Lateral Inhibitory Interactions in the Intermediate Layers of the Monkey Superior Colliculus

DOUGLAS P. MUNOZ AND PETER J. ISTVAN
Department of Physiology, Medical Research Council Group in Sensory-Motor Neuroscience, Queen's University, Kingston, Ontario K7L 3N6, Canada

Munoz, Douglas P. and Peter J. Istvan. Lateral inhibitory interactions in the intermediate layers of the monkey superior colliculus. *J. Neurophysiol.* 79: 1193–1209, 1998. The intermediate layers of the monkey superior colliculus (SC) contain neurons the discharges of which are modulated by visual fixation and saccadic eye movements. Fixation neurons, located in the rostral pole of the SC, discharge action potentials tonically during visual fixation and pause for most saccades. Saccade neurons, located throughout the remainder of the intermediate layers of the SC, discharge action potentials for saccades to a restricted region of the visual field. We defined the *fixation zone* as that region of the rostral SC containing fixation neurons and the *saccade zone* as the remainder of the SC. It recently has been hypothesized that a network of local inhibitory interneurons may help shape the reciprocal discharge pattern of fixation and saccade neurons. To test this hypothesis, we combined extracellular recording and microstimulation techniques in awake monkeys trained to perform oculomotor paradigms that enabled us to classify collicular fixation and saccade neurons. Microstimulation was used to electrically activate the fixation and saccade zones of the ipsilateral and contralateral SC to test for inhibitory and excitatory inputs onto fixation and saccade neurons. Saccade neurons were inhibited at short latencies following electrical stimulation of either the ipsilateral (1–5 ms) or contralateral (2–7 ms) fixation or saccade zones. Fixation neurons were inhibited 1–4 ms after electrical stimulation of the ipsilateral saccade zone. Stimulation of the contralateral saccade zone led to much weaker inhibition of fixation neurons. Stimulation of the contralateral fixation zone led to short-latency (1–2 ms) excitation of fixation neurons. Only a small percentage of saccade and fixation neurons were activated by the electrical stimulation (latency: 0.5–2.0 ms). These responses were confirmed as either orthodromic or antidromic responses using collision testing. The results suggest that a local network of inhibitory interneurons may help shape not only the reciprocal discharge pattern of fixation and saccade neurons but also permit lateral interactions between all regions of the ipsilateral and contralateral SC. These interactions therefore may be critical for maintaining stable visual fixation, suppressing unwanted saccades, and initiating saccadic eye movements to targets of interest.

INTRODUCTION

Saccadic eye movements are used to shift the visual axis rapidly from one point of interest to another. Between saccades the visual axis remains fixed and aligned with the current target of interest to permit detailed analysis of the visual image. During these periods of visual fixation, saccades to irrelevant stimuli must be suppressed. It long has been known that the superior colliculus (SC) is involved in the generation of saccadic eye movements (for review, see Sparks and Hartwich-Young 1989). More recently, the SC also has been identified as an important structure in the control of visual fixation (Munoz and Guitton 1989, 1991; Munoz and Wurtz 1993a,b; Peck 1989). Single-cell recording studies in awake monkeys have identified several different types of neurons in the intermediate layers of the SC the discharges of which are modulated by visual fixation and saccadic eye movements (Glimcher and Sparks 1992; Mays and Sparks 1980; Mohler and Wurtz 1976; Moschovakis et al. 1988b; Munoz and Wurtz 1993a, 1995a; Schiller and Koerner 1971; Sparks 1978; Sparks and Mays 1980; Sparks et al. 1976; Waitzman et al. 1991; Wurtz and Goldberg 1971, 1972). These neurons can be divided into two broad classes based upon their discharge characteristics during various oculomotor paradigms.

Neurons that increase their discharge before and during saccadic eye movements are referred to as saccade neurons (SAC, see Fig. 1*A*). These saccade neurons, distributed throughout the intermediate layers of the SC, discharge preferentially for saccades to a restricted region of the visual field. Each neuron discharges action potentials for saccades of a particular range of amplitudes and directions that define a movement field (Wurtz and Goldberg 1972). Saccade neurons are organized into a motor map that codes for the direction and amplitude of saccades into the contralateral field: small saccades are represented rostrally; large saccades are represented caudally (Robinson 1972). Microstimulation of the SC in the vicinity of saccade neurons elicits saccades the amplitude and direction of which match closely with the optimal amplitude and direction of the neurons lying adjacent to the electrode (Paré et al. 1994; Schiller and Stryker 1972; van Opstal et al. 1990).

Neurons that are tonically active during visual fixation and pause during saccades are referred to as fixation neurons (FIX, see Fig. 1*A*), and they are located in the rostrolateral pole of the SC (Munoz and Wurtz 1993a). These fixation neurons continue to discharge even when the fixation stimulus is removed momentarily from the visual field and the monkey is required to maintain fixation. Fixation neurons cease discharging for all ipsiversive saccades but may continue to discharge for small contraversive saccades. Because many fixation neurons also have movement fields, it has been argued that there is a continuum between saccade and fixation neurons on the SC motor map (Munoz and Wurtz 1995a,b). Low-frequency microstimulation of the SC adjacent to fixation neurons leads to a delay in the time to initiate a saccade to a visual stimulus, and stimulation applied during a saccade leads to its interruption in midflight (Munoz and Wurtz 1993b).

0022-3077/98 $5.00

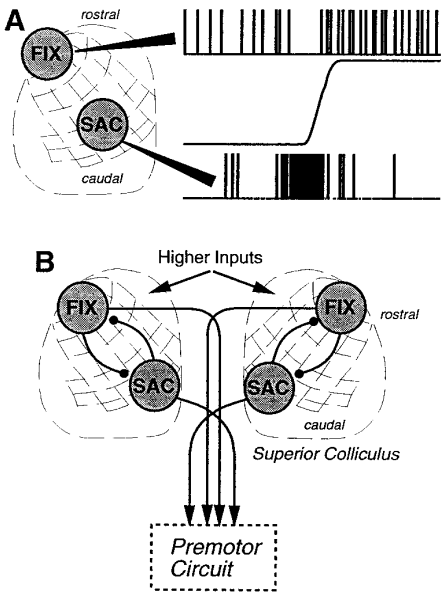

FIG. 1. *A*: reciprocal discharge of a fixation neuron *(top)* and a saccade neuron *(bottom)*, located in the left superior colliculus (SC), when a monkey generates a rightward saccade. *B*: hypothesized collicular circuitry for the control of visual fixation and initiation of saccadic eye movements (Munoz and Guitton 1989, 1991; Munoz and Wurtz 1993b, 1995b). See text for additional details. FIX, fixation neurons; SAC, saccade neurons.

Based upon the reciprocal nature of the discharge patterns between the fixation and saccade neurons (Fig. 1*A*), a hypothesis was proposed to describe the role of the SC in saccade initiation (Munoz and Guitton 1989, 1991; Munoz and Wurtz 1993b, 1995b; Munoz et al. 1991). According to the hypothesis (Fig. 1*B*), inputs to the intermediate layers of the SC from cerebral cortex, basal ganglia, thalamus, brain stem, and cerebellum selectively activate or inhibit either fixation (FIX) or saccade (SAC) neurons. A local network of inhibitory interneurons contributes to shaping the reciprocal patterns of activity. Such connectivity would ensure that during active fixation, saccade neurons would be inhibited, whereas during saccade preparation and generation, fixation neurons would be inhibited. These fixation and saccade neurons then project to the brain stem reticular formation to exert their influence over the saccadic premotor circuitry.

The main goal of this paper is to search for evidence of inhibitory connections between fixation and saccade neurons in the intermediate layers of the monkey SC. The functional identification of each neuron in the SC requires an analysis of the neural discharge recorded while an awake monkey performs various oculomotor tasks. We therefore record from single neurons using extracellular recording techniques and classify them based on their patterns of discharge during the tasks. Brief trains of electrical microstimulation are used to activate neurons at other collicular loci to test for connectivity between different regions of the ipsilateral or contralateral SC. Prolonged stimulation of the fixation and saccade zones also is used to investigate the role of the SC in saccade generation. Prolonged stimulation of the fixation zone of the SC delays saccade initiation (Munoz and Wurtz 1993b). Is this delay mediated by inhibition of collicular saccade neurons? Prolonged stimulation of the saccade zone of the SC elicits repeated fixed-vector saccades with brief periods of no eye motion between each saccade that form a staircase pattern (Robinson 1972; Schiller and Stryker 1972). At present, the mechanism responsible for terminating saccades elicited with collicular stimulation remains unknown. What is the pattern of activity of fixation neurons during these electrically evoked saccades?

We show that stimulation of the rostral SC, adjacent to fixation neurons, leads to short-latency inhibition of saccade neurons, whereas stimulation of the caudal SC, adjacent to saccade neurons, leads to short-latency inhibition of both fixation neurons and saccade neurons distant from the site of stimulation. These data provide additional evidence to support the hypothesis that local inhibitory interneurons help shape not only the reciprocal discharge patterns of fixation and saccade neurons but also permit lateral interactions between all regions of the ipsilateral and contralateral SC. Some of the findings described here have been reported in abstract form (Munoz and Wurtz 1993c).

METHODS

Experiments were performed on six adult rhesus monkeys (1 female, 5 male). Four of the monkeys (*c*, *p*, *g*, and *a*) were used in previous studies performed at the National Eye Institute, and details of the experimental design were described elsewhere (Munoz and Wurtz 1992, 1993a,b, 1995a,b; Munoz et al. 1996). Experiments with two additional monkeys (*l* and *j*) were performed at Queen's University, and detailed methodology is provided in this paper. All experimental protocols were approved by both the National Eye Institute Animal Care and Use Committee and the Queen's University Animal Care Committee and complied with U.S. Public Health Service and Canadian Council on Animal Care policies on use of laboratory animals. The monkeys were under the close supervision of Institute veterinarians.

General

Monkeys were prepared for chronic experiments by undergoing one aseptic surgical procedure. Anesthesia was induced initially with an injection of ketamine-hydrochloride (10 mg/kg im) to allow for preparation of the surgical area and the insertion of an intravenous catheter. An injection of alphaxalone and alphadolone acetate (CT1341; Saffan, 0.5 ml/kg iv) then was given to provide relaxation during the insertion of an endotracheal tube. Surgical levels of anesthesia subsequently were maintained using isofluorane (1–2%) inhaled through the endotracheal tube. Heart rate, respiratory rate, and body temperature were monitored closely for the duration of the surgery.

Using stereotaxic procedures, craniotomies (19 mm diam) were performed to allow access of microelectrodes into the SC. A head implant was constructed from dental acrylic and anchored to the skull with stainless steel screws. A stainless steel post to secure the head was anchored into the acrylic implant. The implant included stainless steel recording chambers over each of the craniotomies. All six monkeys had a recording chamber centered over the midline and angled 38° posterior from vertical to allow access to both SC (stereotaxic coordinates: P1.0, D5.0, RL0). The two monkeys used at Queen's University (*monkeys l* and *j*) had a second recording chamber centered directly above the interaural axis and angled 25° lateral of vertical to allow access to the left SC and paramedian pontine reticular formation (stereotaxic coordinates: P1.0, D5.0, RL0). Preformed eye coils (3 turns of stainless steel wire, 19 or 20 mm diam, Cooner Wire) were implanted into both eyes behind the conjunctiva (Judge et al. 1980) to measure eye movements

using the magnetic search coil technique (Fuchs and Robinson 1966). The coil leads were passed subcutaneously to the acrylic implant that anchored the connectors.

At the end of surgery, the animals received an injection of antibiotics (penicillin intramuscularly) as a prophylactic measure against infection. These antibiotics were administered daily for 10 postoperative days. To alleviate any discomfort in the first week postoperatively, animals also were given analgesic medication (buprenorphine hydrochloride 0.01 mg/kg, Flunixin Meglumine, Banamine 5 mg/kg). Animals were given 1–2 wk to recover from surgery before training began.

Behavioral paradigms

Behavioral paradigms, visual displays, and data acquisition were under the control of a PDP 11/73 computer (experiments at National Eye Institute) or an 80486 computer (experiments at Queen's University) running a UNIX-based real-time data acquisition system (REX) (Hays et al. 1982). Monkeys were seated in a primate chair (Crist Instruments) with their heads restrained for the duration of the experiment (~2–4 hrs). They faced a tangent screen, 86 cm away, so that they had an unobstructed view of 70° x 70° (±35° in any direction from straight ahead). Each behavioral trial was performed in total darkness and lasted ~2–3 s. The intertrial interval varied randomly from 1–2 s, and, during this interval, the screen was illuminated diffusely (1.0 cd/m^2) to prevent the animal from becoming dark adapted. At the start of each trial, the background light was extinguished and, after a period of 250 ms, the trial was initiated by the appearance of a target spot on the screen. The target spots were produced by either light emitting diodes (0.3 cd/m^2) or laser spots (2.0 cd/m^2) that were both rear-projected onto the screen. The position of the visual targets was controlled by the computer via digital-to-analog converters controlling an *x-y* mirror galvanometer (General Scanning).

Monkeys were trained to perform fixation and saccade tasks (Fig. 2) for liquid reward. All trials began with the appearance of a fixation point (FP), usually in the center of the screen. The monkeys had 1,000 ms to begin fixating the FP, and then they had to maintain fixation for 500–1,000 ms before one of several possible events occurred. In the *fixation paradigm* (Fig. 2*A*), the FP remained illuminated for an additional 500–1,000 ms, and the monkey was required to maintain the same gaze position for the duration of the trial unless electrical stimulation of the SC (see further) drove the eyes away from this position. In the *fixation-blink paradigm* (Fig. 2*B*), the FP was extinguished, and the monkey was required to maintain the same gaze position in darkness for an additional 500–1,000 ms unless electrical stimulation of the SC drove the eyes away from the FP. In the *visually guided saccade paradigm* (Fig. 2*C*), the FP was turned off at the same time as an eccentric target (T) appeared on the screen in the peripheral visual field. The monkey had 500 ms to initiate a saccade to T, and then the monkey had to fixate upon T for an additional 300 ms. In the *gap saccade paradigm* (Fig. 2*D*), a period of 0–800 ms was imposed randomly between FP disappearance and T appearance, and during this period the monkey was required to maintain steady fixation at the location of the FP. After T appearance, the monkey had 500 ms to initiate a saccade to T, and then the monkey had to fixate upon T for 300 ms. In the *memory-guided saccade paradigm* (Fig. 2*E*), the T was flashed for 80 ms while the FP remained illuminated. After a randomized period of time (400–800 ms), the FP was turned off and the monkey had 500 ms to initiate a saccade to the remembered location of the T flash and then fixate at this location for 300 ms. In the *target-flash saccade paradigm* (Fig. 2*F*), the FP was turned off and, simultaneously, the T was flashed for 50–80 ms. The monkey had 500 ms to initiate a saccade to the location of the T flash and then had to fixate at this location for an additional 300 ms. Different patterns of electrical stimulation of the SC (see further) were presented before, during, and after the time of saccade generation in the various saccade tasks (Fig. 2, *C–F*). Monkeys were trained on all of the tasks before the onset of cell recording.

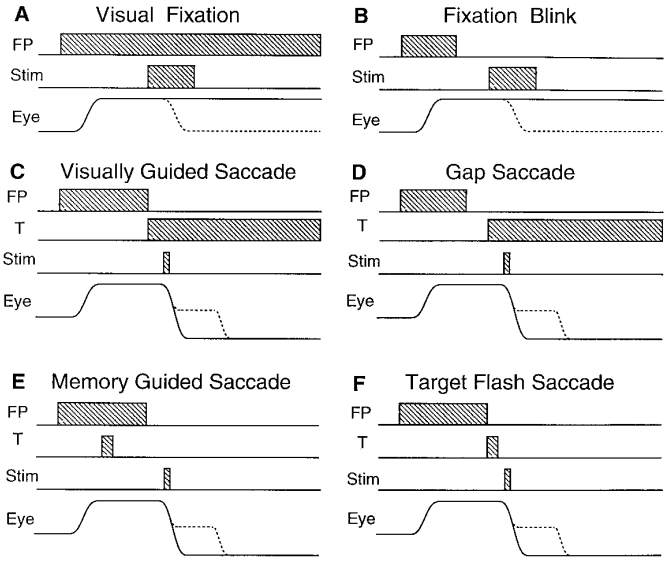

FIG. 2. Behavioral paradigms employed. In all paradigms, the monkey faced a stationary tangent screen that had visual targets projected on it and was rewarded for performance of the task. Electrical stimulation (Stim) to some part of the SC could be delivered at any time during the tasks. In the fixation tasks, stimulation was delivered during fixation, and in the saccade tasks, stimulation usually was delivered immediately before or during saccade initiation. First target to appear, referred to as the fixation point (FP), initiated all behavioral trials. In the visual fixation paradigm *(A)*, the monkey had to maintain fixation upon the visible FP to obtain the reward. In the fixation blink paradigm *(B)*, the monkey had to look at the FP and then maintain that same position while the FP was turned off. In the saccade tasks, the monkey had to first look at the FP and then, when it was turned off, look to the location of a second target (T). In the visually guided saccade paradigm *(C)*, the T appeared at the same time as the FP was turned off. In the gap saccade paradigm *(D)*, the FP was turned some time (usually 200 ms) before T appearance. In the memory-guided saccade paradigm *(E)*, the T was flashed on for 50–80 ms while the FP remained illuminated. After the FP was turned off, the monkey had to look at the remembered location of the T flash. In the target flash saccade paradigm *(F)*, the FP was turned off and the T was flashed for 50–80 ms and the monkey had to look immediately to the location of the T flash.

Recording and stimulation techniques

Before the initiation of neuronal recordings, the recording chambers were fit with delrin grids that secured guide tubes (23-gauge stainless steel tubing) (Crist et al. 1988), which penetrated the dura and extended into the brain to ~5 mm above the SC. Multiple guide tubes could be inserted into the grid at 1-mm intervals. Neuronal discharge was recorded extracellularly with commercially available tungsten microelectrodes (0.5–5 MΩ; Frederick Haer). Conventional recording, amplifying, and display techniques were employed. Initial neuronal recordings were performed to carefully map the coordinates of the SC motor map to the various grid positions.

The SC was stimulated electrically at sites where fixation or saccade neurons already had been recorded. Stimulation was delivered through one of two types of electrodes. We used low-impedance (<0.5 MΩ) tungsten microelectrodes that had been used previously for recording single cell activity, and stimulation with these electrodes was monopolar (*monkey c*). The other type of stimulating electrodes used (*monkeys p, g, a, l,* and *j*) were low-

impedance (~0.1 MΩ) bipolar concentric electrodes (Kopf, SNEX100). The use of bipolar stimulating electrodes reduced both the amplitude and duration of stimulus artifacts. Both types of electrodes were lowered through guide tubes into the SC to the depth that required the lowest intensity to either elicit or interrupt a saccade (see further text). Once the appropriate position in the SC was reached, the stimulating electrodes were secured to the guide tubes with epoxy (Fast Cure Epoxy 45, Loctite) and kept in place for 2–10 days. During the time that the stimulating electrode remained within the SC, stimulation produced a stable response and there was only a nominal increase in threshold current. If there was a large increase in threshold current, the stimulating electrode was removed.

For clarity of presentation we have defined a *fixation zone* and a *saccade zone* within the SC. The fixation zone (shaded region in Fig. 3) was defined as the rostrolateral pole of the SC extending out to 2° on the SC motor map. This region of the colliculus contains fixation neurons (Munoz and Wurtz 1993a), and low-frequency electrical stimulation within this region delays the initiation of saccades (Munoz and Wurtz 1993b). In addition, a population analysis of collicular activity related to fixation and saccades revealed that the region of neurons active during visual fixation extended to the 2° site on the motor map (Munoz and Wurtz 1995b). We defined the saccade zone as the remainder of the motor map of the SC. Stimulating electrodes were implanted into the fixation zone of either the left or right SC in four monkeys (*c*, *p*, *g*, and *a*). Stimulating electrodes were implanted into the saccade zone of four monkeys (*p*, *a*, *l*, and *j*). The location of the stimulation sites within the SC (Fig. 3) were determined by plotting the amplitude and direction of the saccades elicited with a 100-ms train of stimulation pulses (400 Hz, 1.5 times threshold intensity). Note that the location of the stimulating electrodes was always rostral to the 2° isoamplitude line or caudal to the 10° isoamplitude line. To avoid ambiguity in whether the stimulation was confined to either the fixation or saccade zones (Gandhi and Keller 1995), we never attempted electrical stimulation at collicular sites between the 2 and 10° isoamplitude lines.

Each experiment consisted of a block of trials in which the monkey performed one or more of the behavioral paradigms illustrated in Fig. 2. Each block consisted of equal numbers of randomly interleaved control trials (no electrical stimulation) and trials in which some form of electrical stimulation was applied to the SC. Stimulation consisted of trains of biphasic pulses (0.1–0.3 ms anodal and cathodal pulses) with varying intensity, frequency, and train duration. Details of the parameters of electrical stimulation for the individual experiments are given in RESULTS and the figure legends. Stimulation intensity in the saccade zone was set at a level sufficient to elicit eye motion with a 20-ms train at 400 Hz. In the fixation zone, stimulation intensity was set at a level sufficient to interrupt a saccade in midflight with a two- to four-pulse train at 500 Hz (see Munoz and Wurtz 1993b; Munoz et al. 1996). The intensity of stimulation used was always kept <100 μA except when searching for antidromic responses when the intensity of single stimulation pulses may have reached 200 μA.

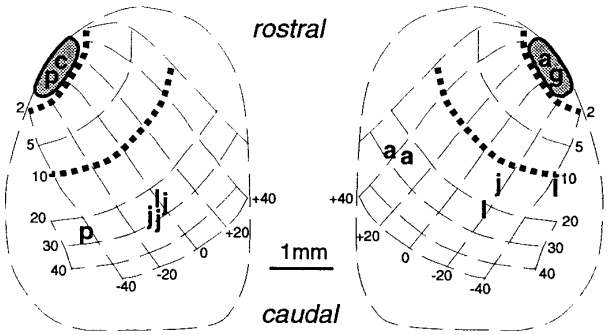

FIG. 3. Location of sites of electrical stimulation in the left and right SC of the 6 monkeys (*c*, *p*, *g*, *a*, *l*, and *j*). Fixation zone (shaded region in rostrolateral pole of the SC, rostral to 2° isoamplitude line) was stimulated in 4 monkeys: *c*, *p*, *g*, and *a*. Saccade zone (caudal to 10° isoamplitude line) was stimulated in 4 monkeys: *p*, *a*, *l*, and *j*. Coordinates of the motor map in the intermediate layers of the rhesus monkey SC were adapted from Robinson (1972).

Changes in cell excitability produced by electrical stimulation were determined from changes in discharge frequency that were recorded extracellularly. To test for inhibitory connections, it was necessary to present electrical stimulation at various times during the saccade and fixation tasks when the different neuronal types were normally active. Inhibitory connections were inferred from sudden drops in discharge frequency that faithfully followed the onset of electrical stimulation. For a saccade neuron, electrical stimulation was usually presented in one or more of the saccade tasks (Fig. 2, *C–F*), around the onset of saccades to the center of the neuron's movement field. Stimulation was triggered after a fixed delay that approximated the saccadic reaction time after FP disappearance or T appearance. For a fixation neuron, stimulation usually was presented during periods of active fixation in the fixation tasks (Fig. 2, *A* and *B*). Excitatory connections were revealed by sudden increases in cell discharge that immediately followed the onset of electrical stimulation. To demonstrate antidromic activation of neurons, we relied on a number of criteria including: constancy of the latency at threshold current, ability of the response to follow high frequencies, and collision of orthodromic and antidromic spike waveforms (Lipski 1981).

Data collection and analysis

Horizontal and vertical eye position were measured from one eye. The magnetic field coils (CNC Engineering) provided a uniform horizontal field to ±180°; the strength of the vertical field decreased in strength with the cosine of the angle. In all monkeys, REX data files consisted of horizontal and vertical eye and target position, digitized at 500 Hz, and the occurrence of single-cell discharges, sampled at 1 kHz after passing through a window discriminator (Bak Electronics). Action potentials that did not meet amplitude and time constraints were excluded. With careful attention, it was usually possible to isolate single neurons on-line without contamination by stimulus artifacts (see further). In the two monkeys studied at Queen's University (*monkeys l* and *j*), brief segments of the extracellular spike waveforms were digitized at 30 kHz using a separate 80486 computer running commercial software for acquisition (DataWave). The sampling of the neuronal discharges by the REX and DataWave computer systems was synchronized so that the time of occurrence of data from the two systems could be aligned accurately. Data was stored on a hard disk for off-line data analysis.

DataWave software was used off-line to sort individual spike waveforms from the raw data stream. Briefly, parameters of spike waveforms were measured that included spike height, peak time, peak amplitude, and spike width. The values of these different parameters were plotted against one another. Spike waveforms with similar parameter measurements formed clusters that represented spike waveforms from a single neuron. A cluster-cutting procedure was used to determine whether spike parameters obtained from a waveform could be generated by a single neuron at a particular recording site. The result of the cluster cutting was verified by viewing the identified spike waveforms along with those that were not identified. From the files saved in DataWave it was usually possible to extract multiple neurons from a single electrode position and reliably identify and remove all stimulus artifacts during off-line analysis.

To determine the latency of the responses to electrical stimula-

tion, we relied upon measurements made from several sources. The latency of antidromic or orthodromic excitatory responses were determined in three ways: on-line, from examining the extracellular records on a storage oscilloscope triggered by stimulation onset, off-line, by measuring the time from stimulation onset to action potential onset on polaroid snapshots taken from the oscilloscope, and off-line, from examining 15-ms segments of spike waveform data (5 ms before stimulation, 10 ms after stimulation) digitized at 30 kHz by the DataWave computer. The latency of an inhibitory response was determined off-line by reviewing perievent time histograms (binwidth 1 ms) aligned on stimulation onset. Inhibitory responses consisted of ≥5 consecutive bins having fewer spike counts than the average of the 10 bins preceding stimulation onset and ≥1 bin having no counts. It was very easy to identify these inhibitory responses in the histograms (e.g., see Figs. 4, 6–9, and 11). The latency to onset of inhibition was measured as the time from stimulation onset to the first of five consecutive bins having a reduction in spike count.

We used two independent methods of recording neuronal discharge (REX and DataWave) to reliably isolate action potentials from stimulus artifacts. However, with these techniques, it was still possible that in some instances we failed to identify some action potentials that occurred simultaneous with a stimulus artifact. Therefore we may have underestimated the occurrence of some action potentials during stimulation. To overcome this limitation, we resorted to using very brief trains of stimulation (usually 2 pulses at 500 Hz) when revealing inhibitory connections to ensure that the resultant decrease in discharge rate of a neuron was not due to obliteration of its action potentials by the stimulus artifacts. For long-duration trains of electrical stimulation, lower frequencies (e.g., 50–200 Hz) usually were employed to reduce the probability of obliteration of action potentials by the stimulus artifacts.

Neuronal classification

We relied on previously described criteria to classify fixation neurons (Munoz and Wurtz 1993a) and saccade neurons (Munoz and Wurtz 1995a). Fixation neurons had the following properties: they were tonically active during periods of visual fixation and this activity continued above 10 spikes/s when the fixation point was momentarily blinked out in a fixation-blink or gap saccade paradigm; there was a discrete pause in their discharge during all ipsiversive and most contraversive saccades; and they were located 1.5–3.0 mm below the dorsal surface of the SC. Fixation neurons were confined to the rostrolateral pole of the SC, anterior to the 2° isoamplitude line (see shaded region of Fig. 3). Microstimulation in this region of the SC delayed the initiation of saccadic eye movements or interrupted saccades in midflight (Munoz and Wurtz 1993b).

Saccade neurons were defined as those neurons that increased their discharge above 100 spikes/s for saccades to a particular region of the visual field. Many saccade neurons were further subdivided into two categories, *burst* and *buildup*, based on the shape of their movement fields and the presence or absence of long-lead prelude activity during the gap period in the gap saccade paradigm (Munoz and Wurtz 1995a). To evaluate the movement field of a neuron, we used the visually guided (Fig. 2*C*) or target flash (Fig. 2*F*) saccade paradigms and target location was varied randomly among one of eight eccentricities in the optimal direction. Typically, each block of trials consisted of the target being presented at the neuron's optimal direction and amplitude, as well as two to four smaller and three to five larger amplitudes. For larger target eccentricities (≥20°), the FP was positioned on one side of the visual screen and the target appeared on the opposite side. Thus target steps of ≤70° eccentricity were possible. The maximum amplitude tested for each neuron was ≥50°. Neurons that discharged for all saccades in the optimal direction with eccentricities equal to or greater than the optimal had open-ended movement fields, whereas neurons that did not discharge for saccades with eccentricities greater than the optimal had closed movement fields (Munoz and Wurtz 1995a). Burst neurons had no significant increase in discharge during the gap period in the gap saccade paradigm and closed movement fields. Buildup neurons had long-lead prelude activity during the gap period in the gap saccade paradigm and open-ended movement fields. We classified saccade neurons as burst or buildup only if they had been recorded during the gap saccade paradigm and the movement field testing was performed.

We occasionally recorded the effects of microstimulation of the intermediate layers on the responses of *visual neurons* in the superficial layers of the SC that had phasic visual responses (Goldberg and Wurtz 1972). These visual neurons lacked any fixation-related responses (i.e., did not discharge after FP disappearance in the fixation-blink or gap saccade tasks) or saccade-related responses (i.e., did not discharge during saccades in the memory guided or target flash saccade paradigms). These experiments on visual neurons were performed to test for the spread of stimulation to the superficial layers of the SC.

RESULTS

Two hundred six collicular neurons were tested for response to electrical stimulation of different regions of the ipsilateral or contralateral SC in six monkeys. Of these 206 neurons, 100 were classified as saccade (42 burst neurons, 18 buildup neurons, 40 unclassified saccade neurons), 84 were classified as fixation, and 22 were classified as visual (see Table 1). Figure 3 illustrates the location of the stimulation sites in the six monkeys. We first describe the effects of stimulation of the ipsilateral and contralateral fixation and saccade zones on saccade neurons and fixation neurons and the lack of effect of stimulation on visual neurons. We then describe the responses of some neurons to prolonged stimulation of the SC.

Effects of stimulation on saccade neurons

STIMULATION OF THE IPSILATERAL FIXATION ZONE. Microstimulation of the ipislateral fixation zone led to short-latency inhibition of saccade neurons (Fig. 4). The clearest

TABLE 1. *Summary of neurons tested with electrical stimulation*

Stimulation Site	Total	Saccade	Burst	Buildup	Fixation	Visual
Ipsi fixation	33	28	10	6	—	5
Contra fixation	36	17	6	6	13	6
Ipsi saccade	90	35	16	4	47	8
Contra saccade	47	20	10	2	24	3
Total	206	100	42	18	84	22

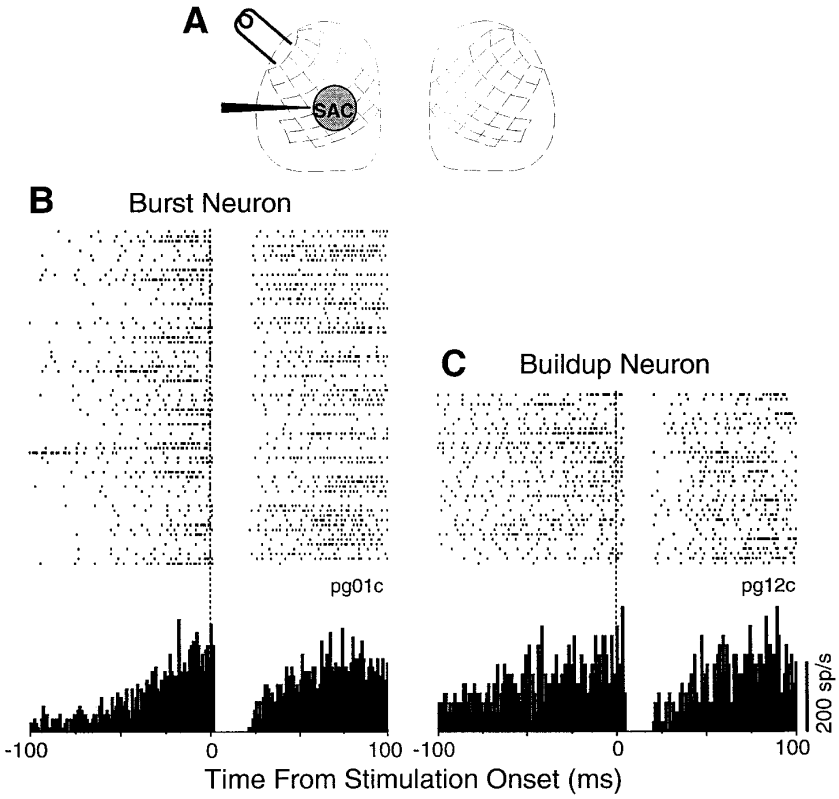

FIG. 4. Recording from a burst neuron *(B)* and a buildup neuron *(C)* in the saccade zone of the left SC of *monkey p* during electrical stimulation of the ipsilateral fixation zone. Individual rasters and histogram (binwidth 1 ms) aligned on the onset of a brief (7 ms), high-frequency (500 Hz) train of 4 pulses. Stimulation was presented while the monkey executed saccades of direction and amplitude that matched each cell's optimal saccade vector.

way to demonstrate this inhibition with extracellular recording was to deliver the electrical stimulation at the time the monkey was initiating a saccade of the optimal amplitude and direction to activate the neuron being studied. Presentation of electrical stimulation at this time led to an immediate deceleration of the saccade (Munoz and Wurtz 1993b). The extent of the interruption of the saccade and the latency to onset of the modified saccade were dependent on parameters of stimulation and were described previously (Munoz et al. 1996). Here we focus on the initial response of the neuron being recorded immediately after onset of stimulation of the ipsilateral fixation zone. Figure 4 shows the responses of a burst neuron and a buildup neuron that were both recorded from the same grid location in the caudal left SC of *monkey p* on different days. A brief train of stimulation applied to the ipsilateral fixation zone during saccades of the optimal amplitude and direction for each neuron led to a sudden reduction in discharge frequency of both neurons. The burst neuron illustrated in Fig. 4*B* had a sharp drop in discharge 1 ms after stimulation onset, and the buildup neuron shown in Fig. 4*C* had a similar drop after 3 ms. Both neurons subsequently resumed their discharge shortly after the end of the stimulation. The duration of cessation of the burst neuron discharge that followed the stimulation outlasted that of the buildup neuron.

All 28 saccade neurons tested for response to stimulation of the ipsilateral fixation zone were inhibited at short-latency (Table 2). The latency to onset of inhibition was measured for 24 saccade neurons. All of these neurons had a sharp drop in discharge frequency that began 1–3 ms after stimulation onset (Fig. 5*A*). The mean latency (±SD) for the 24 neurons was 1.8 ± 0.6 ms. There was no significant difference (*t-test*, $t = 0.0$, df = 5, $P > 0.05$) in the mean latency to inhibition between the classified burst (2.0 ± 0.6 ms, $n = 6$) and buildup (2.0 ± 0.6 ms, $n = 6$) neurons.

STIMULATION OF THE CONTRALATERAL FIXATION ZONE. Microstimulation of the contralateral fixation zone also led to short-latency inhibition of saccade neurons. Figure 6 illustrates the short-latency inhibition of a burst neuron and a buildup neuron, recorded from the same grid location in the caudal left SC of *monkey a* on different days, after stimulation of the contralateral fixation zone. Both neurons resumed their saccade-related discharge after the stimulation-induced pause. Once again the duration of the pause in discharge of the burst neuron (Fig. 6*B*) was longer than that of the buildup neuron (Fig. 6*C*).

Of the 17 saccade neurons tested for response to stimulation of the contralateral fixation zone, 15 were inhibited at short latency (Table 2). The latency to onset of inhibition was measured for 14 saccade neurons. The mean latency (±SD) to onset of inhibition was 3.6 ± 1.4 ms, and Fig. 5*B* shows the distribution of latencies. There was no significant difference (*t-test*, $t = 0.57$, df = 5, $P > 0.05$) in the latency

TABLE 2. *Summary of responses recorded from saccade neurons*

Stimulation Site	Neurons Tested	Inhibition	Excitation	Antidromic
Ipsi fixation	28	28	0	0
Contra fixation	17	15	0	0
Ipsi saccade	35	27	3	1
Contra saccade	20	18	0	1

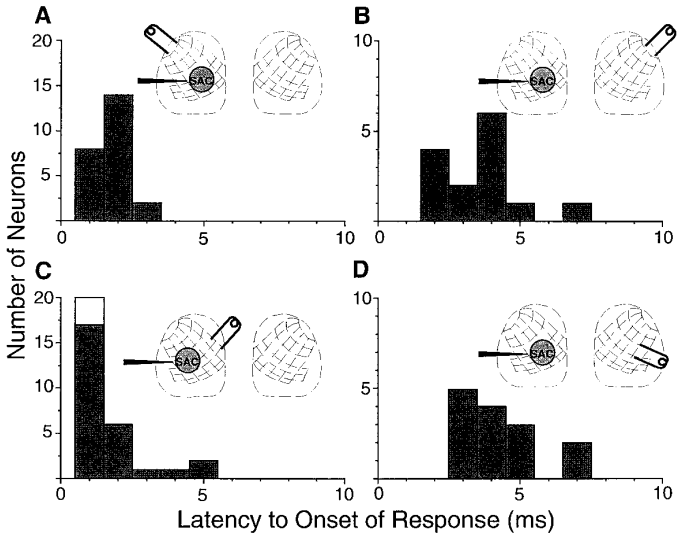

FIG. 5. Histograms showing the distribution of latencies to inhibition (▨) or excitation (□) of saccade neurons after stimulation of the ipsilateral fixation zone *(A)*, the contralateral fixation zone *(B)*, the ipsilateral saccade zone *(C)*, and the contralateral saccade zone *(D)*. Latency was measured from the beginning of stimulation to onset of the response.

to onset of inhibition for classified burst (3.3 ± 1.2 ms, $n = 6$) and buildup (3.8 ± 1.8 ms, $n = 6$) neurons after stimulation of the contralateral fixation zone.

STIMULATION OF THE IPSILATERAL SACCADE ZONE. The closest distance between stimulation and recording electrodes in the ipsilateral saccade zone tested was 1 mm, corresponding to the minimum distance between adjacent grid locations. However, the majority of the neurons tested were located ≥2 mm away from the site of stimulation. Figure 7*B* illustrates the short-latency inhibition of a saccade neuron after stimulation of the ipsilateral saccade zone. There was an abrupt cessation of cell discharge 1 ms after the onset of stimulation. The neuron resumed its discharge shortly thereafter. Figure 7*C* illustrates the short-latency excitation of a saccade neuron in the left SC of *monkey j* after stimulation of the ipsilateral saccade zone with single pulses. This neuron was activated 1.4 ms after the onset of stimulation. The latency and threshold of the response were somewhat variable, and collision testing failed to eliminate the response. The orthodromic responses were more reliable when stimulation intensity was increased from 70 to 90 μA.

Of 35 saccade neurons tested for response to stimulation of the ipsilateral saccade zone, 27 neurons were inhibited, 2 neurons were excited, and 1 neuron was antidromically activated (see Table 2). There were not enough observations to determine whether the location of the stimulating electrode relative the recording site influenced the distribution of these responses. The short-latency inhibitory and excitatory orthodromic responses of 30 saccade neurons are shown in Fig. 5*C*. The mean latency (±SD) to onset of the inhibition or excitation of saccade neurons after stimulation of the ipsilateral saccade zone was 1.6 ± 1.0 ms. All excitatory orthodromic responses had latencies between 1.0 and 1.5 ms. Inhibitory responses ranged from 1 to 5 ms. There was no significant difference (*t-test*, $t = 0.25$, df = 2, $P > 0.05$) in the latency to onset of inhibition for burst (1.4 ± 0.7 ms, $n = 11$) and buildup (1.3 ± 0.6 ms, $n = 3$) neurons. The latency of the one antidromic response was 0.85 ms.

STIMULATION OF THE CONTRALATERAL SACCADE ZONE. Electrical stimulation to the contralateral saccade zone led to inhibition of saccade neurons, as shown in Fig. 8. There was a sudden drop in discharge frequency within 3 ms of stimulation onset. The degree of inhibition produced with

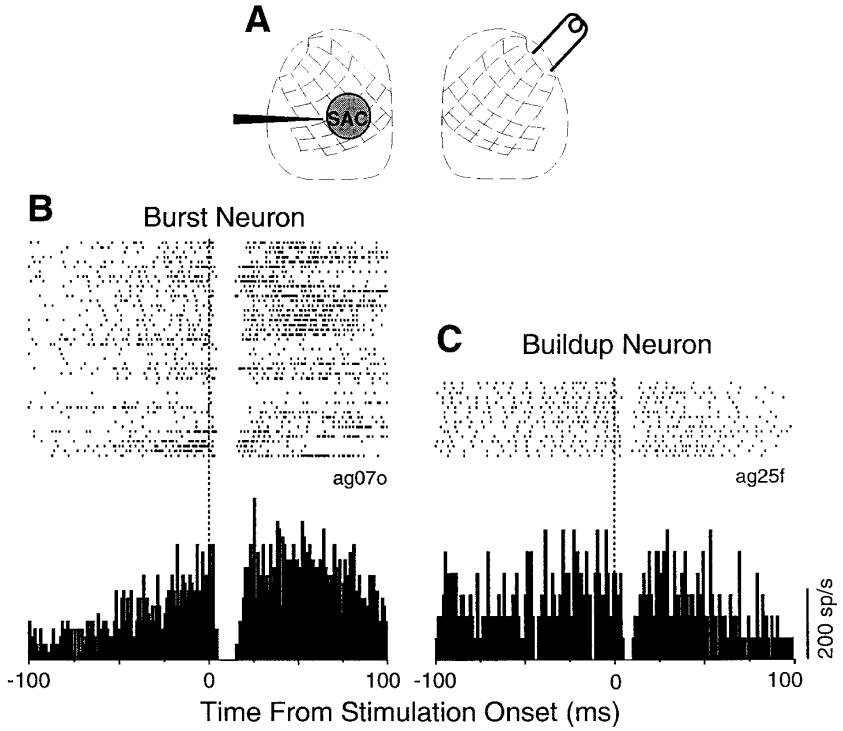

FIG. 6. Recording from a burst neuron *(B)* and a buildup neuron *(C)* in the saccade zone of the left SC of monkey a during electrical stimulation of the contralateral fixation zone. Individual rasters and histogram (binwidth 1 ms) aligned on the onset of a brief (3 ms), high-frequency (500 Hz) train of 2 pulses. Stimulation was presented while the monkey executed saccades of direction and amplitude that matched each cell's optimal saccade vector.

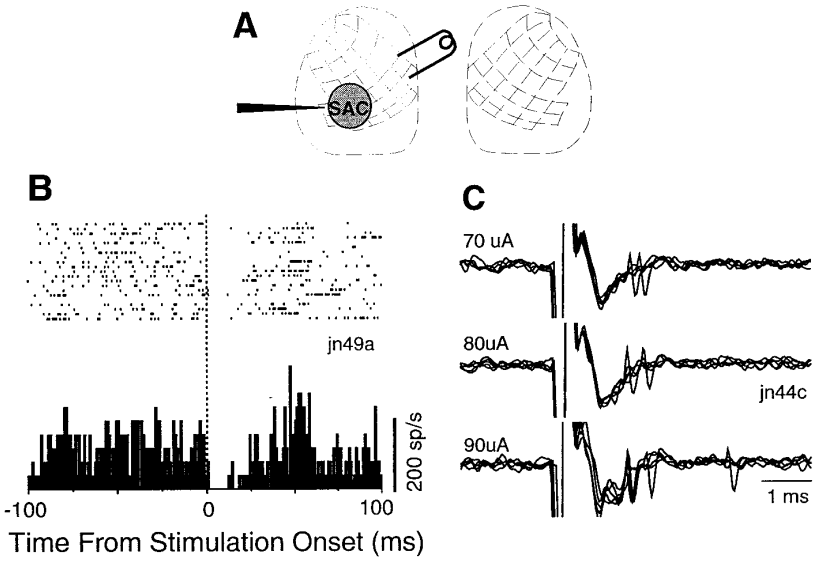

FIG. 7. Responses of 2 saccade neurons after stimulation of the ipsilateral saccade zone. *B*: saccade neuron located in the left SC of *monkey j* was inhibited after stimulation of the left saccade zone with a brief (3 ms), high-frequency (500 Hz) train of 2 pulses. Rasters and histograms (binwidth 1 ms) are aligned on stimulation onset. *C*: saccade neuron located in the left SC of *monkey j* was excited orthodromically with a single stimulus pulse delivered to the left saccade zone.

stimulation of the contralateral saccade zone tended to be weaker than that produced after stimulation of either fixation zone or the ipsilateral saccade zone. However, it was not possible to quantify this effect because neurons were recorded from different monkeys, on different days, and the stimulating electrodes used were varied.

Of the 20 saccade neurons tested for response to stimulation of the contralateral saccade zone, 18 were inhibited at short latency, and 1 neuron was activated antidromically (see Table 2). The mean latency (±SD) to onset of the inhibition for 14 saccade neurons was 4.3 ± 1.4 ms, and the distribution of latencies is shown in Fig. 5*D*. The one antidromic response had a latency of 1.2 ms. Once again, the latency to onset of inhibition for burst (3.1 ± 1.8 ms, $n = 10$) and buildup (3 ms, $n = 1$) neurons was very similar.

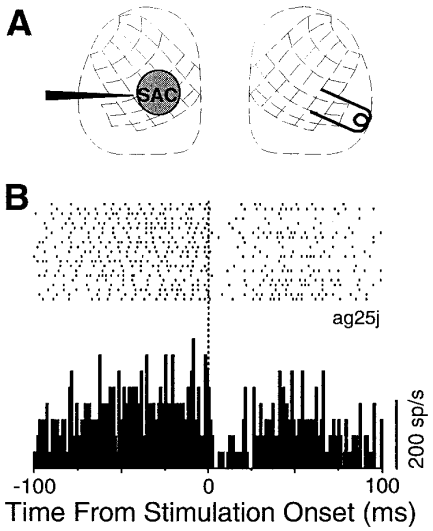

FIG. 8. Recording from a saccade neuron during electrical stimulation of the contralateral saccade zone with a brief (7 ms), high-frequency (500 Hz) train of 4 pulses. Neuron was located in the caudal left SC, and the stimulating electrode was positioned in the caudal right SC of *monkey a.* Rasters and histogram (1-ms binwidth) aligned on stimulation onset.

Effects of stimulation on fixation neurons

STIMULATION OF THE IPSILATERAL SACCADE ZONE. Most fixation neurons were inhibited at short latency after stimulation of the ipsilateral saccade zone (Table 3). Figure 9 illustrates the responses of two fixation neurons that were recorded simultaneously in the rostral left SC of *monkey j*. Stimulation led to short-latency inhibition of both neurons. Of the 47 fixation neurons tested for responses to stimulation of the ipsilateral saccade zone, 36 were inhibited, 2 were excited, and 4 were antidromically activated (see Table 3). The mean latency (±SD) to onset of inhibition or excitation for 34 fixation neurons was 1.6 ± 0.7 ms. Inhibitory response latencies ranged from 1 to 4 ms, whereas excitatory response latencies were 1.0 and 1.5 ms. The distribution of latencies is illustrated in Fig. 10*A*. Antidromic latencies ranged from 0.5 to 1.2 ms.

STIMULATION OF THE CONTRALATERAL SACCADE ZONE. Stimulation of the contralateral saccade zone had only a modest influence upon some fixation neurons. Figure 11 illustrates the responses of two fixation neurons after stimulation of the contralateral saccade zone. The fixation neuron shown in Fig. 11*B* did not alter its discharge after the stimulation, whereas the fixation neuron shown in Fig. 11*C* was inhibited. Of the 24 fixation neurons tested for their response to stimulation of the contralateral saccade zone, only 33% (8/24) were inhibited (Table 3). Figure 10*B* shows the distribution of latencies to inhibition for the eight fixation neurons. The mean latency (±SD) was 4.6 ± 1.3 ms and the latencies ranged from 3 to 7 ms.

TABLE 3. *Summary of responses recorded from fixation neurons*

Stimulation Site	Neurons Tested	Inhibition	Excitation	Antidromic
Ipsi saccade	47	36	2	4
Contra saccade	24	8	0	0
Contra fixation	13	0	7	2

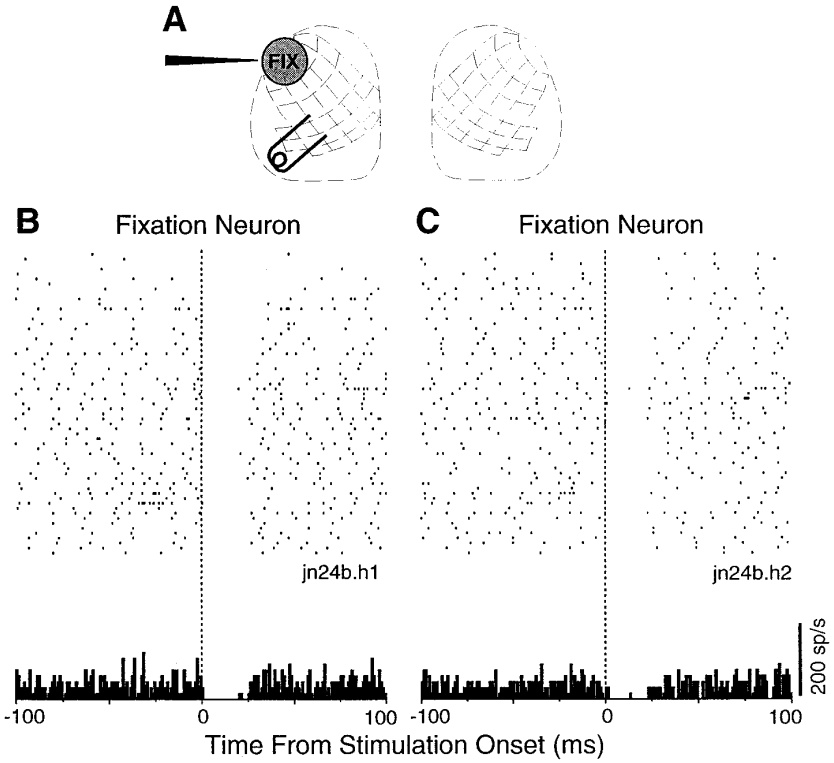

FIG. 9. Recording from 2 fixation neurons (recorded simultaneously) during electrical stimulation of the ipsilateral saccade zone. Both fixation neurons were located in the rostral left SC of *monkey j*. Rasters and histograms (1-ms binwidth) aligned on onset of a 3-ms train of 2 pulses (500 Hz).

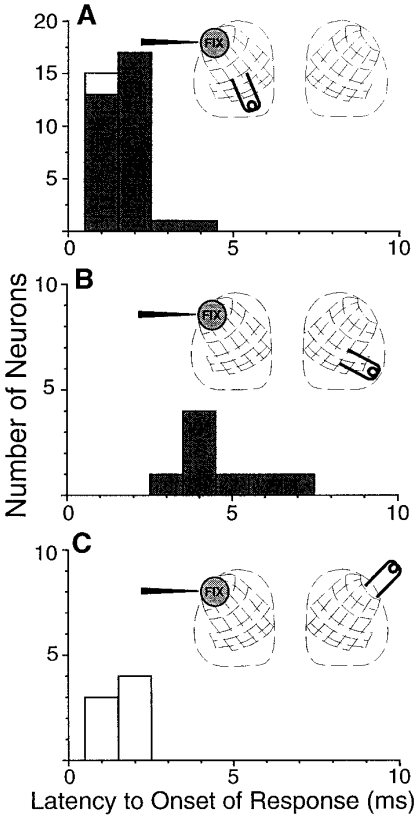

FIG. 10. Histograms showing the distribution of latencies to inhibition (▨) or excitation (□) of fixation neurons after stimulation of the ipsilateral saccade zone *(A)*, the contralateral saccade zone *(B)*, and the contralateral fixation zone *(C)*. Latency was measured from the beginning of stimulation to the onset of the response.

STIMULATION OF THE CONTRALATERAL FIXATION ZONE. Stimulation of the contralateral fixation zone lead to excitation of fixation neurons (see Table 3). Figure 12 illustrates the evidence for monosynaptic excitatory connections between neurons in the two fixation zones. Figure 12*B* shows the responses of a fixation neuron that was activated orthodromically by a single pulse of electrical stimulation to the contralateral fixation zone. Increasing stimulation intensity from 20 to 50 μA led to a reduction in latency from >2 to 1.3 ms. This short latency implies only one synaptic connection between the recording and stimulation sites. Fifty-four percent (7/13) of the fixation neurons tested were activated orthodromically at latencies between 1.2 and 2.5 ms. The mean latency ($\pm$SD) was 1.8 $\pm$ 0.5 ms, and the distribution of latencies is shown in Fig. 10*C*.

Figure 12*C* shows the responses of a fixation neuron that was activated antidromically by stimulation of the contralateral fixation zone. The antidromic response had a latency of 1.0 ms. The antidromic response was verified by collision testing (Fig. 12*C*). Decreasing the interval between a spontaneously occurring orthodromic action potential and the triggering of stimulation of the contralateral fixation zone led to collision of the orthodromic and antidromic waveforms (*top 2 traces* in Fig. 12*C*). Two fixation neurons were activated antidromically after stimulation of the contralateral fixation zone. Four fixation neurons were not activated either orthodromically or antidromically by stimulation of the contralateral fixation zone.

Contrast of responses of saccade and fixation neurons

The distribution of inhibitory and excitatory responses differed across the SC. Figure 13 shows the percentage of excitatory and inhibitory responses of saccade (Fig. 13*A*)

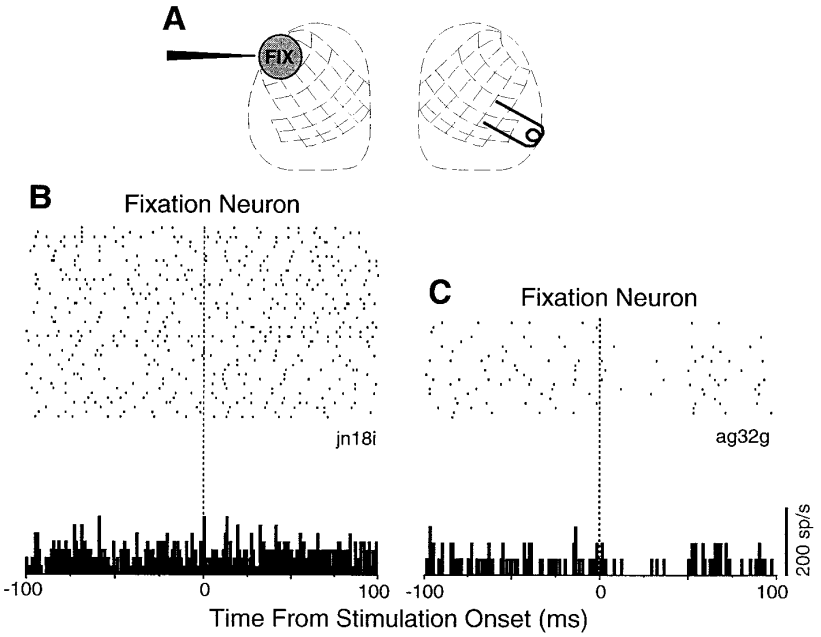

FIG. 11. Recording from 2 fixation neurons during electrical stimulation of the contralateral saccade zone with a brief (7 ms), high-frequency (500 Hz) train of 4 pulses. Fixation neuron in *B* was not influenced by the electrical stimulation, whereas the neuron illustrated in *C* was inhibited. Rasters and histograms (1-ms binwidth) aligned on stimulation onset.

and fixation (Fig. 13*B*) neurons produced by stimulation of the ipsilateral and contralateral saccade and fixation zones. Only one combination of recording (fixation neurons) and stimulation site (contralateral fixation zone) failed to produce inhibitory responses. For all other combinations of recording and stimulation, inhibitory responses predominated.

The latency to onset of inhibition or excitation was very similar between saccade (Fig. 13*C*) and fixation (Fig. 13*D*) neurons. There were no significant differences between fixation and saccade neurons in the latency to onset of inhibition or excitation from either the contralateral or ipsilateral SC (*t-test*, $P > 0.05$). Therefore the responses of fixation and saccade neurons were combined for the following analysis. The latency of inhibitory responses from the contralateral and ipsilateral SC were 4.1 ± 1.4 ms ($n = 36$) and 1.7 ± 0.7 ms ($n = 83$), respectively, and this difference was highly significant (*t-test*, $t = 9.77$, df = 35, $P < 0.0005$). The latency of excitatory responses from the contralateral and ipsilateral SC were 1.8 ± 0.4 ($n = 7$) and 1.3 ± 0.3 ($n = 5$), respectively, and this difference was also significant (*t-test*, $t = 2.47$, df = 4, $P < 0.05$). The difference in the latency of excitatory and inhibitory responses from the

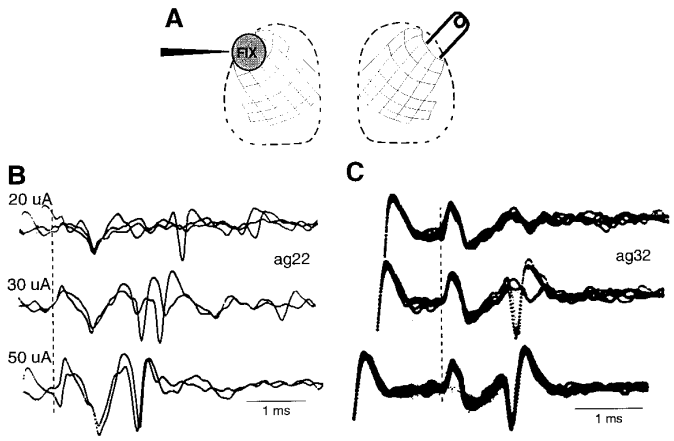

FIG. 12. Recording from fixation neurons during electrical stimulation of the contralateral fixation zone. *A*: cells were located in the rostral pole of the left SC and the stimulating electrode was positioned in the rostral pole of the right SC on *monkey a. B*: orthodromic excitation of a fixation neuron after stimulation with a single monophasic pulse (¦). Latency of orthodromic response is reduced with increased intensity of stimulation. *C*: antidromic activation of a fixation cell after stimulation with a single monophasic pulse (¦). Reducing the interval between the orthodromic spikes (*left edge* of *traces*) and the stimulation pulses led to collision of orthodromic and antidromic waveforms (*bottom 2 traces*), verifying the antidromic nature of the response. Waveforms in *B* and *C* initially were captured on polaroid film and later scanned into a computer.

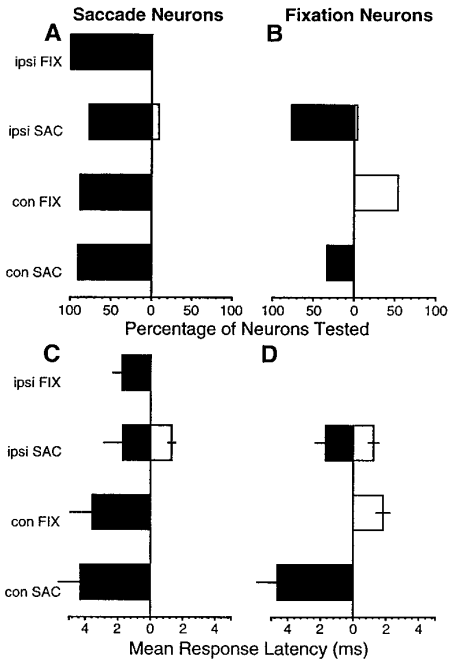

FIG. 13. Contrast of inhibitory (■) and excitatory (□) responses of saccade neurons (*A* and *C*) and fixation neurons (*B* and *D*). *A* and *B*: percentage of neurons tested with excitatory or inhibitory responses. *C* and *D*: mean latency (±SD) to onset of excitatory or inhibitory responses. Ipsi, ipsilateral; con, contralateral; FIX, fixation neurons; SAC, saccade neurons.

ipsilateral SC was significant (*t-test*, $t = 2.59$, df = 4, $P < 0.05$), and the difference in latency of excitatory and inhibitory responses from the contralateral SC was highly significant (*t-test*, $t = 8.27$, df = 6, $P < 0.0005$).

Effects of stimulation on visual neurons

We also recorded from some visual neurons in the superficial layers of the SC while electrical stimulation was applied to the contralateral and ipsilateral saccade and fixation zones in the intermediate layers. The discharge of visual neurons was not affected by stimulation of any SC zone: ipsilateral fixation (5 neurons tested), contralateral fixation (6 neurons tested), ipsilateral saccade (8 neurons tested), or contralateral saccade (3 neurons tested). We conclude from these results that the microstimulation applied to the fixation and saccade zones did not modify the discharge of all collicular neurons. Rather, it was selective for neurons in the intermediate layers of the SC.

Effects of prolonged stimulation

FIXATION ZONE STIMULATION. Although both burst and buildup neurons were inhibited by electrical stimulation of either the ipsilateral or contralateral fixation zone, the effect was usually greater on burst neurons (see Figs. 4 and 6). This observation was difficult to quantify because the neurons were usually recorded on different days, from different monkeys, with different stimulating electrodes. This difference in the magnitude of inhibition was revealed most prominently when prolonged low-frequency stimulation was used to delay saccade initiation. Figures 14 and 15, respectively, illustrate the responses of a burst neuron and a buildup neuron after prolonged stimulation of the contralateral fixation zone. Both neurons were active in the control (no stimulation) visually guided saccade condition (Figs. 14*A* and 15*A*). They were both activated shortly after target appearance, and they continued to discharge until after completion of the 20° rightward saccades. In the memory-guided saccade paradigm, the burst neuron discharged a weak phasic burst after the T flash (Fig. 14*B*), was silent until FP disappearance, and then discharged a burst of action potentials associated with the memory-guided saccade, which followed FP disappearance (Fig. 14*C*). In contrast, the buildup neuron was active at a low sustained frequency for most of the time between the T flash (Fig. 15*B*) and saccade initiation (Fig. 15*C*). A brief train of electrical stimulation of the contralateral fixation zone led to short-latency inhibition of both neurons (see Fig. 6). Stimulation at the same site with a long-duration (500 ms), low-frequency train (50 Hz) produced ripples in the spike density waveforms of both neurons (Figs. 14*D* and 15*D*), and a modest delay in the time to saccade initiation. Each ripple in the spike density waveform was the direct result of a single stimulation pulse. When saccade initiation was delayed with a 500-ms train at 125 Hz, the buildup neuron continued to discharge at a low frequency until the saccade was initiated (Fig. 15*E*), whereas the burst neuron remained almost silent during the stimulation-induced delay period (Fig. 14*E*). The discharge of both burst and buildup neurons during the stimulation-induced delay (Figs. 14*E* and 15*E*) was very similar to the discharge recorded during the instructed delay period in the memory-guided saccade paradigm (Figs. 14*B* and 15*B*). Similar results were obtained from the five burst and five buildup

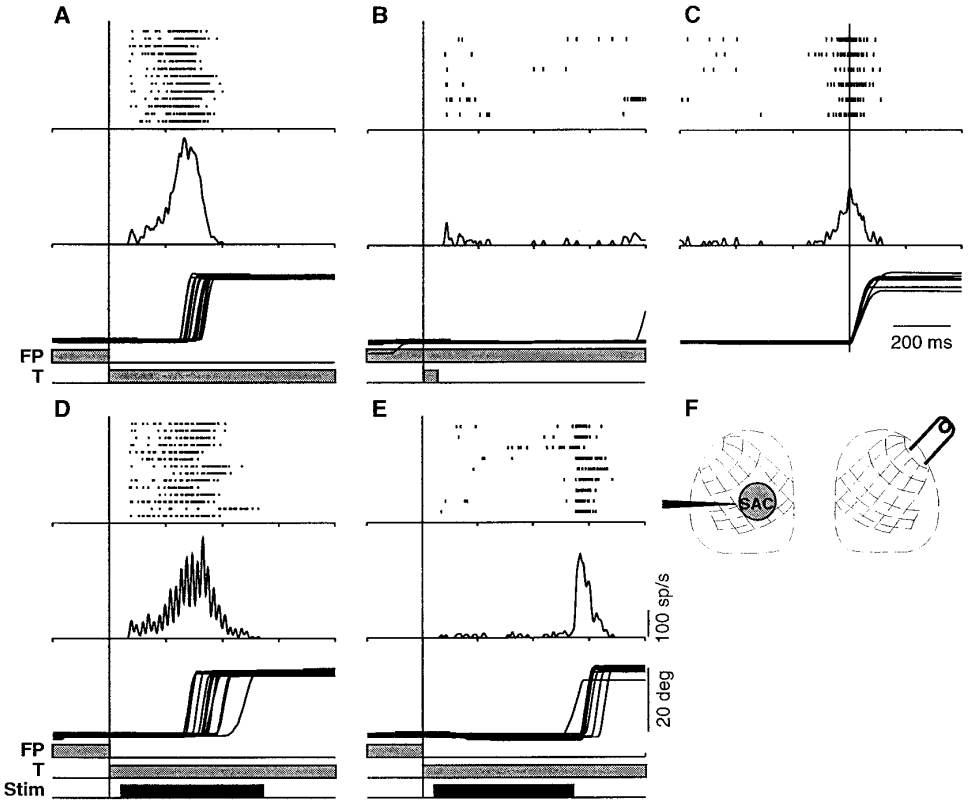

FIG. 14. Activity of a burst neuron during control and prolonged stimulation trials. Same neuron as shown in Fig. 6*B*. *A*: control trials in the visually guided saccade paradigm. Rasters, spike density waveform, and horizontal eye position aligned on target appearance in the movement field of the neuron. *B* and *C*: control trials in the memory-guided saccade paradigm aligned on onset of the target flash *(B)* and saccade onset *(C)*. *D* and *E*: effects of the neuron during a low-frequency (*D*, 50 Hz; *E*, 125 Hz), long-duration (500 ms) train of stimulation delivered to the contralateral fixation zone in the visually guided saccade paradigm. Traces aligned on target appearance. Stimulation train began 40 ms after target appearance. Spike-density function was generated by substituting a Gaussian pulse of 4 ms for each action potential, and then summing all Gaussians together (Richmond et al. 1987).

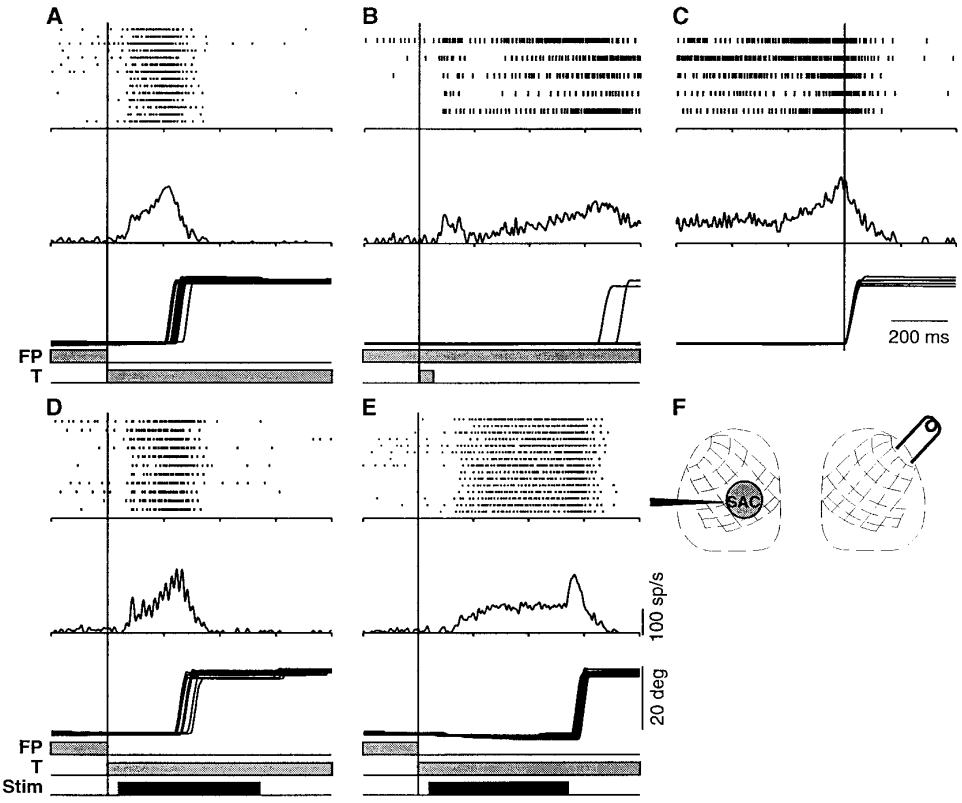

FIG. 15. Activity of a buildup neuron during control and prolonged stimulation trials. Same neuron as shown in Fig. 6*C*. *A*: control trials in the visually guided saccade paradigm. Rasters, spike density waveform, and horizontal eye position aligned on target appearance in the movement field of the neuron. *B* and *C*: control trials in the memory-guided saccade paradigm aligned on onset of the target flash *(B)* and saccade onset *(C)*. *D* and *E*: effects of the neuron during a low-frequency (*D*, 50 Hz; *E*, 125 Hz), long-duration (500 ms) train of stimulation delivered to the contralateral fixation zone in the visually guided saccade paradigm. Traces aligned on target appearance. Stimulation train began 40 ms after target appearance. Spike-density function was generated by substituting a Gaussian pulse of 4 ms for each action potential, and then summing all Gaussians together (Richmond et al. 1987).

neurons tested with low-frequency, long-duration stimulation of the contralateral fixation zone.

SACCADE ZONE STIMULATION. We investigated whether the reactivation of fixation neurons occurred at the end of each saccade elicited by prolonged electrical stimulation of the saccade zone of the SC. Figure 16 illustrates two examples of a fixation neuron recorded from the rostral pole of the left SC in *monkey p* during prolonged stimulation of the ipsilateral saccade zone. This fixation neuron was inhibited 2 ms after onset of a brief high-frequency train of electrical stimulation (not shown). The neuron was inhibited at a very short latency after onset of a 200-Hz train of stimulation pulses delivered to a region of the ipsilateral (left) SC that elicited saccades ~30° in amplitude to the right and down. A 135-ms train (Fig. 16*B*) elicited one saccade, whereas a 400-ms train (Fig. 16*C*) elicited two saccades. The fixation neuron stopped discharging shortly after the onset of electrical stimulation, but it came back on after the end of the first saccade regardless of whether the train of stimulation had ended (Fig. 16*B*) or was ongoing (Fig. 16*C*). Thus during prolonged stimulation of the SC, the activity of the fixation neuron illustrated in Fig. 16 was modulated with the occurrence of the saccadic eye movements elicited by the stimulation. Activity was not suppressed during the entire time of stimulation but evolved as a result of the pattern of eye movements. All 18 fixation neurons tested discharged action potentials at the end of saccades elicited by prolonged stimulation of the ipsilateral saccade zone even if the train of electrical stimulation continued.

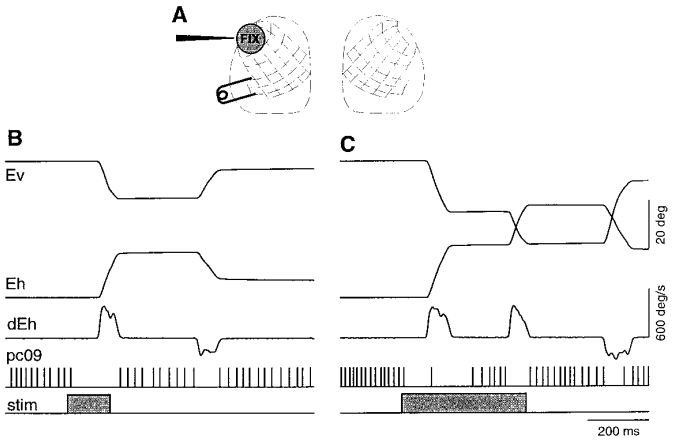

FIG. 16. Recording from a fixation neuron during prolonged electrical stimulation of the ipsilateral saccade zone. *A*: neuron was located in the rostral pole of the left SC of *monkey p* and the stimulating electrode was positioned in the ipsilateral saccade zone. *B* and *C*: individual trials showing how stimulation led to cessation of discharge and initiation of a saccade. Stimulation consisted of a train of pulses at 200 Hz just above threshold intensity that was presented while monkey performed the fixation blink paradigm (train duration: 135 ms in *B*, 400 ms in *C*). Traces shown from *top* to *bottom* are: vertical (Ev) and horizontal (Eh) eye position, and horizontal eye velocity (dEh), individual action potentials, and representation of the stimulation train (stim).

Figure 17 shows the responses of a fixation neuron recorded from the rostral right SC during prolonged stimulation of the contralateral saccade zone. This neuron was not inhibited by a brief, high-frequency train of stimulation applied to the contralateral saccade zone (same neuron in Fig. 11*B*). During prolonged stimulation in the fixation task, the fixation neuron remained active except when a saccade was elicited. Thus the discharge of the fixation neuron was modulated with saccade occurrence and not stimulation onset. All

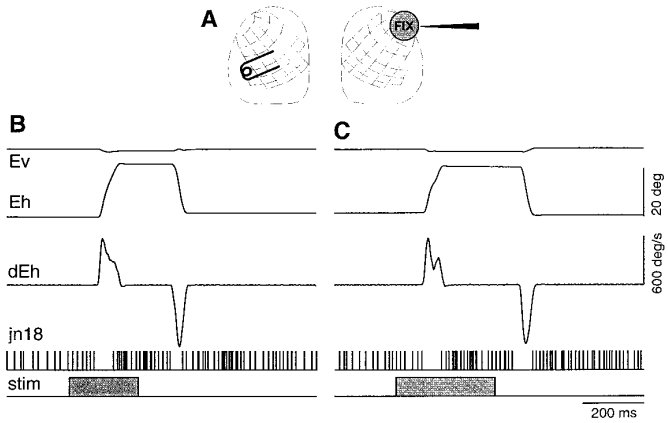

FIG. 17. Recording from a fixation neuron during prolonged electrical stimulation of the contralateral saccade zone. *A*: neuron was located in the rostral pole of the right SC of *monkey j* and the stimulating electrode was positioned in the caudal right SC. *B* and *C*: individual trials showing how stimulation did not influence the discharge of the neuron unless a saccade was elicited. Stimulation consisted of a train of pulses at 200 Hz at threshold intensity that was presented while monkey performed the fixation paradigm (train duration: 220 ms in *B*, 320 ms in *C*). Traces shown from *top* to *bottom* are: vertical (Ev) and horizontal (Eh) eye position, and horizontal eye velocity (dEh), individual action potentials, and representation of the stimulation train (stim).

11 fixation neurons tested discharged action potentials at the end of saccades elicited by prolonged stimulation of the contralateral saccade zone even if the train of electrical stimulation continued.

DISCUSSION

We have shown that most saccade and fixation neurons in the intermediate layers of the monkey SC were inhibited at short latency after microstimulation of other regions of the ipsilateral and contralateral SC. Although these observations support the hypothesis outlined in Fig. 1*B*, they also demonstrate that there were strong inhibitory connections among all regions of the ipsilateral and contralateral SC. The only exception was the interaction between the two fixation zones where we only recorded excitatory responses. Because the efficacy of the inhibition was so strong and widespread, we believe that local inhibitory interneurons form an important part of the collicular circuitry. Such a network of inhibitory interneurons may help shape, not only the reciprocal discharge patterns between fixation and saccade neurons, but also lateral interactions between saccade neurons in different parts of the ipsilateral and contralateral SC. We first discuss our data in relation to other anatomic and physiological studies of intracollicular connectivity. We then speculate on the role of intrinsic collicular circuitry in saccade control.

Relation to previous studies

Several different patterns of connectivity could account for the inhibitory responses we described here for fixation and saccade neurons, and some of these possibilities are illustrated in Fig. 18. Because latencies for many of the inhibitory responses after ipsilateral stimulation were of such short latency (see Figs. 5 and 10), it is unlikely that they were the result of stimulation leading to activation of fibers leaving the SC, being transmitted through a distant synapse and innervating neurons in another part of the brain, which then project back to the SC. Rather, we posit that the majority of responses recorded from collicular fixation and saccade neurons after electrical stimulation were the result of activation of monosynaptic inhibitory connections within the SC. This is not to say that all responses were generated by intrinsic collicular neurons. It is possible that the microstimulation could have activated an axon reflex if inhibitory afferent fibers collateralize to other areas in the SC distant from the site of electrical stimulation (e.g., Fig. 18*A*). For example, the substantia nigra pars reticulata, the zona incerta, and the nucleus of the optic tract contain GABAergic neurons that project to the SC (Appell and Behan 1990; Büttner-Ennever et al. 1996; Ficalora and Mize 1989; May et al. 1997). It is not clear how widespread these neurons collateralize within the SC. Nonetheless, it is possible that electrical stimulation of the SC may have led to activation of at least some of these inhibitory afferents, which then could collateralize elsewhere to generate short-latency inhibitory responses via an axon reflex (Fig. 18*A*). However, a similar mechanism also could have led to excitation of fixation and saccade neurons if the electrical stimulation activated excitatory afferents to the SC that collateralize within the SC. The fact that, except between the two fixation zones, an overwhelming number of inhibitory responses were recorded (see Fig. 13, *A* and *B*) suggests that much of the inhibition was mediated via local inhibitory connections.

It is also possible that some of the fixation and saccade neurons we recorded had horizontal projections to elsewhere within the SC to either terminate with inhibitory connections (Fig. 18*B*) or excitatory connections onto local inhibitory interneurons (Fig. 18*C*) to produce the inhibitory responses we observed among fixation and saccade neurons. Although a small percentage of the neurons were activated antidromically from elsewhere within the ipsilateral and contralateral SC (see Tables 2 and 3), the vast majority of the neurons tested were not antidromically activated. The extracellular recording techniques that were employed favored the recording of the largest neurons in the intermediate layers of the SC that tend to project out of the SC (May and Porter 1992). In squirrel monkey, these large efferent neurons may

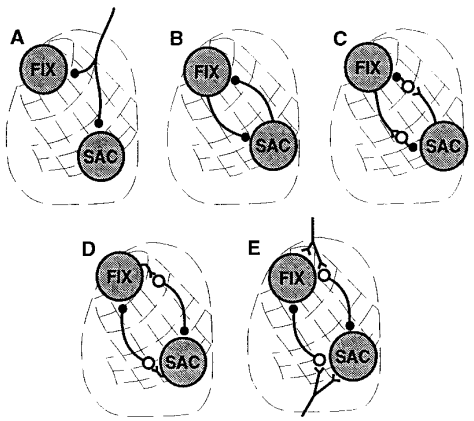

FIG. 18. Possible patterns of connections that could produce the monosynaptic inhibitory responses that we described here. See DISCUSSION for details.

have a recurrent collateral back to the same region of the SC containing the soma, a commissural projection to the opposite SC, or no local projection at all (Moschovakis et al. 1988a). They do not have horizontal projections to other regions of the ipsilateral SC. Behan and Kime (1996a) studied intrinsic circuitry in the deeper layers of the cat SC by injecting the neuroanatomic tracer biocytin into the deeper layers and examining the distribution of labeled axons and terminals. These authors found evidence for a broadly distributed network of intrinsic projections. The highest density of labeled terminals was 1–2 mm away from the site of the injection, but labeled terminals were present ≤5 mm away from the site of injection. The mean diameter of labeled neurons was 14.7 μm, but they ranged in size from 5.6 to 71 μm. Mize and colleagues (Mize et al. 1991) used immunocytochemical techniques to study characteristics of GABAergic neurons in the SC of rhesus monkeys and found that γ-aminobutyric acid (GABA) immunoreactive neurons were present throughout all layers of the SC. These neurons were small, ranging in size from 6 to 16 μm (mean 10.6 μm), and presumably do not project out of the SC. Most of the neurons we recorded were presumed to be the large efferent neurons (May and Porter 1992; Moschovakis et al. 1988a) and not the small local interneurons, many of which are GABAergic (Mize et al. 1991). We therefore conclude that the majority of fixation and saccade neurons we recorded did not have horizontal inhibitory (Fig. 18*B*) or excitatory (Fig. 18*C*) projections to other regions of the ipsilateral SC.

The most parsimonious explanations to account for our data and that of other studies are shown in Fig. 18, *D* and *E*. It is most probable that electrical stimulation led to the direct activation of inhibitory interneurons that projected horizontally across the SC to exert an inhibitory influence on fixation or saccade neurons distant from the site of electrical stimulation. This would account for the short-latency responses we observed, many of which were in the monosynaptic range (i.e., <2 ms). Physiological evidence for horizontal inhibitory connections also has been observed in the intermediate collicular layers of the ferret (Meredith and Ramoa 1996). The inhibitory interneurons could be activated by recurrent collaterals from fixation and saccade neurons (Fig. 18*D*), or they may share similar inputs as the fixation and saccade neurons (Fig. 18*E*) or both. Therefore, the local interneurons would have similar discharge characteristics as the adjacent fixation and saccade neurons. The small percentage of neurons that were activated antidromically may have been these local interneurons.

Electrical stimulation of the ipsilateral SC led to predominantly inhibitory responses in both saccade and fixation neurons (Fig. 13, *A* and *B*). In these experiments, the distance between the stimulation and recording sites was almost always ≥2 mm. McIlwain (1982) applied brief trains of electrical stimulation to the intermediate layers of the ipsilateral cat SC and observed predominantly short-latency excitatory responses. In this study, the distance between the stimulation and recording sites was varied systematically, and it was observed that the percentage of excitatory responses was greatest when the stimulation and recording sites were close together (<1 mm). We suggest that the infrequent excitatory responses we observed may be due to the relatively long distances between the stimulation and recording sites rather than any species difference. In support of this interpretation, Douglas and Vetter (1986) applied electrical stimulation to the intermediate layers of the cat and rat SC and observed inhibition throughout the ipsilateral and contralateral SC. The onset of the ipsilateral inhibition sometimes was obscured by short-latency excitation. In a separate study using slices of ferret SC, Meredith and Ramoa (1998) found evidence for both excitatory and inhibitory short-latency responses after ipsilateral SC stimulation. With pharmacological manipulations, it was concluded that the inhibitory responses were conveyed by inhibitory interneurons. It remains to be determined whether the distribution of intrinsic excitatory and inhibitory connections onto collicular neurons in the monkey varies systematically with distance between the recording and stimulation sites. The averaging saccades produced by two-point electrical stimulation in the SC (Robinson 1972) have been modeled using lateral spatial interactions within the SC that result in nearby excitation and remote inhibition (Van Opstal and Van Gisbergen 1989).

Electrical stimulation of the contralateral SC produced a nonuniform pattern of excitatory and inhibitory responses among fixation and saccade neurons. Among fixation neurons, stimulation of the contralateral fixation zone produced orthodromic excitation at monosynaptic latencies and antidromic responses. We therefore conclude that the two fixation zones are coupled together via excitatory interconnections. Stimulation of the contralateral saccade zone produced only weak inhibition of fixation neurons and this effect may have been mediated via the contralateral fixation zone. Among saccade neurons, stimulation of the contralateral fixation zone produced inhibition, and it is at least possible that some of this effect may have been mediated via the ipsilateral fixation zone. We cannot speculate on the precise nature of the inhibitory connection from the contralateral saccade zone onto saccade neurons. Previous physiological studies in cat and monkey have described inhibitory and excitatory responses of collicular neurons after stimulation of the contralateral SC (Maeda et al. 1979; Moschovakis et al. 1988a). Anatomic studies also have revealed evidence for both excitatory and inhibitory projections across the collicular commissure (Behan 1985; Behan and Kime 1996b; Olivier et al. 1997). Therefore at least some of the inhibitory responses we recorded after stimulation of the contralateral SC may have been mediated by inhibitory commissural neurons.

The latency to inhibition that we observed by stimulating the contralateral SC (Figs. 5, 10, and 13) was similar to that described by Moschovakis and colleagues (Moschovakis et al. 1988a), who used intracellular recording techniques. They reported that 71% (15/21) of the neurons tested were inhibited by electrical stimulation of the contralateral SC. Most of these neurons were the large efferent neurons located in the stratum opticum and stratum griseum intermedium of the SC. Stimulation of the contralateral SC evoked inhibitory postsynaptic potentials in these neurons with latencies ranging from 0.6 to 3.0 ms (mean ± SD; 1.73 ± 0.85 ms). The range of latencies to inhibition reported by Moschovakis and colleagues (Moschovakis et al. 1988a) is shorter than what we recorded after stimulation of the contralateral SC using extracellular recording techniques (range 2–7 ms; see Figs. 5, *B* and *D*, and 12, *B* and *C*).

The longer latencies we recorded were presumably the result of measuring the time to a reduction in discharge rate that would follow an inhibitory postsynaptic input after some delay.

SC and saccade control

The observations we have described provide new insight into the role of the SC in saccade generation. In the time leading up to the generation of a saccadic eye movement, saccade neurons (both burst and buildup neurons) in the caudal SC at the locus coding the direction and amplitude of the next saccade become active, and fixation neuron activity is diminished. Because of the tight coupling of these events, it is difficult to determine the precise sequence of events among fixation neuron deactivation, buildup neuron activation, and burst neuron activation. Processes related to fixation disengagement can be dissociated from those related to saccade initiation in a gap saccade paradigm in which the initial fixation target disappears for some time prior to target appearance. During the gap period, fixation neurons in the SC reduce their tonic discharge rate, buildup neurons are activated at low sustained frequencies, and burst neurons remain silent (Dorris and Munoz 1995; Dorris et al. 1997; Munoz and Wurtz 1995a). We speculate that the reduction in fixation neuron activity during the gap leads to a global disinhibition of saccade neurons via the intracollicular mechanisms described earlier. Although both burst and buildup neurons were inhibited by electrical stimulation of either fixation zone, the effect was usually greater on burst neurons (see Figs. 4 and 6). In addition, prolonged, low-frequency stimulation of the fixation zone, which is known to delay saccade initiation (Munoz and Wurtz 1993b), also led to a delay in the activation of burst neurons (Fig. 14*E*) but not buildup neurons (Fig. 15*E*). We therefore conclude that the efficacy of inhibition from the fixation zone onto burst neurons is much greater than onto buildup neurons. Burst and fixation neurons cannot be active simultaneously for any prolonged period of time and potent local inhibitory interconnections within the SC prevent this. In contrast, buildup neurons and fixation neurons can be active simultaneously, for example, during the stimulation-induced delay period (Fig. 15*E*) or during the gap period in the gap saccade paradigm (Dorris et al. 1997; Munoz and Wurtz 1995a). The activities of fixation and buildup neurons may compete against one another via local inhibitory connections to determine the future behavior of the animal: fixate or make a saccade. Once the animal is committed to making a saccade, the burst neurons are activated and fixation neurons stop discharging.

Our results also revealed strong inhibitory connections between different loci within the collicular saccade zones (see Fig. 13). These local inhibitory connections may play a very important role in selection of the next saccade target, enabling the different collicular sites to interact with each other before saccade initiation. We suggest that such a network may serve as a winner-take-all mechanism before the onset of the saccade-related burst of the saccade neurons. The buildup activity of buildup neurons may represent this process. In support of this hypothesis, the level of buildup neuron activity during the gap period has been correlated to saccadic reaction time (Dorris et al. 1997). The more intense the buildup activity is at a particular point within the SC, the shorter the reaction time is for saccades driven by that site.

At the start of a saccade, neural activity is centered at a point in the saccade zone of the SC coding the direction and amplitude of the impending saccade and both burst and buildup neurons at this site are maximally active (Munoz and Wurtz 1995b). As a saccade progresses there are two important changes in activity within the SC: the high-frequency burst discharge of burst neurons is clipped (Waitzman et al. 1991) and there is a rostral spread of activity within the buildup layer of the SC toward the fixation zone (Munoz and Wurtz 1995b). At the time of saccade termination, burst neurons are nearly silent and fixation neurons are reactivated. These changes in activity on the SC map may help terminate the saccade.

Prolonged stimulation of the saccade zone of the intermediate layers of the monkey SC leads to generation of repeated fixed-vector saccades that are separated by brief periods of no eye movement, which produces a staircase shape in the eye position record (Robinson 1972; Schiller and Stryker 1972). The amplitude of the evoked saccade matches closely with the optimal amplitude of the saccade neurons lying adjacent to the stimulating electrode (Paré et al. 1994; Schiller and Stryker 1972; van Opstal et al. 1990). It is therefore possible that a similar mechanism may terminate both natural and electrically evoked saccades. Prolonged electrical stimulation of the saccade zone of the SC presumably leads to prolonged activation of saccade neurons within the SC. Why does this saccade terminate even though electrical stimulation continues to activate saccade neurons directly? Because fixation neurons pause for both natural (Munoz and Wurtz 1993a) and electrically evoked saccades (Figs. 16 and 17) and resume their tonic discharge around the end of both natural and electrically evoked saccades, it is possible that both of these types of saccades may be terminated, at least in part, by the reactivation of fixation neurons. The rostral spread of activity across the buildup layer may provide the mechanism for reactivation of fixation neurons at saccade termination. Alternatively a signal from outside of the SC may reactivate fixation neurons at saccade termination. Regardless of the precise mechanism, reactivation of the fixation neurons may help terminate the saccade even if electrical stimulation continued. There then would be a refractory period before the fixation neurons can again be inhibited and another saccade triggered. Such a mechanism could account for the staircase pattern of eye motion produced with prolonged stimulation. From the results we have presented here, we can conclude that prolonged electrical stimulation of the saccade zone of the SC does not produce a static condition within the SC. Rather, there is a dynamic change in neuronal excitability across the SC during the generation of electrically evoked saccades. Fixation neurons in the rostral pole of the SC modulated their activity with the occurrence of saccades: they were active when the eyes were stationary and they paused when the eyes moved.

Conclusion

Inputs to the SC selectively activate either fixation neurons or subpopulations of saccade neurons. Our results show that

lateral inhibitory interactions within the SC may play a very important role in shaping the reciprocal discharges of these neurons. In addition, lateral inhibitory interactions between distant regions of the ipsilateral and contralateral saccade zones may play a role in saccade target selection. Future work is required to elucidate the discharge characteristics of the local circuit neurons and their precise connectivity.

We thank A. Lablans, D. Hamburger, and K. Powell for technical assistance. We are also grateful to Dr. R. H. Wurtz for the use of the resources of the Laboratory of Sensorimotor Research at the National Eye Institute in Bethesda, MD. We thank B. Corneil, S. Everling, M. Dorris, M. Paré, E. Olivier, and J. Broughton for comments on an earlier version of the manuscript.

This work was supported by a group grant from the Medical Research Council of Canada.

Address reprint requests to D. P. Munoz.

Received 18 September 1997; accepted in final form 25 November 1997.

REFERENCES

APPELL, P. P. AND BEHAN, M. Sources of subcortical GABAergic projections to the superior colliculus in the cat. *J. Comp. Neurol*. 302: 143–158, 1990.

BEHAN, M. An EM-autoradiographic and EM-HRP study of the commissural projection of the superior colliculus in the cat. *J. Comp. Neurol.* 234: 105–116, 1985.

BEHAN, M. AND KIME, N. M. Intrinsic circuitry in the dep layers of the cat superior colliculus. *Vis. Neurosci*. 13: 1031–1042, 1996a.

BEHAN, M. AND KIME, N. M. Spatial distribution of tectotectal connections in the cat. In: *Progress in Brain Research*, edited by M. Norita, T. Bando and B. Stein. Amsterdam: Elsevier, 1996b, vol. 112, p. 131–142.

BÜTTNER-ENNEVER, J. A., COHEN, B., HORN, A.K.E., AND REISINE, H. Efferent pathways of the nucleus of the optic tract in monkey and their role in eye movements. *J. Comp. Neurol*. 373: 90–107, 1996.

CRIST, C. F., YAMASAKI, D. S., KOMATSU, H., AND WURTZ, R. H. A grid system and a microsyringe for single cell recording. *J. Neurosci. Methods* 26: 117–122, 1988.

DORRIS, M. C. AND MUNOZ, D. P. A neural correlate for the gap effect on saccadic reaction times in monkey. *J. Neurophysiol.* 73: 2558–2562, 1995.

DORRIS, M. C., PARÉ, M., AND MUNOZ, D. P. Neuronal activity in monkey superior colliculus related to the initiation of saccadic eye movements. *J. Neurosci*. 17: 8566–8579, 1997.

DOUGLAS, R. M. AND VETTER, M. Widespread inhibition and target selection in the superior colliculus *Soc. Neurosci. Abstr*. 12: 458, 1986.

FICALORA, A. S. AND MIZE, R. R. The neurons of the substantia nigra and zona incerta which project to the cat superior colliculus are GABA immunoreactive: a double-label study using GABA immunocytochemistry and lectin retrograde transport. *Neuroscience* 29: 567–581, 1989.

FUCHS, A. F. AND ROBINSON, D. A. A method for measuring horizontal and vertical eye movement chronically in the monkey. *J. Appl. Physiol.* 21: 1068–1070, 1966.

GANDHI, N. J. AND KELLER, E. L. Interrupting saccades by electrical stimulation of the superior colliculus determines an extended fixation zone. *Soc. Neurosci. Abstr.* 21: 1193, 1995.

GLIMCHER, P. W. AND SPARKS, D. L. Movement selection in advance of action in the superior colliculus. *Nature* 355: 542–545, 1992.

GOLDBERG, M. E. AND WURTZ, R. H. Activity of superior colliculus in behaving monkey. I. Visual receptive fields of single neurons. *J. Neurophysiol*. 35: 542–559, 1972.

HAYS, A. V., RICHMOND, B. J., AND OPTICIAN, L. M. A UNIX-based multiple process system for real-time data acquisition and control. *WESCON Conf. Proc*. 2: 1–10, 1982.

JUDGE, S. J., RICHMOND, B. J., AND CHU, F. C. Implantation of magnetic search coils for measurement of eye position: an improved method. *Vision Res.* 20: 535–538, 1980.

LIPSKI, J. Antidromic activation of neurones as an analytic tool in the study of the central nervous system. *J. Neurosci. Methods* 4: 1–32, 1981.

MAEDA, M., SHIBAZAKI, T., AND YOSHIDA, K. Labyrinthine and visual inputs to the superior colliculus neurons. In: *Reflex Control of Posture and Movement*, edited by R. Granit and O. Pompeiano. Amsterdam: Elsevier, 1979, p. 735–743.

MAY, J. P., SUN, W., AND HALL, W. C. Reciprocal connections between the zona incerta and the pretectum and superior colliculus of the cat. *Neuroscience* 77: 1091–1114, 1997.

MAY, P. J. AND PORTER, J. D. The laminar distribution of macaque tectobulbar and tectospinal neurons. *Vis. Neurosci* 8: 257–276, 1992.

MAYS, L. E. AND SPARKS, D. L. Dissociation of visual and saccade-related responses in superior colliculus neurons. *J. Neurophysiol.* 43: 207–232, 1980.

MCILWAIN, J. T. Lateral spread of neural excitation during microstimulation in intermediate gray layer of cat's superior colliculus. *J. Neurophysiol.* 47: 167–178, 1982.

MEREDITH, M. A. AND RAMOA, A. S. Intrinsic circuitry of the superior colliculus: pharmacophysiological identification of horizontally-oriented inhibitory interneurons. *J. Neurophysiol*. 79: 1597–1602, 1998.

MIZE, R. R., JEON, C. J., HAMADA, O. L., AND SPENCER, R. F. Organization of neurons labeled by antibodies to gamma-aminobutyric acid (GABA) in the superior colliculus of the rhesus monkey. *Vision Res.* 6: 75–92, 1991.

MOHLER, C. W. AND WURTZ, R. H. Organization of monkey superior colliculus: intermediate layer cells discharging before eye movements. *J. Neurophysiol.* 39: 722–744, 1976.

MOSCHOVAKIS, A. K., KARABELAS, A. B., AND HIGHSTEIN, S. M. Structure-function relationships in the primate superior colliculus. I. Morphological classification of efferent neurons. *J. Neurophysiol.* 60: 232–262, 1988a.

MOSCHOVAKIS, A. K., KARABELAS, A. B., AND HIGHSTEIN, S. M. Structure-function relationships in the primate superior colliculus. II. Morphological identity of presaccadic neurons. *J. Neurophysiol.* 60: 263–302, 1988b.

MUNOZ, D. P. AND GUITTON, D. Fixation and orientation contol by the tecto-reticulo-spinal system in the cat whose head is unrestrained. *Rev. Neurol.* 145: 567–579, 1989.

MUNOZ, D. P. AND GUITTON, D. Control of orienting gaze shifts by the tectoreticulospinal system in the head-free cat. II. Sustained discharges during motor preparation and fixation. *J. Neurophysiol.* 66: 1624–1641, 1991.

MUNOZ, D. P., GUITTON, D., AND PELISSON, D. Control of orienting gaze shifts by the tectoreticulospinal system in the head-free cat. III. Spatiotemporal characteristics of phasic motor discharges. *J. Neurophysiol.* 66: 1642–1666, 1991.

MUNOZ, D. P., WAITZMAN, D. M., AND WURTZ, R. H. Activity of neurons in monkey superior colliculus during interrupted saccades. *J. Neurophysiol.* 75: 2562–2579, 1996.

MUNOZ, D. P. AND WURTZ, R. H. Role of the rostral superior colliculus in active visual fixation and execution of express saccades. *J. Neurophysiol.* 67: 1000–1002, 1992.

MUNOZ, D. P. AND WURTZ, R. H. Fixation cells in monkey superior colliculus. I. Characteristics of cell discharge. *J. Neurophysiol.* 70: 559–575, 1993a.

MUNOZ, D. P. AND WURTZ, R. H. Fixation cells in monkey superior colliculus. II. Reversible activation and deactivation. *J. Neurophysiol.* 70: 576–589, 1993b.

MUNOZ, D. P. AND WURTZ, R. H. Interactions between fixation and saccade neurons in primate superior colliculus. *Soc. Neurosci. Abstr.* 19: 787, 1993c.

MUNOZ, D. P. AND WURTZ, R. H. Saccade-related activity in monkey superior colliculus. I. Characteristics of burst and buildup cells. *J. Neurophysiol.* 73: 2313–2333, 1995a.

MUNOZ, D. P. AND WURTZ, R. H. Saccade-related activity in monkey superior colliculus. II. Spread of activity during saccades. *J. Neurophysiol.* 73: 2334–2348, 1995b.

OLIVIER, E., PAULIUS, Q., HARDY, O. AND CORVISIER, J. Evidence for excitatory tectotectal neurons in the cat superior colliculus: an immunohistochemical study. *Soc. Neurosci. Abstr*. 23: 1295, 1997.

PARÉ, M., CROMMELINCK, M., AND GUITTON, D. Gaze shifts evoked by stimulation of the superior colliculus in the head-free cat conform to the motor map but also depend on stimulus strength and fixation activity. *Exp. Brain Res.* 101: 123–139, 1994.

PECK, C. K. Visual responses of neurones in cat superior colliculus in relation to fixation of targets. *J. Physiol. (Lond)*. 414: 301–315, 1989.

RICHMOND, B. J., OPTICAN, L. M., PODELL, M., AND SPITZER, H. Temporal encoding of two-dimensional patterns by single units in primate inferior temporal cortex. *J. Neurophysiol.* 57: 132–146, 1987.

ROBINSON, D. A. Eye movements evoked by collicular stimulation in the alert monkey. *Vision Res.* 12: 1795–1808, 1972.

SCHILLER, P. H. AND KOERNER, F. Discharge characteristics of single units in superior colliculus of the alert rhesus monkey. *J. Neurophysiol.* 34: 920–936, 1971.

SCHILLER, P. H. AND STRYKER, M. Single-unit recording and stimulation in superior colliculus of the alert rhesus monkey. *J. Neurophysiol.* 35: 915–924, 1972.

SPARKS, D. L. Functional properties of neurons in the monkey superior colliculus: coupling of neuronal activity and saccade onset. *Brain Res.* 156: 1–16, 1978.

SPARKS, D. L. AND HARTWICH-YOUNG, R. The deep layers of the superior colliculus. In: *The Neurobiology of Saccadic Eye Movements*, edited by R. H. Wurtz and M. E. Goldberg. Amsterdam: Elsevier, 1989, p. 213–255.

SPARKS, D. L., HOLLAND, R., AND GUTHRIE, B. L. Size and distribution of movement fields in the monkey superior colliculus. *Brain Res.* 113: 21–34, 1976.

SPARKS, D. L. AND MAYS, L. E. Movement fields of saccade-related burst neurons in the monkey superior colliculus. *Brain Res.* 190: 39–50, 1980.

VAN OPSTAL, A. J. AND VAN GISBERGEN, J.A.M. A nonlinear model for collicular spatial interactions underlying the metrical properties of electrically elicited saccades. *Biol. Cybern*. 60: 171–183, 1989.

VAN OPSTAL, A. J., VAN GISBERGEN, J.A.M., AND SMIT, A. C. Comparison of saccades evoked by visual stimulation and collicular electrical stimulation in the alert monkey. *Exp.Brain Res.* 79: 299–312, 1990.

WAITZMAN, D. M., MA, T. P., OPTICIAN, L. M., AND WURTZ, R. H. Superior colliculus neurons mediate the dynamic characteristics of saccades. *J. Neurophysiol.* 66: 1716–1737, 1991.

WURTZ, R. H. AND GOLDBERG, M. E. Superior colliculus responses related to eye movement in awake monkeys. *Science* 171: 82–84, 1971.

WURTZ, R. H. AND GOLDBERG, M. E. Activity of superior colliculus in behaving monkey. III. Cells discharging before eye movements. *J. Neurophysiol.* 35: 575–586, 1972.