

Neck Muscle Responses to Stimulation of Monkey Superior Colliculus. I. Topography and Manipulation of Stimulation Parameters

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¹Canadian Institutes of Health Research Group in Sensory-Motor Systems, Centre for Neuroscience Studies, Department of Physiology, Queen's University, Kingston, Ontario K7L 3N6, Canada; and ²Laboratory of Neurophysiology, School of Medicine, University of Louvain, 1200 Brussels, Belgium

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Corneil, Brian D., Etienne Olivier, and Douglas P. Munoz. Neck muscle responses to stimulation of monkey superior colliculus. I. Topography and manipulation of stimulation parameters. *J Neurophysiol* 88: 1980–1999, 2002; 10.1152/jn.00959.2001. The role of the primate superior colliculus (SC) in orienting head movements was studied by recording electromyographic (EMG) activity from multiple neck muscles following electrical stimulation of the SC. Combining SC stimulation with neck EMG recordings provides an objective and sensitive measure of the SC drive onto neck muscle motoneurons, particularly in relation to evoked gaze shifts. In this paper, we address how neck EMG responses to SC stimulation in head-restrained monkeys depend on the rostrocaudal, mediolateral, and dorsoventral location of the stimulating electrode within the SC and vary with manipulations of the eye position prior to stimulation onset and changes in stimulation current and duration. Stimulation predominantly evoked EMG responses on the muscles obliquus capitis inferior, rectus capitis posterior major, and splenius capitis. These responses became larger in magnitude and shorter in onset latency for progressively more caudal stimulation locations, consistent with turning the head. However, evoked responses persisted even for more rostral stimulation locations usually not associated with head movements. Manipulating initial eye position revealed that the magnitude of evoked responses became stronger as the eyes attained positions contralateral to the side of stimulation, consistent with a summation between a generic command evoked by SC stimulation and the influence of eye position on tonic neck EMG. Manipulating stimulation current and duration revealed that the relationship between gaze shifts and evoked EMG responses is not obligatory: short-duration (<20 ms) or low-current stimulation evoked neck EMG responses in the absence of gaze shifts. However, long-duration stimulation (>150 ms) occasionally revealed a transient neck EMG response aligned on the onset of sequential gaze shifts. We conclude that the SC drive to neck muscle motoneurons is far more widespread than traditionally supposed and is relayed through intervening elements which may or may not be activated in association with gaze shifts.

INTRODUCTION

The role of the primate superior colliculus (SC) in the generation of saccades and combined eye-head gaze shifts has been widely studied in head-restrained and -unrestrained preparations, respectively (see Munoz et al. 2000; Sparks 1999;

Sparks and Hartwich-Young 1989 for review) (here gaze shifts refer to rapid movements of the eyes in space, regardless of whether the head is restrained or not). Neurons in the deeper layers of the SC are organized topographically into a motor map coding gaze shift direction and amplitude (Robinson 1972). Small-amplitude gaze shifts encoded in the rostral SC are generally accomplished by eye movements alone, whereas larger gaze shifts encoded in the caudal SC are composed of coordinated eye and head movements (Freedman and Sparks 1997b; Phillips et al. 1995; Tomlinson and Bahra 1986). Much remains to be learned about the circuitry between the SC and head plant, particularly compared with what is known about the circuitry between the SC and eye plant (see Moschovakis et al. 1996 for review). For example, during volitional gaze shifts, the SC command must be transformed into the appropriate spatial (i.e., which muscles) and temporal (i.e., recruitment timing) patterns of neck muscle activity. It is not clear how this transformation is accomplished, although work in nonprimates suggests a segregation of the SC command into orthogonal components (owls: Masino and Knudsen 1993; cats: Fukushima 1987; Grantyn et al. 1992; Isa and Naito 1994, 1995; Isa and Sasaki 1992a,b; Sasaki et al. 1999). It is also not known how this transformation is adjusted for gaze shifts that begin from different eye or head positions nor whether an SC drive to the head plant in behaving monkeys is obligatorily linked to gaze shift onset.

One way to study gaze shifts and head movements is to deliver electrical stimulation to the deeper layers of the SC because this evokes gaze shifts that conform to its motor map (provided appropriate parameters are used: Robinson 1972; Schiller and Stryker 1972; Stanford et al. 1996; van Opstal et al. 1990) and are composed of coordinated and seemingly natural eye and head movements (Freedman et al. 1996; Klier et al. 2001; Segraves and Goldberg 1992). In this paper and its companion (Corneil et al. 2002), we combined electrical stimulation of the SC with the recording of the electromyographic (EMG) responses in neck muscles. The head-neck system is a complex multiarticular structure endowed with substantial inertia (Winters 1988; Zangemeister and Stark 1981) and is

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controlled by more than two dozen neck muscles (Corneil et al. 2001; Richmond et al. 2001). Unlike the intuitive neuromuscular patterns underlying eye movements, it is impossible to use head kinematics to infer the spatiotemporal EMG patterns that result from the command to move the head because of the redundancy of the system for orienting movements (e.g., Hooper and Weaver 2000; Zajac and Gordon 1989). Recording neck EMG enables sensitive, precise, and objective quantification of the final neural signal issued to the head plant. This paper examines neck EMG responses evoked while the monkey's head is restrained, a justifiable approach because changes in neck EMG precede evoked head movements. We apply our technique to a head-unrestrained preparation in the companion paper (Corneil et al. 2002).

The first objective of this paper is to map the topography of the SC drive onto neck muscle motoneurons. As mentioned in the preceding text, SC stimulation evokes movements that conform to its known motor topography: smaller gaze shifts without head movements are evoked from the rostral SC; larger gaze shifts composed of both eye and head movements are evoked from the more caudal SC (Freedman et al. 1996; Klier et al. 2001; Segraves and Goldberg 1992). Two explanations are possible for the absence of evoked head movements from the rostral SC: either stimulation does not evoke neck muscle EMG responses or the muscle forces generated in response to SC stimulation do not overcome the head's inertia. To discern between these alternatives, we varied systematically the rostrocaudal and mediolateral location of the stimulating electrode to identify functional recruitment synergies for horizontal and vertical head movements. We also varied the dorsoventral location of the stimulating electrode because some physiological (Cowie and Robinson 1994) and anatomical (May and Porter 1992) data suggest that dorsal and ventral regions of the deeper layers of the SC project preferentially to the eye and head, respectively.

The second objective of this paper is to examine how the evoked neck EMG responses vary with manipulations known to affect the metrics of evoked gaze shifts and/or head movements. For example, caudal SC stimulation in head-restrained animals can evoke "goal-directed" gaze shifts that converge toward a specific position regardless of initial head-fixed gaze position (cats: Guitton et al. 1980; monkeys: Azuma et al. 1996; Freedman et al. 1996; Segraves and Goldberg 1992). Recording neck EMG can resolve whether the SC drive to the head plant covaries with the metrics of the head-fixed gaze shift or not. Recording neck EMG can also address how the SC drive to the head plant relates to the command to shift gaze: are neck EMG responses necessarily dependent on the generation of gaze shifts or can neck EMG responses be evoked without gaze shifts? Further, during longer stimulation trains that evoke sequential gaze shifts, is there a transient increase in neck EMG that accompanies each gaze shift? Assessing the variations in the evoked neck EMG with parametric manipulations in stimulation current or duration can provide insights into the functional properties of the SC drive to neck muscle motoneurons. We relate such insights to evoked head movements in the companion paper (Corneil et al. 2002).

Some results have been reported previously in abstract form (Corneil et al. 1998, 1999).

METHODS

Experimental procedures

Three male monkeys (*Macaca mulatta*, monkeys *f*, *z*, and *r*) weighing 5.4–6.7 kg were used in these experiments following procedures approved by the Queen's University Animal Care Committee in compliance with the guidelines of the Canadian Council on Animal Care. The monkeys' weights were monitored daily, and their general health was under the close supervision of the university veterinarian. Each monkey underwent two surgeries as described previously (Corneil et al. 2001). Briefly, the first surgery prepared the monkey for chronic recording of gaze position and extracellular recording and microstimulation within the SC (Munoz and Istvan 1998). A cylinder was positioned over a craniotomy allowing access to both SC, and was oriented 38° posterior of vertical so that electrode penetrations were perpendicular to the surface of the SC. A delrin grid (1 mm spacing; Crist Instruments) inside the cylinder held 23-gauge guide tubes through which the stimulating electrode was lowered (Crist et al. 1988). In the second surgery, chronically indwelling patch or hook EMG electrodes were implanted in 10–12 neck muscles under aseptic conditions (Table 1; Fig. 1). Anatomical description of these muscles has been provided previously (Richmond et al. 2001) as have the details of electrode design (Loeb and Gans 1986). All leads were tunneled subcutaneously to and buried in the previously implanted skull pedestal and soldered onto a connector. All animals appeared to be making normal head movements by the second or third postoperative day. EMG recordings began on the fifth postoperative day.

Monkeys were placed with their heads and torsos restrained in a primate chair and wheeled into a dark, sound-attenuated room. The monkeys either faced an array of 49 light-emitting diodes (LEDs; 4.7 cd/m²) or a tangent screen onto which a red laser (8.4 cd/m²) was back-projected. Both displays spanned about ±35° of the central visual field. A Pentium computer running a real-time data acquisition system (REX) (Hays et al. 1982) controlled all aspects of the experimental paradigms and visual displays at a rate of 1,000 Hz.

Microstimulation parameters

Stimulation was generated by a stimulator (model S88, Grass Instruments) and constant-current stimulus isolation units (model PSIU6, Grass Instruments) and delivered through tungsten microelectrodes (~0.2–1 MΩ at 1 kHz; Frederick Haer and Co.). To reduce possible tissue damage and avoid electrode polarization, stimulation consisted of biphasic pulses delivered at a pulse rate of 300 Hz, with an individual pulse duration of 0.3 ms. These settings have been shown to be the minimal values required to evoke kinematically consistent saccades with low current levels (Paré et al. 1994; Stanford et al. 1996). Stimulation duration ranged between a minimum of 0.6

TABLE 1. Listing of the recorded muscles, abbreviations, and the side and type of electrode that was implanted

Muscle	Monkey <i>f</i>	Monkey <i>z</i>	Monkey <i>r</i>
Splenius capitis (SP cap)	L R	x r	l r
Biventer cervicis (BC)	L	r	l r
Complexus (COM)	L R	r	l r
Atlanto-scapularis anterior (AS ant)		l	
Rectus capitis posterior major (RCP maj)		l	l r
Obliquus capitis inferior (OCI)	L R	l r	l r
Sternocleidomastoid (SCM)	l r	r	

Upper and lower case letters denote muscles that were implanted with patch and hook electrodes, respectively. The side of the implanted device is designated by either *L* or *l* for left muscles and *R* or *r* for right muscles. *X* or *x* indicates a muscle that was excluded from analysis because of electrode breakage. See Richmond et al. (2001) for morphometric descriptions of these muscles.

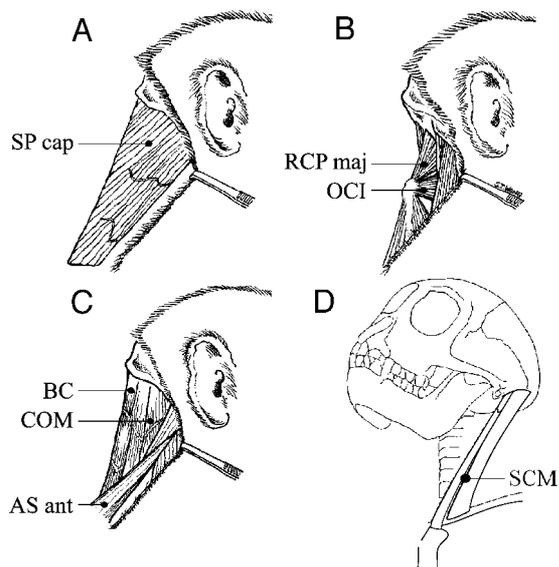


FIG. 1. Schematic line drawings of implanted neck muscles examined in this and the companion paper. Adapted with permission from Richmond and colleagues (2001), showing dorsal (A–C) and ventral neck muscles (D). A comprehensive summary of the activation patterns of these muscles is found in Corneil and colleagues (2001). Briefly, the suboccipital muscles obliquus capitis inferior (OCI) and rectus capitis posterior major (RCP maj) are active for the smallest head turns, and splenius capitis (SP cap) and sternocleidomastoid (SCM) are additionally active for progressively larger head turns. Anlantoscappularis anterior (AS ant) is active during centripetal head turns. Biventer cervicis (BC), complexus (COM), RCP maj, and SP cap are active to varying degrees for upward head movements, and SCM is active for only very vigorous downward head movements.

ms (1 biphasic pulse) to a maximum of 420 ms. The threshold current was defined as that which elicited a short-latency gaze shift (less than ~ 50 ms) on 50% of stimulation trials with a 100-ms train. This current threshold was termed the *GT100* (i.e., gaze threshold at 100 ms). A current level $1.5 \times GT100$ was used in all experiments (range 2.5–50 μA) unless otherwise noted. The *GT100* threshold current was either determined uniquely for each penetration or at each unique stimulation site (described in more detail below). We decided to determine such thresholds, as opposed to adopting a fixed current level (e.g., a level of 50 μA is typical) because preliminary experiments demonstrated frequently *GT100* levels of $< 10 \mu A$. We felt that introducing large currents into such a low-threshold area would activate an unnecessarily large volume of tissue.

For clarity, we have adopted the following terminology. *Stimulation site* refers to a unique stimulation position within the three dimensions of the SC (rostrocaudal, mediolateral, and dorsoventral). *Electrode penetration* denotes a dorsoventral collection of stimulation sites that were visited during the same experimental session as the electrode was moved through a given guide tube. *Stimulation location* denotes the unique two-dimensional position (rostrocaudal and mediolateral) of the electrode penetration on the SC map as determined by the position of the guide tube. Over different days, repeated electrode penetrations could be made at the same stimulation location by lowering the electrode into the same guide tube.

Behavioral paradigms

Monkeys were trained on a fixation task requiring them to look at a fixation point (FP) for a predetermined amount of time to obtain a liquid reward. Trial onset was signaled by the removal of a background diffuse white light (1.0 cd/m^2). The FP (variable positions, described in the following text) appeared 250 ms later, and the monkeys had 1,000 ms to look to it. The monkeys were then required

to keep their gaze within a computer-controlled fixation window (between 3×3 to $5 \times 5^\circ$ depending on FP position) for between 800 and 1,500 ms. SC stimulation (variable duration, described in the following text) was delivered on 80–90% of all trials between 500 and 1,000 ms after the onset of fixation. Stimulation was delivered either while the FP remained visible (*fixation trials*; 40–45% of all trials) or 200 ms after the FP was extinguished (*fixation-blink trials*, 40–45% of all trials). Monkeys were still required to maintain fixation while the FP was extinguished in the fixation-blink trials, and the FP reappeared after stimulation offset. The monkeys were rewarded even if stimulation drove gaze outside the fixation window. Control trials without stimulation were run in ~ 10 –20% of all trials. The neck EMG evoked by SC stimulation in fixation and fixation-blink trials differed slightly in response magnitude, but this will not be discussed in the present papers. However, we confirmed that the baseline level of neck EMG immediately prior to stimulation onset did not differ between the fixation and fixation-blink trials.

The three-dimensional topography of the SC drive onto neck muscles was studied by systematically positioning guide tubes in different locations in the delrin grid above the SC. The term *depth series* refers to an electrode penetration in which stimulation was delivered at different sites in 500 μm increments to examine the evoked responses as a function of the dorsoventral location of the electrode. Depth series usually employed a central FP and a stimulation duration of 100 ms, although stimulation duration could be lengthened to 150 ms to ensure the entire gaze shift amplitude was realized before the end of the stimulation train. A block of 20–40 stimulation trials was delivered at every site between the dorsal and ventral extents of the intermediate and deep layers of the SC. The dorsal extent was identified as the dorsal-most site at which gaze shifts and/or EMG responses were evoked using at most 50 μA of current with a train duration of 100 ms.¹ We assumed the electrode had progressed through the ventral extent of the SC if one of the following conditions was met:² neither a gaze nor an EMG response was evoked with stimulation of 50 μA and 100 ms; stimulation evoked movements of the face, body, limb, or pinna (monitored via an infra-red camera) or vocalizing responses; or the qualitative pattern of evoked neck EMG changed. For example, stimulation beyond the ventral-most site could facilitate muscles that had been suppressed at all more dorsal stimulation sites.

In *monkeys f* and *z*, the stimulating current was kept constant at $1.5 \times GT100$ throughout the entire depth series, based on the *GT100* determined at the second or third depth. If stimulation evoked a gaze shift without an EMG response, the site was termed a “gaze site.” If stimulation evoked neck EMG without a gaze shift, the site was termed an “EMG site.” If stimulation evoked both a gaze shift and an EMG response, the site was termed a “gaze and EMG site.” The sites that evoked the shortest gaze shift latencies were noted.

In *monkey r*, the current thresholds required to evoke one or both of an EMG and gaze response were determined at each stimulation site within a depth series, and the classification of the site was based on a comparison of these thresholds. If the current threshold for evoking an EMG response was $\geq 25\%$ less than *GT100*, the site was termed an EMG site. If the *GT100* was $\geq 25\%$ less than the current threshold for evoking an EMG response, the site was termed a gaze site. If EMG and gaze shift thresholds were approximately equal, the site was

¹ Other stimulation studies have used higher current intensities in the superficial layers of the SC (Robinson 1972; Segraves and Goldberg 1992; Stryker and Schiller 1975). We chose an arbitrary maximum of 50 μA in agreement with recent stimulation studies in head-unrestrained primates (Cowie and Robinson 1994; Freedman et al. 1996; Klier et al. 2001).

² Although the dorsal surface of the SC is easily recognized in chronic recording experiments, the ventral extent of the SC cannot be discerned without histological examinations. From a physiological standpoint, the cells in the deeper layer of the SC share functional properties with cells in the underlying central mesencephalic reticular formation (Ma et al. 1991; Werner et al. 1997b). Because we had no objective criteria for determining the ventral border of the SC, we stopped the depth series according to the listed criteria.

termed a gaze and EMG site. The sites endowed with the lowest GT100s were noted.

Following completion of the depth series, the stimulating electrode was returned to the dorsal-most depth at which stimulation evoked either the shortest-latency gaze shifts (*monkeys f* and *z*) or had the lowest GT100 (*monkey r*), and these responses to stimulation were confirmed. Variants of the fixation task were then run to study the effects of manipulations in eye position or stimulation parameters, always using current levels at $1.5 \times$ GT100. Manipulations of eye position were studied in blocks of 150–200 trials with stimulation duration set to 100 ms, and the FP was moved to one of nine possible locations randomly selected from a 3×3 grid of 15 or 30° steps. In another block of 50–100 trials, we determined the minimum number of pulses required to elicit a neck EMG response by varying randomly the stimulation duration among five intervals between 0.6 ms (1 biphasic pulse) and 10 or 20 ms (4 or 8 pulses, respectively). In a third block of 50–100 trials, longer-duration stimulation trains were varied randomly among intervals of 20, 120, 220, 320, and 420 ms. Because longer trains evoked sequential “staircases” of gaze shifts (Robinson 1972; Schiller and Stryker 1972), this block was run only when stimulation evoked gaze shifts less than $\sim 15^\circ$ in amplitude, and the FP was positioned 15 or 30° contralateral to the direction of the ensuing gaze shift.

Data collection and analysis

Digitized signals of integrated EMG activity (described in the following text) and the gaze (eye-in-space) positions derived from the magnetic coil system were acquired simultaneously at 500 Hz. A flexible ribbon-cable linked the EMG connector to preamplifiers and low-pass filters (MAX274 integrated IC filter, $f_c = 8$ kHz, roll-off = 24 dB/octave, Maxim Electronics) that filtered out the coil frequencies. EMG signals were then fed into an Analog Preprocessor and Timer (Aztec Associates) that enabled computer-programmable amplification, filtering (100–5,000 Hz), rectification, integration and digitization of the signals into 2-ms bins. The rectification and amplification in such conditioning attenuated the peak-to-peak amplitude of the raw EMG signals by approximately a factor of 10 (Bak and Loeb 1979).

Off-line, computer software determined the beginning and end of each gaze shift using velocity and acceleration thresholds and template-matching criteria (Waizman et al. 1991) and were verified by an experimenter to ensure accuracy. Average evoked EMG responses were calculated by aligning repeated trials on stimulation onset and averaging every 2 ms. The mean and SD of the baseline activity in the 100 ms preceding stimulation onset was calculated. The latency of facilitation or suppression of the evoked EMG response was determined as the bin following stimulation onset that was the first of at least five consecutive bins either 2 SDs above or below the average baseline activity, respectively. Determination of a suppressive response was therefore only possible in the presence of notable baseline activity. The peak magnitude of the EMG response was taken as the highest average bin value after stimulation onset minus the average baseline activity. Because the magnitude of neck EMG activity varies with different eye-in-head positions (Lestienne et al. 1984; Werner et al. 1997a) (see also Fig. 9A), the search for the peak EMG magnitude evoked by SC stimulation ranged from stimulation onset to the onset of the evoked gaze shift.

A scoring criteria quantified the proportion of EMG sites and gaze sites within a depth series and was used to map the topography of these different classes of SC sites. EMG sites were given a score of +1, gaze sites a score of –1, and gaze and EMG sites a score of 0. These scores were summed for all sites within a depth series to yield a representative score. For example, a depth series score of –3 signifies an electrode penetration in which three more gaze sites were observed than EMG sites. This score was then divided by the total

number of sites within the depth series to yield a score normalized to the number of stimulation sites.

To visualize the properties of evoked EMG as a function of stimulation location within the SC, maps were constructed in the following manner. For every stimulation location in which a gaze shift was evoked, the approximate two-dimensional position of the electrode (u , v) on the SC motor map was obtained using the equations of van Gisbergen et al. (1987) and the metrics of the gaze shift derived from the most dorsal site evoking either the shortest gaze shift latency or lowest GT100

$$u = B_u \ln \left[\frac{\sqrt{R^2 + A^2 + 2AR \cos \theta}}{A} \right] \quad (1)$$

$$v = B_v \arctan \left[\frac{R \sin \theta}{R \cos(\theta) + A} \right] \quad (2)$$

where u = anatomical distance from the foveal representation in the SC measured along the horizontal meridian (in mm), v = anatomical distance along the v axis which runs perpendicular to the u axis (mm), B_u = a scaling constant (1.4 mm) determining the size of the SC map along its u axis, B_v = a scaling constant (1.8 mm/rad) determining the size of the SC map along its v axis, A = a constant (3°) that, together with the ratio B_u/B_v , determines the mapping shape, R = vectorial amplitude of the evoked head-fixed gaze shift, in degrees,³ and θ = direction of evoked gaze shift, in degrees.

The parameter in question (response latency, magnitude, or normalized score) was plotted at the estimated stimulation location (u , v), pooled across both SC in all monkeys, and then plotted onto a single representative SC map.

RESULTS

General patterns of neck EMG evoked by SC stimulation

We stimulated the SC of head-restrained monkeys in 361 unique stimulation sites distributed throughout 35 different stimulation locations (10 in *monkey f*, 13 in *monkey z*, and 12 in *monkey r*). At most sites, stimulation evoked neck EMG and gaze shifts (see following text). Only small quantitative differences in the evoked gaze shifts and neck EMG were observed when stimulation locations were revisited. The initial EMG response to SC stimulation consisted of a facilitation in the activity of agonist neck muscles that turned the head in the direction contralateral to the stimulating site and a suppression in the activity of antagonist muscles on the opposite side. Stimulation evoked neck EMG responses most commonly in splenius capitis (SP cap; Fig. 1A) and in the suboccipital muscles obliquus capitis inferior (OCI) and rectus capitis posterior major (RCP maj; Fig. 1B). Our quantitative analyses focus on these three muscles. Stimulation evoked EMG responses less frequently in sternocleidomastoid (SCM), biventer cervicis (BC), complexus (COM), and atlantoscapularis anterior (AS ant; Fig. 1, C and D), and these patterns are described at the end of RESULTS.

Examples of evoked neck EMG in OCI, RCP maj, and SP

³ Using head-restrained gaze shifts to map out the location of the stimulating electrode likely distorts the resulting SC map because caudal SC stimulation evokes larger gaze shifts in the unrestrained versus restrained preparation given an increased head contribution (Freedman et al. 1996). However, the amount by which such distortion changes the estimated location of the stimulation electrode is small given the logarithmic nature of the SC map. For example, we compared the metrics of evoked gaze shifts in the restrained and unrestrained preparation and found only 1 example of 13 in which the estimated location of the stimulating electrode on the SC map differed by >0.3 mm across the restrained and unrestrained preparations.

cap are shown in Fig. 2, *A* and *B*. Stimulation ($15 \mu\text{A}$) through a caudally located electrode (Fig. 2*A*) evoked a 15° right 10° down gaze shift ~ 25 – 30 ms after stimulation onset and also evoked EMG responses consisting of a facilitation in R-OCI, R-RCP maj, and R-SP cap and a concomitant suppression in ipsilateral L-OCI, L-RCP maj and L-SP cap. The evoked EMG responses began ~ 10 ms after stimulation onset and always preceded gaze shift onset. Stimulation at more rostral sites also evoked neck EMG, as shown in Fig. 2*B* when stimulation ($20 \mu\text{A}$) evoked 5° right 2° down gaze shifts. Here the evoked activity in R-OCI and R-RCP maj was very weak but still significantly above baseline. The facilitation latency for R-OCI was longer in Fig. 2*B* than 2*A* (22 vs. 10 ms) but still preceded gaze shift onset by ~ 10 – 20 ms. Rostral stimulation did not

evoke a concomitant suppression in the antagonist muscles presumably due to a lack of baseline activity.

The spatiotemporal pattern of neck EMG activity during and immediately after SC stimulation presented as one of two forms. In approximately half of all sites, stimulation evoked a reciprocal pattern in which the initial EMG response to stimulation reversed ~ 50 ms after stimulation onset, facilitating the antagonist muscles and returning the agonist muscles to or below their baseline levels (e.g., Fig. 2, *A* and *B*). In the other half, the agonist muscle response to stimulation consisted of an initial phasic burst followed by a generalized facilitation in the agonist muscles and a complete suppression of EMG activity in the antagonist muscles (e.g., Fig. 3, *B*–*E*). We could not predict which of these two patterns would be evoked at a given stimulation site as they did

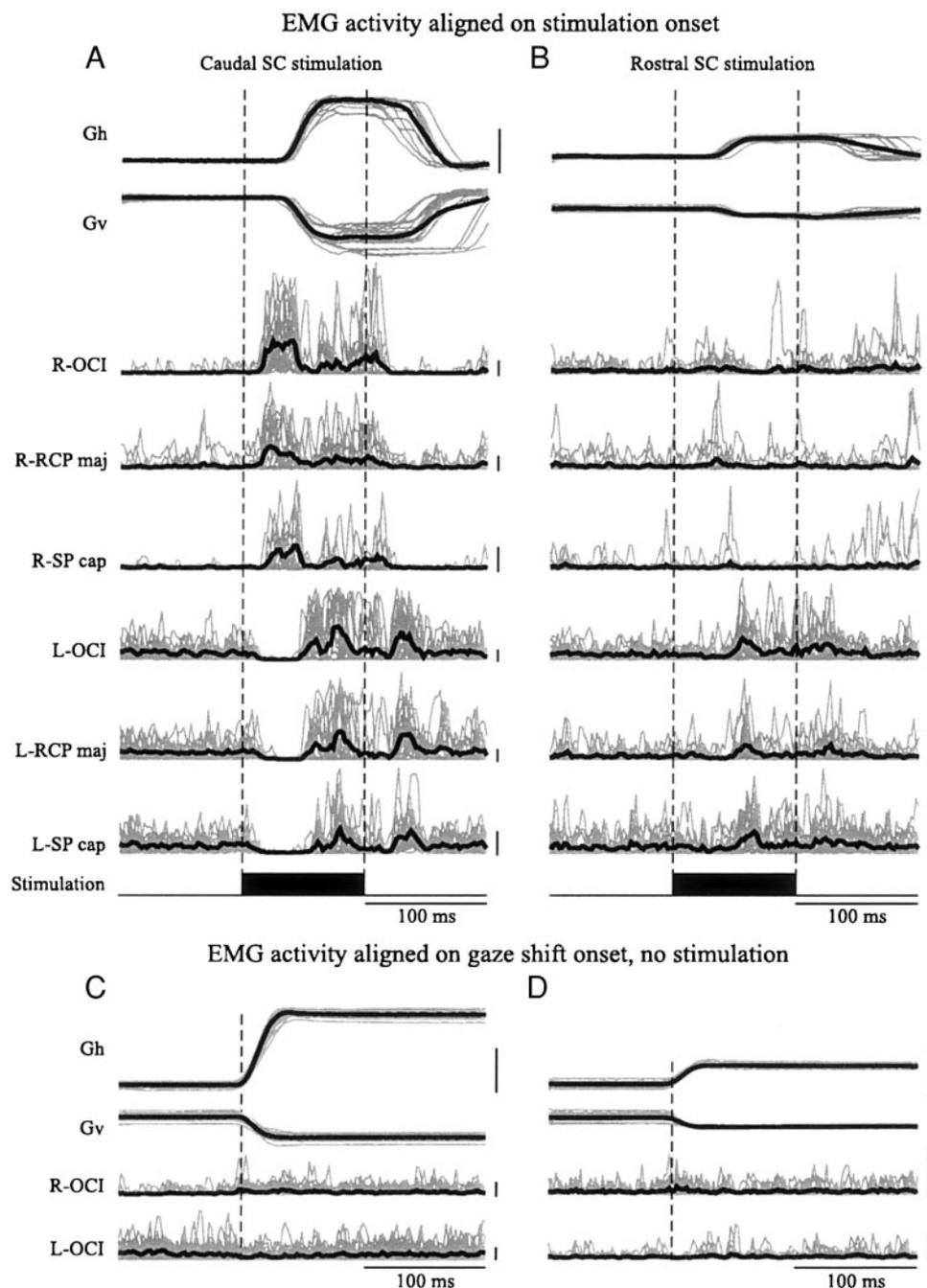


FIG. 2. Comparison of gaze and EMG traces either evoked by superior colliculus (SC) stimulation (*A*: caudal site, *B*: rostral site) or generated voluntarily (*C* and *D*). Data from *monkey r*. The pairs *A* and *C* and *B* and *D* were matched approximately for gaze shift metrics. Thick, black lines trace the average EMG and gaze shift responses, averaged over each of the component EMG and gaze responses (thin, gray lines; 20 in *A*, 19 in *B*, 29 in *C*, 20 in *D*). R- and L- in front of each muscle denotes right and left, respectively. Gh and Gv denote horizontal and vertical gaze position traces, respectively. Positive deflections of these traces indicate rightward and upward movements, respectively. Black rectangle and vertical dashed lines in *A* and *B* denote the stimulation train. Vertical dashed lines in *C* and *D* denote gaze shift onset. Scale bars for gaze traces denote 10° . Scale bars for EMG traces denote $25 \mu\text{V}$.

not depend on gaze shift metrics, stimulation current, or stimulation location. Another characteristic EMG response to SC stimulation appeared 20–40 ms after stimulation offset and consisted of a suppression of agonist muscle activity and a facilitation of antagonist muscle activity. This stimulation offset transient did

not always coincide with returning gaze shifts (Figs. 2A and 3, D and E). As will be presented in the companion paper (Cornel et al. 2002), both the reciprocal pattern of EMG activity during stimulation and the stimulation offset transients are not artifacts of head restraint.

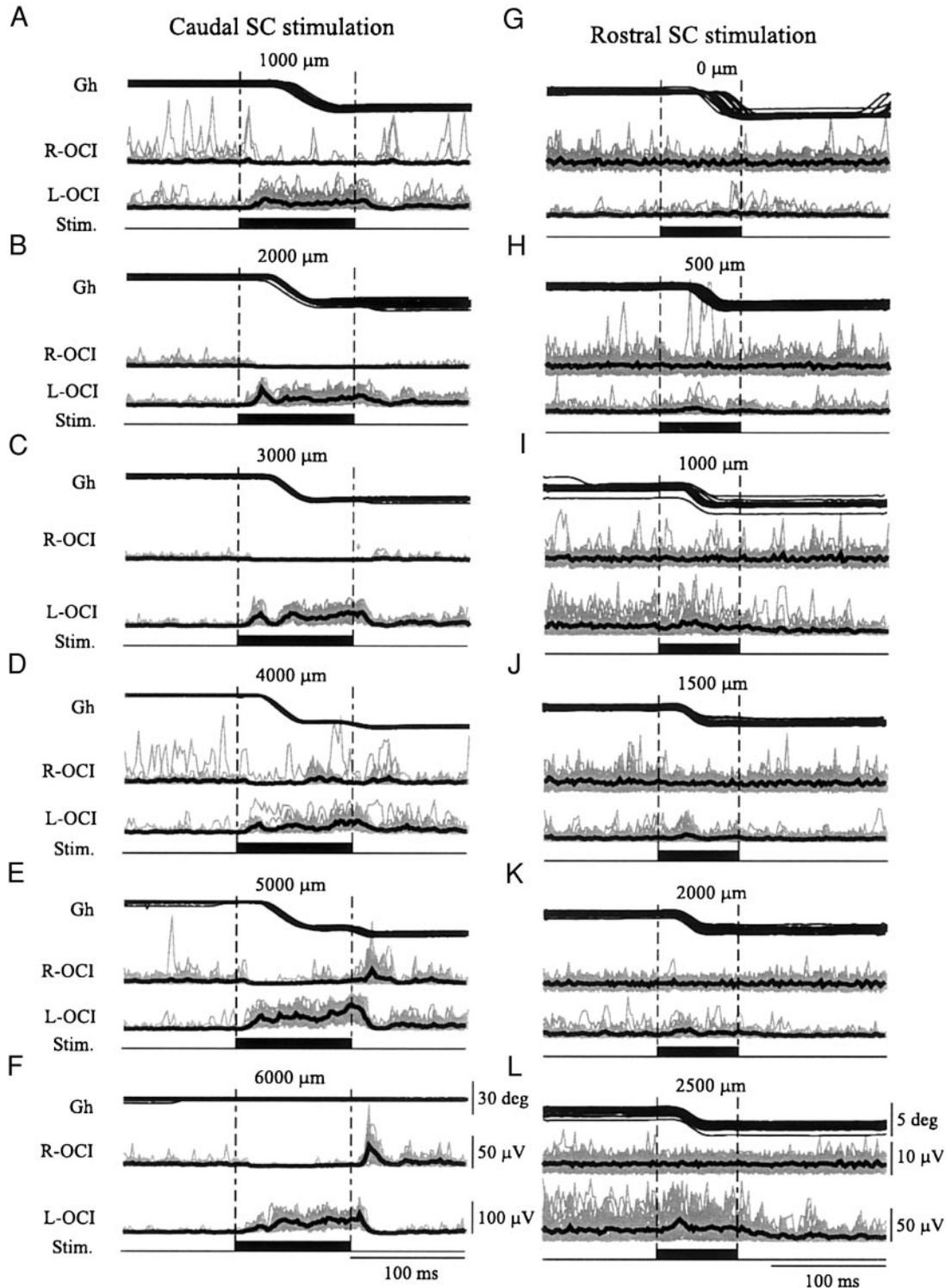


FIG. 3. Horizontal gaze position (Gh) and neck EMG responses in R- and L-OCI following stimulation at different dorsal-ventral depths within the SC for a track from the caudal (A–F) and rostral SC (G–L). Data from *monkey z*. The numbers above each subplot indicate the depth below the dorsal-most stimulation site. The scale bars in F and L apply to all depths for the given track. Same format as Fig. 2.

We compared the EMG patterns evoked by stimulation to those accompanying volitional head-fixed gaze shifts (Corneil et al. 2001). The pattern of EMG activity during volitional head-fixed gaze shifts was relatively small in magnitude (Fig. 2, *C* and *D*) and never displayed the reciprocal switching of agonist and antagonist muscle activity nor the offset transients typical of SC stimulation.

Topography of SC drive onto neck muscles

We adopted a systematic approach to map the SC drive onto neck muscle motoneurons in three-dimensions by performing depth series throughout different parts of the SC. The average length of such depth series was 4,500 μm (range: 1,500–8,500 μm). Portions of two depth series are shown in Fig. 3 to illustrate representative results observed for OCI from either a caudal (Fig. 3, *A–F*) or rostral (*G–L*) stimulation location (similar results were observed in RCP-maj and SP cap but are not shown). Stimulation in most sites in the caudal SC evoked both gaze shifts and EMG responses, and such sites were termed gaze and EMG sites (Fig. 3, *A–E*). However, stimulation in other sites in the caudal SC evoked neck EMG responses either without evoking a gaze shift (Fig. 3*F*) or at lower current levels than the GT100. Such sites were termed EMG sites. Note that although a gaze shift was not evoked in Fig. 3*F*, the spatiotemporal pattern of the evoked EMG responses appeared very similar to that evoked at more dorsal sites. Further, we found that stimulation in most EMG sites in monkey *r* could elicit gaze shifts if the stimulation current was increased but still kept $<50 \mu\text{A}$.

In the rostral SC, most sites were also classified as gaze and EMG sites (Fig. 3, *H–L*). However, stimulation at some dorsal sites evoked either gaze shifts without neck EMG (Fig. 3*G*) or at lower current levels than that required to evoke EMG responses. Such sites were termed gaze sites. As in the caudal SC, both the spatiotemporal form of the evoked EMG response and the evoked gaze shift metrics remained fairly constant throughout the depth series.

We devised a system to quantify the proportion of gaze sites and EMG sites within the 26 sites in which depth series were completed (see METHODS), and represented these quantities as a function of stimulation location (Fig. 4*A*). Rostral depth series attained more negative scores, indicating more gaze sites. Caudal depth series attained more positive scores, indicating more EMG sites. To visualize these data further, we represented the classification of every site within all depth series, leveled relative to the most dorsal depth at which either the lowest gaze shift latency or GT100 was observed (Fig. 4*B*). Most stimulation sites were classified as gaze and EMG sites (yellow squares: 149/218 = 68.3%). Gaze sites (blue squares: 20/218 = 9.2%) were more prevalent in the rostral SC, and EMG sites (red squares: 49/218 = 22.5%) were more prevalent in the caudal SC and occurred more often at ventral sites. We did not observe a strict dichotomy in the dorsoventral distribution of either gaze sites or EMG sites; examples of each could be found in either the dorsal or ventral extremes of individual depth series. Overall, stimulation evoked EMG responses (i.e., both EMG sites and gaze and EMG sites) at most stimulation sites (198/218 = 90.8%) in these depth series. Further, EMG responses appeared in the sites endowed with the shortest gaze shift latencies or lowest GT100 (gray shaded

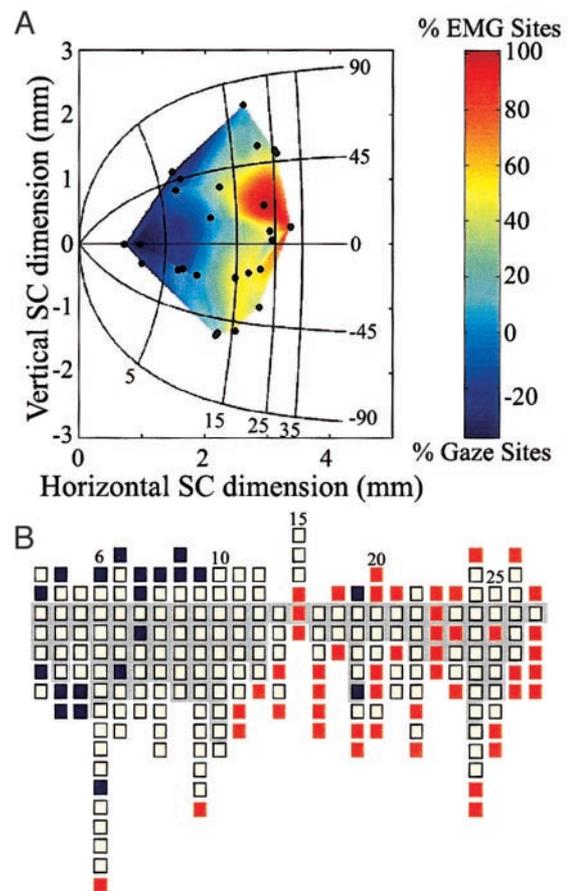


FIG. 4. *A*: SC contour map of the representative scores tabulated for contralateral OCI for all depth series in all monkeys. The abscissa represents the rostrocaudal (horizontal) axis of the SC; the ordinate represents the mediolateral (vertical) axis of the SC. Iso-amplitude and -direction lines are superimposed with the corresponding values of each line placed within either the lower or rightward portion, respectively. Dots denote the estimated location of the stimulating electrode, based on the gaze shift evoked from the dorsal-most site endowed with the shortest gaze shift latency or lowest GT100. The contour plots interpolate data between filled dots. The representative score was derived by tallying a score of +1 for all EMG sites with a score of -1 for all gaze sites for all sites, then dividing this total by the total number of sites within the depth series. *B*: for the same data, each column represents a single depth series, with each square denoting the classification for sites visited within 500- μm increments. Every site was assigned a blue, yellow, or red square depending on whether the site was classified as a gaze site, a gaze and EMG site, or an EMG site, respectively. Columns are arranged from left to right in order of the increasing amplitude of the evoked gaze shift (the amplitude is denoted above some columns) and are leveled to the most dorsal site within each depth series endowed with the shortest gaze shift latencies or lowest GT100 (shaded gray contour). See METHODS for further details.

regions). We conducted all subsequent experiments at these depths.

To quantify the evoked neck EMG responses, we compared the response latencies (Fig. 5) and magnitudes (Fig. 7) across all stimulation locations in which gaze shifts were evoked. A strong rostrocaudal trend was apparent in the facilitation and suppression response latencies, ranging from ~ 8 ms for caudal stimulation locations ≤ 25 –30 ms for rostral stimulation locations (Fig. 5). Notably, a significant EMG response in at least one muscle was evoked by stimulation in 34 of 35 stimulation locations; SC stimulation failed to evoke an EMG response in only one far rostral location (\circ in Fig. 5*A*; a depth series was not completed for this site). For small gaze shifts, stimulation

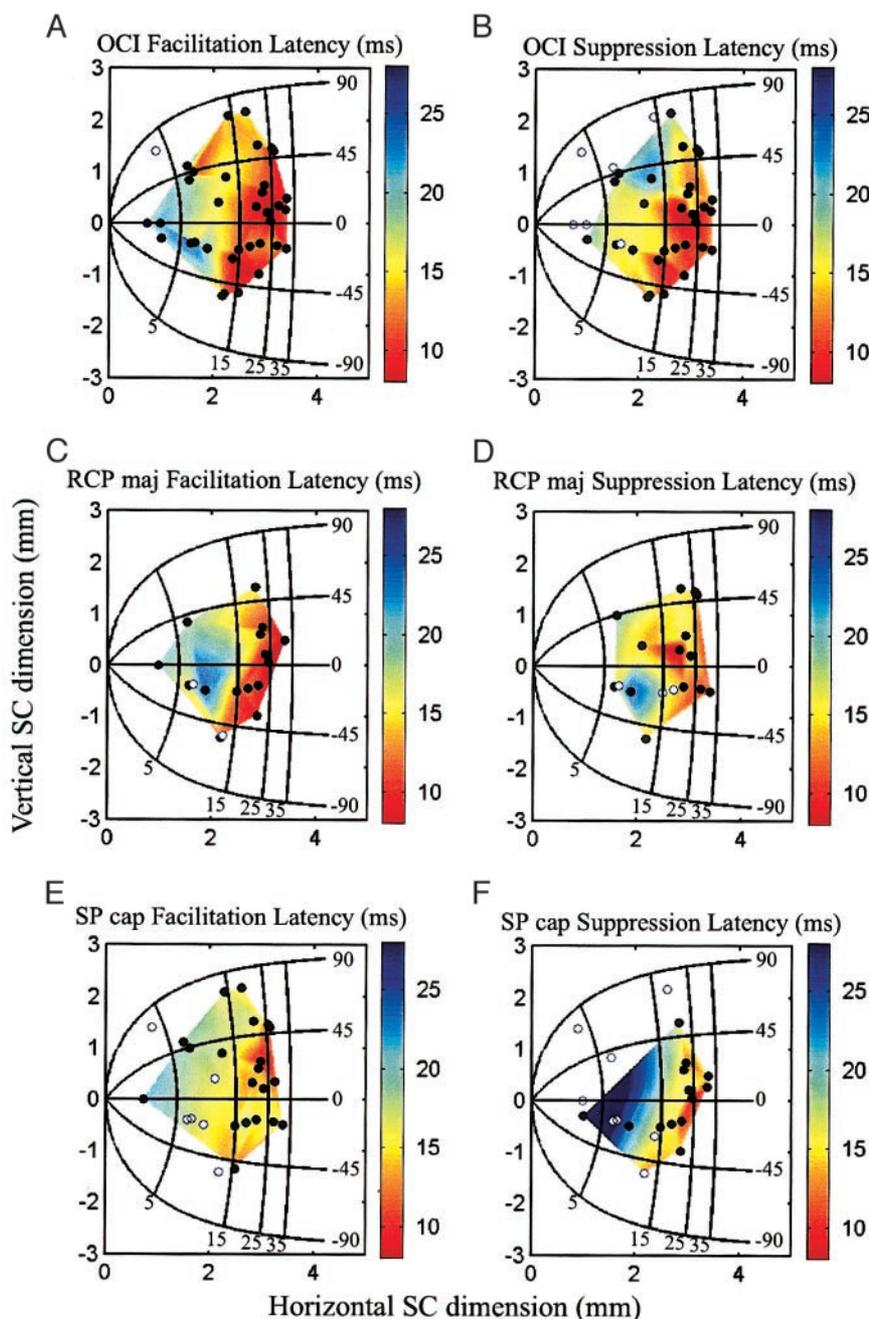


FIG. 5. SC maps of the facilitation (A, C, and E) and suppression (B, D, and F) latencies for OCI (A and B), RCP maj (C and D), and SP cap (E and F). Same format as Fig. 4A. ●, locations at which the given EMG responses were observed; ○, locations at which the given EMG response was not observed. Results were pooled across both SC in all 3 monkeys. The number of data points differs in the graphs because some muscles were implanted unilaterally in some monkeys (Table 1).

evoked responses more frequently in OCI and RCP maj than SP cap, resembling the recruitment pattern seen during volitional head movements (Corneil et al. 2001). SC stimulation also evoked more instances of facilitation than suppression, presumably because the determination of suppression depended on sufficient baseline activity. Somewhat surprisingly, we did not observe any mediolateral trend in the latency data as might have been expected because RCP maj and SP cap contribute to inclining head movements (Corneil et al. 2001) (t -test on sites $>10^\circ$ from horizontal meridian, $P > 0.5$ for all comparisons).

Even with the rostrocaudal variations in the EMG response, the onset of EMG responses always preceded or equaled gaze shift onset (Fig. 6A). Gaze shift latencies were longer and much more variable (mean: 36.3 ± 11.7 ms, range: 21–70) than OCI

facilitation latencies [mean: 13.4 ± 4.5 ms, range: 8–24. Paired t -test, $t(33) = -9.37$, $P < 0.0001$], demonstrating that the EMG responses did not result from changes in eye position. We also compared response latencies among different muscles. In OCI, the latency of suppression was significantly greater than the latency of facilitation [Fig. 6B; paired t -test, $t(26) = -2.58$, $P = 0.016$, mean difference = 2.0 ms]. Further, the latency of facilitation in agonist OCI was equal to that for agonist RCP maj [Fig. 6C, paired t -test, $t(13) = -0.894$, $P = 0.39$, mean difference = 0.5 ms], but significantly shorter than that for agonist SP cap [Fig. 6D, paired t -test, $t(17) = -7.74$, $P < 0.0001$, mean difference = 3.5 ms].

We also plotted the peak magnitudes of evoked neck EMG responses above baseline as a function of electrode location (Fig. 7). Facilitatory responses became progressively stronger

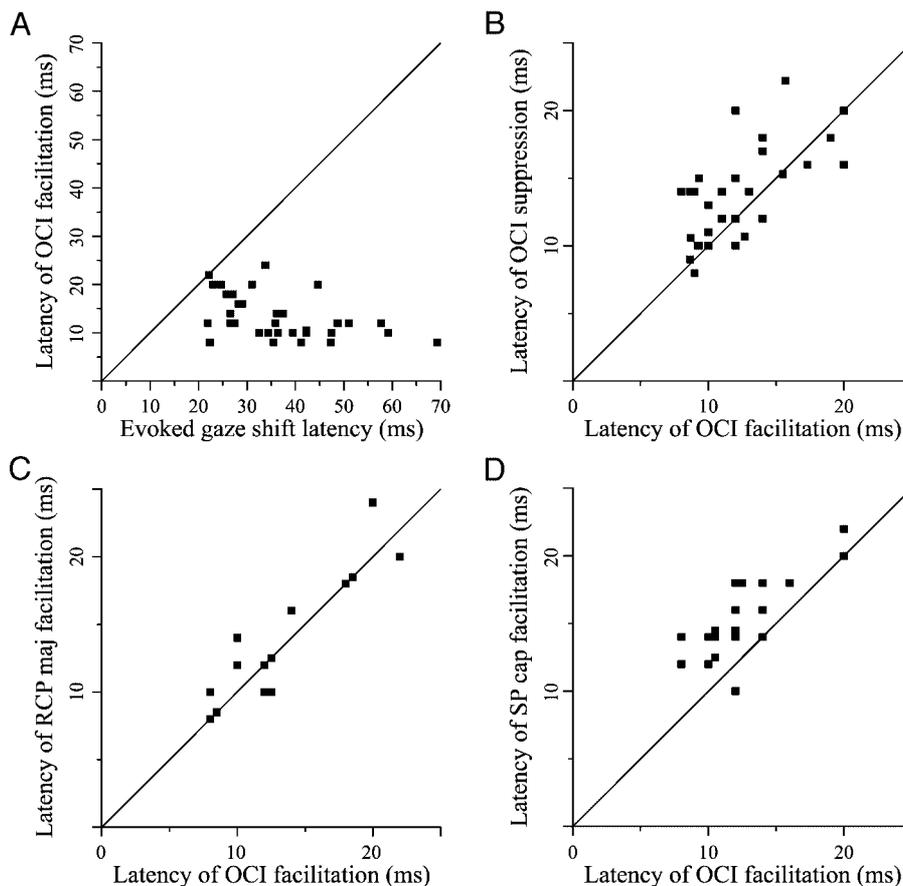


FIG. 6. Comparison of latency of facilitation in contralateral OCI vs. the gaze shift latency (A), the latency of suppression in ipsilateral OCI (B), the latency of facilitation in contralateral RCP maj (C), and the latency of facilitation in contralateral SP cap (D). Each point represents data from a different stimulation location, and the results are pooled across all 3 monkeys. —, the unity lines.

for more caudal stimulation locations and, as mentioned before, SP cap was not recruited from some rostral stimulation locations (Fig. 7C). We also found that the magnitudes of the EMG responses did not vary with the mediolateral location of stimulation (t -test on sites $>10^\circ$ from horizontal meridian, $P > 0.5$ for all comparisons).

When the topography of the peak EMG magnitude (Fig. 7) is considered along with the dorsal-ventral distributions of sites (Fig. 4) and the SC distribution of EMG response latencies (Fig. 5), a topography emerges suggesting that the drive onto neck muscles persisted throughout almost the entire SC, but had a shorter latency (Fig. 5), and got progressively stronger (Fig. 7) and more prevalent (Fig. 4, A and B) for more caudal stimulation locations. To summarize these data, we plotted each of these parameters versus the rostrocaudal location of the stimulating electrode, as indexed by the amplitude of the evoked gaze shift (Fig. 8). The transition in these parameters from the rostral to caudal SC was monotonic, emphasizing the notion of a continuous drive throughout almost the entire SC onto neck muscle motoneurons.

Manipulation of behavioral or stimulation parameters

VARIATIONS IN EYE POSITION. To address whether evoked neck EMG responses varied with eye position, we stimulated the SC after the monkeys attained different eye positions. The baseline level of neck EMG prior to stimulation varied with eye position, becoming progressively more active as the eye attained ipsiversive positions relative to the muscle under consideration and inactive for contraversive positions (Fig. 9A for R-OCI).

Similar results were observed in RCP maj and SP cap in all monkeys and agree with previous work (Lestienne et al. 1984; Werner et al. 1997a). The variations in the baseline neck EMG with eye position provided the framework for interpreting how evoked neck EMG responses changed with eye position. In the example shown in Fig. 9B, the gaze vectors evoked by stimulation ($45 \mu\text{A}$ for 100 ms) varied somewhat as the monkey adopted one of nine different fixation positions. The evoked patterns of synchronous facilitation and suppression persisted in agonist and antagonist neck muscles, respectively, but became more or less apparent depending on the baseline level of EMG activity (Fig. 9C). For example, the activity evoked in R-OCI and R-SP cap was greater when the animal fixated 30° right than when the animal fixated center and was small or absent when the animal fixated 30° left. Suppression in antagonist L-OCI was strong when the animal looked 30° left but could not be demonstrated when the animal looked 30° right given the lack of baseline activity.

Figure 10 displays the results from seven stimulation sites in the left SC of *monkey r* (similar results were obtained for the other SC and from *monkey f*). We expressed the peak magnitude of evoked activity above baseline in agonist R-OCI (Fig. 10, D and F) and R-SP cap (Fig. 10, E and G) as a function of eye position prior to stimulation onset. Along the horizontal meridian (Fig. 10, D and E), the peak magnitude of evoked activity in these muscles increased significantly for more rightward positions [i.e., contralateral to the side of stimulation. Kruskal-Wallis (KW) on repeated-measures ranks. R-OCI: $\chi^2(4) = 16.5$, $P < 0.01$. R-SP: $\chi^2(4) = 25.1$, $P < 0.0001$]. This

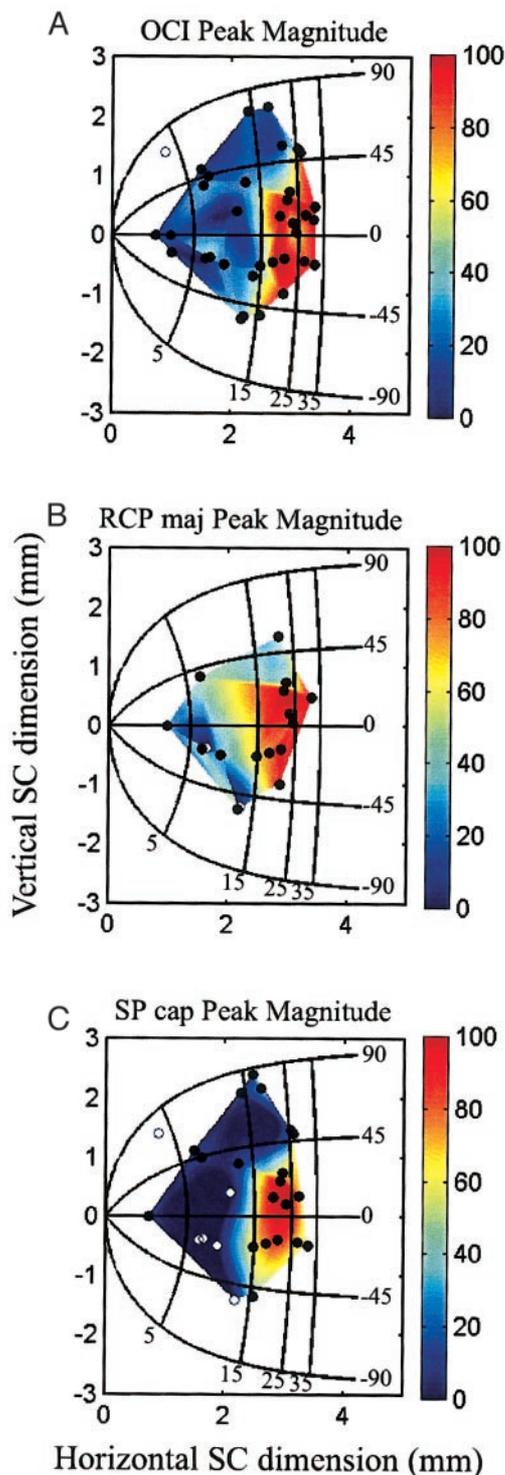


FIG. 7. SC maps of the normalized peak magnitude of evoked neck EMG above baseline for OCI (A), RCP maj (B), and SP cap (C). Same format as Fig. 4A. Peak EMG magnitude was normalized to the maximum response evoked in a given muscle, allowing data to be pooled across both SC in 3 monkeys. Stimulation current was always $1.5 \times GT100$.

response pattern was observed regardless of whether the vector of the evoked gaze shifts varied mildly with eye position (Fig. 10B) or converged strongly toward a certain eye position (Fig. 10C). In the vertical plane, the evoked R-OCI response did not vary with eye position [Fig. 10F; $\chi^2(4) = 4.4$, $P = 0.35$], but

the evoked R-SP cap response became significantly greater with more upward eye positions [Fig. 10G; $\chi^2(4) = 21.1$, $P < 0.001$]. Thus regardless of the metrics of the evoked gaze shift, the magnitude of the evoked EMG responses became stronger when the monkey adopted more contralateral (OCI and SP cap) or upward (SP cap only) eye positions, consistent with the changes in the baseline activities of these muscles.

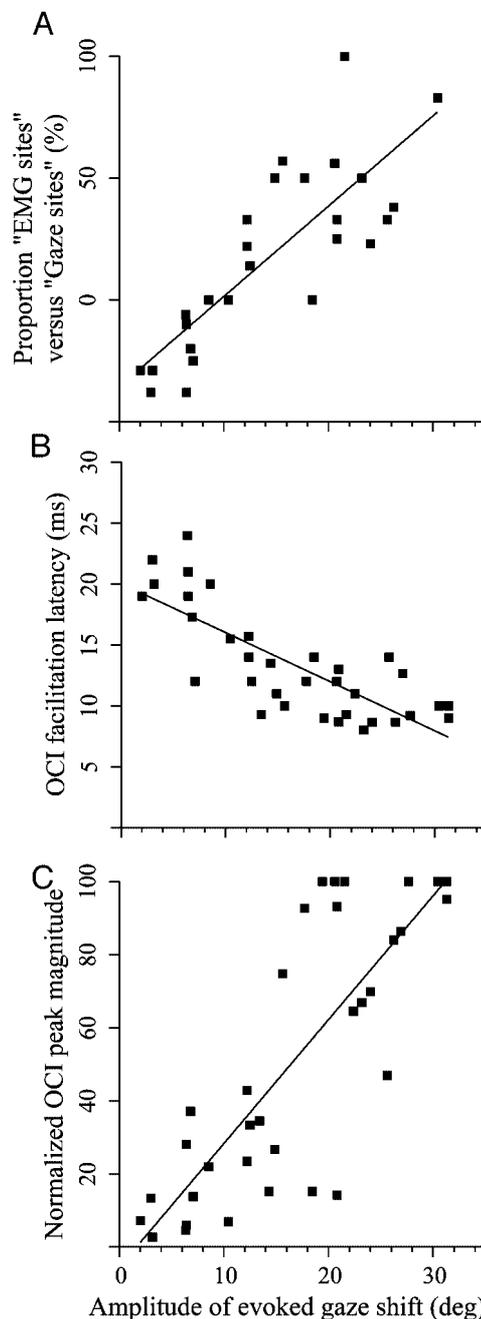


FIG. 8. Representation of parameters of EMG responses evoked in OCI by SC stimulation, contrasting the proportion of EMG sites vs. gaze sites (A), the facilitation latency (B), and the normalized peak EMG magnitude above baseline (C) as a function of the amplitude of the evoked gaze shift. ■, data from a different stimulation location. —, statistically significant linear regression lines ($P < 0.05$). For regression line in A: $r = 0.81$, $m = 3.70$, $y\text{-int} = -35.61$, $n = 26$; B: $r = -0.78$, $m = -0.40$, $y\text{-int} = 20.05$, $n = 34$; C: $r = -0.80$, $m = 3.39$, $y\text{-int} = -5.55$, $n = 34$.

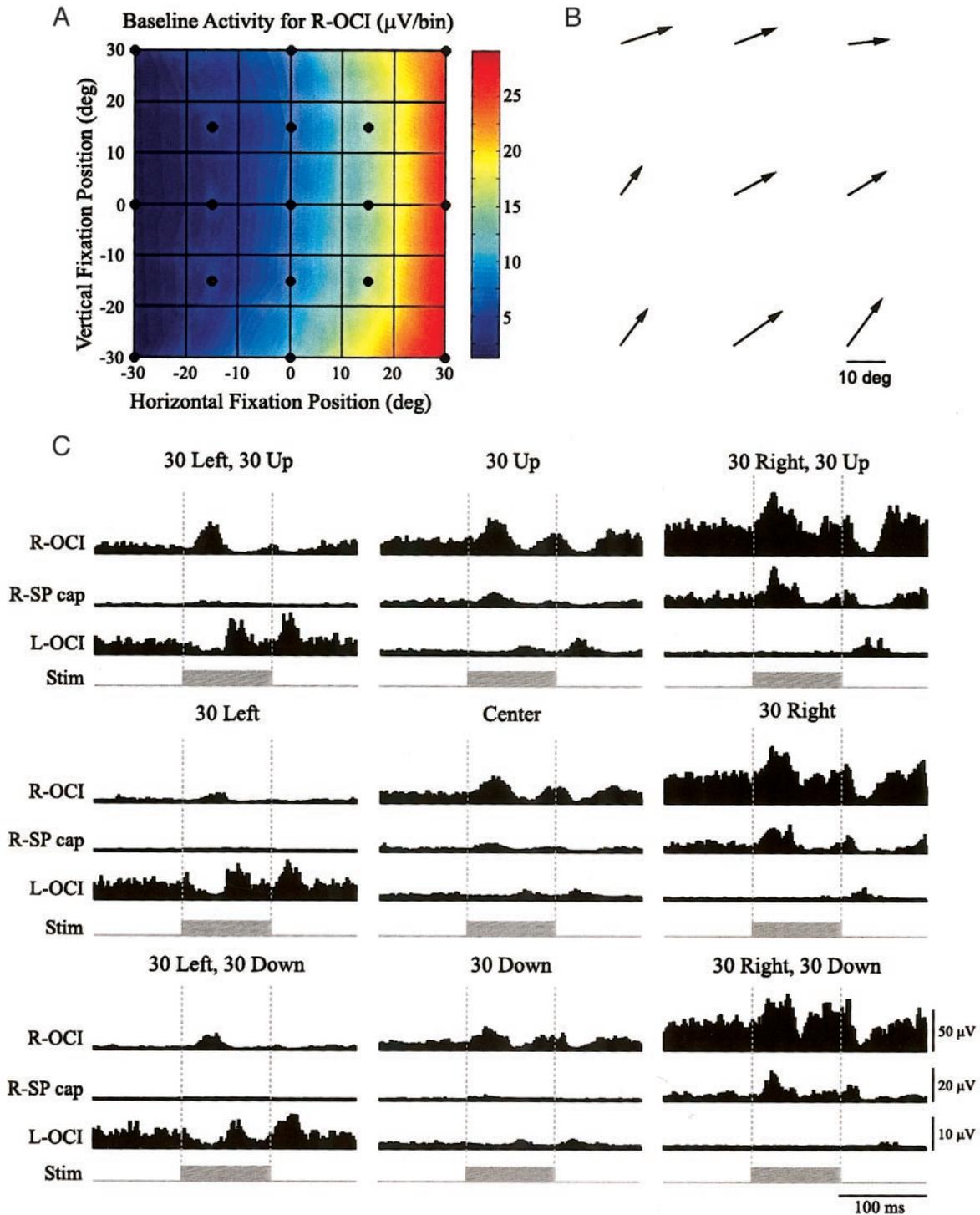


FIG. 9. Variations in evoked neck EMG with different initial eye positions. *A*: contour plots expressing baseline neck EMG as a function of the eye position for R-OCI in monkey *r*. Data obtained by averaging the baseline neck EMG in the 100 ms prior to stimulation while the monkey fixated different FP locations (\bullet). *B* and *C*: results of gaze (*B*) and EMG (*C*) responses evoked by a 100-ms stimulation train while monkey *r* fixated 9 different positions in a 3×3 grid, with a 30° spacing between adjacent fixation locations. *B*: representation of the average gaze shift vector evoked by stimulation. The origin of each line indicates the initial eye position, and is joined to the end of the arrowhead representing the averaged endpoint of the evoked gaze shifts. *C*: averaged neck EMG responses to stimulation (\square and $--$), represented as histograms with 2-ms bins. Each subplot is laid out relative to FP location. The scale bars in the lower right subplot apply to all subplots.

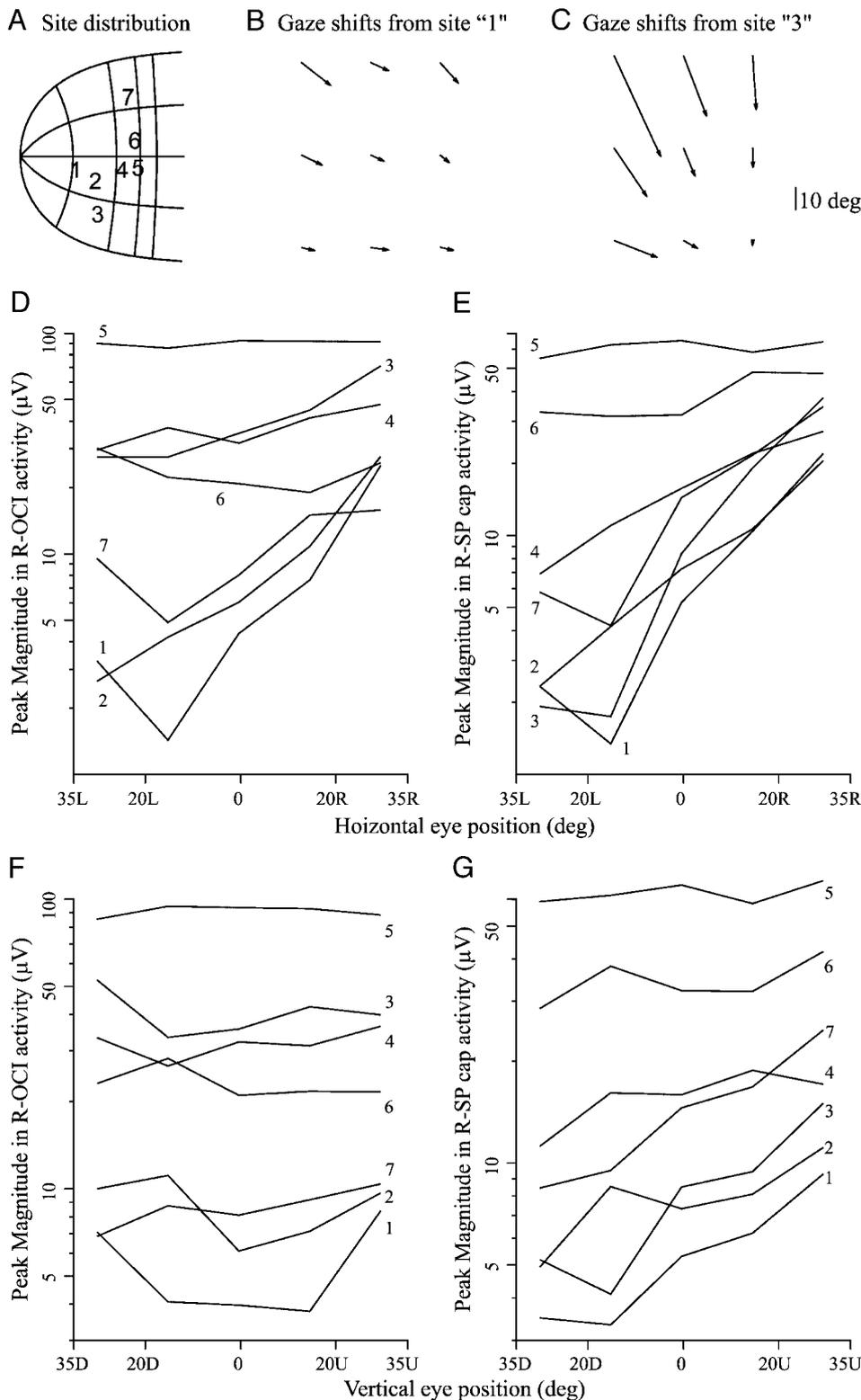


FIG. 10. Plots of averaged peak EMG magnitude above baseline evoked by stimulation as a function of eye position in the horizontal (*D* and *E*) or vertical (*F* and *G*) planes for R-OCI (*D* and *F*) and R-SP cap (*E* and *G*). Data from *monkey r* following stimulation in the left SC. —, the data points obtained at a given stimulation site. Note that the ordinate is plotted as a logarithmic scale, permitting the comparison of small and large peak values. The numbers beside the lines reveal the location of the stimulating electrode within the SC, as shown in *A* (see Fig. 4 for values of the isoamplitude and isodirection lines). *B* and *C* show the pattern of evoked gaze shifts over the 30° grids that were evoked from sites "1" and "3," respectively. The gaze shifts evoked from site "1" were relatively constant, whereas those evoked from site "3" varied dramatically depending on initial eye position.

SHORT-DURATION STIMULATION TRAINS. We consistently observed in 119 different stimulation sites distributed over 33 stimulation locations in all monkeys that a stimulation train of ≤ 20 ms evoked strong EMG responses in both agonist and antagonist muscles without evoking gaze shifts. To ascertain the minimum number of stimulation pulses required to elicit a change in neck EMG, we delivered between one and four

individual stimulation pulses to sites in 13 different stimulation locations in two monkeys. Figure 11 shows representative agonist OCI responses to stimulation delivered to either rostral or caudal SC locations. At both sites, 100-ms stimulation at $1.5 \times \text{GT}100$ reliably drove both gaze shifts and neck EMG responses (not shown). A 10-ms train of stimulation (4 biphasic pulses at 300 Hz, $1.5 \times \text{GT}100$) evoked large and consis-

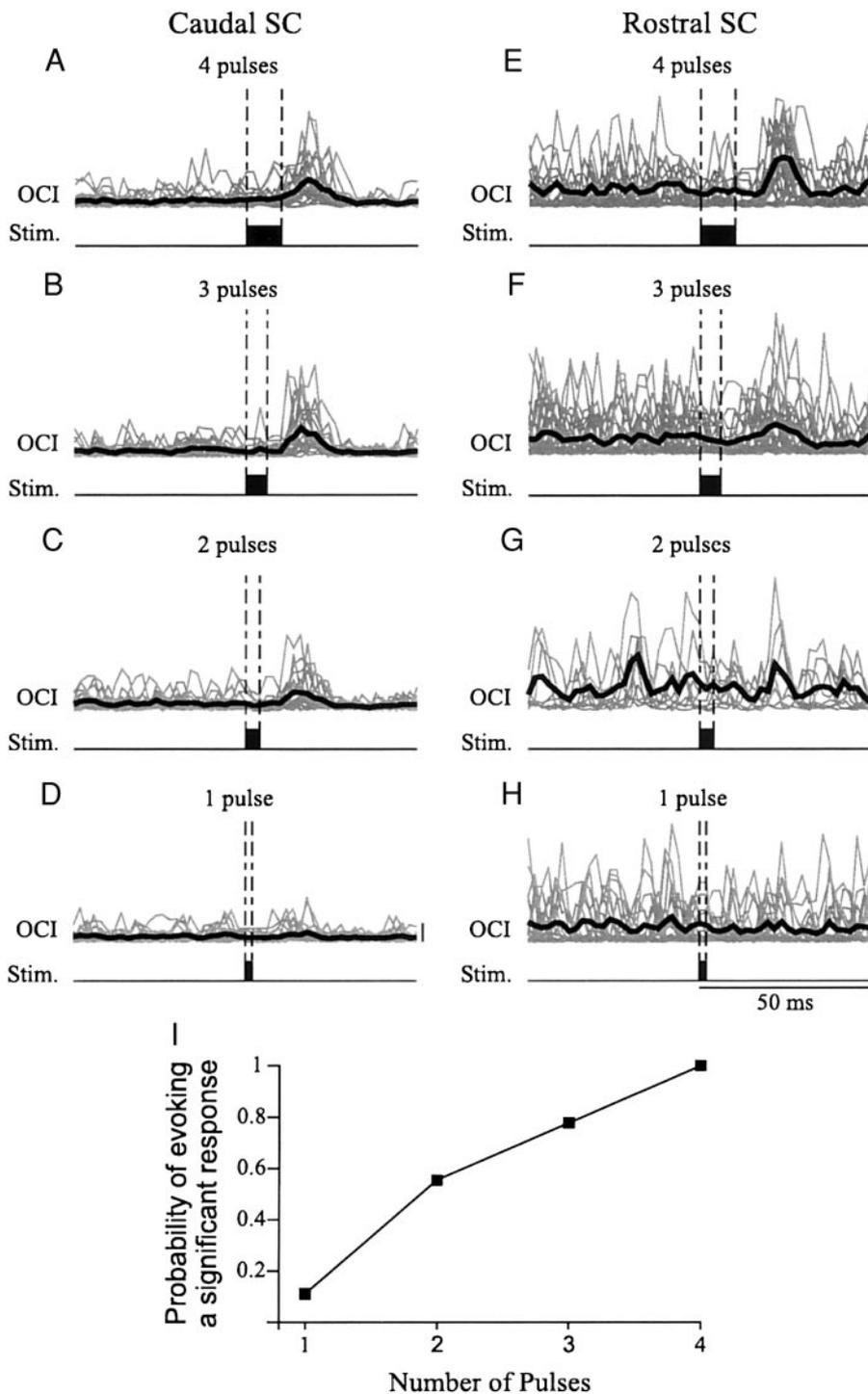


FIG. 11. A–H: variations in magnitude of the peak EMG responses following stimulation trains that pass 4, 3, 2, or 1 biphasic pulses of stimulation. A–D are from a caudal stimulation site in the right SC of *monkey r*, demonstrating neck EMG evoked by 1 to 2 pulses. E–H are from a rostral stimulation location in the left SC of *monkey r*, demonstrating neck EMG evoked by a minimum of 3 pulses. Scale bars in D and H denote 10 μ V and apply for all above traces. Same format as Fig. 2. I: probability of evoking a significant response in contralateral OCI as a function of the number of stimulation pulses, pooled across 13 different stimulation locations in *monkeys f* and *r*.

tent neck EMG responses, again without evoking gaze shifts (Fig. 11, A and E; gaze traces not shown). The magnitude of the evoked EMG response diminished as the number of pulses decreased. In the caudal SC, two pulses of stimulation elicited an OCI response in all individual trials (Fig. 11C), but a single stimulation pulse evoked responses only in a few individual trials (Fig. 11D). Such inconsistent responses to a single stimulation pulse were prevalent only at the caudal-most portions of the SC; the more typical pattern resembled that shown in Fig. 11, E–H, in which a reliable EMG response could only be elicited with a minimum of three or more pulses (Fig. 11, E and

F). Over all 13 stimulation locations, a minimum of three or four stimulation pulses was required to reliably evoke neck EMG on individual trials (Fig. 11I). Again, such short-duration stimulation never evoked gaze shifts.

LONG-DURATION STIMULATION TRAINS. Prolonged stimulation trains greater than ~ 150 ms evoked repeated “staircases” of gaze shifts that persisted for the duration of the stimulation train (Fig. 12A) (see also Robinson 1972; Schiller and Stryker 1972). To examine whether a similar sequential drive accessed the head plant, we realigned the EMG responses evoked by

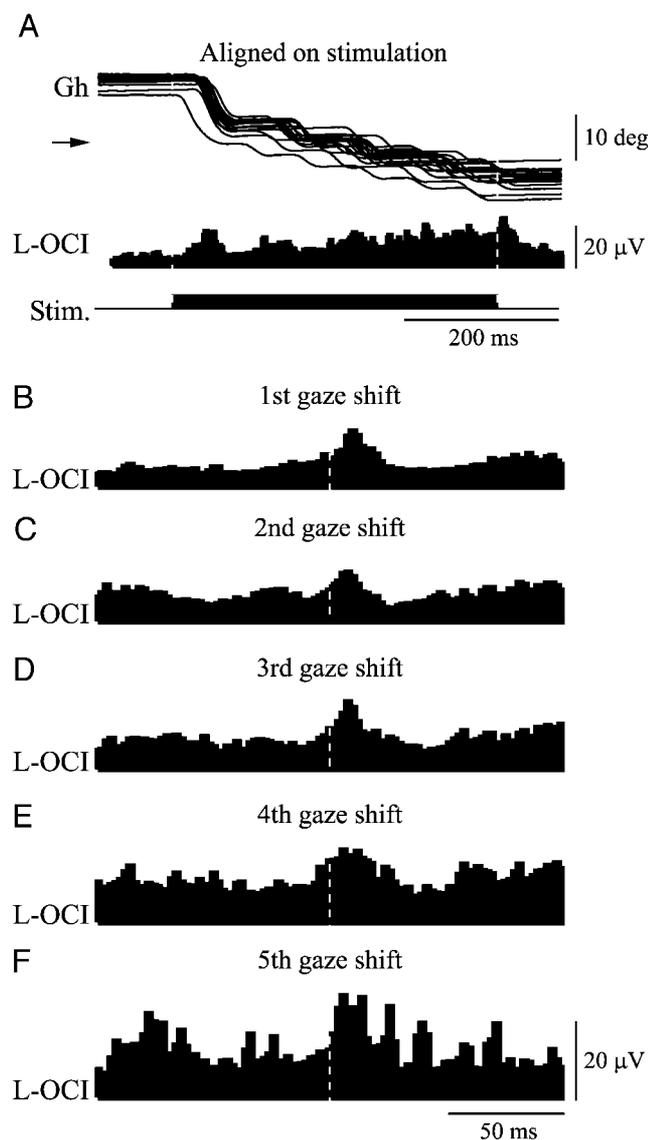


FIG. 12. Horizontal gaze position (Gh) and average EMG histograms (2-ms bins) following long-duration stimulation trains. *Monkey r* fixated a FP 15° to the right (A, arrow denotes straight ahead), and prolonged stimulation (420 ms) evoked repeated gaze shifts until stimulation ceased. B–F: EMG data aligned on the onset of the sequential gaze shifts. Note a transient increase in L-OCI activity appears around the onset of the sequential gaze shifts. Scale bars in F also apply for B–E.

stimulation on the onset of each sequential gaze shift. In the example shown in Fig. 12, the monkey began by looking 15° right to minimize the obscuring postural activity on L-OCI as the eyes were driven leftward. This realignment revealed a transient increase in agonist L-OCI aligned to gaze shift onset that began ≤ 15 ms before gaze shift onset and lasted ~ 30 ms (Fig. 12, B–F). This increase was present even up to the fifth gaze shift (Fig. 12F) and was accompanied by a small decrease in antagonist R-OCI activity (not shown).

Long-duration stimulation evoked sequences of at least two gaze shifts in a total of 10 different stimulation locations in two monkeys. In seven of these sites, gaze shift onset was usually linked to a phasic activation of the agonist OCI. To quantify this, we integrated the EMG activity over three different 30-ms intervals relative to gaze shift onset while stimulation was

ongoing (Fig. 13A): -45 to -15 ms (pregaze interval), -15 to $+15$ ms (perigaze interval), and $+15$ to $+45$ ms (postgaze interval), and then graphed the perigaze activity as a function of either the pregaze (Fig. 13B) or postgaze activity (Fig. 13C). Most data points lay above the unity line, implying that the perigaze activity exceeded both the pregaze and postgaze activity for sequential gaze shifts. However, the exceptions (i.e., the points lying on or near the unity line) indicated examples where gaze shift onset did not coincide with a transient EMG response. Stimulation at such sites evoked the smallest or most vertically oriented gaze shifts, consistent with a smaller magnitude drive onto the agonist motoneurons from the rostral SC, and also evoked the lowest levels of pregaze and postgaze activity. Higher levels of perigaze activity were associated with correspondingly higher levels of pregaze and postgaze activity and, although the magnitude of the perigaze EMG response that was aligned to gaze shift onset might seem modest, recall that these experiments were conducted only when the gaze shift amplitude was less than $\sim 15^\circ$. These results suggested that a portion of the SC drive onto neck muscles coincided with gaze shift onset, particularly for stimulation sites not confined to the rostral SC. Another portion of the drive onto neck muscles was not associated with gaze shifts and determined the magnitude of the pregaze and postgaze activity. The strength of both drives varied with the location of the electrode within the SC, becoming stronger for more caudal stimulation locations.

Evoked activity in other muscles

We observed EMG responses to SC stimulation in muscles other than OCI, RCP maj, and SP cap, but could not thoroughly quantify their evoked activities because they were either not implanted frequently (Table 1) or did not display a systematic relationship with stimulation location. For example, both SCM and AS ant link the skull to the shoulder girdle (Fig. 1) and contribute to volitionally generated horizontal head movements (Corneil et al. 2001). EMG responses in SCM and AS ant derived exclusively from the caudal half of the SC. In *monkey z* (the only monkey in which AS ant was implanted), EMG activity in L-AS ant was evoked in four of the six stimulation locations in the right SC and was usually synchronous with activity in L-OCI. Activity in SCM was most commonly evoked by stimulation in the caudal parts of the *ipsilateral* SC and accompanied activity in the agonist OCI and SP cap muscles, consistent with the role of the SCM contralateral to the direction of volitional head turns (Corneil et al. 2001). Surprisingly, SCM responses to stimulation could also be elicited from the *contralateral* SC. Further, we did not observe any relationship between evoked SCM activity and downward gaze shifts as was expected given SCM's role as an occasional head flexor (Corneil et al. 2001).

The muscles COM and, to a lesser extent BC, are involved principally during inclining movements of the head (Corneil et al. 2001). The pattern of evoked neck EMG in these muscles did not relate simply to stimulation location and sometimes lagged the onset of evoked gaze shifts. Further, although evoked responses in BC and COM usually accompanied upward gaze shifts, activity in these muscles also accompanied

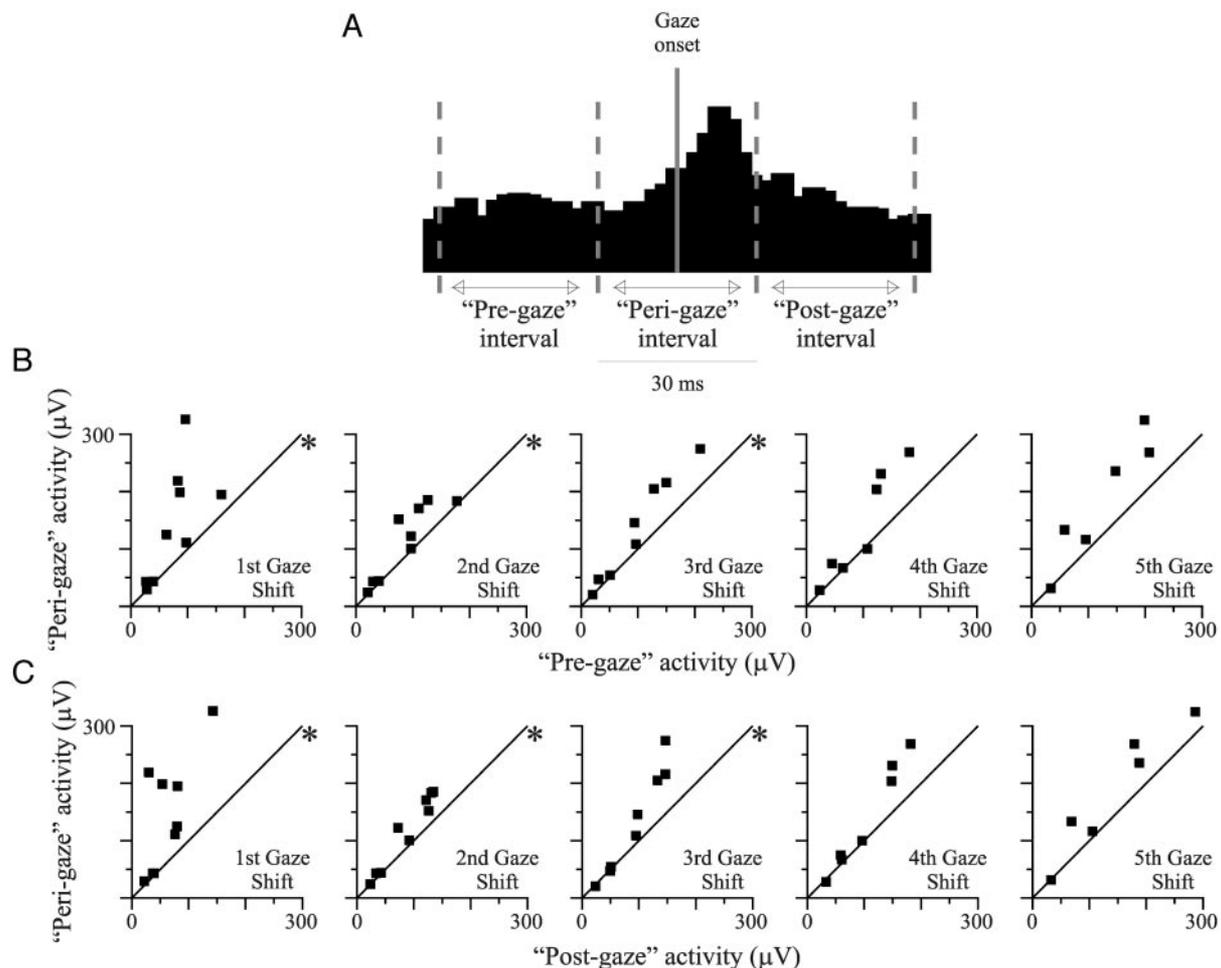


FIG. 13. *A*: depiction of the 3 30-ms intervals over which the EMG activity was integrated. Relative to gaze shift onset (solid gray line), the pregaze interval spans -45 to -15 ms, the perigaze interval spans -15 to $+15$ ms, and the postgaze interval spans $+15$ to $+45$ ms (dashed gray lines denote the boundaries of these intervals). *B* and *C*: relationships between the EMG activity integrated over the perigaze interval vs. either the pregaze (*B*) or postgaze (*C*) intervals for sequential gaze shifts. Each square denotes data from a different stimulation site, and the solid black line denotes the unity line. Asterisks, those graphs in which the perigaze activity was the significantly greater value as determined by a signed-rank test ($P < 0.05$).

downward directed gaze shifts and was even seen during some purely horizontal gaze shifts.

DISCUSSION

This report is the first to describe patterns of neck muscle activity following SC stimulation in head-restrained monkeys. We stress four important results. First, the drive to neck muscle motoneurons is widely distributed throughout almost the entire SC. Second, this drive conforms to a clear topography, becoming faster, stronger and more prevalent for more caudal stimulation locations. Third, evoked neck EMG responses are systematically influenced by eye position prior to stimulation. Fourth, variations in stimulation duration and current show that evoked neck EMG responses are not obligatorily dependent on evoked gaze shifts but also suggest that a component of the EMG response is augmented by gaze shift generation. These results affirm that combining SC stimulation with recording neck muscle activity can address important issues regarding the role of the SC in the generation of head movements and gaze shifts.

Before delving into the implications of our results, we first consider the limitations of our approach.

Methodological considerations

Electrical stimulation introduces current into an area with nonhomogeneous tissue resistivities and affects an unknown number of cellular processes (Ranck 1975). The parameters of SC stimulation (current, duration, frequency) dictate many facets of the behavioral response to stimulation, and summaries of these effects can be found for multiple species (owl: du Lac and Knudsen 1990; cat: Paré et al. 1994; monkey: Freedman et al. 1996; Stanford et al. 1996). For simplicity, we did not alter stimulation frequency. However, these previous reports emphasized that the number of suprathreshold stimulation pulses (the product of frequency and duration) determines the metrics of saccadic eye movements. We suspect the use of different frequencies would have altered the latencies and magnitudes of the evoked EMG responses via altered rates of temporal summation at intervening synapses downstream from the SC without changing the observed topography.

One of the difficulties in interpreting stimulation data lies in

differentiating directly excited element(s) from those that ultimately mediate the observed responses. For example, stimulation in cortical gray matter preferentially excites axonal branches as opposed to cell bodies or axon initial segments (Nowak and Bullier 1998a,b), and the observed responses to stimulation reveal more about the organization of inputs onto an output element than the output elements immediately in the vicinity of the electrode (e.g., see Lemon 1988). In regards to our experiment, the current levels (2.5–50 μ A) likely directly excited elements within a sphere of 45–200 μ m (Stoney et al. 1968). Further, because stimulation could have been delivered to either gray or white matter, indirect activation of other elements could occur via afferent axons, recurrent or ascending collaterals of tectal efferents, axons of passage, or lateral excitation through intrinsic SC interneurons (McIlwain 1982; Meredith and Ramoa 1998; Munoz and Istvan 1998). In light of these mechanisms, can we be certain that the observed responses are mediated by tectal efferents? Further, is the concept of a rostrocaudal topography relevant?

To both of these questions we answer a qualified yes. Anatomically, it is hard to imagine how an alternative mechanism not involving tectal efferents, such as the excitation of fibers of passage or axon reflexes through collaterals of spinotectal or reticulospinal cells, could generate the topography of the evoked neck EMG responses. If fibers of passage were excited, then the topography should reflect the lateral positioning of these fibers to the SC (Moschovakis et al. 1988a). If stimulation elicited axon reflexes, then only ipsilateral EMG responses should have been observed because contralateral EMG responses depend on the integrity of the predorsal bundle (Anderson et al. 1971). Hence the signals ultimately influencing neck muscle motoneurons most probably exited the SC along tectal efferents. It has also been suggested that rostral SC stimulation may induce neck muscle responses via the activation of ascending collaterals of caudal tectofugal neurons (Alstermark et al. 1992). We do not believe this mechanism underlies our results because ascending collaterals branch from the main axon ventrally near the predorsal bundle (Grantyn and Grantyn 1982; Moschovakis et al. 1988a), whereas rostral stimulation of the SC evoked neck muscle responses at nearly all dorsoventral depths (Fig. 4).

Physiologically, the metrics of saccades evoked by SC stimulation are known to resemble the movement field properties of the neurons in the vicinity of the electrode (Freedman and Sparks 1997a; Schiller and Stryker 1972; van Opstal et al. 1990), suggesting that indirect excitation does not greatly distort the output of the SC motor map. At the current levels we used, lateral excitation would be expected to spread ≤ 1.5 mm away from the electrode (McIlwain 1982), beyond which a predominantly inhibitory effect dominates (Munoz and Istvan 1998). Further, the spread of lateral excitation induced by stimulation approximates the area of tissue active in the SC during volitional saccades (Munoz and Wurtz 1995), suggesting that stimulation does not induce a wholly unnatural spatial profile of activity in the SC. Moreover, the pattern of evoked EMG responses corresponded closely to the known topography of the SC motor map. Evoked EMG responses followed a recruitment sequence similar to voluntary head movements (Corneil et al. 2001) and scaled to the size of the gaze shift: responses in the smaller suboccipital muscles were evoked from the rostral SC, to which responses in the larger, multiar-

ticular muscles were added from the caudal SC. Although we cannot definitively exclude the possibility that rostral stimulation indirectly excited tectal efferents that originate from the caudal SC, we speculate that such a mechanism would have evoked a more generic response pattern that included the larger muscles. As with all stimulation studies, our results await confirmation with other techniques; spike-triggered averaging of neck muscle activity would be particularly useful to resolve the rostrocaudal topography of SC projections onto neck muscles (Olivier et al. 1995).

One final point is that our methodology cannot resolve the number of synapses intervening between the directly excited elements within the SC and neck motoneurons. The digitizing rate of the EMG data is too slow (500 Hz); therefore the EMG response latencies could result either from a slowly conducting mono- or disynaptic pathway or a rapidly conducting oligosynaptic pathway. Obviously, pathways other than a direct tectospinal pathway (see following text) must be excited by SC stimulation to explain both the variation of the EMG activity during SC stimulation and the large ranges in facilitation latencies (8–24 ms for OCI and RCP maj, 10–24 ms for SP cap; Fig. 6). While the pathways from the rostral SC could involve more synapses, the large variation in response latencies probably relates to a weaker projection from the rostral SC that requires more temporal summation to reach threshold within relays of the pathway (e.g., see Moschovakis et al. 1998). A similar explanation probably underlies the longer (≤ 6 ms) facilitation latencies for SP cap than for OCI (Fig. 6D).

Three-dimensional topography of SC drive onto neck muscles

ROSTROCAUDAL TOPOGRAPHY. SC stimulation increased EMG activity in agonist muscles that contribute to head turns contralateral to the electrode and suppressed activity in the antagonist muscles. The companion paper (Corneil et al. 2002) shows that these patterns are almost certainly the muscular correlates of head movements evoked by stimulation in unrestrained monkeys in previous studies (Cowie and Robinson 1994; Freedman et al. 1996; Klier et al. 2001; Segraves and Goldberg 1992). The topography of evoked neck EMG resembled the motor map reported for saccades (Robinson 1972) but extended surprisingly far rostral: neck EMG accompanied gaze shifts of $< 5^\circ$, even though the head does not normally contribute to such small gaze shifts (Freedman and Sparks 1997b; Phillips et al. 1995; Tomlinson and Bahra 1986; but see Land 1992). This extensive drive is consistent with anatomical data from cats in which the density of tectoreticulospinal cells is constant along the rostrocaudal axis of the SC (Olivier et al. 1991) rather than being limited to zones within the caudal SC. The variations in EMG response latency (Fig. 5) and magnitude (Fig. 7) suggest this drive gets progressively stronger for more caudal stimulation locations. Presumably, this explains why the head movement evoked by SC stimulation gets progressively smaller and evoked at longer latency for more rostral SC stimulation locations (Freedman et al. 1996).

The observed topography differs dramatically from the view proposed by Stryker and Schiller (1975) that the primate SC does not *directly* contribute to head movements but rather is “pulled along” as stimulation-induced saccades approached the limits of the oculomotor range. Our results suggest the stimu-

lation delivered by Stryker and Schiller (1975) may have been too rostral to elicit observable head movements given the head's inertia but nevertheless evoked neck EMG responses prior to gaze shift onset. Further, the observed latencies of facilitation are quite different from those reported in cats (Guitton et al. 1980; Roucoux et al. 1980) in which the latencies ranged between 10 and 250 ms depending on the initial positions of the eye and head. Rostral SC stimulation in head-fixed cats evoked responses in BC (the only muscle implanted) when the eyes were driven past a given orbital position (Guitton et al. 1980), whereas the EMG response latencies reported here preceded or equaled gaze shift latencies. Compared to cats, the facilitation latencies from the rostral SC reported here seem surprisingly short, although we suspect similar results would be observed in cats if the suboccipital muscles were implanted.

Multiple areas targeted by tectal efferents could underlie the short-latency SC influence on neck motoneurons. First, our technique cannot exclude a tectospinal projection that connects to motoneurons either directly or through intercalated spinal interneurons, although this seems unlikely given the weak or absent monosynaptic connections of the feline SC with neck muscle motoneurons (Alstermark et al. 1992; Anderson et al. 1971; Gura and Limanskii 1986) and the paucity of tectospinal projections in the monkey (Nudo et al. 1993; Robinson et al. 1994). Even in cats, the role of intercalated spinal interneurons that receive tectal excitation and project to neck motoneurons (Muto et al. 1996) is likely minor given the deficits in orienting head movements caused by lesions of the paramedian pontine reticular formation (Sasaki et al. 1999). The more likely scenario in primates is that the influence of SC efferents acts through brain stem relays. For example, the crossed tectoreticular pathway projects to reticular areas in the pons (nucleus pontis oralis and caudalis) and medulla (nucleus gigantocellularis) that give rise to reticulospinal pathways (Cowie et al. 1994; Grantyn and Berthoz 1985; Harting 1977; Huerta and Harting 1982; May and Porter 1992; Robinson et al. 1994; Scudder et al. 1996a,b). Tectal efferents also contribute an ascending branch running to areas such as the interstitial nucleus of Cajal and the adjacent rostral mesencephalic reticular formation, which have been implicated in the control of vertical head movements (Fukushima 1987; Harting et al. 1980; Isa and Naito 1994; Isa et al. 1992b; Moschovakis et al. 1988a) and project to the spinal cord either directly or via relays in some of the aforementioned pontine and medullary reticular formations (Castiglioni et al. 1978; Cowie et al. 1994; Isa and Naito 1995; Kokkoroyannis et al. 1996; May and Porter 1992; Robinson et al. 1994; Sasaki et al. 1999). Collaterals of tectoreticular cells also project to the ipsilateral central mesencephalic reticular formation (cMRF) and portions of the nucleus subcuneiformis, which may also play a role in head movement (Castiglioni et al. 1978; Chen and May 2000; Cohen et al. 1985; Cowie et al. 1994; May and Porter 1992; Moschovakis et al. 1988a,b; Robinson et al. 1994; Silakov et al. 1999; Waitzman et al. 2000). Obviously, more refined techniques will have to be applied to parse out the contributions of these pathways to SC mediated effects on neck muscle motoneurons.

DORSOVENTRAL TOPOGRAPHY. Evoked gaze shifts and EMG responses were observed over long dorsoventral expanses. Although sites were encountered where only one of a gaze or

EMG response was evoked, stimulation at most sites evoked both gaze shifts and EMG responses (Fig. 4B). The ventral border of the SC cannot be determined easily *in vivo*, particularly because this border varies with the mediolateral position of the penetration (e.g., May and Porter 1992). As noted by Robinson (1972), the most parsimonious explanation for the long depth series is that stimulation was delivered to tectal efferents as they course to the deep layers of the SC before assuming a rostral, lateral and ventral trajectory to circumscribe the periaqueductal gray (Moschovakis et al. 1988a). This trajectory is consistent with the longest depth series (8.5 mm), recorded from a rostral and lateral stimulation location (Fig. 4B). A coronal section of the monkey SC (see Fig. 1 of May and Porter 1992) demonstrates that the parasagittal distance from the top of the superficial layers to the deep gray and white layers can exceed 8 mm. Cowie and Robinson (1994) reported somewhat shorter stimulation tracks, but their results are not directly comparable to ours because they used a shorter train duration (40 ms) and did not record neck EMG. Regardless, the results obtained from ventral sites does not alter the interpretation of our results because we cannot differentiate between the direct or indirect excitation of tectal efferents in the first place and because the full range of gaze and/or EMG responses was observed at all depths, including those endowed with either the shortest gaze shift latencies or the lowest gaze shift current thresholds (Fig. 4B).

Our results also cannot address whether there are functionally segregated sublamina within the intermediate and deep layers of the SC specialized for the control of eye and head movements, as suggested from previous studies (Cowie and Robinson 1994; May and Porter 1992; but see Freedman and Sparks 1997a). Electrical stimulation does not have the spatial selectivity to resolve this issue, although recording neck EMG in multiple muscles in conjunction with spike-triggered averaging would be very useful (Olivier et al. 1995).

The studies of Hoffmann and colleagues (Stuphorn et al. 1999, 2000; Werner et al. 1997a,b) found that neural activity in the deep SC and underlying cMRF related to the EMG activity in proximal forelimb muscles. A direct comparison with our results is difficult because we used microstimulation and examined a different set of muscles. It is possible that our protocol evoked forelimb muscle responses that went unnoticed. In contrast to what we observed, arm-movement related neurons reside deeper than oculomotor movement-related neurons, do not correlate to the discharge of SP cap, and do not conform to the topography of the SC motor map (Stuphorn et al. 1999, 2000; Werner et al. 1997a,b). Thus it is likely that arm-movement neurons represent a separate population than those that underlie evoked neck EMG responses.

MEDIOLATERAL TOPOGRAPHY. Somewhat surprisingly, mediolateral variations in the electrode location did not evoke different patterns of neck EMG as expected given the EMG records during volitional head movements (Corneil et al. 2001). We anticipated that medial or lateral SC stimulation would preferentially recruit muscles involved in inclining (e.g., COM, BC, RCP maj, and SP cap) or declining (e.g., SCM) movements, respectively. It is quite possible that no mediolateral topography was observed because stimulation was applied unilaterally, whereas volitional inclining or declining movements involve coordinated activity in both SC. Coordinated

activity across both SC may be essential for establishing muscular synergies during vertical movements (Olivier et al. 2000).

Properties of the SC drive to neck muscle motoneurons

ALTERATIONS IN EYE POSITION MODULATE EVOKED EMG RESPONSES. The adoption of different initial eye positions caused large-scale modulations in the pattern of evoked neck EMG; the magnitude of agonist muscle responses increased when the eyes were deviated contralateral to the side of stimulation, regardless of the size of the evoked gaze shift (Figs. 9 and 10). These responses appeared to change in accordance to the size of the head movement that would be required for a gaze shift if the head were free to move (i.e., for the same gaze amplitude, an increased contribution of the head is required if the eyes begin deviated in the direction of the ensuing gaze shift). A more straightforward alternative is that the initial eye position induced changes in the baseline level of EMG activity (Fig. 9A) to which the generic stimulation-evoked response was added. This topic is considered more thoroughly in the companion paper along with the effects of altering initial head position (Corneil et al. 2002).

EVOKED NECK EMG RESPONSES CAN OCCUR WITHOUT GAZE SHIFTS. Stimulation of low current (Fig. 4B) or short duration (Fig. 11) can evoke neck EMG responses without evoking gaze shifts. Given the mechanics of force development in primate extraocular muscles (see Goldberg et al. 1998 for review), it is improbable that such stimulation excited extraocular muscle motoneurons without evoking eye movements. The lag between activation of saccade-related neurons and the onset of eye movements is very short: activity in the abducens nucleus precedes saccades by ~ 7.5 ms (Robinson 1970), and stimulation of the premotor burst generator in the PPRF can induce eye movements in < 10 ms (Keller 1974; Miyashita and Hikosaka 1996; Scudder et al. 1988). Apparently, short-duration or sustained low-current SC stimulation does not engage premotor saccade burst elements.

These results imply independence between the signals that access the eye and head plants. Such independence may have more to do with the circuitry gating saccadic eye movements because spurious activity in this pathway could degrade retinal stability, whereas vestibular reflexes and the head's inertia accommodate for spurious activity in the head premotor pathway. The SC drive to extraocular muscle motoneurons is relayed sequentially through long-lead and medium-lead burst neurons (Keller et al. 2000; Miyashita and Hikosaka 1996; Raybourn and Keller 1977; Scudder et al. 1996a), and activity in premotor medium-lead burst neurons is observed only if another population of neurons, the pontine omni-pause neurons (OPNs), become silent (cats: Evinger et al. 1982; Nakao et al. 1980; monkeys: Everling et al. 1998; Strassman et al. 1987). OPNs are thought to act as a gate preventing saccade generation when active (see Moschovakis et al. 1996 for review). We speculate that low-current or short-duration stimulation did not silence the OPNs and release the burst generator from OPN inhibition, leading us to conclude that the SC drive to neck muscle motoneurons is mediated, at least in part, by elements not subject to the circuits that gate saccadic eye movements.

EVOKED NECK EMG RESPONSES ARE AUGMENTED BY GAZE SHIFT GENERATION. In contrast to the independence revealed by short or subthreshold SC stimulation, long-duration stimu-

lation that evoked patterns of sequential gaze shifts demonstrated a transient increase in neck EMG activity that was usually aligned to the onset of each gaze shift (Figs. 12 and 13). The magnitude and preponderance of this aligned EMG activity was modest, but recall that we applied prolonged stimulation only when the evoked gaze shift amplitude was $< 15^\circ$. These results address a long-standing issue concerning whether a transient drive to the head plant occurs with sequential gaze shifts (Freedman et al. 1996; Stryker and Schiller 1975) and provide experimental support for models of eye-head control that distribute an augmented drive to the head at the time of gaze shift initiation (Galiana and Guitton 1992; Guitton et al. 1990). We conclude that neck EMG responses evoked by SC stimulation are augmented by, but not dependent on, gaze activity.

Overall, head-restrained stimulation suggests a parallel nature in the influence of SC activity on neck muscle motoneurons, being both independent and dependent on gaze shift initiation. Primate SC neurons have been shown to encode gaze shifts rather than the component eye or head movement (Freedman and Sparks 1997a). Thus the dual influence of SC activity on neck muscle motoneurons probably arises downstream from the SC providing head premotor areas (or different populations of neurons within the same premotor area) demonstrate differential firing relationships with gaze shifts. There is ample anatomical and physiological evidence that tectal efferents project to both saccadic and head premotor areas and that reticulospinal cells discharge in conjunction with gaze shifts (cats: Grantyn and Berthoz 1987a,b; Grantyn and Grantyn 1982; Isa and Naito 1995; Vidal et al. 1983; monkeys: Scudder et al. 1996a,b; Whittington et al. 1984). Regardless of the precise anatomical underpinnings, our results allow specific predictions about the relationship between evoked neck EMG, head movements and gaze shifts in a head-unrestrained preparation. First, if SC stimulation evokes neck EMG without gaze shifts, it should also drive head movements without gaze shifts. Second, if another component of the SC drive to the head is linked to the circuitry mediating gaze shifts, then a transient increase in neck EMG, and an acceleration of the head, should accompany gaze shift generation. These predictions are tested directly in the companion paper (Corneil et al. 2002).

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