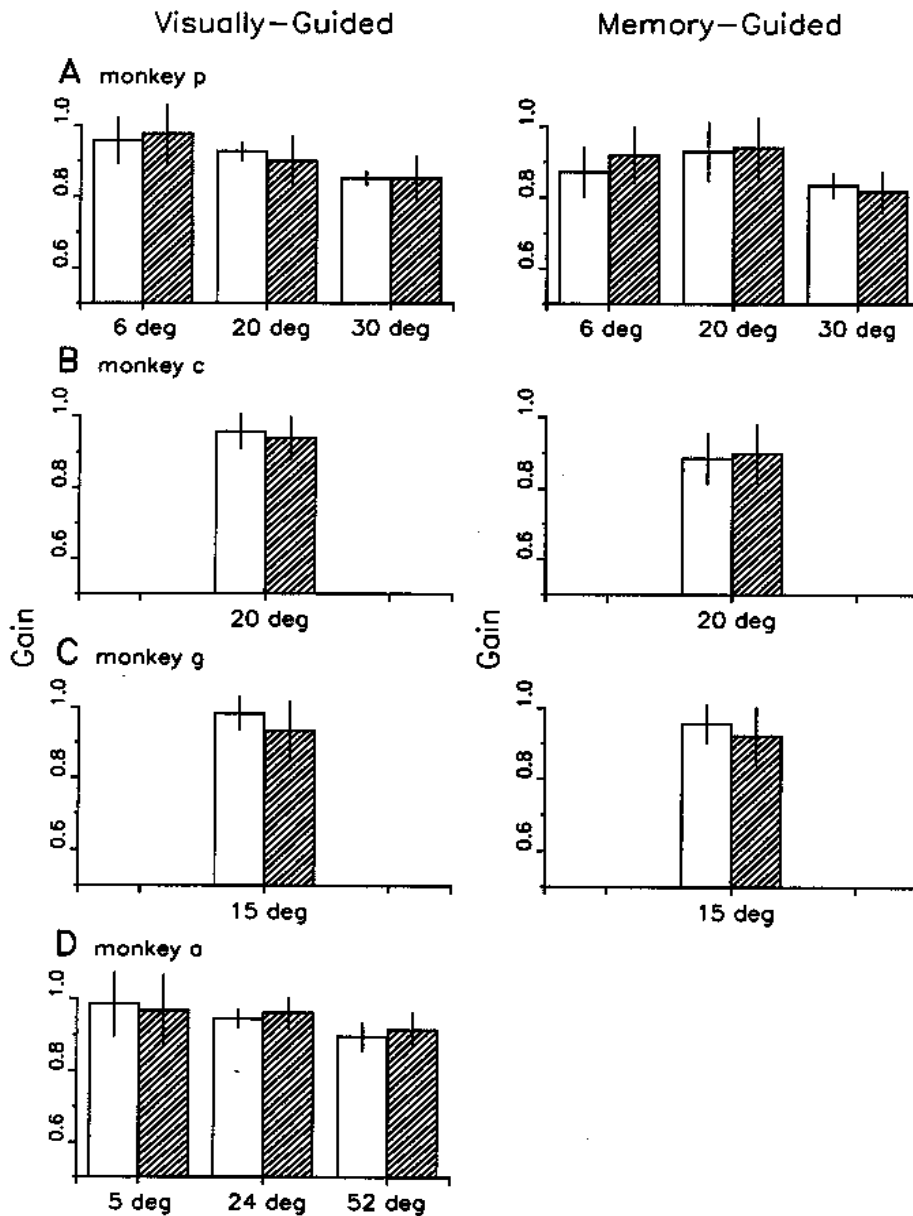


FIG. 2. Control and interrupted saccades have similar amplitudes. Gain (saccade end position/target position) is shown for control (open bars) and interrupted (hatched bars) saccades to some of the different targets in the visually guided and memory-guided paradigms for the 4 monkeys used in this study. The number of trials in each histogram ranged from 20 to 87 in the visually guided condition and from 13 to 48 in the memory-guided condition.

Both the resumption of the saccade and the neuronal firing of burst neurons depended on the time between the onset of electrical stimulation and the start of the preinterruption saccade. Figure 5 shows the responses of the same burst neuron as in Fig. 4, with stimulation delivered at successive times before and during visually guided saccades. We found that stimulation altered the saccade only when delivered <20–25 ms before saccade onset. The neuron was only reactivated after stimulation if a saccade was still required to drive the eyes to the target (Fig. 5, B–E). If the stimulation occurred long before the saccade (Fig. 5A), late in the saccade (Fig. 5F), or after the end of the saccade (not shown), then an additional saccade was not required and the neuron did not resume firing. The interruption of the neuronal discharge followed the time course of the saccadic interruption. The resumption of firing was not simply the rebound from stimulation-induced inhibition, but rather was temporarily linked with the execution of the postinterruption saccade.

The resumption of firing of the burst neurons during interrupted saccades was not due to any visual input to the neuron during the saccade, because burst neurons resumed firing during interruption of memory-guided saccades when no target was visible. Figure 6 shows the responses of the same burst neuron shown in Figs. 4 and 5 when the monkey made memory-guided saccades. The cell resumed firing before the postinterruption component of the memory-guided saccade, even though this movement was generated while there was no visual target and the monkey was in complete darkness. This result was confirmed in all 15 burst neurons that were tested in the memory-guided saccade paradigm in three monkeys.

The alteration of burst neuron firing with saccadic interruption also did not require electrical stimulation of the rostral pole of the SC. We saw a similar pause and resumption of activity of burst neurons during spontaneous interruptions (no electrical stimulation) in saccades that occasionally oc-

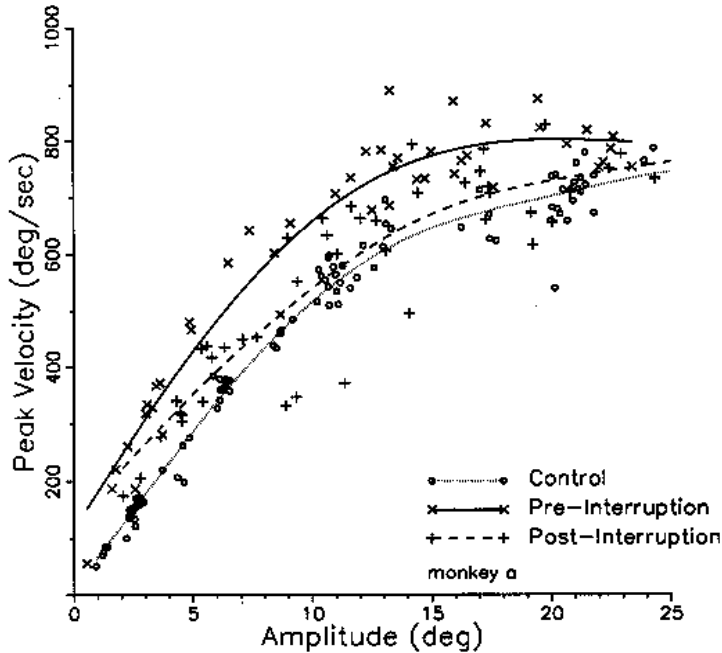


FIG. 3. Main sequence of interrupted saccades. Plot of peak velocity vs. amplitude for control saccades (\circ), preinterruption saccades (\times), and postinterruption saccades ($+$) in the visually guided saccade paradigm. The data from control saccades were to targets located 0.5° – 60° to the right, and the dotted line represents a spline function fit to the data. The data points from the preinterruption and postinterruption saccades were obtained from interrupting saccades to targets located 24° to the right. The solid and dashed lines represent spline fits through the preinterruption and postinterruption data points, respectively. The preinterruption saccades tend to lie above the control main sequence, whereas the postinterruption saccades are similar to control saccades.

curred in the memory-guided saccade paradigm. Figure 7 shows an example for the same burst neuron illustrated in Figs. 4–6. The neuron began to burst before saccade onset, reduced its discharge immediately before the deceleration of the saccade, and then increased its discharge immediately before the reacceleration of the saccade. Note that the duration of both the saccade and the burst increased during this spontaneous interruption, just as happened after electrical stimulation.

Quantification of burst neuron responses

We obtained sufficient data from 22 burst neurons in four monkeys to allow for a detailed analysis of the discharge during control and stimulation-interrupted saccades. The neurons had optimal saccadic amplitudes ranging from 3° to 40° . These analyses show that the change in activity of burst neurons parallels the changes in the interrupted saccades: the total number of spikes remained constant, as did the saccade amplitude; the duration of the spike activity was prolonged, as was the saccade duration; and the resumed spike activity was temporally correlated with the dynamics of the saccade trajectory in the postinterruption saccade.

SPIKE COUNT. The area under the spike density waveforms in Figs. 4 and 5 appeared similar for control and interrupted saccades, suggesting that the number of spikes generated by the burst neuron may have been held constant for a specific amplitude of saccade despite the stimulation-induced interruption of the saccade. To verify this observation, we counted the number of spikes from 8 ms before saccade onset to 8 ms before the end of the visually guided control saccade, and we compared this with the number of spikes

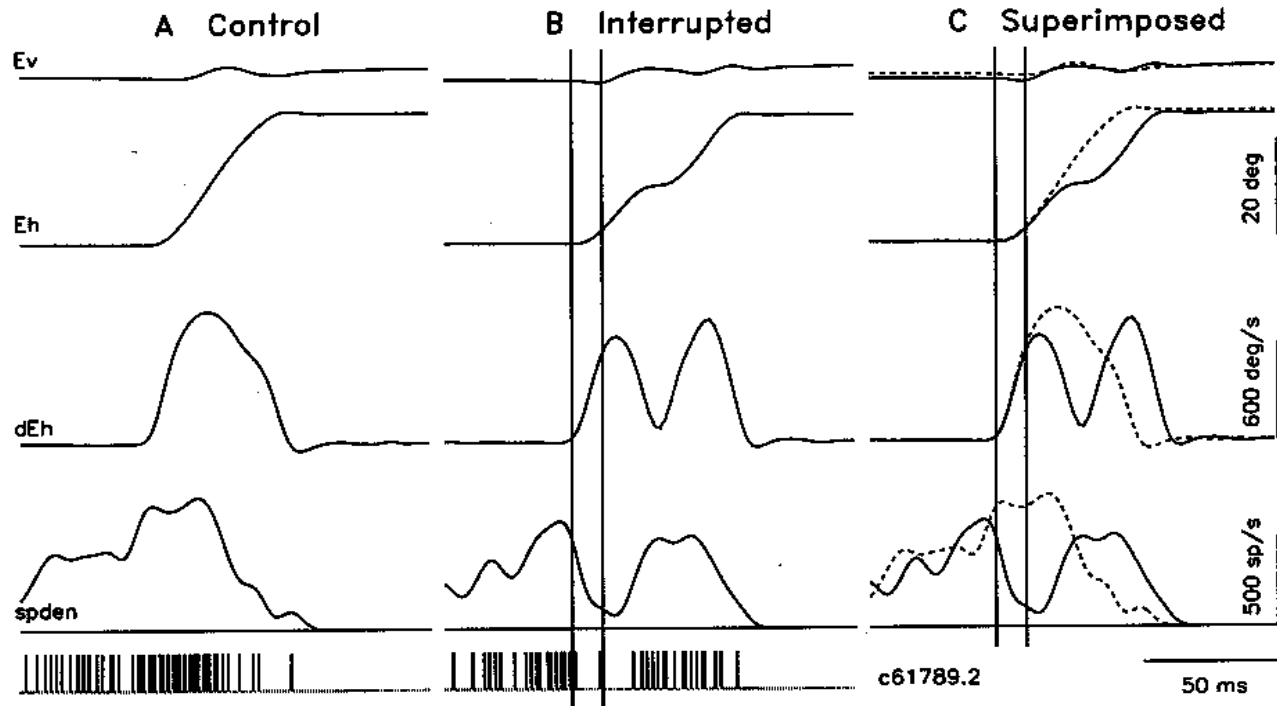


FIG. 4. Burst neuron activity pauses and resumes during interrupted saccades. Activity of the neuron was recorded during a visually guided saccade of the optimal amplitude and direction (A) and an interrupted saccade to the same visual target (B). The traces are superimposed in C. Shown are the spike density for the single trial ($\sigma = 4$ ms), and representations of the individual action potentials. The neuron responded best to saccades of 30° amplitude. Electrical stimulation, consisting of 6 pulses at 500 Hz delivered to the rostral left SC, was presented between the 2 vertical lines. Neuron was located in the left SC of monkey c.

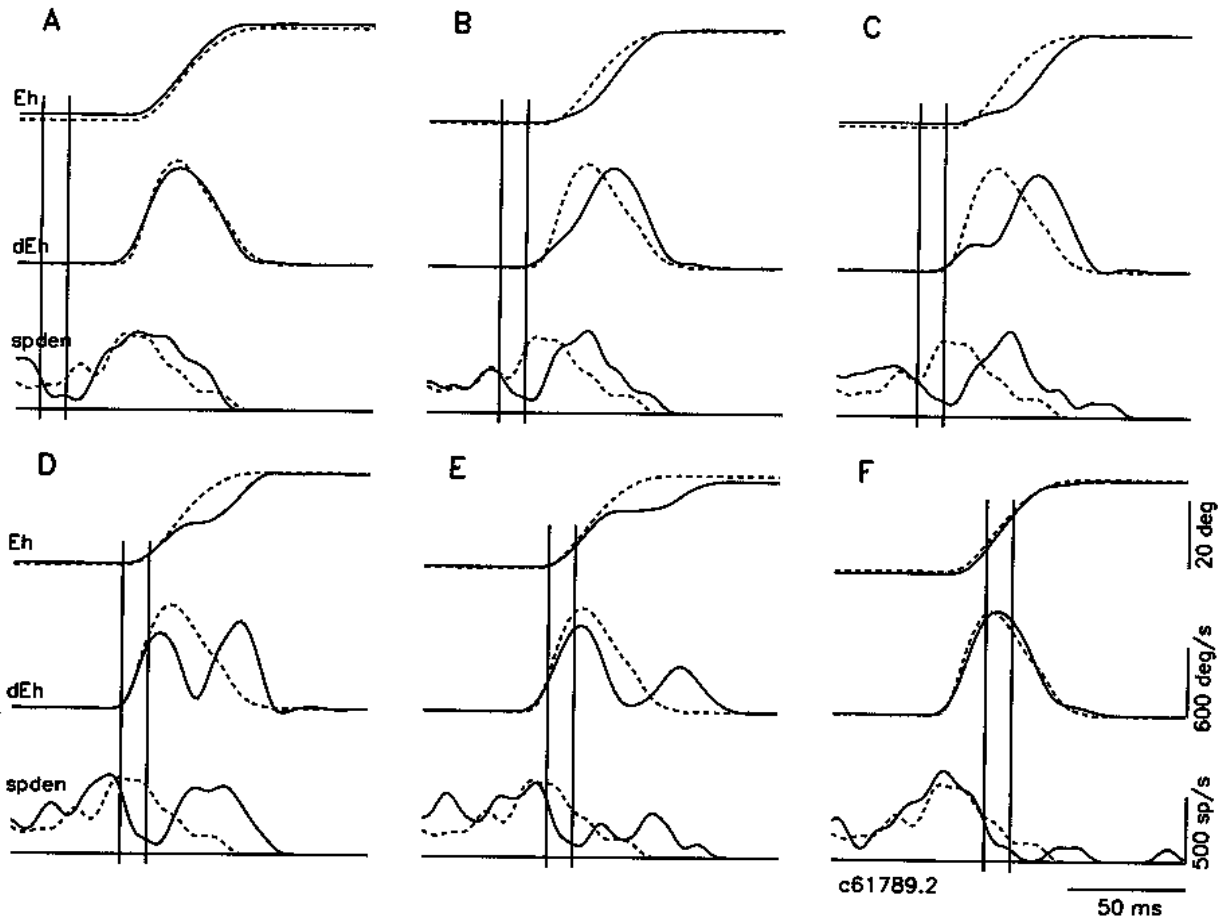


FIG. 5. Interruption of saccade and burst cell activity only occurred after stimulation given at the time of saccade generation. The 6 examples in the visually guided paradigm show stimulation progressively closer to the time of saccade onset (*A-D*), overlapping the saccade onset (*E*), and after saccade onset (*F*). Eye position, eye velocity, and spike density (*spden*) waveforms related to individual interrupted saccades (—) are superimposed on those for a control saccade (---). The traces of action potentials are from the interrupted trials. Same cell and stimulation parameters as in Fig. 4.

that occurred from 8 ms before the onset of the preinterruption saccade to 8 ms before the end of the postinterruption saccade. We shifted the sampling period backward in time by 8 ms because we inferred that this was the minimum period in which collicular activity contributed to a saccade, because stimulation of the deeper layers of the extrafoveal SC in the monkey altered the ongoing saccade within 8–10 ms (Munoz and Wurtz, unpublished observations). Figure 8 shows the distribution of spike counts of a burst neuron for 30° visually guided control (Fig. 8*A*) and stimulation-interrupted (Fig. 8*B*) saccades. An approximately equal number of action potentials were recorded in the two conditions: the mean was 17.8 ± 1.5 (SD) ($N = 14$) for control saccades and 16.2 ± 3.8 (SD) ($N = 34$) for interrupted saccades. This close relationship held for all 22 burst neurons studied, as shown in Fig. 9, which plots the mean number of spikes in control saccades against interrupted saccades for movements of the optimal amplitude and direction for each neuron. The regression line has a slope of 0.84 and a correlation coefficient of 0.94, indicating a close relationship between the number of spikes of burst neurons with the control and interrupted saccades.

BURST DURATION VERSUS SACCADE DURATION. The interruption of the saccade after stimulation increased the time from saccade onset to the time the eyes reached the target.

If the burst neurons contribute to the generation of the postinterruption saccades, then there should also be an increase in the duration of neuronal discharge. Burst duration was measured from 8 ms before saccade onset to the time when the discharge fell below 10% of the peak value of the spike density. In the case of interrupted saccades, we determined the time at which activity accompanying the postinterruption saccade fell below 10% of the peak value.

Figure 10*A* plots the total eye movement duration versus total burst duration for one burst neuron for saccades of optimal amplitude and direction. A linear regression analysis through all of the data points had a slope of 1.29 with a strong correlation coefficient ($r = 0.93$), indicating a clear relation between burst duration and saccade duration. Figure 10, *B* and *C*, shows histograms of the slopes and correlation values for all 22 burst neurons analyzed. For most burst neurons, there was a clear correlation between total eye movement duration and total burst duration.

DYNAMICS OF SACCADIC AND NEURONAL RESPONSES. Waitzman et al. (1988, 1991) described the clipping in burst neuron discharge that occurred during a saccade and suggested that the sharp reduction in burst neuron discharge that occurred at the end of a saccade was an active process related to controlling saccade trajectory. We investigated whether this relationship was maintained for the saccades interrupted

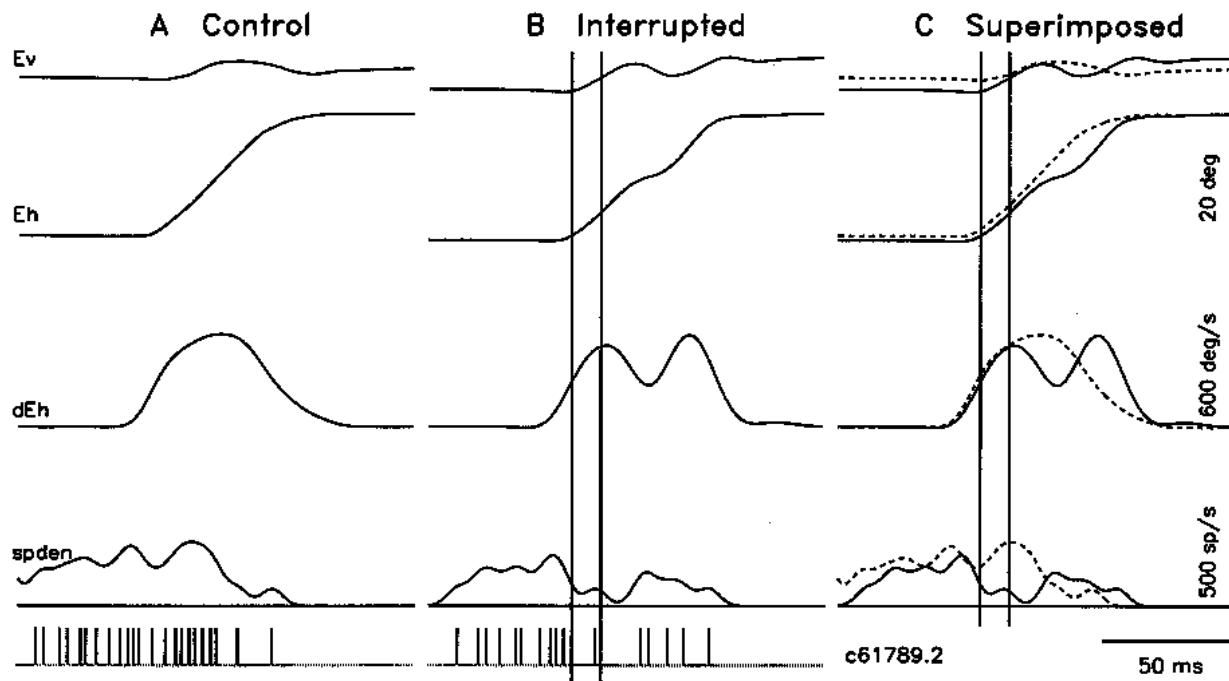


FIG. 6. Burst neuron activity associated with a postinterruption saccade was not affected by visual stimulation during the saccade. A memory-guided saccade of optimal amplitude for a burst neuron (A) and an interrupted memory-guided saccade of optimal amplitude (B) are superimposed in C. Note that the cell was active for the postinterruption saccade. Same cell and stimulation parameters as in Fig. 4.

with stimulation of the rostral SC. Figure 11 shows plots of spike density versus saccade amplitude for a representative burst neuron (same neuron as shown in Figs. 4–7) whose optimal saccade amplitude was $\sim 30^\circ$. The activity of the neuron decreased as the saccade progressed from 0° toward 30° (Fig. 11A). On interruption trials (Fig. 11B, $\cdot\cdot\cdot$),

the burst neuron resumed its discharge after the interruption, and the value of spike density was close to that appropriate for the continuing saccadic trajectory (compare $\cdot\cdot\cdot$ in Fig. 11B with —, which is the mean of the control trials).

We found that 16 of the 22 burst neurons analyzed were similar to the neuron shown in Fig. 11. That is, after the

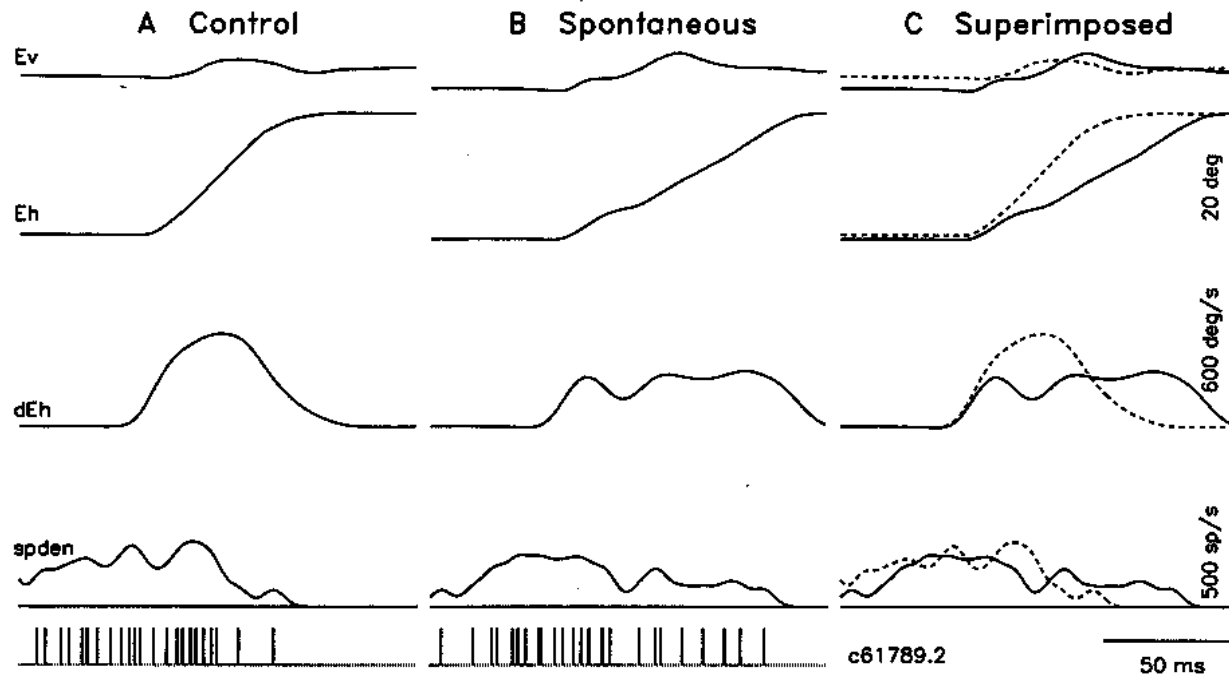


FIG. 7. Activity of a burst neuron was altered during spontaneously interrupted memory-guided saccade. A memory-guided saccade of optimal amplitude for a burst neuron (A) and a spontaneously interrupted memory-guided saccade of optimal amplitude (B) are superimposed in C. No electrical stimulation was given. Note that the cell was active for the postinterruption saccade. Same cell as in Fig. 4.

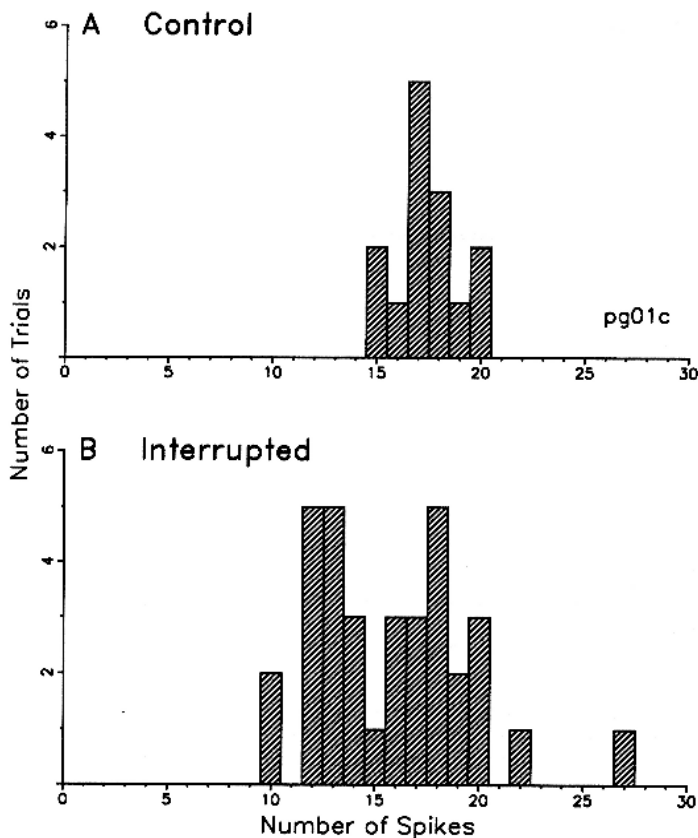


FIG. 8. Similar number of spikes recorded from a burst neuron during interrupted and normal visually guided saccades. *A*: number of spikes recorded in the saccade burst for control trials. *B*: number of spikes for interrupted saccades. The mean numbers of spikes counted in the 2 conditions were 17.8 ± 1.5 (SD) ($N = 14$) in control trials and 16.2 ± 3.8 (SD) ($N = 34$) in the stimulation trials. The neuron, recorded in *monkey p*, responded best to saccades that were 30° in amplitude. Stimulation consisted of 4 pulses at 500 Hz delivered to the ipsilateral rostral SC during saccades of optimal amplitude.

interruption in burst neuron discharge and saccade trajectory, the relationship between spike density and saccade trajectory was reinstated. For five other neurons there was an overshoot after the interruption above the value for a control saccade, and for one neuron there was a considerable undershoot in the spike density. Thus, for most burst neurons, the instantaneous discharge of the SC burst neurons returns to or approaches that of the control saccade after the interruption produced by stimulation.

Spatial distribution of activity in the burst cell layer

We have already noted that the burst neurons active for the preinterruption saccade resumed firing during the postinterruption saccade, but we also wanted to determine whether burst neurons located elsewhere on the SC motor map were activated for the postinterruption saccade. We know from previous experiments that a constant-sized population of burst neurons is activated for a saccade and that there is no change in the spatial distribution of activity during control saccades (Munoz and Wurtz 1995b). To determine whether the locus of activity remained fixed on the motor map during the preinterruption and postinterruption saccades, we first recorded activity of a burst neuron for control and interrupted

saccades of the optimal amplitude and direction for the neuron. We verified that the neuron was not active for very large saccades of the optimal direction but outside the neuron's movement field. We then determined whether the cell was active after interruption of these large-amplitude saccades when the postinterruption saccades were of the optimal amplitude for the neuron under study. Figure 12 shows the activity of one burst neuron that preferred saccades of $\sim 20^\circ$ amplitude, as indicated by the cross section of the movement field for saccades of increasing amplitude along the optimal saccadic direction (Fig. 12*A*). The movement field of the burst neuron was closed, that is, the neuron did not discharge action potentials for saccades greater than the optimal amplitude (i.e., $>40^\circ$ amplitude). Figure 12*B* shows neuronal activity associated with a 22° visually guided saccade, for which it was maximally active, and Fig. 12*C* shows the lack of activity associated with the large 54° saccade. When stimulation interrupted a 22° saccade (Fig. 12*D*), the burst neuron was silenced and then resumed firing for the ensuing postinterruption saccade. When stimulation interrupted a 54° saccade, to produce a postinterruption movement of 20° , there was no high-frequency burst when the postinterruption saccade was triggered 60 ms after the stimulation-induced interruption (Fig. 12*E*). The same neuron, however, did burst when the same 20° postinterruption saccade was triggered 230 ms after the interruption (Fig. 12*F*). Thus, although the cell was maximally active for 20° saccades, it was not activated for 20° postinterruption saccades unless there was a considerable delay before the onset of this postinterruption saccade. The long delay in onset of the postinterruption saccade in Fig. 12*F* suggests that the first movement was aborted after interruption and a new saccade was triggered.

Figure 13 emphasizes the generality of this result by showing activity from a different burst neuron whose optimal

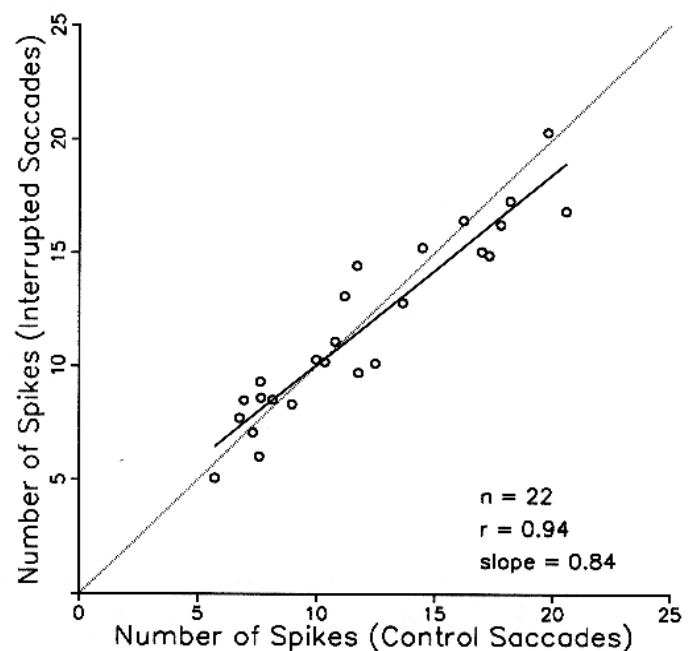


FIG. 9. Similar numbers of spikes during interrupted (*ordinate*) and control (*abscissa*) saccades in the sample of 22 burst neurons. The neurons included had optimal saccadic amplitudes ranging from 3° to 40° , and for all neurons the number of spikes was very similar under the 2 conditions.

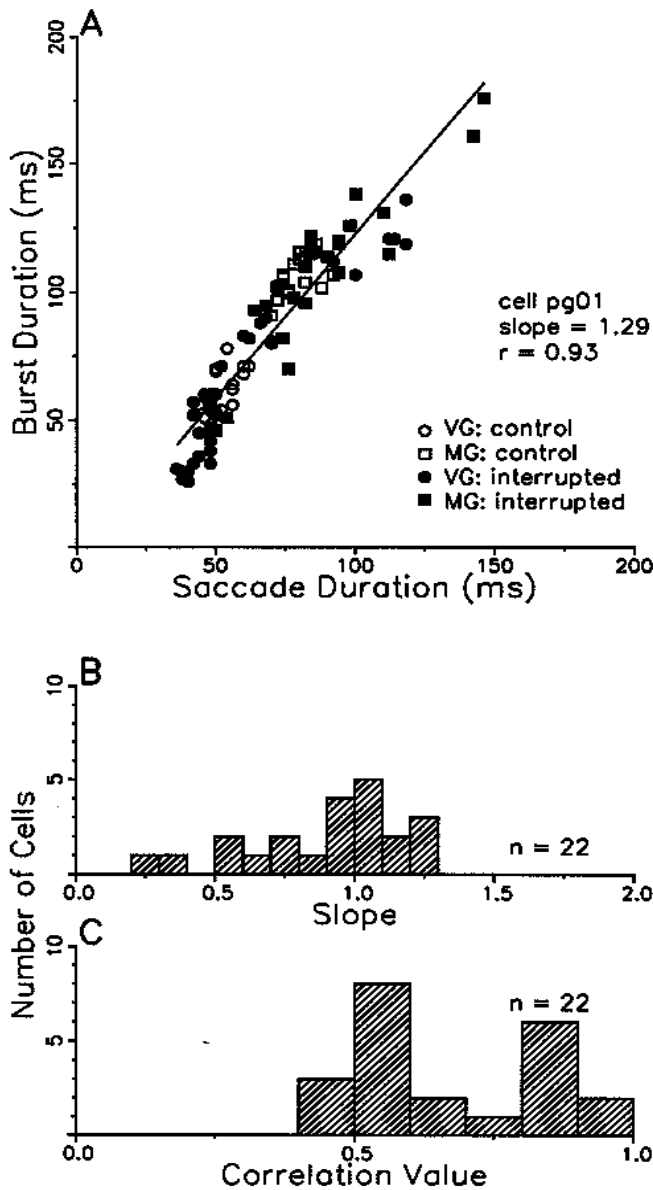


FIG. 10. Duration of the saccade and the duration of the burst neuron activity increase linearly during interrupted saccades. **A**: plot of total burst duration vs. total saccade duration for control and stimulated trials for 1 burst neuron in *monkey p*. For interrupted saccades, the duration of the saccade was from the beginning of the preinterruption saccade to the end of the postinterruption saccade. The solid line was generated from a linear regression analysis through all data points (slope = 1.29; correlation coefficient = 0.93; Y -intercept = -6.11). Note that on trials when duration was prolonged by the stimulation-induced interruptions, there was a comparable increase in the duration of cell activity. VG, visually guided saccades; MG, memory-guided saccades. The neuron responded best to saccades that were 30° in amplitude. Stimulation consisted of a brief train of 4 pulses at 500 Hz, delivered to the ipsilateral rostral SC. **B** and **C**: bar graphs showing the range of slopes and correlation values for all 22 burst neurons analyzed. The slopes ranged from 0.36 to 1.29, and the correlation coefficients ranged from 0.42 to 0.94. Note that the slopes cluster near 1 and that the correlation values largely extend above 0.5.

amplitude was $\sim 5^\circ$ (Fig. 13A). This neuron also had a closed movement field and was not active for saccades $> 15^\circ$ in amplitude. The neuron was maximally active for the 4°

saccade (Fig. 13B) and silent for the 22° saccade (Fig. 13C). When the 4° saccade was interrupted, the burst from the neuron was truncated but the cell then resumed its burst for the postinterruption movement (Fig. 13D). The neuron was silent for 22° interrupted saccades having a 4° postinterruption component triggered 25 ms after the interruption (Fig. 13E), but was active for the 3° postinterruption movement when the movement was initiated 170 ms after the interruption (Fig. 13F). This result once again shows that burst neurons at the initial site of activation were reactivated for the postinterruption saccade and not neurons at a new site in the SC. Only after a sufficient time had elapsed was a new site in the SC activated corresponding to the new saccade.

To quantify the time necessary for this shift in the locus of burst activity following a stimulation-induced interruption in saccade trajectory, we recorded from neurons whose optimal saccade was appropriate for the amplitude of the uninterrupted saccade (the initial site in Fig. 14A) and from those at the site of the activity associated with the amplitude of the postinterruption saccade (the new site in Fig. 14A). We plotted the activity at these two sites (average firing frequency in the burst) against the time from the interruption to the onset of the postinterruption saccade (latency to postinterruption saccade; Fig. 14, B and C). The activity of burst neurons at the initial site (●), coding the

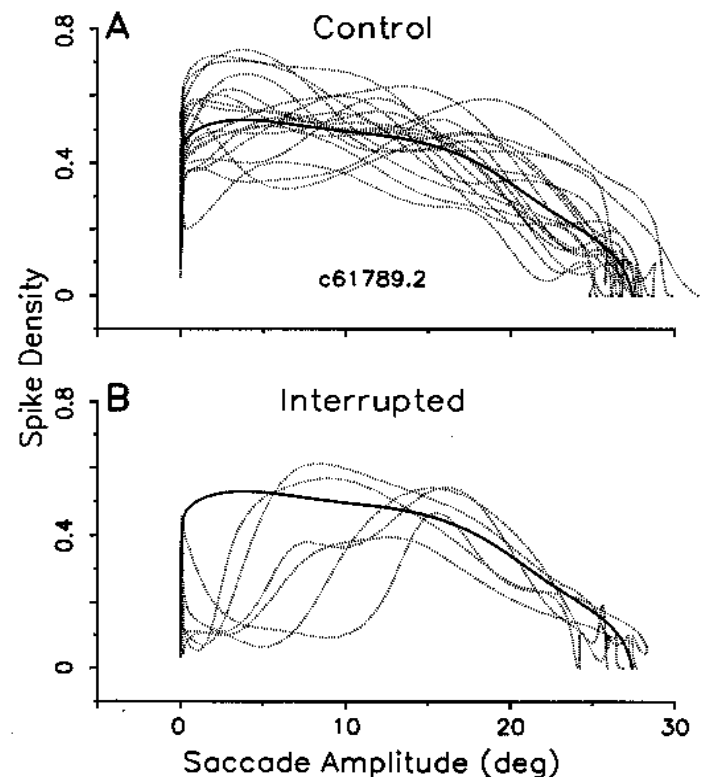


FIG. 11. Plots of spike density versus trajectory of visually guided saccades for a typical burst neuron (same neuron as in Figs. 4–7). **A**: individual (· · ·) and mean (—) traces from control trials. **B**: superposition of individual trials from interrupted trials (· · ·) and the mean curve from the control trials (—). The curves begin at 0° and proceed toward 30°; time is implicit in the plots. The spike density function was shifted backward in time by 7 ms (see Waitzman et al. 1991 for more details). The interruption trials are similar to those shown in Fig. 5, B–E. Note that after the stimulation deflects the curves return to the original trajectory.

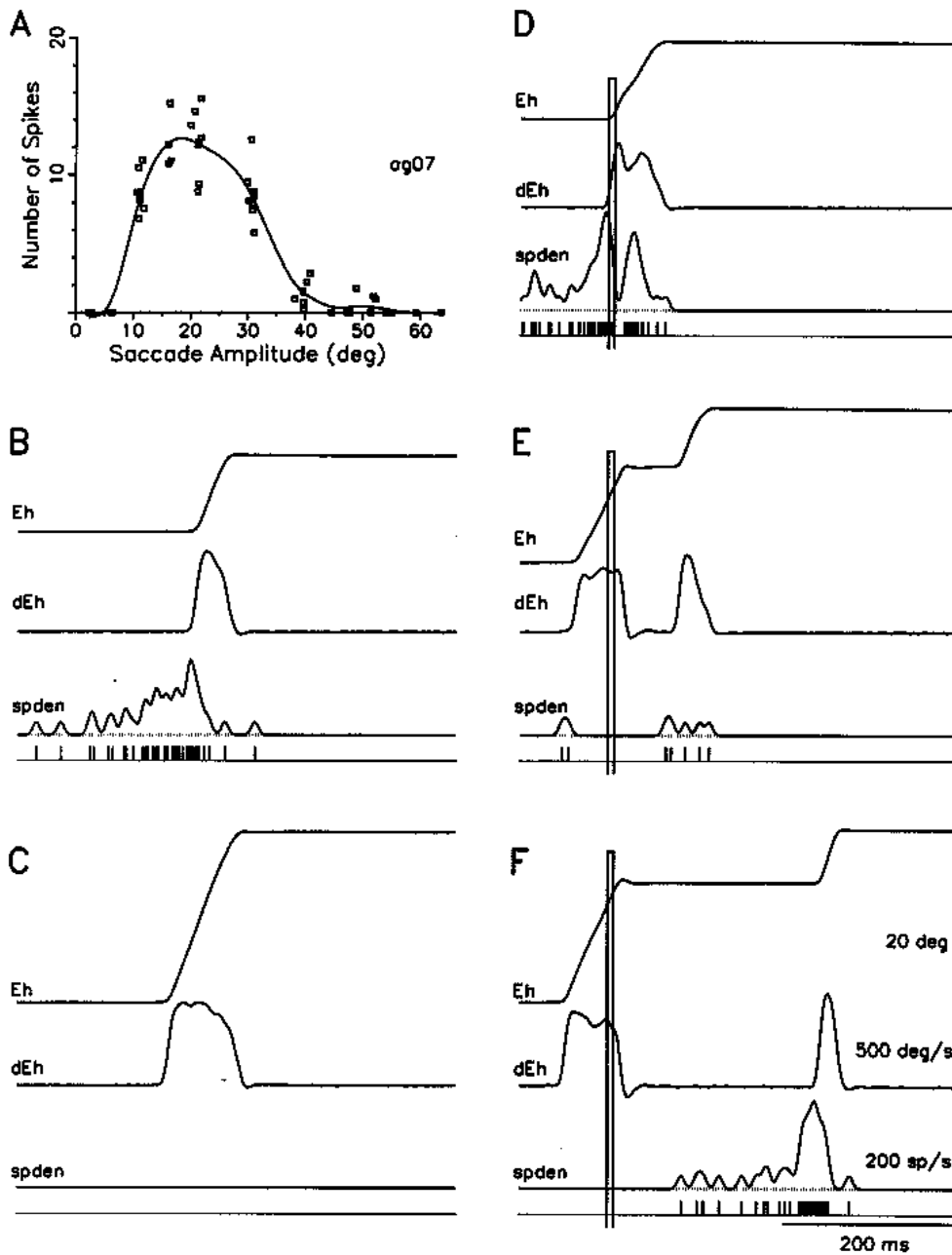


FIG. 12. Activity of a burst neuron in the caudal left SC discharging maximally for $\sim 20^\circ$ rightward visually guided saccades. *A*: cross section of the movement field for visually guided saccades along the optimal saccadic direction. *B*: maximal discharge for 22° control saccades. *C*: no activity for 54° control saccades. *D*: cell was active for 22° saccades and had a characteristic pause in discharge during saccade interruption. *E*: cell was almost silent during interruption of a 54° saccade, even though the postinterruption saccade triggered 72 ms after the interruption was $\sim 20^\circ$. *F*: cell discharged a high-frequency burst when the postinterruption saccade occurred 230 ms after the interruption. Stimulation consisted of a brief train of 4 pulses at 500 Hz, delivered to the rostral right SC.

amplitude and direction of the initial (preinterruption + postinterruption) saccade, dropped off when the postinterruption saccade occurred >100 – 150 ms after the interruption. In sharp contrast, the burst neurons at the new site (\circ) became activated only when the postinterruption saccade was initiated >100 ms after the interruption. Thus there was a shift in activity from one site on the SC to another when the poststimulation saccade occurred after an interruption of 100 – 150 ms.

Buildup neuron activity during interrupted saccades

We also recorded the activity of buildup neurons while we stimulated the rostral SC to interrupt saccades. Figures 15 and 16 show the open-ended movement fields and discharge of two buildup neurons, whose optimal saccade amplitudes were $\sim 20^\circ$ (Fig. 15) and 5° (Fig. 16). We selected these buildup neurons because their optimal amplitudes were

very similar to those of the two burst neurons shown in Figs. 12 and 13. The buildup neuron in Fig. 15 had a typical open-ended movement field: it was active for all rightward saccades that were $>10^\circ$ in amplitude (Fig. 15*A*). For control saccades, this neuron achieved a higher frequency of discharge for 20° saccades (Fig. 15*B*) than for 50° saccades (Fig. 15*C*), and this is characteristic of many buildup neurons (Munoz and Wurtz 1995a). When saccades of 20° (Fig. 15*D*) or 55° (Fig. 15, *E* and *F*) were interrupted with electrical stimulation of the contralateral rostral SC, there was a brief cessation in the discharge of the buildup neuron. However, the buildup neuron resumed its discharge shortly after the stimulation and well before the initiation of the postinterruption saccade. During the interruption of the 55° saccades, the neuron only discharged a high-frequency burst of action potentials when the 20° postinterruption saccade was triggered 180 ms after the interruption (Fig. 15*F*). If the postin-

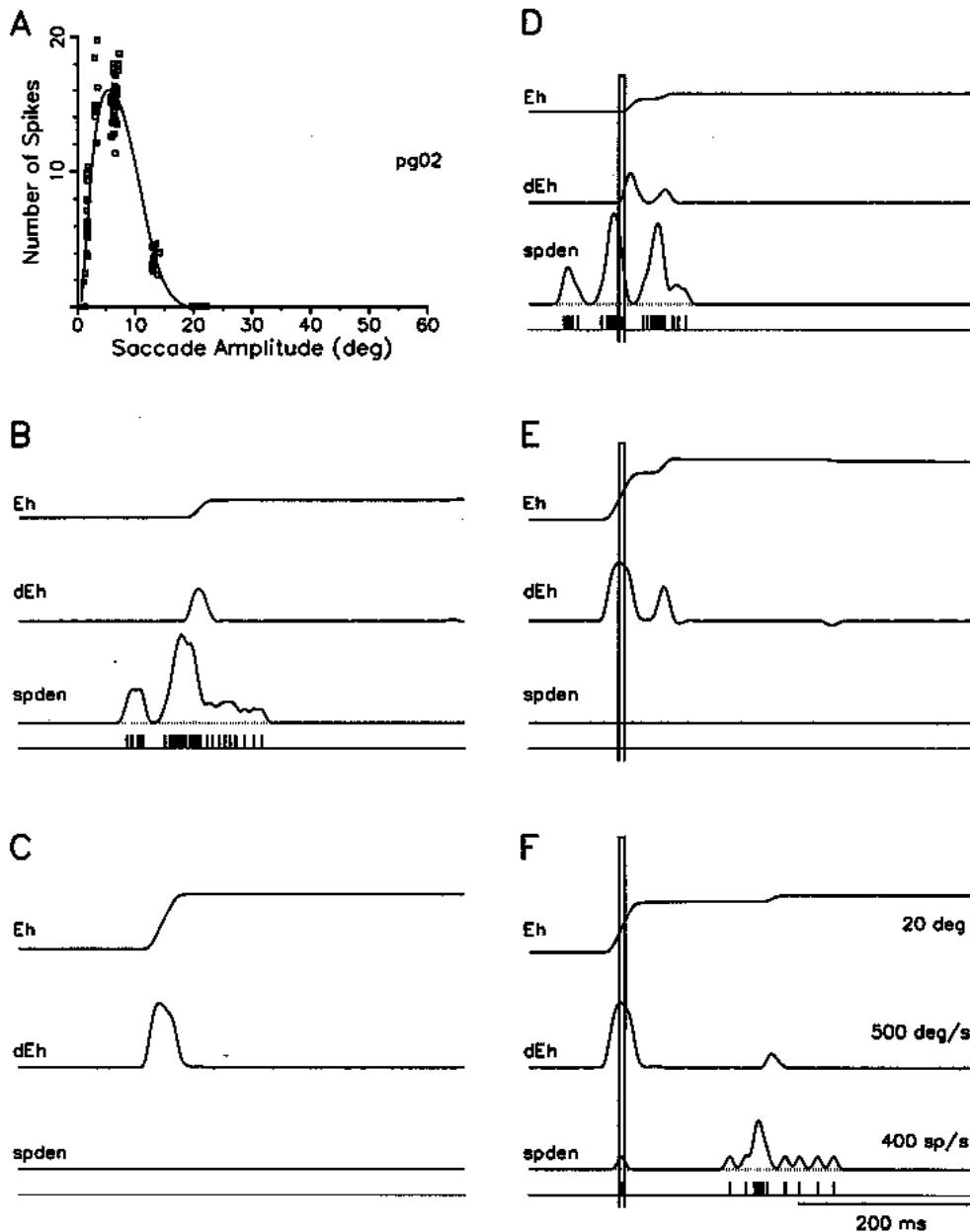


FIG. 13. Activity of a burst neuron located in the left SC discharging for $\sim 5^\circ$ amplitude visually guided saccades. *A*: movement field of the neuron, which discharged maximally for 5° control visually guided saccades (*B*) and was silent for 22° control saccades (*C*). *D*: cell was active for 6° saccades and had a characteristic pause in discharge during saccade interruption. *E*: cell was silent during interruption of a 22° saccade, even though the postinterruption saccade triggered 44 ms after the interruption was $\sim 4^\circ$, clearly inside the cell's movement field. *F*: cell discharged a high-frequency burst when a 3° postinterruption saccade occurred 170 ms after the interruption. Stimulation consisted of a brief train of 4 pulses at 500 Hz, delivered to the rostral pole of the left SC. The initial burst in *B* and *D* was a visual response to onset of the target in the neuron's visual receptive field.

interruption saccade was triggered 55 ms after the interruption, then the buildup neuron was reactivated immediately after the stimulation, but it did not achieve the level of discharge that was present for 20° control saccades (compare Fig. 15, *E* and *B*).

Figure 16 shows the activity of the buildup neuron that was maximally active for saccades 5° in amplitude. This neuron discharged for all saccades $>5^\circ$ in amplitude, and was presumed to have an open-ended movement field (Fig. 16*A*). Although we only tested this neuron for saccades out to 22° in amplitude, the shape of its movement field was clearly different from the burst neuron with the closed movement field in Fig. 13. The discharge of this buildup neuron was only momentarily interrupted after stimulation of the contralateral rostral SC (Fig. 16, *D-F*), and the neuron resumed its discharge well before the initiation of the post-interruption saccade, regardless of whether the postinterruption

saccade was triggered immediately (Fig. 16, *D* and *E*) or long after (Fig. 16*F*) the interruption. Once again, note that the high-frequency response of the neuron's discharge was only observed when the postinterruption saccade was triggered >150 ms after the interruption (Fig. 16*F*).

One additional aspect of buildup neuron activity was quite comparable with that of the burst neurons. It was previously reported that many buildup neurons also discharged a high-frequency burst of action potentials for saccades of the optimal amplitude and direction. This high-frequency discharge did not accompany saccades with amplitudes greater than the optimal amplitude (Munoz and Wurtz 1995a). It is worth noting that, for the buildup neurons illustrated in Figs. 15 and 16, the times at which the discharge exceeded 200 spikes/s were very similar to those of the burst neurons (Figs. 12 and 13). It was as if the buildup neurons carry an additional low-frequency component to their discharge that produces

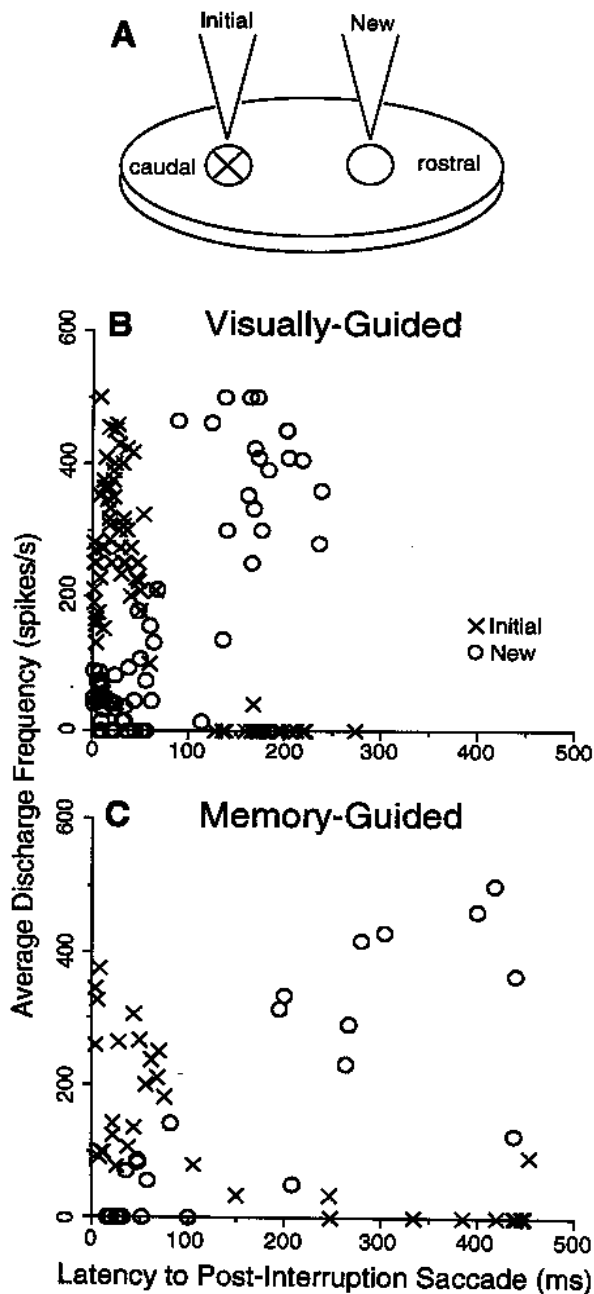


FIG. 14. Shift in locus of activity of burst neurons from 1 area of SC to another when the postinterruption saccade was delayed. *A*: schematic to show the position of the neurons recorded in relation to the initially studied interrupted saccade (Initial) in the caudal SC and the area of the SC that became newly active (New) in the more rostral SC when the postinterruption saccade was delayed. *B* and *C*: plots of firing frequency of 6 burst neurons vs. latency from the interruption of the saccade to the onset of the postinterruption saccade. ●, activity at the initial site; ○, activity at the new site, for both visually guided saccades (*B*) and memory-guided saccades (*C*). Data from initial site are from neurons whose optimal amplitudes matched the initial (preinterruption + postinterruption) amplitude. Data from the new site are from neurons whose optimal amplitudes matched the amplitude of the postinterruption saccade only. The firing frequency was computed by counting the number of spikes from 8 ms before the start of the postinterruption saccade to 8 ms before its termination and dividing by the duration of the saccade. Note that at the initial site, burst neurons are active for the postinterruption saccade, provided it is triggered within 100 ms of the interruption. At the new site, burst neurons are only activated when the postinterruption saccade was triggered >100 ms after the interruption.

the open-movement fields, and makes them distinct from the burst neurons.

We were able to record from nine buildup neurons while interrupting saccades, and comparable results were obtained for all neurons. Although we were unable to demonstrate whether electrical stimulation delayed the spread of activity among buildup neurons, we were able to see that all buildup neurons stopped discharging briefly during the electrical stimulation and resumed their discharge immediately after the period of stimulation.

Fixation neuron activity during interrupted saccades

We also recorded from four fixation neurons in the rostral left SC of one monkey (*monkey g*) while we interrupted saccades by electrically stimulating the rostral right SC. Figure 17 shows the discharge of one fixation neuron when stimulation was given at various times relative to the saccade. The neuron had the characteristic pause in its discharge associated with the saccade. After stimulation, the activity of the neuron increased in the interval between the pre- and postinterruption saccades, provided this interval was beyond ~40 ms (Fig. 17, *D* and *E*). Note also that the stimulation did not modify the discharge of the neuron when it was presented before (Fig. 17*A*) or after (Fig. 17*F*) the saccade.

Figure 18 compares the discharge of another fixation neuron during visually guided saccades with the discharge during interrupted saccades. The traces are aligned on the end of the saccade. This neuron paused for the duration of the control saccade and resumed activity shortly before the eyes achieved the new target (Fig. 18*A*). The electrical stimulation delayed the time that the eyes reached the target and delayed the resumption of discharge of the fixation neuron (Fig. 18*B*). The only difference in the firing of the neuron between the two conditions (Fig. 18*C*) was the prolonged pause during the interrupted trials, related to a comparable increase in the duration of the saccade (preinterruption saccade + postinterruption saccade).

DISCUSSION

Stimulation among the fixation cells in the rostral SC not only interrupted saccades in midflight, but it also altered the discharge of SC burst neurons, buildup neurons, and fixation neurons. We found that 1) burst neuron activity decreased while the saccade was interrupted; 2) if the postinterruption saccade was triggered <100 ms after the stimulation-induced perturbation, then burst neuron activity resumed at the same SC locus; 3) burst neuron activity was initiated at a different SC locus when the postinterruption saccade was triggered >100–150 ms after the interruption; and 4) the buildup neurons were only transiently interrupted by the electrical stimulation, and resumption of fixation neuron activity remained synchronized with the end of the postinterruption saccade. We believe that each of these observations clarifies our understanding of the contribution of the SC to the generation of saccades, and we will discuss each in turn.

Interruption of burst neuron discharge

The most parsimonious interpretation of the stimulation of the rostral SC on the burst neurons within the SC is that the brief train of electrical stimulation directly inhibited these

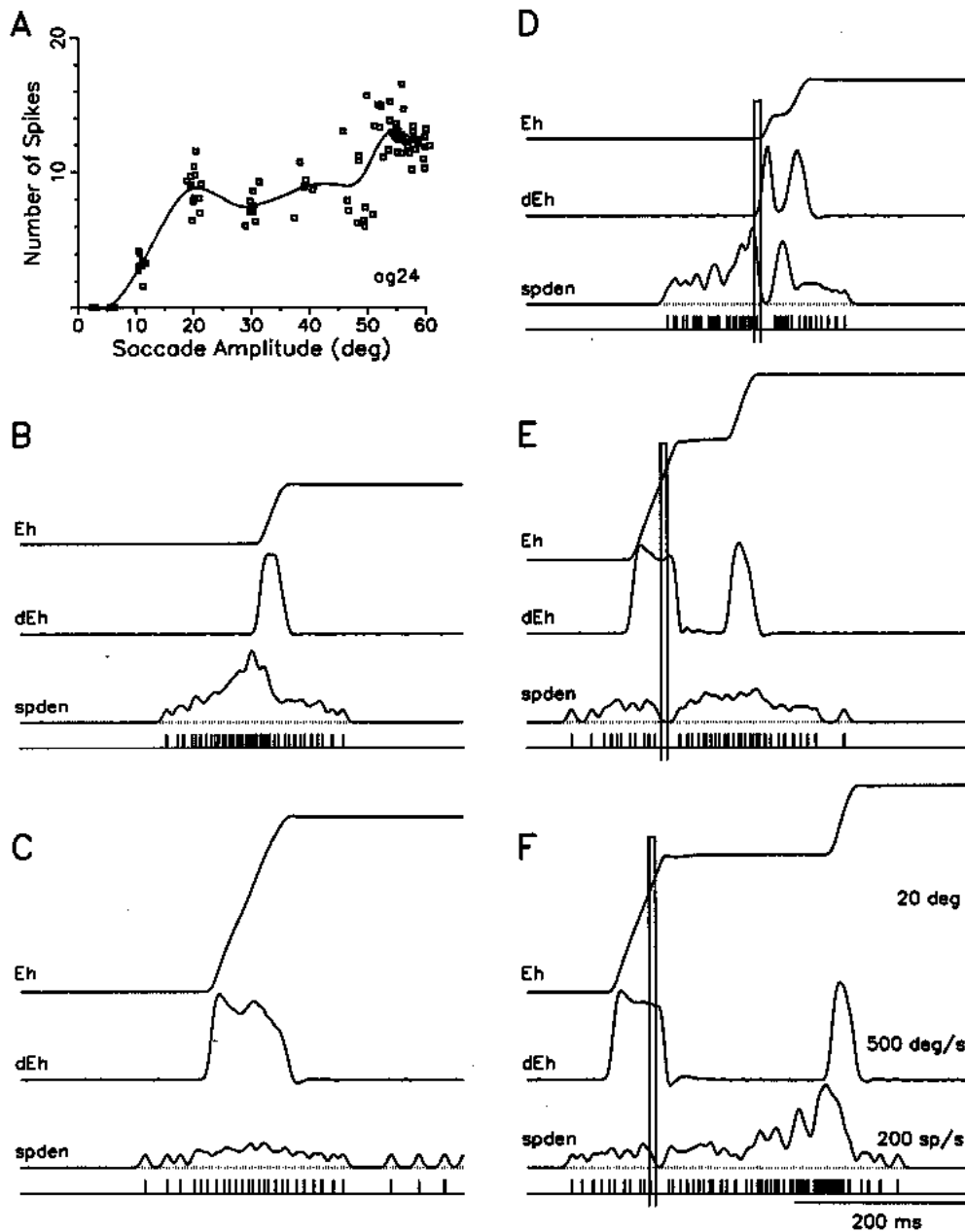


FIG. 15. Buildup neuron in the caudal left SC pauses and resumes its discharge during interrupted saccades. *A*: movement field of the neuron that discharged maximally for 20° control visually guided saccades (*B*), but continued to discharge for all rightward saccades whose amplitudes were larger than the optimal (e.g., 50°; *C*). *D*: discharge accompanying 20° saccades was momentarily interrupted after stimulation of the contralateral rostral SC. *E*: cell was active during interruption of a 55° saccade, even though the postinterruption saccade was triggered 72 ms after the interruption. *F*: cell discharged a high-frequency burst when the postinterruption saccade occurred 230 ms after the interruption. Stimulation consisted of a brief train of 4 pulses at 500 Hz, delivered to the rostral right SC.

neurons via intracollicular inhibitory connections. Stimulation of the ipsilateral rostral SC led to inhibition of burst neurons and buildup neurons within 1–2 ms (Munoz and Wurtz 1993c). The short latency of these responses strongly suggests that the electrical stimulation led to the activation of a monosynaptic inhibitory intracollicular connection onto the burst neurons. Such a connection has been proposed because of the reciprocal discharge patterns of burst and fixation neurons (Munoz and Guitton 1991; Munoz and Wurtz 1993a, 1995a). The inhibition of the burst and buildup neurons would presumably remove the input from the brain stem neurons that provide the primary excitatory drive onto the burst neurons in the reticular formation of the monkey (Moschovakis et al. 1991a,b; Strassman et al. 1986a,b), which would lead to an immediate deceleration of saccades. The saccade would then only resume when the collicular burst signal resumes.

An alternative mechanism could be that the brief electrical stimulation in the rostral SC may have produced an orthodromic volley in fixation neurons that project an axon into the region of the omnipause neurons in the pons (Istvan et al. 1994; Munoz and Guitton 1991). Omnipause neurons are excited at monosynaptic latencies following collicular stimulation (Pare and Guitton 1994; Raybourn and Keller 1977), so that the orthodromic volley from the fixation neurons may have led to activation of the omnipause neurons. These omnipause neurons have an inhibitory projection onto the excitatory and inhibitory burst neurons (Strassman et al. 1987), which would lead to an immediate deceleration of saccades. However, the omnipause neurons do not project to the SC. Therefore activation of omnipause neurons can account for the deceleration of saccades, but it cannot account for the short-latency inhibition we observed for burst

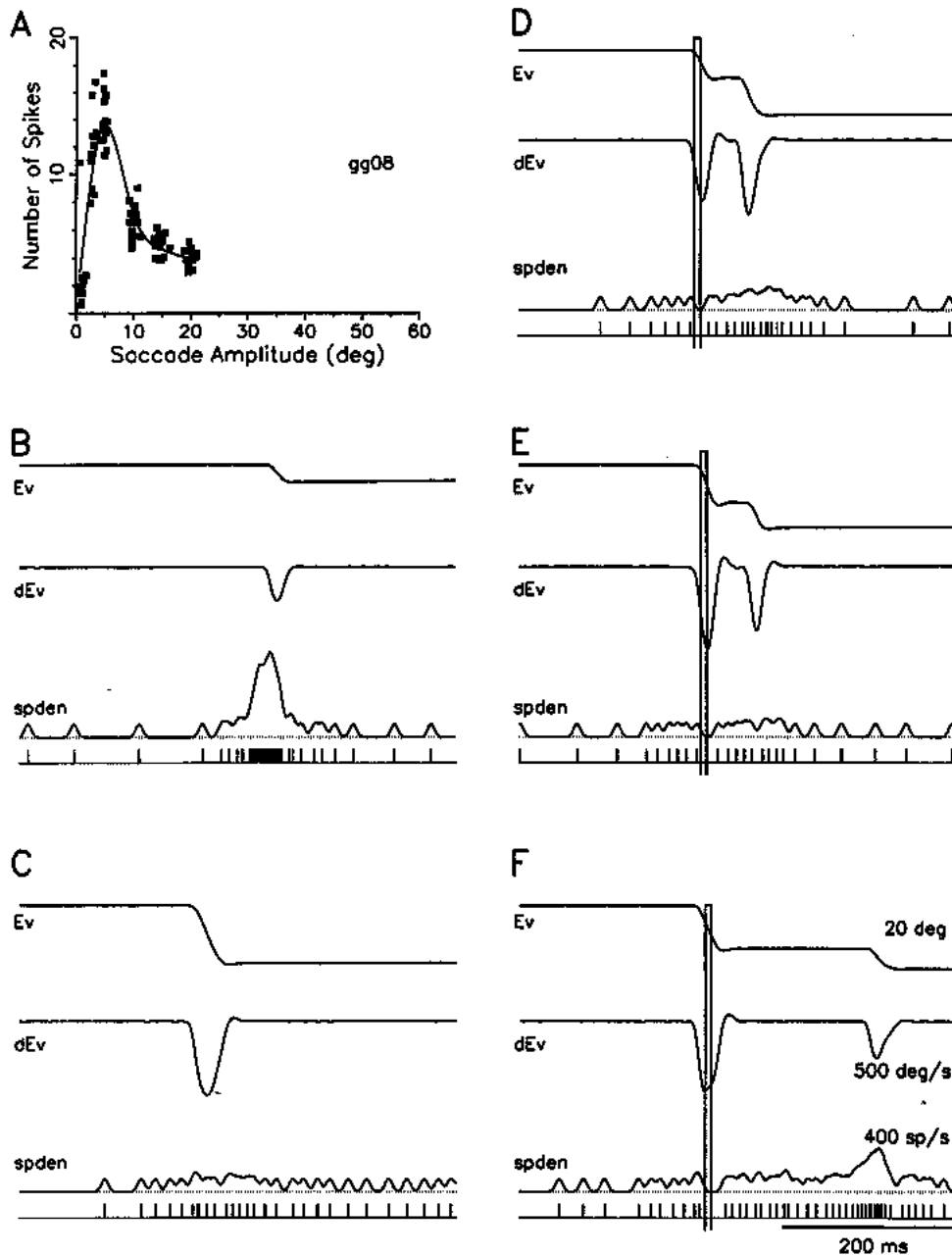


FIG. 16. Buildup neuron in the left SC pauses and resumes its discharge during interrupted saccades. *A*: movement field of the neuron, which discharged maximally for 5° control visually guided saccades (*B*) but continued to discharge for all rightward saccades whose amplitudes were larger than the optimal (*C*). *D* and *E*: cell was active during interruption of 22° saccades, even though the postinterruption saccade was triggered shortly after the interruption. *F*: cell discharged a high-frequency burst when the postinterruption saccade occurred 170 ms after the interruption. Stimulation consisted of a brief train of 4 pulses at 500 Hz, delivered to the rostral right SC.

and buildup neurons following electrical stimulation of the rostral SC.

Our results on burst neurons are very similar to those of Keller and Edelman (1994), who stimulated the omnipause region of the pons to interrupt saccades during recording from collicular burst neurons. Both studies found that the stimulation led to cessation in collicular burst neuron discharge. The inhibition of the burst neurons occurred with a mean latency of 3.8 ms following stimulation of the omnipause region, and Keller and Edelman (1994) suggested that the inhibition of the SC burst neurons may have resulted from stimulation of the collicular fixation neurons projecting into the omnipause region. They speculated that antidromic activation of fixation neurons with recurrent collaterals could have led to activation of a local collicular inhibitory interneuron producing the short-latency inhibition of burst neurons (see Fig. 13 of Keller and Edelman 1994). The

remarkable similarity of our results from SC stimulation and the results of Keller and Edelman from omnipause stimulation is consistent with this possibility. If this interpretation is correct, the difference between the studies would be that we applied the electrical stimulation to the cell bodies of fixation neurons, whereas Keller and Edelman (1994) applied the stimulation to the axons of fixation neurons.

One hypothesis about the activity of the burst neurons within the SC has been that they convey the motor error signal (how much of the saccade remains to be executed) to the saccadic burst generator. This hypothesis arose from the observation that many burst neurons in the SC had activity that ended with the end of the saccade and that showed a monotonic decay of the cell discharge with the approaching end of the saccade (Waitzman et al. 1988, 1991). If this were the case, when the saccade was interrupted by electrically stimulating the rostral SC (the present study) or the omni-

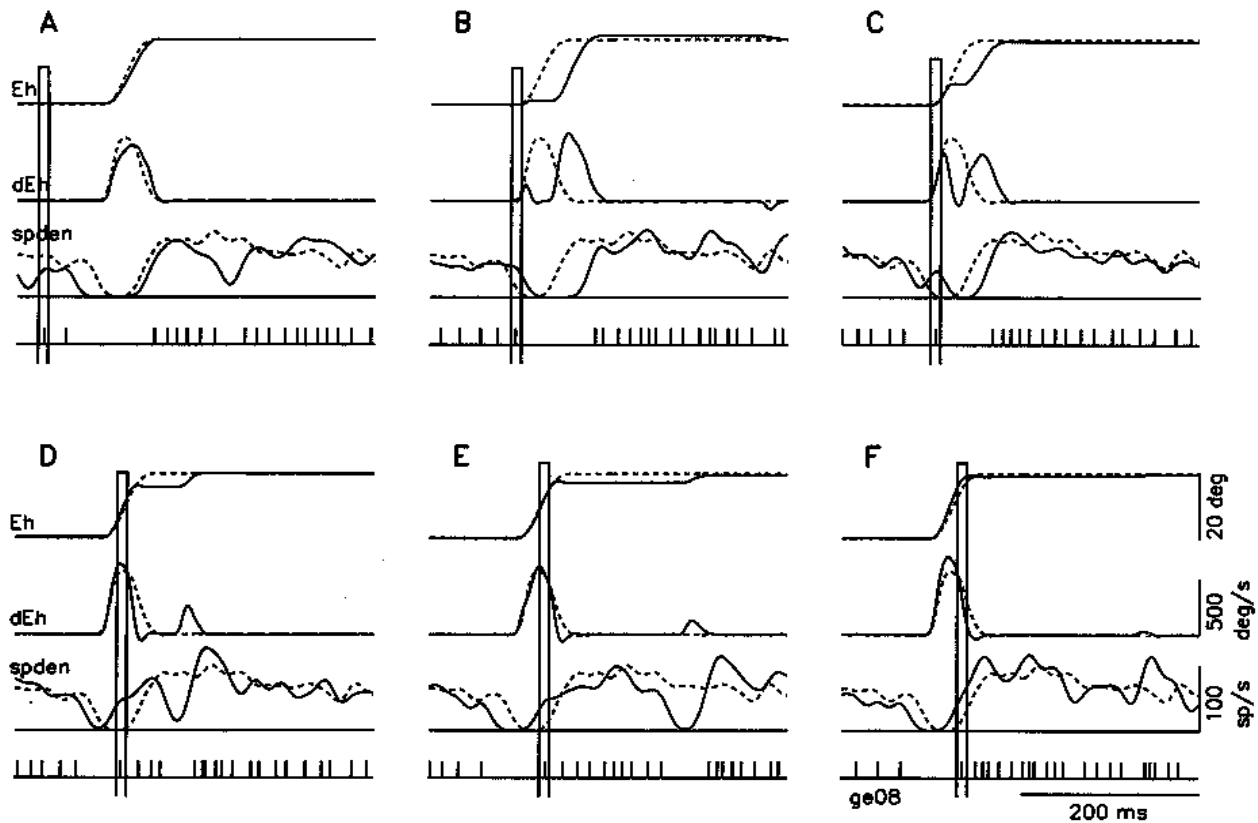


FIG. 17. Fixation neuron that pauses for saccades and is active during the interval between the preinterruption and postinterruption saccades. Cell was recorded in the rostral left SC of *monkey g* and electrical stimulation, consisting of a brief train of 4 pulses at 500 Hz delivered to the rostral right SC. A control visually guided trial (---) is superimposed on interruption trials (—). The action potentials are from the stimulated trials. For the spike density calculation, $\sigma = 10$ ms.

pauser region (Keller and Edelman 1994), the burst neurons should have continued to discharge or should have immediately resumed their discharge after brief inhibition in order to continue to provide the residual motor error signal. Because their discharge ceased until just before the postinterruption saccade began, these neurons do not by themselves fit the requirements for the motor error signal. During the interruption, the motor error was still present, but the cell discharge was not. In addition, the degree of clipping of the discharge of the population of burst neurons varied with the amplitude of the saccade (Munoz and Wurtz 1995b), which is also not consistent with the burst neurons alone providing the motor error signal.

In contrast, the view that the locus of burst neuron activity specifies the desired change in eye position (Lee et al. 1988) is entirely consistent with the interruption of the burst neuron activity: when the burst neuron firing was interrupted by the stimulation, the saccade was also interrupted. This is exactly what would be expected of the signal conveying desired change in eye position, and we take this as evidence that the locus of burst neuron activity on the SC map conveys the signal for the desired change in eye position.

Resumption of burst neuron discharge

The activity of the burst neurons resumed before the initiation of the postinterruption saccades, as happened after stimulation in the omnipausers region (Keller and Edelman

1994), provided that the postinterruption saccade was triggered <100 – 150 ms after the interruption. This implies that there is an excitatory input impinging on these burst neurons that remains after the interruption. This reactivation of burst neurons presumably indicates that the input to these cells, requesting a saccade of a given amplitude and direction, remains despite the interruption in burst neuron discharge and saccade trajectory.

It seems unlikely that this resumption of burst neuron activity represents simply a rebound of excitation following stimulation of the rostral SC for three reasons. First, a similar pattern of interruption and resumption of burst neuron discharge was observed for memory-guided movements that were interrupted spontaneously (Fig. 7). Second, when electrical stimulation was given during periods of fixation, we never observed rebound activation of the burst neurons. Third, a number of the parameters of the resumed activity were closely related to the parameters of the saccade: 1) the number of spikes in the preinterruption and postinterruption saccades equaled that of normal saccades (Figs. 8 and 9); 2) the total saccadic duration (preinterruption + interruption + postinterruption) matched total burst duration (Fig. 10); and 3) the time course of the cell discharge and the time course of the postinterruption saccade frequently followed the same monotonic trajectory (Fig. 11). Keller and Edelman (1994) described similar correlations when burst neuron discharge resumed after stimulation of the omnipausers region. There was, however, a slight difference: Keller and

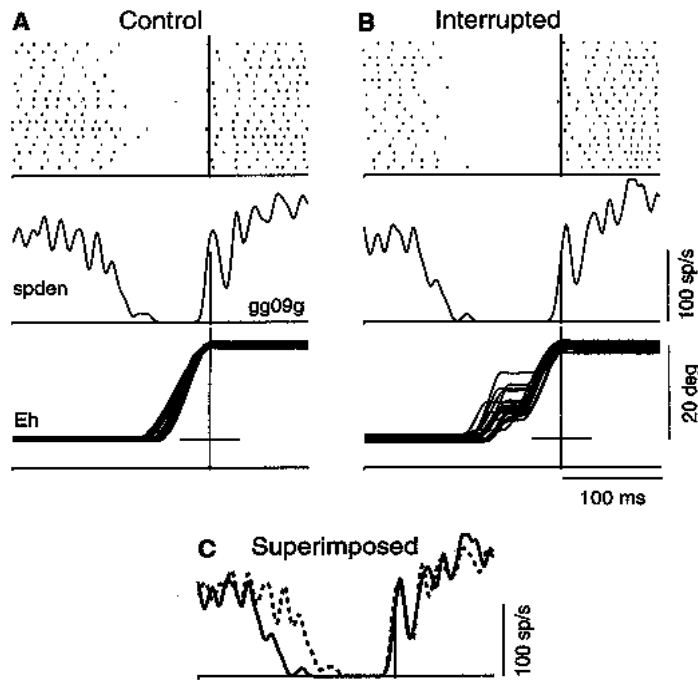


FIG. 18. Saccade-related pause in fixation neuron discharge ends when the postinterruption saccade ends. *A*: discharge of a fixation neuron, located in the rostral left SC of monkey *g*, during interruption of visually guided saccades following a brief train of 4 pulses at 500 Hz applied to the rostral right SC. Individual rasters, mean spike density plots, and horizontal eye position traces from control saccades are aligned on saccade end. *B*: same traces from interrupted saccades are aligned on saccade end. *C*: superposition of the spike density functions from control (---) and interrupted (—) saccades. Note that the only difference in fixation neuron discharge was the increased duration of the pause during interrupted saccades.

Edelman found that the discharge of most burst neurons was greater for the initial part of the postinterruption saccade than what we described (compare their Figs. 11 and 12 with our Fig. 11). However, in the study of Keller and Edelman, for a given amplitude saccade, the peak velocity of the post-interruption saccade was lower than that for control saccades, whereas in our study the peak velocity of the post-interruption saccade was indistinguishable from that in control saccades (see our Fig. 3).

It is generally believed that saccades are generated and controlled by a closed-loop control system (Jürgens et al. 1981; Robinson 1975), and several models have emerged that place the SC within a feedback loop controlling saccade accuracy (Arai et al. 1994; Droulez and Berthoz 1991; Lefèvre and Galiana 1992; Munoz and Wurtz 1995b; Munoz et al. 1991a; Optican 1994; van Opstal and Kappen 1993; Waitzman et al. 1988, 1991). Because of the tight correlations between burst neuron activity and the poststimulation saccade, we believe that the resumption of activity after the stimulation-induced interruption provides evidence that these neurons are receiving a feedback signal regarding the ongoing saccade. It is conceivable that the burst neurons could be reactivated because of the persistence of an excitatory input even if the SC were not receiving any feedback regarding the interruption of the saccade. However, it seems unlikely that the resumed discharge could be so closely scaled to the postinterruption saccade unless the SC was receiving information about how much of the initial saccade

was completed before the interruption, and how much remains to be completed after the interruption to bring the eyes on target. Furthermore, the two neuronal events synchronized with the end of the saccade in the control condition, the cessation of the high-frequency discharge of burst neurons (Munoz and Wurtz 1995b; Waitzman et al. 1991) and the resumption of the sustained discharge of fixation neurons (Munoz and Wurtz 1993a), remain synchronized with the end of the postinterruption saccade. Although alternative explanations could be offered to account for each of these observations, taken together, we think they offer strong evidence that the SC lies in a feedback loop controlling the amplitude and direction of saccades.

Shift in the locus of SC burst activity

At the time of a saccade, only one locus is active within the burst neuron layer of the SC (Munoz and Wurtz 1995b; Sparks and Mays 1980; Waitzman et al. 1991). When the saccade was interrupted by electrically stimulating the rostral pole of the SC, the same collicular locus of burst neurons was reactivated to drive the postinterruption saccade, provided this movement was initiated <100 ms after the interruption. If the ensuing saccade was initiated >100–150 ms after the interruption, then cells at the initially active site were not reactivated, and instead burst neurons at a new site, coding the direction and amplitude of the new saccade, were activated within the SC (see Fig. 14). In the study of Keller and Edelman (1994), only saccades >12° were studied and the postinterruption saccades were always generated within 100 ms of stimulation, so that Keller and Edelman were unable to extend their observations on both these spatial and temporal variables. Our observations suggest that there is a fixed time during which a saccade command can be effective for triggering movement, and when this time period is exceeded, a new command must be issued from a new site within the SC.

Recent experiments (Kustov and Robinson 1995; Nichols and Sparks 1995) have revealed that electrical stimulation of the SC <100 ms after the end of a control saccade led to a systematic deviation in the direction and amplitude of the evoked saccade. This effect was not present when the stimulation was applied >100 ms after the end of the control saccade. The authors of these studies concluded that the gradual decay in this effect was due to the gradual resetting of a neural integrator that has been hypothesized to reside within the feedback loop controlling saccade accuracy. The similarity between the time to reset integrator and the shift in activity within the burst neuron layer after saccade interruption (Fig. 14) is intriguing. In our experiments, the resumption of activity of the burst neurons at the same location on the SC motor map if the saccade resumed within ~100 ms might also be due to the continued input from the same neural integrator. Only after the integrator is reset would a new locus within the burst neuron layer be activated. In our experiments we would not have seen any gradual decay, because the burst neurons were still receiving input but being held off by the stimulation of the fixation neurons. In contrast, in the experiments of Nichols and Sparks (1995) and Kustov and Robinson (1995), the decay of the integrator was evident because stimulation was occurring when the burst neuron activity related to the preceding saccade was over.

Modification of buildup and fixation neuron activity

We recorded from some individual buildup neurons during the stimulation-induced interruption of saccade trajectory, and found that they were also inhibited at short latency following the electrical stimulation of the rostral SC. However, unlike the burst neurons, buildup neurons immediately resumed their discharge, regardless of whether the poststimulation saccade was triggered immediately or delayed beyond 100 ms (see Figs. 15 and 16). This continued discharge of the buildup neurons, even though the eyes had stopped moving, is consistent with these cells conveying a motor error signal. Munoz and coworkers (Munoz et al. 1991a,b) suggested that the tectoreticulospinal neurons in the cat might be providing a spatial code of motor error, and our observation on the buildup neurons is consistent with their hypothesis. Munoz et al. envisioned the motor error to be represented by the spatial distribution of neural activity on the motor map during a saccade, and the movement terminated when the fixation neurons in the rostral SC were reactivated. More recently, Munoz and Wurtz (1995b) described a rostral spread of activity across the buildup neuron layer of the monkey SC. An alternative interpretation of this spread of activity is that it represents a spatial integrator for the duration of the saccade (Optican 1994). Both views are dependent on the rostral movement of activity within the SC during the course of the saccade, but in our present experiments we did not ascertain whether the stimulation-induced interruption of the saccade led to a slowing or stopping of the spreading activity. Experiments that determine whether the stimulation of the fixation cells during the saccade actually interrupted or slowed this spread of activity should provide a critical test of these ideas.

Stimulation of the rostral SC leads to antidromic or orthodromic excitation of at least some fixation neurons in the opposite rostral pole of the SC at monosynaptic latencies (Munoz and Wurtz 1993c). Although the electrical stimulation we used in this study reactivated some fixation neurons in the contralateral SC during the interruption of the saccade (Fig. 17), the fixation neurons ceased discharging for the postinterruption saccade and only resumed their tonic discharge at the end of the postinterruption saccade (Figs. 17 and 18). Because the change in fixation neuron discharge remained synchronized with the end of the postinterruption saccade, it once again suggests that neuronal elements within the SC received feedback about the interruption in saccade trajectory, and the change in the saccade-related pause of fixation neurons reflected this. Because of the reciprocal activation of burst and fixation neurons, it remains to be determined whether the feedback affected both cell types directly, or whether it was mediated from one cell type to the other through the inhibitory connections within the SC.

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