Widespread Presaccadic Recruitment of Neck Muscles by Stimulation of the Primate Frontal Eye Fields

James K. Elsley,1,2 Benjamin Nagy,1,4 Sharon L. Cushing,5 and Brian D. Corneil1,2,3,5

1Canadian Institutes of Health Research Group in Action and Perception, 7Departments of Physiology & Pharmacology and 3Psychology, University of Western Ontario, London, Ontario; 4Graduate Program in Neuroscience, University of Western Ontario, London, Ontario; and 5Department of Otolaryngology Head and Neck Surgery, University of Toronto, Toronto, Ontario, Canada

Submitted 4 April 2007; accepted in final form 10 July 2007

Elsley JK, Nagy B, Cushing SL, Corneil BD. Widespread presaccadic recruitment of neck muscles by stimulation of the primate frontal eye fields. J Neurophysiol 98: 1333–1354, 2007. First published July 11, 2007; doi:10.1152/jn.00386.2007. We studied the role of the primate frontal eye fields (FEFs) in eye-head gaze shifts by recording EMG activity from multiple dorsal neck muscles after electrical stimulation of a broad distribution of sites throughout FEF. We assess our results in light of four mechanisms forwarded to account for why eye and head movements follow FEF stimulation. Two mechanisms propose that movements are generated indirectly by FEF stimulation in response to either a percept or an eccentric orbital position. Two other mechanisms propose that movements are evoked directly through the issuance of either a gaze command or separate eye and head commands. FEF stimulation evoked short-latency (~20 ms) neck EMG responses from the vast majority (>95%) of stimulation sites. Evoked responses usually preceded the gaze shift by ~20 ms, even for small gaze shifts (<10°) not typically associated with head motion. Evoked responses began earlier and attained a larger magnitude when accompanied by larger gaze shifts and took a form consistent with the recruitment of the appropriately directed head movements to accompany the evoked gaze shift. We also observed robust neck EMG even when stimulation failed to evoke a gaze shift and occasionally observed head-only movements when the head was unrestrained. These results resemble neck EMG evoked from the superior colliculus (SC). Neck EMG response latencies approached the minimal conduction time to the motor periphery and hence are not consistent with either of the indirect mechanisms. The widespread nature of the cephalomotor drive from the FEF, the scaling of neck EMG responses with gaze magnitude, and the consistently earlier generation of the EMG versus gaze response are difficult to reconcile with suggestions that separate FEF channels encode eye and head motion independently. The most parsimonious interpretation is that a gaze command issued by the FEF is decomposed into eye and head commands downstream of the SC. The relative timing of the neck EMG and gaze shift responses, and the presence of neck EMG responses on trials without gaze shifts, implies that head premotor elements are not subjected to the same brain stem control mechanisms governing gaze shifts.

INTRODUCTION

The frontal eye fields (FEFs) are an integral part of the saccadic network. The FEF integrates sensory, contextual, and premotor inputs from parietal, prefrontal, and premotor cortices and sends signals appropriate for saccade control to subcortical structures such as the superior colliculus (SC) (for review, see Lynch and Tian 2005; Schall 2002; Wurtz et al. 2001). The primate SC is thought to control the orientation of the visual axis (gaze), regardless of the component movements of the eyes and head (Freedman and Sparks 1997; Freedman et al. 1996; Klier et al. 2001), raising the question of whether the FEF controls gaze shifts in a similar manner.

To date, this question has not been adequately resolved. Chronic lesions of the FEF produce a gaze strategy in which the head plays an increased role (van der Steen et al. 1986), but this strategy emerges after a substantial recovery period. Single units correlated to either eye or head movements have been reported (Bizzi and Schiller 1970; Guitton and Mandl 1978b), but no study has dissociated the encoding of the eye component versus the entire gaze shift. Stimulation studies have arrived at surprisingly different conclusions, based in part on how much the head either did or did not move during evoked gaze shifts. Some studies concluded that the FEFs controls gaze shifts in a manner similar to the SC (Guitton and Mandl 1978a; Knight and Fuchs 2007; Tu and Keating 2000) but another concluded that eye and head control is independent in the FEFs (Chen 2006).

There are a number of mechanisms by which FEF stimulation could generate eye and head motion, two of which were forwarded in Chen (2006). First, stimulation in the FEF may activate separate channels that independently control eye and head motion. Second, FEF stimulation may issue a gaze command to a single gaze controller that drives both eye and head motion. If so, the dynamics of the gaze drive should be reflected in the trajectory of head motion. Because Chen (2006) observed evoked gaze shifts that consisted primarily of eye-only movements that were temporally uncoupled from subsequent head motion, he concluded that the drive to the eyes and head were driven by separate channels.

There are alternatives to the type of gaze control mechanism considered by Chen (2006). Freedman et al. (1996) proposed a mechanism wherein a gaze command issued by SC stimulation is distributed to downstream controllers that separately drive the eye and head, with each controller governed by separate properties (e.g., gating elements and relative activation thresholds). We will consider only this type of gaze control mechanism in this manuscript, because it is consistent with a number of models and observations (Corneil and Elsley 2005; Corneil et al. 2002b, 2004, 2007; Galiana and Guitton 1992; Gandhi and Sparks 2007; Goossens and Van Opstal 1997; Pélisson et al. 2001; Phillips et al. 1995, 1999) and explains why every
aspect of a gaze shift need not be reflected in the head movement trajectory. For example, the persistence of head motion for the duration of SC or FEF stimulation, regardless of gaze shift cessation (Chen 2006; Corneil et al. 2002a,b; Freedman et al. 1996; Knight and Fuchs 2007), is equally consistent with a separate channels mechanism and a gaze control mechanism, providing the head drive in the latter mechanism persists for the duration of stimulation.

Both the separate channels and gaze control mechanisms assume that FEF stimulation evokes movements causally through effenter connections to the oculomotor brain stem. A recent review (Chen and Tehovnik 2007) raised two additional indirect mechanisms. One proposes that the generated movements may be in response to a sensory percept evoked by FEF stimulation, such as a phasense. The FEF is interconnected with sensory areas (Stanton et al. 1995), and FEF stimulation can modulate processing in higher visual areas (Moore and Armstrong 2003). A second mechanism suggests that the eye movement is directly evoked by stimulation but that any subsequent head movement limits orbital deviation and re-centers the eyes in the orbit. Preliminary evidence suggests that an area near the supplementary eye fields, rather than the FEFs, may implement such a strategy (Chen and Walton 2005; Sparks et al. 2001).

Thus the nature of head movements after FEF stimulation remains unclear. Here, we combine FEF stimulation with the recording of EMG activity from dorsal neck muscles in both head-restrained and unrestrained primates. Neck EMG recordings have provided insights into volitional movements (Cornell et al. 2001, 2004) and movements evoked from the SC (Cornell et al. 2002a,b, 2007). Neck EMGs originate upstream from biomechanical complexities of head motion and provide a precise assessment of the spatial (i.e., which muscles) and temporal patterns of any cephalomotor command.

Such precise assessment provides an opportunity to test the different mechanisms outlined above, because they predict different patterns of evoked neck EMG. A separate channels mechanism predicts evoked eye-only movements in the absence of evoked neck EMG (presuming the current would not spread into adjacent “head” channels). Chen (2006) showed that eye-only sites accounted for 75% of all FEF stimulation sites. Accordingly, neck EMG should be evoked from the minority of FEF stimulation sites. One would also predict a lack of temporal coordination between the evoked gaze shift and neck EMG, given the dissociated patterns of eye and head motion reported by Chen (2006). In contrast, a gaze control mechanism (with separate eye and head controllers downstream from the SC) predicts that evoked neck EMG should resemble that evoked from the SC (Cornell et al. 2002a,b). Hence, neck EMG evoked from the FEFs should precede evoked gaze shifts (as in cats; Guitton and Mandl 1978a), co-vary in magnitude with a wide variety of small, medium, and large gaze shifts, persist for the duration of stimulation, and be present when stimulation fails to evoke a gaze shift. Finally, the percept and postural mechanisms both predict that the neck EMG response latencies should exceed the minimal conduction time for the polysynaptic pathway from the FEFs to the neck muscle motoneurons; at the very least, neck EMG responses should either follow or occur simultaneously with evoked eye movements.

Portions of this manuscript have appeared in abstract form (Elsley et al. 2006a,b).

Methods

Surgical and experimental procedures

Two male monkeys (Macaca mulatta, monkeys j and m), weighing 5.4–6.8 kg were used in these experiments. All training, surgical, and experimental procedures were in accordance with the Canadian Council on Animal Care policy on the use of laboratory animals and approved by the Animal Use Subcommittee of the University of Western Ontario Council on Animal Care. The monkeys’ weights were monitored daily, and their health was under the close supervision of the university veterinarians.

Each animal underwent two surgeries. In both surgeries, anesthesia was induced with ketamine and a loading dose of propofol and maintained with a drip infusion of propofol and midazolam. Heart rate, blood pressure, respiratory rate, and body temperature were monitored closely throughout the surgery. Antibiotics (cefazolin) were administered pre- and postoperatively, and anti-inflammatories (metacam) and analgesics (buprenorphine) were administered postoperatively. Animals were given ≥1 wk to recover from each surgery before other experimental procedures began. The animals were trained on a variety of behavioral tasks between the first and second surgery. The goal of the first surgery was to prepare the animal for chronic monitoring of gaze position and extracellular recording and microstimulation within the FEFs. A head implant constructed from dental acrylic was anchored to the skull via titanium screws. For access to the left FEF, a recording cylinder (Crist Instruments) embedded in the acrylic was positioned stereotactically through a 19-mm craniotomy over the left frontal lobe (interaural coordinates: A24.0, L19.0, D34.0) and angled ~20° to lie flush with the skull to permit a surface normal approach to the frontal cortex. During the experiments, a delrin grid (grid holes at 1-mm spacing, Crist Instruments) was secured within this recording chamber to standardize our exploration of the frontal cortex. A titanium head bolt to restrain the head was also anchored to the acrylic implant. Preformed eye coils [3 turns of stainless steel, Teflon coated wire (Cooner Wire or Baird wire), 19 or 20 mm diam] were implanted subconjunctivally into both eyes (Judge et al. 1980) to measure gaze shifts using the magnetic search coil technique (Fuchs and Robinson 1966). Coiled leads were passed subcutaneously to connectors embedded within the acrylic implant. A similar coil could be secured to the acrylic implant in the frontal plane to measure head movements.

In the second surgery, chronically indwelling bipolar hook electrodes were implanted bilaterally into five muscles under aseptic conditions (10 electrodes total), using an approach modified from that used in cats (Richmond et al. 1992). The muscles targeted were: obliquus capitis inferior (OCI), rectus capitis posterior major (RCP), splenius capitis (SP cap), biventer cervicis (BC), and complexus (COM; see Fig. 1A). All muscles are referred to as being contralateral or ipsilateral to the side of stimulation. In both monkeys, recordings from ipsi-SP cap were unavailable because of electrode failure noted after the EMG surgery. Anatomical and functional descriptions of these muscles have been provided previously (Cornell et al. 2001; Richmond et al. 2001). The muscles were approached through a dorsal midline incision and isolated by first separating the muscle layers from the dorsal midline raphe to gain access to the cleavage planes between the muscles. Hook electrodes were constructed from stainless steel, Teflon-coated wire (Cooner Wire) as described elsewhere (Loeb and Gans 1986) and consisted of recording contacts (~3 mm long) staggered by ~3 mm. Hook electrodes were coated obliquely through the muscle such that the staggered contacts were oriented perpendicularly to the long axis of the muscle fiber fascicles. Muscle layers were reaproximated with a midline closure. In one monkey, a ground wire consisting of a single, partially bared loop of Teflon-
coated multistranded stainless steel was secured to subcutaneous fascia. In the other, the ground was taken from a bare wire peeled around a titanium skull screw (sandblasted to remove the coating). There was no noticeable effect of ground location on our results. All leads were tunneled subcutaneously to the preexisting acrylic implant and connected to a 26-pin connector that was embedded into the acrylic implant. All animals appeared to be making normal head movements by the first postoperative day.

Before EMG recordings, the monkeys were placed in a primate chair (Crist Instruments) designed to permit completely unrestrained head movement. Both monkeys wore a customized vest (Lomir Biomedical) that permitted them to be tethered to the primate chair. Our chair features horizontally oriented neck plates, and the monkeys’ position within the chair was such that these plates were placed near the bottom of the neck. This arrangement was effective at preventing trunk rotation (estimated to be at most ±10°) without restraining the head or neck. The monkeys were wheeled into a dark, sound-attenuated room, and placed within the center of a 3–ft² coil system (CNC Engineering). The monkeys faced an array of 49 tricolor light-emitting diodes (LEDs; Fairchild Semiconductors MVS437) arranged in a radial fashion surrounding a central LED. LEDs were positioned at visual angles that corresponded to a two-dimensional (2-D) polar coordinate system to six radial eccentricities (5, 10, 15, 20, 27, and 35°) and eight radial angles (0°, 45°, 90°, 135°, 180°, 225°, 270°, and 315°; 0° = rightward, and 90° = upward). All aspects of the experiment were controlled at 1,000 Hz by customized real-time LabView programs interfacing with the hardware through a PXI controller (National Instruments). The monkeys were monitored throughout the experiment through infrared cameras positioned outside of the line of sight.

Microstimulation parameters

Stimulation was generated by a stimulator and two constant-current stimulus isolation units (model S88 and PSU-6; Grass Instruments) and delivered through a tungsten microelectrode (~0.2–1 MHz at 1 kHz, Frederick Haer and Co.). The electrode was lowered by a low-weight (100 g) hydraulic microdrive customized for head-unrestrained experiments (Narishige Instruments). To reduce 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 per phase. Stimulation duration was controlled by our experimental computer and was usually set to 100 ms, although this value was prolonged to 125 or 150 ms when necessary to ensure that the evoked gaze shift was not truncated prematurely by stimulation offset. For some head-unrestrained experiments, stimulation duration was prolonged to 300 ms to ensure that head movements were realized.

The neck EMG and movements presented in this report were evoked by a fixed current level of 50 μA. To qualify as a valid stimulation site, 50 μA of current had to evoke gaze shifts on ≥50% of all stimulation trials at short latencies (<100 ms). Such a criterion has become a standard means of functionally identifying the low-threshold portion of the FEF, because such low currents occur when the electrode is localized within the gray matter (Bruce et al. 1985). This current level is on the lower range of that used in recent studies of the primate FEF in head-unrestrained animals (Tu and Keating 2000) used current levels usually between 100 and 200 μA; Chen (2006) used a range of 50–150 μA, with a typical level of 80 μA; Knight and Fuchs (2007) used a level twice as high as the ≤50-μA threshold required to evoke short-latency gaze shifts. At 60 of the stimulation sites presented in this report, we first determined the
current threshold necessary to evoke gaze shifts on 50% of all stimulation trials in 5-μA steps (30 trials per current). Gaze shift thresholds over these sites averaged 25.8 ± 11.9 (SD) μA. Given such low thresholds, and the timing and metrics of the evoked movements presented in RESULTS, we are confident that stimulation was delivered to the low-threshold region of the FEF. A future manuscript will examine the effects of variations in stimulation current on the evoked patterns of neck EMG and gaze shifts.

For clarity, we refer to a stimulation site as a unique stimulation location within the FEF. Although we usually only recorded data at one stimulation site on a given day, we occasionally stimulated at multiple locations within a given electrode penetration. Stimulation locations had to be separated by a minimum of 500 μm to be considered a unique stimulation site; this criteria was chosen based on an estimated current spread of 200 μm for a 50-μA stimulation intensity (Stoney et al. 1968) and is consistent with recently published reports (Chen 2006; Corneil et al. 2002a). When the electrode was lowered through previously visited locations on the recording grid, we only accepted stimulation sites where stimulation evoked a notably different vector than those evoked on previous days.

Behavioral paradigm

Monkeys were trained on a gap-saccade task that required them to look from a fixation point (FP) to a peripheral target (T) to obtain a liquid reward. They were trained to perform this task with either the head restrained or unrestrained. On a given experimental session, we first localized the FEF with the head restrained and then sometimes unrestrained the head. When the head was unrestrained, the reward was delivered through a sipper tube that moved with the implant.

Two types of trials were run, stimulation and control trials, distinguished by whether FEF stimulation was delivered or not, respectively, in the interval between FP disappearance and T presentation. Stimulation trials made up one half of all trials. Control trials were incorporated into our experimental design to ensure the subjects could not anticipate stimulation on every trial. Both trial types began with the removal of a diffuse background white light. The FP was presented at a central location directly in front of the monkey. The monkeys were required to look at the FP within 1,000 ms and hold gaze within a computer-controlled fixation window (3° radius) for an interval of 750, 875, 1,000, 1,125, or 1,250 ms. The FP point was removed, and monkeys were trained to maintain fixation within the fixation window. On stimulation trials, the stimulation train started 200 ms after FP disappearance and continued for ≥100 ms, up to a maximum of 300 ms. Regardless of stimulation duration, a peripheral target was presented immediately after stimulation offset at one of eight potential target locations located on the concentric ring 10° eccentric from the central FP when the head was restrained and at one of eight potential targets located on the concentric ring 20° eccentric from the central FP when the head was unrestrained. Therefore on stimulation trials, the gap between FP disappearance and T presentation was 200 ms greater than the stimulation duration. An equivalent gap interval was used during control trials. All variables within this task (e.g., fixation duration, target location, trial type) were presented in a pseudorandom fashion. Hence, we obtained ~30 stimulation trials for each unique stimulation site.

Although this task was designed to deliver FEF stimulation at an optimal time in terms of fixation disengagement (Dorris and Munoz 1995; Opris et al. 2001; Tehovnik et al. 1999), the multiple potential target locations discourages the preparation of a particular motor program (Basso and Wurtz 1997; Dorris and Munoz 1998). Thus we do not believe that our results are unduly influenced by a potential overlap between stimulation location and the preparation of an impending gaze shift, even though the animals could anticipate the time of target presentation.

Data collection and analysis

The processing of the EMG signals commenced at a headstage plugged directly onto the EMG connector embedded within the acrylic implant. This headstage (Plexon) performed differential amplification of the EMG signals (20× gain) and filtering (bandwidth, 20 Hz to 17 kHz). A flexible ribbon cable linked the headstage to the Plexon preamplifier, which contained a signal processing board custom- made for EMG recordings (50× gain; bandwidth, 100 Hz to 4 kHz). All analog signals (e.g., conditioned EMG signals, coil signals) were digitized at 10 kHz.

Off-line, coil signals were downsampled by a factor of 10 to 1 kHz. EMG signals were notch filtered to remove 60-Hz noise, rectified, and integrated into 1-ms bins using a rationale described previously (Bak and Loeb 1979). These steps attenuated the digitized peak-to-peak amplitudes by a factor of ~3×.

Computer algorithms were used to determine the beginning and end of evoked movements using velocity criteria (30°/s for gaze and eye movements; 10°/s for head movement), which were later verified by an experimenter and corrected if necessary within a customized graphical user interface written in Matlab (The Mathworks). This interface permitted the experimenter to inspect all trials and discard trials if, for example, there was aberrant patterns of gaze movements or excessive background EMG activity across the recorded muscles (e.g., if the animal was shifting position or chewing the sipper tube). Trials with gaze shifts occurring just before or <5 ms after stimulation onset were also rejected. Overall, trials were rejected at a rate of <3%.

After this trial-by-trial inspection, customized Matlab programs extracted the parameters of the evoked movements (e.g., onset latency relative to stimulation onset, vector of evoked movement). We identified trials in which the evoked gaze shift ended either before or shortly after (<20 ms) stimulation offset, because such movements were not truncated prematurely by stimulation offset and therefore represent the characteristic vector associated with the given stimulation site. When the head was unrestrained, we also determined the latency and amplitude of the evoked head movement, the amount the head contributed to a gaze shift (for nontruncated gaze shifts only), and the onset latency of the head movement relative to the gaze shift.

We performed a number of analyses of the evoked neck EMG responses. To be consistent with previous reports from the SC (Corneil et al. 2002a,b), we calculated the mean evoked neck EMG for each muscle by aligning repeated trials on stimulation onset. The mean and SD of the baseline activity in the 100 ms preceding stimulation onset were calculated. The latency of facilitation or suppression of the evoked EMG response was determined as the first of at least five consecutive bins either 2 SD above or 1 SD below the average baseline activity, respectively. Determination of a suppressive response was possible only in the presence of considerable background activity. The peak magnitude of the EMG response was taken as the highest mean bin value after stimulation onset minus the average baseline activity. Because the peak magnitude of neck EMG activity varies with different eye-in-head positions (Corneil et al. 2002a; Lestienne et al. 1984; Werner et al. 1997), we extended the search for the peak EMG magnitude only out to the time of gaze shift initiation.

We also performed a second analysis to extract the onset of the neck EMG response on a trial-by-trial basis. The logic and derivation of this analysis is described in RESULTS (see Timing of evoked neck EMG responses in relation to gaze shift onset).

Results

Stimulation was delivered throughout a wide distribution of sites within the frontal cortex in two monkeys (Fig. 1, B and C). A subset of these stimulation sites evoked short-latency gaze shifts with stimulation parameters customarily used to
localize FEFs (see METHODS). With this criterion, we determined that FEF stimulation was delivered to a total of 140 unique sites in two monkeys (31 in monkey m and 109 in monkey j). One hundred three of these sites were studied only with the head restrained, 14 were studied with only the head unrestrained, and 23 were studied with the head both restrained and unrestrained. Based on anatomical MRIs taken in each monkey before the start of the experiment, most if not all sites lay within the anterior bank of the arcuate sulcus (note that the sulci traced in Fig. 1C show the surface normal appearances, and do not capture the 3-D geometry). Longer duration stimulation of 300 ms was also applied with the head-unrestrained at 28 of these sites. To facilitate comparison of our results with previous literature, we first provide a description of the kinematics of the evoked movements.

The timing and metrics of evoked gaze shifts conformed with previous findings in head-unrestrained primates (Chen 2006; Knight and Fuchs 2007; Tu and Keating 2000), in that larger gaze shifts were evoked from more dorsomedial locations, and smaller gaze shifts were evoked from more ventrolateral location (Fig. 1C). Consistent with other reports (Gotlieb et al. 1993), stimulation at a relatively ventrolateral site elicited a smooth pursuit movement, whereas stimulation at a more caudal site evoked an observable arm movement (Fig. 1C). We also encountered many dorsomedial sites where 50 μA of stimulation current evoked neck muscle activity without an accompanying gaze shift (“n” in Fig. 1C). Briefly, the timing and patterns of evoked neck EMG in these nongaze sites resembled those reported below, with the exception of being greater in magnitude, and associated with the recruitment of a larger head movement when the head was unrestrained.

Timing and metrics of evoked movements

Stimulation in the FEFs evoked a wide range of gaze shifts (Fig. 1D). The vast majority of evoked gaze shifts (137/140) were driven contralateral to the side of stimulation. On three occasions, evoked gaze shifts contained an ipsilateral horizontal component relative to the side of stimulation, consistent with some previous reports (Chen 2006; Knight and Fuchs 2007; Robinson and Fuchs 1969). Two of these examples contained a predominantly vertical component, but one was predominantly horizontal. All subsequent analyses focus on the remaining 137 sites from which contralateral gaze shifts were evoked.

We were able to evoke a large range of contralateral gaze shift vectors from the FEF [Fig. 1D; segregated by whether the site was studied only with the head-restrained (left subplot) or with the head-unrestrained for at least one file (right subplot)], ranging from 2 to 30° in radial magnitude [12.8 ± 6.2° (SD)] and −72 (i.e., downward) to 87° in radial angle (16 ± 40°). Over this sample, gaze shifts were always initiated during the stimulation train, beginning from between 19 and 65 ms after stimulation onset (40 ± 10 ms).

We next focus on the timing and metrics of eye-head gaze shifts evoked from the 36 sites from which contralateral gaze shifts were evoked with the head unrestrained. On average, the initial eye-in-head and head-in-space positions were near midline before stimulation (mean horizontal eye-in-head position = −2.8 ± 1.9°; range −5.1 to 3.2°; mean horizontal head-in-space position = 3.3 ± 1.7°, range: −4.3 to 6.3; similar values were obtained for initial vertical positions); hence eye, head, and gaze positions were approximately aligned at the time of stimulation onset. The pattern of evoked gaze shifts differed very little from when the head was restrained (gaze initiation latency = 39 ± 9 ms; gaze magnitude = 14.1 ± 5.1°; gaze direction = 4.0 ± 29.1°). With the 100- to 150-ms stimulation train, total head movement amplitude was 8.4 ± 5.7° angled approximately along the horizontal (head movement direction = 4.5 ± 15.5°). Consistent with previous results (Chen 2006; Knight and Fuchs 2007; Tu and Keating 2000), the amount of the evoked gaze shift that was caused by the motion of the head (i.e., head contribution) was very modest, averaging 2.1 ± 1.9° of the horizontal component and 0.4 ± 0.4° of the vertical component. Head movements were initiated 73 ± 32 ms after stimulation onset, on average starting 23 ± 34 ms after the evoked gaze shift (range: −46 to 92 ms).

We observed a number of straightforward relationships between the timing and metrics of eye-head gaze shifts. First, we observed a positive correlation between head contribution and the magnitude of the evoked gaze shift (Fig. 2A). In our sample, the head started to contribute to gaze shifts greater than −15–20° in amplitude. Second, we observed that the evoked head movement comprised a proportionally larger amount of the evoked gaze shift the earlier the head movement began relative to gaze shift onset. This observation was revealed by plotting the proportional head contribution (normalized to the magnitude of the evoked gaze shift) as a function of the gaze-head lead time (Fig. 2B, derived as Head RT – Gaze RT; hence positive values represent sites where gaze onset lead head movement onset). The two outliers come from the sites with the longest gaze initiation latencies, presumably because the 50-μA current was close to gaze threshold). Third, we found that total head movement amplitude was ~40% and peak head velocity was ~25% greater when the stimulation train duration was prolonged to 300 ms (Fig. 2, C and D; 22 sites studied with both a 100- and 300-ms train duration). This is because the head continued to move, and usually continued to accelerate, for the duration of the stimulation train. All of these relationships are consistent with previous reports in head-unrestrained primates (Chen 2006; Knight and Fuchs 2007; Tu and Keating 2000).

As mentioned above, stimulation was passed with both the head restrained and unrestrained at a total of 23 different FEF sites. This subset of stimulation sites permit a direct comparison of evoked movements made across head restraint. We found no significant difference in gaze initiation latencies (head-restrained gaze initiation latency = 45 ± 11 ms; head-unrestrained gaze initiation latency = 44 ± 18 ms; paired t-test: P = 0.70). Of more interest, we found that overall gaze magnitudes were systematically larger when stimulation was delivered with the head-unrestrained (Fig. 2E; head-restrained gaze magnitudes = 10.9 ± 3.7°; head-unrestrained gaze magnitudes = 14.4 ± 5.4°; paired t-test: P < 0.005). Closer examination of this dataset revealed that the increase in the magnitude of head-unrestrained gaze shifts was caused in part by the head’s contribution (Fig. 2F). Although this plot reveals substantial site-by-site variability, the head did tend to contribute more when evoked from stimulation sites with larger differences in gaze magnitude across head restraint. Consistent with this, we observed no systematic difference between head-
the more variable recruitment synergy accompanying gaze quantification of the horizontal turning synergy and its variation with the parameters of the evoked gaze shift. We quantify the more variable recruitment synergy accompanying gaze shifts with substantial vertical components later.

Patterns of neck EMG evoked by FEF stimulation

Stimulation of the FEF evoked robust changes in EMG activity recorded from many neck muscles. The overall pattern of evoked neck EMG consisted of the recruitment of a synergy that would turn the head in a direction contralateral to the side of stimulation, to which a more variable recruitment synergy was added depending on the vertical component of the evoked gaze shift. The majority of our analyses will focus on the quantification of the horizontal turning synergy and its variation with the parameters of the evoked gaze shift. We quantify the more variable recruitment synergy accompanying gaze shifts with substantial vertical components later.

Representative examples of the turning synergy evoked by FEF stimulation are shown in Fig. 3, accompanying a large gaze shift (Fig. 3A), a medium-sized gaze shift (Fig. 3B), or a very small gaze shift (Fig. 3C). Each of these examples was recorded while monkey j was head-restrained, but as described below, we saw no evidence that head restraint modified the overall profile of evoked neck EMG. FEF stimulation at sites evoking large gaze shifts (Fig. 3A) evoked a rapid facilitation in agonist neck muscles such as the OCL, RCP maj, and SP cap muscles contralateral to the side of stimulation, and a concomitant suppression in antagonist neck muscles such as OCI and RCP maj ipsilateral to the side of stimulation (see Fig. 1A for anatomical sketches of these muscles; recordings from ipsi-SP cap were not successful). These evoked EMG responses began very soon after stimulation onset. From the stacked 3-D color plots in Fig. 3A (where each row conveys the EMG activity on a single trial, ordered by the initiation latency of the evoked gaze shift), it is obvious that the evoked EMG responses preceded the evoked gaze shift on every trial. The initial response in this case was followed by a period of agonist muscle facilitation and antagonist muscle suppression that persisted for the duration of stimulation. In other cases (e.g.,...
Fig. 3, B and C), the initial response to stimulation was followed by a pattern in which agonist and antagonist muscles returned to prestimulation activity levels even though stimulation was on-going. We could not predict which of these two patterns would be present for a given stimulation site and location, head restraint, or the metrics of the evoked gaze shift. After the cessation of stimulation, the EMG activity of the agonist muscles returned very quickly to prestimulation levels (Fig. 3A); we also occasionally observed a brief rebound excitation of the antagonist muscles (Fig. 3B). Again, this feature was also not simply related to stimulation location, head restraint, or the metrics of the evoked gaze shift.

Perhaps more surprising are the patterns of EMG activity that accompanied both medium- and small-sized gaze shifts. In the representative examples shown in Fig. 3, B and C, FEF stimulation evoked a similar pattern of neck EMG, although with more moderate magnitudes. For example, a clear facilitation on agonist OCI and RCP maj is apparent on all trials evoking the medium-sized gaze shift (Fig. 3B) and on most trials where the small-sized gaze shift was evoked (Fig. 3C). Facilitation of agonist SP cap is absent in each of these examples, consistent with previous reports of how SP cap recruitment only accompanies relatively larger head movements (Corneil et al. 2001, 2002a). Most impressively, robust suppression responses are seen on the antagonist muscles on almost all stimulation trials (differences in prestimulation levels of activity in the antagonist muscles in Fig. 3, B and C, are caused by different idiosyncratic body-under-head postures adopted during the different experimental sessions). Once again, these facilitation and suppression responses began well in advance of the evoked gaze shift. These evoked responses are quite surprising given that the presumed head motion, if the head was unrestrained, would be small in the case of the medium-sized gaze shift and nonexistent for the small evoked gaze shift.

In Fig. 4, we show data from the other monkey (monkey m) obtained when the head was unrestrained. These data are arranged in a similar format as in Fig. 3 and have been selected to represent the activity associated with similarly sized gaze vectors. Although the absolute magnitudes of EMG activity are not comparable across the two monkeys (given the idiosyncratic properties of different EMG electrodes), the patterns of EMG recruitment (shown here from bilateral OCI for simplicity) are very similar. For example, the same rapid facilitation of the agonist OCI and rapid suppression of the antagonist OCI muscles is present when the head is unrestrained, almost always preceding gaze shift onset regardless of the size of the evoked gaze shift. Furthermore, the changes in neck EMG activity preceding the medium- and small-sized evoked gaze shift occur even though head movements are detected rarely (2 head movements were detected after the medium-sized gaze shift in Fig. 4B, and no head movements were detected after the small-sized gaze shift in Fig. 4C). These examples confirm that neck EMG responses can be evoked despite the absence of head motion.

FEF stimulation at sites that evoked larger gaze shifts commonly evoked head motion. In the representative example shown in Fig. 4A, the onset of head motion typically started ~50–80 ms after stimulation onset (Fig. 4A, black circles), sometimes lagging gaze shift onset and sometimes leading gaze shift onset. More impressively, this representative example depicts trials in which stimulation failed to evoke a gaze shift but still evoked both a neck EMG response and a contralateral head movement (see top rows of 3-D color plots, which do not have a white square but do have a black circle). Gaze remained stable during these head-only movements because the eyes counter-rotated in the opposite direction, presumably because of the vestibulo-ocular reflex (see arrows in Fig. 4A, top left).
placed on Eh traces in Fig. 4A). We will describe such head-only movements in more detail below.

**Effect of head restraint on parameters of evoked neck EMG**

Before quantifying the parameters of evoked neck EMG, we first examine the effect of head restraint more directly. To do this, we analyzed the 23 examples where we obtained both head-restrained and head-unrestrained data from the same stimulation site (i.e., data were collected first with the head-restrained and then the head was released and data were collected with the head-unrestrained). Figure 5A shows data obtained from the same stimulation site as Fig. 3B (i.e., the medium-sized gaze shift), showing that a qualitatively similar pattern of neck EMG was evoked regardless of head restraint:

FEF stimulation always elicited a facilitation or suppression of neck EMG activity on contralateral or ipsilateral turners, respectively. In the example shown in Fig. 5A, FEF stimulation drove gaze shifts with a moderate head contribution (in this case ~3°), with the evoked head movement continuing after gaze shift offset.

To quantify the effect of head restraint on the evoked neck EMG response, we compared both the peak magnitude of evoked activity and the facilitation latency for contralateral turning muscles across the 23 stimulation sites from which both head-restrained and -unrestrained data were collected. For OCI, RCP maj, and SP cap, the peak magnitude of evoked activity was similar regardless of head restraint (Fig. 5B; paired t-test: $P = 0.34$, 0.23 and 0.24 for OCI, RCP maj, and SP cap,

---

**FIG. 5.** Comparison of EMG activity evoked with either the head-restrained or -unrestrained. A: horizontal gaze (Gh) and head (Hh) position traces and EMG activity evoked with the head-unrestrained, taken from the same site as shown in Fig. 3B. Same format as Figs. 3 and 4. B and C: comparison of EMG response parameters on contralateral muscles, taken from the subset of stimulation sites that were studied with both the head-restrained and -unrestrained. Each point denotes mean value [either peak evoked magnitude (B) or facilitation latency (C)] obtained with the head-unrestrained plotted as a function of mean value obtained with the head-restrained for a single stimulation site. Filled symbols in B denote peak magnitudes that were significantly different across restraint condition. Statistical testing is not possible in C because response latencies were derived from the mean EMG waveforms and do not come with a variance. Diagonal dashed line shows line of unity. Peak evoked magnitudes (B) tended to cluster near line of unity (paired t-test, $P = 0.34$, 0.23, and 0.24 for OCI, RCP maj, and SP cap, respectively), whereas facilitation latency tended to be significantly shorter when stimulation was passed with head-unrestrained (paired t-test, $P = 0.001$, 0.01, and 0.04 for OCI, RCP maj, and SP cap, respectively).
respectively). We did find that the facilitation latency of these muscles were significantly shorter when the head was unrestrained (paired t-test: all $P < 0.05$). However, the difference in facilitation latency across head restrained was modest for OCI and RCP maj, averaging $\sim 3$ ms, and larger for SP cap ($\sim 10$ ms).

Comparison of EMG activity accompanying evoked versus volitional gaze shifts

We sought to compare the EMG patterns accompanying gaze shifts evoked by FEF stimulation to those accompanying volitional gaze shifts made during control trials. This comparison was fairly limited, because target placement during control trials could be at one of eight positions $10^\circ$ eccentric from the fixation point when the head was restrained and at one of eight positions $20^\circ$ eccentric from the fixation point when the head was unrestrained (see METHODS). Although we would have liked to have performed a detailed quantitative comparison of neck EMG accompanying head movements matched for amplitude, velocity, and acceleration, we could not find enough volitional head movements that matched the kinematic profile of evoked head movements. This is in part because of the variability of head acceleration during volitional head turns (Corneil et al. 2001) and because of the dependency of head movement amplitude and peak velocity with stimulation duration (see Fig. 2).

We therefore concentrated on stimulation sites where the evoked gaze shift vector brought final gaze position near one of the contralateral targets on either the $10^\circ$ (when head-restrained) or the $20^\circ$ (when head-unrestrained) concentric ring location. In Fig. 6A, we contrast one representative example of EMG data aligned on the onset of head-unrestrained evoked gaze shifts (here $18^\circ$ to the right) to EMG data from control trials, aligned on when the animal looked to the target placed $20^\circ$ to the right. The evoked EMG activity attained greater magnitudes and was clearly more aligned to stimulation onset than gaze shift onset. The contralateral muscles also displayed much more phasic patterns, decreasing in activity after the initial facilitation, and subsequently peaking in activity for a second time $\sim 80$ ms into stimulation onset. In contrast, although EMG activity did peak in the peri-gaze shift interval on control trials, this magnitude of this peak was far more modest. Furthermore, there was no tendency for subsequent bursts of EMG activity after the initial activation in the peri-gaze shift interval on control trials. These trends persisted across our sample, with the activation of all three contralateral turner muscles being substantially greater on stimulation versus control trials (Fig. 6B).

Quantification of evoked neck EMG responses from the FEF

The analyses presented above show that there was little systematic difference in the parameters of evoked neck EMG...
when the head was restrained or unrestrained. For the population analyses that follow, we pooled the data in the following manner, to ensure that all data came from unique stimulation sites. We pooled data collected from sites studied with the head-restrained only (100 sites total, discarding the 3 sites from which ipsilateral gaze vectors were evoked), data collected from sites studied with the head-unrestrained only (14 sites), and data from the 23 sites studied with both the head restrained and unrestrained (using only the head-restrained data from these 23 sites). Across the 137 unique stimulation sites from where a contralateral gaze shift was evoked, we almost always observed an evoked neck EMG response, and this evoked neck EMG response usually preceded the evoked gaze shift. In general, this evoked neck EMG response was larger and started earlier when accompanying a larger evoked gaze shift, but as shown above (e.g., Figs. 3C and 4C), we frequently observed evoked neck EMG responses that accompanied smaller gaze shifts not usually associated with head motion.

As stated above, FEF stimulation consistently recruited a neck EMG synergy comprised of facilitation and/or suppression of the activity of contralateral or ipsilateral turner muscles, respectively. We constructed averages of evoked EMG activity by constructing the mean stimulation-aligned waveform across all stimulation trials, and observed a significant evoked neck EMG response (see METHODS for definition of a significant facilitation or a suppression of EMG activity) on at least one neck muscle in 97.8% (134/137) of our stimulation sites (a significant facilitation of contra-OCI, contra-RCP maj, and contra-SP cap was seen in 93.4 (128/137), 80.3 (110/137), and 35.8% (49/137) of all stimulation sites, respectively; a significant suppression of ipsi-OCI and ipsi-RCP maj was seen in 82.5 (113/137) and 73.7% (101/137) of all stimulation sites, respectively). Most facilitation latencies were <25 ms [16.5 ± 6.9 ms (median 15 ms) for contra-OCI, 18.5 ± 9.3 ms (median 17 ms) for contra-RCP maj, 26 ± 10.0 ms (median 24 ms) for SP cap]. Similar values were obtained for the suppression latencies [17.7 ± 7.2 ms (median 16 ms) for ipsi-OCI and 17.3 ± 6.1 ms (median 16 ms) for ipsi-RCP maj].

The facilitation latencies for all three muscles displayed straightforward relationships with the horizontal component of the evoked gaze vector, being evoked earlier for gaze shifts with larger horizontal components (Fig. 7, A–C). Similarly, we also observed that the peak magnitude of facilitation increased for gaze shifts with progressively larger horizontal components (Fig. 7, D–F). Both of these results are consistent with a FEF drive to the cephalomotor system that gets progressively stronger for gaze shifts with progressively larger horizontal components.

Another feature that can be appreciated from Fig. 7, consistent with a cephalomotor drive that scales with the horizontal gaze component, is that those stimulation sites from which an EMG response could not be evoked tended to drive gaze shifts with horizontal components <10° (denoted by “x”s” on the horizontal axis in Fig. 7). Gaze shifts with horizontal components <10° in amplitude were seen in 7 of 8 of the nonresponsive sites for contra-OCI, 23 of 26 of the nonresponsive sites for contra-RCP maj, and 67 of 87 of the nonresponsive sites for SP-cap. It is important, however, to stress that it was far more common to observe EMG responses that accompanied such modest gaze shifts. For example, a significant facilitation was observed on contra-OCI from 20 of 26 stimulation sites from which horizontal gaze components <5° were evoked and 62 of 63 times for gaze components that fell between 5 and 10°. Similar numbers were observed for RCP maj (17 of 26 sites for Gh < 5°; 62/63 for 5° < Gh < 10°). SP cap, however, was not systematically recruited in association with such small gaze shifts (3/26 for Gh < 5°; 19/63 for 5° < Gh < 10°), consistent with previous results from the SC (Cornell et al. 2002a). Overall, these results attest to a persistent frontal drive to neck muscle motoneurons, albeit of a low magnitude, even for sites evoking gaze shifts not typically associated with head motion.

**Timing of evoked neck EMG responses in relation to gaze shift onset**

We now focus on the timing of the evoked neck EMG responses relative to the timing of the gaze shift. In particular, does the onset of the evoked neck EMG response occur before, in synchrony with, or after the accompanying evoked gaze shift?

To assess this question, we first compared the facilitation latencies of the mean EMG responses on the contralateral
agonist muscles to the mean onset latency of the evoked gaze shift. The results of this comparison are shown in Fig. 8 across all stimulation sites and clearly show that the onset of the mean EMG response preceded the mean gaze shift onset [for all muscles, the mean facilitation latency was significantly less than mean gaze shift onset (paired t-test, all \( P < 10^{-5} \)]. The mean facilitation latency on contra-OCI, contra-RCP maj, and contra-SP cap preceded the mean gaze shift latency by 25.4 ± 12.4, 23.6 ± 14.5, and 14.5 ± 15.1 ms, respectively. We observed a significant correlation between these measures, such that the mean facilitation latencies tended to be longer for stimulation site-evoke gaze shifts at longer onset latencies (all regressions shown in Fig. 8 are significant at \( P < 0.05 \)). The slopes of these regression lines ranged between 0.15 and 0.20, meaning that the EMG facilitation latency increased by ∼1 ms for every 5- to 6-ms increase in gaze shift onset latency.

One shortcoming of the above analysis is that it may exaggerate the difference between mean EMG facilitation latency (determined through an average of ∼30 stimulation trials) and mean gaze onset (determined on a trial-by-trial basis), because the derivation of the mean EMG facilitation latency will be biased by those trials with a rapid EMG facilitation latency. To overcome this problem, we performed a second analysis wherein we determined the onset of the EMG response on a trial-by-trial basis. To do this, we summed the normalized EMG records from agonist muscles with the inverted normalized EMG records from antagonist muscles (depicted graphically in Fig. 9A for contra-OCI, contra-RCP maj, and ipsi-OCI; EMG magnitudes normalized to the maximal level recorded during a given experimental session). This derivation results in a trace representing the cumulative change in EMG activity across multiple muscles in response to stimulation onset on a single trial. Using this trace, we determined the onset of the EMG response on a trial-by-trial basis by identifying the first of three of five points after stimulation onset that exceeds the mean prestimulation level of activity by 2 SD.

The results of this analysis are shown for a single stimulation site in Fig. 9B (using the same data as that shown in Fig. 3B). Here, we contrast EMG onset latency to gaze shift onset latency on a trial-by-trial basis (i.e., each square in Fig. 9B is derived from an individual trial), and from this example, it is clear that the onset of the EMG response preceded the onset of the gaze shift for every individual trial (this feature was also apparent in Fig. 3B).

Across our sample of stimulation sites, we analyzed the relative onset of the EMG response with gaze shift onset in two ways. First, for each stimulation site, we plotted the mean single-trial EMG onset as a function of the mean gaze shift onset (Fig. 9C). Once again, EMG responses preceded the gaze shift onset at the majority (116 of 133) of stimulation sites from which an EMG response was evoked. Using this analysis, the mean EMG onset preceded the mean gaze shift onset by 15 ± 15 ms. Because a trial-by-trial onset can be derived for both the EMG and a gaze shift response, we can also derive the variability of each measure. This feature is presented in Fig. 9D, which also plots the relative timing of the onset of the EMG and gaze shift response. In this figure, error bars to the left denote the SD of the EMG response, whereas error bars to the right denote the SD of the gaze shift response.

Second, we also examined the relative timing of the EMG and gaze shift onset across all stimulation trials on which both were evoked (i.e., pooling across all monkeys and stimulation sites, \( n = 3,069 \)). A histogram of the difference between EMG and gaze shift onset latencies is shown in Fig. 9E. Across all stimulation trials, the onset of the EMG response preceded the onset of the gaze shift by an average of 17.0 ± 19.3 ms, with negative values (i.e., when the EMG response preceded the gaze shift) occurring on 85.7% (2631/3069) of all stimulation trials. Overall, these analyses show that the neck EMG response evoked by FEF stimulation was initiated much earlier than the gaze shift response.

**Correlation of evoked neck EMG responses to evoked head movements**

The derivation of a trial-by-trial EMG response permits us to analyze the relationship between evoked neck EMG activity and the ensuing head movement. In Fig. 10, we show a number of relationships between the parameters of the evoked neck
EMG response and those of the evoked head movement. First, we compared the onset time of the EMG response to the onset of the movement. On a site-by-site basis, we found that the neck EMG response always led the onset of the evoked head movement (Fig. 10A), on average by \(~40\) ms. In Fig. 10B, we present the relative timing of the neck EMG to head movement response, as well as the variability of each measure. From this plot, it is again clear that the neck EMG response led the onset of head motion; moreover, the variability of the onset of the neck EMG response was much less than the variability of onset of head motion (the EMG variability is much less in Fig. 10B than Fig. 9C because sites were constrained to those from which a head movement was evoked). We also examined the relative timing of the onset of the neck EMG head movement on a trial-by-trial basis for all trials in which both a head movement and neck EMG response were observed and found that the onset of the EMG response preceded the onset of a head movement by \(40.6 \pm 16.3\) ms, with values less than \(-10\) (i.e., when the EMG response preceded head motion by \(\geq 10\) ms) occurring on \(>99\)% of all trials.

We also analyzed how well aspects of the EMG response predicted the parameters of the evoked head movement. To do this, we calculated the normalized integral of the composite EMG response on a trial-by-trial basis (imagine extracting the area under the composite EMG response shown in Fig. 9A for each trial) and plotted this value against either the amplitude and peak head velocity to be strongly correlated with this measure of the EMG response (e.g., the \(R^2\) values in Fig. 10, \(D\) and \(E\), exceed 0.45), showing that the EMG responses we measured are very good predictors of ensuing head motion (because targets were always presented at \(20^\circ\), an analogous analysis of volitional head movements made during control trials could not be performed given the lack of variability in head movement amplitude).

**Evoked neck EMG responses on stimulation trials without an evoked gaze shift**

As mentioned in the Introduction, we passed a fixed stimulation current of \(50\) \(\mu\)A at all of our stimulation sites. Our criterion that a given stimulation site lay within the FEF was that gaze shifts had to be evoked on at least one half of all
stimulation trials (see METHODS). Across all 137 stimulation sites that met this criterion, gaze shifts were evoked on 87.3 ± 14.9% of all trials (range, 50–100%; median, 94%). Thus, although it was far more common for FEF stimulation to evoke a gaze shift, an evoked gaze shift was not observed on a substantial proportion of stimulation trials. We now examine the neck EMG responses that accompanied such trials without gaze shifts.

A representative example of a stimulation site from where gaze shifts were either evoked (n = 18) or not evoked (n = 11) is shown in Fig. 11A. Here, we segregated the EMG records for those trials with or without gaze shifts (termed “gaze” and “no-gaze,” respectively). Prominent EMG responses were observed on both gaze and no-gaze trials. The onset latencies, peak magnitudes, and spatio-temporal profile appear quite similar across both trial types (i.e., agonist muscle facilitation and antagonist muscle suppression were observed on both gaze and no-gaze trials).

Across our sample of stimulation sites, we compared the EMG responses on gaze versus no gaze trials for those sites in which a minimum of five no-gaze trials were elicited (hence, gaze shifts were evoked on between ~50 and 83% of all stimulation trials). The results of this quantitative analysis are shown in Fig. 11, comparing the onset latency (Fig. 11B) and the normalized integral (Fig. 11C) of the composite EMG response.

There are a number of points to emphasize from this quantitative analysis. First, a significant neck EMG response was always observed on no-gaze trials (if neck EMG responses were not evoked on no-gaze trials, the data points in Fig. 11, B and C, would have fallen on the x-axis). Second, the facilitation latency was significantly shorter on trials in which an accompanying gaze shift was elicited (i.e., gaze trials) by 4.8 ± 13.3 ms (paired t-test, P < 0.05; Fig. 11B). Third, the EMG response tended to be stronger on gaze trials than no-gaze trials by 8.9 ± 8.2% (paired t-test, P < 10^{-5}; Fig. 11C). These results show that the FEF-mediated recruitment of neck muscles does not require an accompanying gaze shift, even if the EMG response starts slightly sooner and is slightly larger on trials with gaze shifts.

**Evoked head movements on stimulation trials without an evoked gaze shift**

Our observation that FEF stimulation evokes neck EMG even in the absence of accompanying gaze shifts raises the prediction...
that FEF stimulation in the head-unrestrained animal should be capable of driving head movements in the absence of gaze shifts. We did observe a number of such head-only movements, as shown in Fig. 12A. In this example, 100 ms of FEF stimulation on some occasions drove head movements accompanied by a rightward gaze shift (19 trials), and on other occasions evoked head movements but failed to evoke a gaze shift during the stimulation interval (17 trials). Importantly, robust neck EMG responses and small rightward head movements were evoked regardless of whether a gaze shift was evoked or not. Gaze remained stable during the head-only movements on trials without gaze shifts because of a compensatory movement of the eyes in the opposite direction. At a qualitative level, the parameters of the evoked head movement and neck EMG response appear quite similar across gaze and no-gaze trials.

To analyze such head-only movements across our sample of FEF sites studied with the head unrestrained, we first identified sites from which a substantial portion of head movements with or without gaze shifts could be evoked. From our sample of 36 sites that evoked contralateral movements with the head unrestrained, stimulation at a total of 10 sites evoked at least five examples of head movements either without gaze shifts or where the onset of head motion led the gaze shift by ≥40 ms (we recognize that this 40-ms criteria is arbitrary, but given the results shown in Fig. 10C, we feel that the relative timing of the gaze and head drives are highly asynchronous on such trials). A comparative analysis of head motion on gaze versus no-gaze trials showed that the head moved further and faster on trials accompanied by a gaze shift (Fig. 12, B and C; paired t-test, \( P < 0.05 \) for both comparisons), although the timing of head movement onset did not differ from trials without a gaze shift (results not shown, paired \( t \)-test, \( P = 0.26 \)). A comparative analysis of the evoked composite EMG response showed that the EMG responses tended to be slightly larger on trials with gaze shifts (Fig. 12D), although this trend did not reach significance (paired \( t \)-test, \( P = 0.09 \)). There was no difference in the timing of the onset of EMG activity across trials with and without gaze shifts (results not shown; paired \( t \)-test, \( P = 0.82 \)).

Overall, our analysis of EMG activity and head motion on trials with and without gaze shifts shows clearly that a FEF drive to the head plant is not dependent on the presence of a gaze shift. However, the drive to the head plant tends to be slightly stronger on stimulation trials where a gaze shift is evoked.

**Neck EMG responses evoked on the extensor musculature**

In addition to the responses on the turner muscles described above, FEF stimulation commonly evoked neck EMG responses on the extensor muscles biventer cervicis (BC) and complexus (COM; Fig. 1A), particularly (although not exclusively) for those gaze shifts with large vertical components. In Fig. 13, we present the EMG activity recording from these muscles for a large upward gaze shift (Fig. 13A) and a large downward gaze shift (Fig. 13B). Both of these examples were recorded with the head restrained. Despite such restraint, clear EMG responses are seen on the four extensor muscles.
A bilateral COM (Fig. 13A) vector, we observed strong facilitation on bilateral BC and head movement amplitude (D), peak head velocity (scale for Eh on gaze vs. no-gaze trials and for Hh. and counter-rotation of the eye to ensure gaze stability. Note also the different presence of prominent neck EMG responses head movements on no-gaze trials (green traces) and 17 no-gaze trials (red traces) were evoked. Note the presence of prominent neck EMG responses head movements on no-gaze trials and counter-rotation of the eye to ensure gaze stability. Note also the different scale for Eh on gaze vs. no-gaze trials and for Hh. B–D: comparison of evoked head movement amplitude (B), peak head velocity (C), and mean integral (D) of composite EMG response for gaze and no-gaze trials. Each square taken from a different stimulation site, with filled squares showing measures that were significantly different within a given stimulation site (2-tailed \( t \)-test, \( P < 0.05 \)). Integral data are normalized to maximum integral recorded within each monkey. Across our sample, head movement amplitude and peak velocity were significantly greater on gaze vs. no-gaze trials (paired \( t \)-test, \( P < 0.05 \) for both comparisons). Value of EMG integral tended to be larger for gaze vs. no-gaze trials but did not reach significance (paired \( t \)-test, \( P = 0.09 \)).

After FEF stimulation, which drove the sharp upward gaze vector, we observed strong facilitation on bilateral BC and bilateral COM (Fig. 13A). In this example, extensor muscle activity began after the gaze shift and well after the onset activity on contra-OCI and contra-RCP maj (data not shown). This extensor muscle facilitation persisted for the duration of the stimulation train, although a slight decrement in EMG activity was observed during the stimulation train, beginning \( \sim 60 \) ms after stimulation onset.

After FEF stimulation which drove the downward gaze vector, we observed a slightly more complicated pattern of extensor muscle activity (Fig. 13B). A suppression of activity was clear on bilateral BC and ipsi-COM, which was approximately synchronous with gaze shift onset. However, we observed a seemingly paradoxical facilitation in the activity of contra-COM.

Over our sample, stimulation at a total of 50 sites drove gaze shifts with a larger vertical than horizontal component (i.e., angled at \( >45^\circ \) from the horizontal). The responses on the extensor musculature was mostly predictable based on the vertical component of the evoked gaze shift, although there were a number of occurrences, such as that shown in Fig. 13B, of seemingly paradoxical responses (e.g., extensor muscle facilitation accompanying downward gaze shifts, or extensor muscle suppression accompanying upward gaze shifts). Furthermore, the facilitation and suppression latencies on the extensor musculature tended to be longer than those observed for the turner muscles. The mean facilitation latencies for contra-BC, contra-COM, ipsi-BC, and ipsi-COM were 33.3 \pm 18.0 (median, 28 ms), 25.0 \pm 16.9 (median, 20 ms), 37.5 \pm 16.2 (median, 35 ms), and 38.8 \pm 15.1 ms (median, 39 ms), respectively. For contra-BC, ipsi-BC, and ipsi-COM, the facilitation response tended to start earlier and reach larger peak values when accompanying gaze shifts with larger upward components (Fig. 14, A and B). Surprisingly, such relationships were not seen for contra-COM, where the EMG response was mostly invariant with vertical gaze component (Fig. 14, A and B, 2nd column from the left).

A suppression of EMG activity was usually seen on these muscles when they accompanied gaze shifts with a downward component. The mean suppression latencies for contra-BC, contra-COM, ipsi-BC, and ipsi-COM were 33.1 \pm 13.2 (median, 30 ms), 46.2 \pm 12.5 (median, 44 ms), 28.3 \pm 17.3 (median, 22 ms), and 24.6 \pm 11.2 ms (median, 21 ms), respectively. This suppressive response tended to begin earlier on bilateral BC and ipsi-COM when they accompanied gaze shifts with larger downward components (Fig. 14C). There was no obvious relationship between suppression latency and the vertical component of the evoked gaze shift on contra-COM.

**Comparison of EMG activity on control and stimulation trials**

We compared the EMG activity on control and stimulation trials to examine whether there were any systematic differences that would suggest that the animal was anticipating stimulation. First, we compared the EMG activity from the sample immediately preceding stimulation onset to the EMG activity taken from the same sample on control trials (i.e., 199 ms into gap interval) and found that the levels of activity on all muscles were indistinguishable for control and stimulation trials (paired \( t \)-test, \( P > 0.40 \) for all muscles). This result is consistent with the structure of our paradigm, because the monkeys did not know whether stimulation would be delivered on a given trial. Second, for both control and stimulation trials, we compared the EMG activity from the sample immediately before stimulation onset to the EMG activity from the sample immediately before the offset of the fixation point and found no evidence that EMG activity increased during the gap interval on any muscle as would be expected if the monkeys were using the gap interval to anticipate the timing of stimulus onset or in the anticipation of target presentation at a particular location (paired \( t \)-test, \( P > 0.34 \) for all muscles). These results are consistent with patterns of prestimulation neck EMG reported previously (Corneil et al. 2007).

**Discussion**

We described neck EMG evoked by stimulation of the primate FEF. Stimulation throughout the FEF evoked neck
Overall, the pattern of the cephalomotor drive evoked from the FEF is very similar to that evoked from the SC, showing that these structures play a similar role in evoked eye-head gaze shifts.

**Comparisons to previous studies in the FEF**

Regardless of head restraint, evoked neck EMG responses preceded evoked gaze shifts by ~15–20 ms (Fig. 9). These

![Diagram of gaze shifts and EMG activity evoked by stimulation in 2 different FEF locations driving either a large upward gaze shift (A) or a large downward gaze shift (B), with the head restrained. Same format as Fig. 3, showing EMG activity for contralateral and ipsilateral extensor muscles.](http://jn.physiology.org/)

**FIG. 13.** Gaze shifts and EMG activity evoked by stimulation in 2 different FEF locations driving either a large upward gaze shift (A) or a large downward gaze shift (B), with the head restrained. Same format as Fig. 3, showing EMG activity for contralateral and ipsilateral extensor muscles.

EMG responses, even from sites evoking small gaze shifts. Neck EMG responses persisted on stimulation trials without an evoked gaze shift, culminating occasionally in head-only movements with the head unrestrained. The relative timing of neck EMG and gaze shift responses suggest that elements downstream from the FEF delay gaze shift initiation without imparting a comparable delay on the cephalomotor command. Overall, the pattern of the cephalomotor drive evoked from the FEF is very similar to that evoked from the SC, showing that these structures play a similar role in evoked eye-head gaze shifts.

**FIG. 14.** A and B: correlations between parameters of evoked responses on extensor muscles (A: facilitation latencies; B: normalized peak evoked magnitude; C: suppression latencies) with vertical component of evoked gaze shift. Same format as Fig. 7. Subplots with * in top left portion show regressions that were significant. (A, proceeding left to right): Pearson’s $r = -0.17, P = 0.20, n = 63$; Pearson’s $r = 0.17, P = 0.14, n = 77$; Pearson’s $r = -0.28, P = 0.05, n = 45$; Pearson’s $r = -0.63, P < 10^{-5}, n = 53$. B: proceeding left to right: Pearson’s $r = 0.63, P < 10^{-5}, n = 63$; Pearson’s $r = -0.09, P = 0.44, n = 77$; Pearson’s $r = 0.74, P < 10^{-5}, n = 45$; Pearson’s $r = 0.73, P < 10^{-5}, n = 53$. C: Pearson’s $r = 0.25, P = 0.12, n = 39$; Pearson’s $r = 0.10, P = 0.76, n = 12$; Pearson’s $r = 0.41, P = 0.006, n = 44$; Pearson’s $r = 0.31, P = 0.02, n = 53$.)
findings resemble those from the feline FEF (Guitton and Mandl 1978a) and have important implications because most FEF stimulation studies are conducted head restrained, particularly because head restraint does not grossly alter the evoked neck EMG (Fig. 5). The absence of a gaze shift after FEF stimulation in the primate does not infer the absence of a motor command, even for relatively small gaze shifts (Fig. 11), but likely results as a consequence of the head’s substantial inertia. Preliminary evidence shows that neck EMG responses persist for stimulation currents far <50 μA (Elsley et al. 2006a). This cephalomotor component should be recognized, and if possible controlled for, in stimulation paradigms that manipulate high-level cognitive processes through sub-gaze threshold stimulation of the oculomotor system (see Cohen and Newsome 2004 for review).

Consistent with previous reports (Bruce et al. 1985), larger or smaller gaze shifts were evoked generally from more medial or lateral locations, respectively (Fig. 1C). Our results show that the cephalomotor drive varies continually with the size of the evoked gaze shift (Fig. 7). Very large neck EMG responses with similar qualitative patterning could also be evoked from areas rostral to the superior arm of the arcuate sulcus (Fig. 1C). Future recording studies will have to determine the role of this area in eye-head gaze shifts.

The timing and kinematics of evoked eye-head movements (Figs. 2 and 3) compare well with previous reports. Evoked gaze shifts began ~40 ms after stimulation onset, in good agreement with Tu and Keating (2000) (47.0 ± 2.4 ms) and Knight and Fuchs (2007) (31 ± 12 ms) but not Chen (2006) (91 ± 50 or 81 ± 48 ms, depending on task). Evoked head movements were initiated ~75 ms after stimulation onset, slightly longer than reported by Tu and Keating (2000) (58.3 ± 5.3 ms) and Knight and Fuchs (2007) (60 ± 16 ms) but shorter than reported by Chen (2006) (178 ± 60 ms). Finally, head motion contributed modestly to evoked gaze shifts, averaging 2.1 ± 1.9° of the horizontal component and 0.4 ± 0.4° of the vertical component.

Our trial-by-trial analysis of evoked neck EMG (Fig. 10) implies that it is causal to the ensuing head movement. Evoked neck EMG responses led head movements by ~40 ms, estimating the neuromuscular and biomechanical delays in head motion within our experiment. This 40-ms lag should not be regarded as a fixed value, because it will likely vary with different behavioral constraints and stimulation frequency and current. Regardless, the correlations between evoked neck EMG and the associated gaze shift (Fig. 7) are consistent with a functional relationship between evoked gaze shifts and head movements.

Our results agree with the conclusions of Tu and Keating (2000) and Knight and Fuchs (2007) that the primate FEF plays a role in controlling eye-head gaze shifts. How can we reconcile our findings with those arguing for independent control of the eyes and head in the FEF (Chen 2006)? We share the opinion of Knight and Fuchs (2007) that the differences may be caused in part by the paradigm used by Chen (2006) to dissociate the eye and head position before stimulation onset. Chen (2006) delivered FEF stimulation when head position was constrained within a computer-controlled window. Such stabilization may dampen the cephalomotor command and/or increase the stiffness of the head plant through co-contraction of the neck muscles. Either explanation is consistent with the prolonged lead times reported by Chen (2006) (head movements started on average 88 ± 53 ms after gaze shifts compared with 23 ± 34 ms reported here) and the shorter lead times (57 ± 59 ms) reported by Chen (2006) when stimulation was delivered when head position was unconstrained.

Large head movements can be evoked from the supplementary eye fields (SEFs) (Chen and Walton 2005) using the same behavioral paradigm as in Chen (2006). We have no explanation for this difference, but suspect it says more about the SEF, which seems to control movements differently than the SC and FEFs (Martinez-Trujillo et al. 2004; Monteon et al. 2006)

We also evoked head-only movements from the primate FEF that resemble those evoked from the SC (Corneil et al. 2002b; Pélisson et al. 2001). Head-only movements follow logically from the presence of neck EMG responses in the absence of gaze shifts (Fig. 11). Previous FEF studies have reported head-only movements (Chen 2006; Knight and Fuchs 2007; Tu and Keating 2000), particularly when the eye is deviated contralateral to the side of stimulation (such eye positions are associated with greater levels of neck EMG on the contralateral muscles before stimulation onset; Corneil et al. 2002a).

Comparison to previous studies from the SC

Head movements evoked by FEF stimulation fall consistently below the amplitude-velocity main sequences curves for volitional head movements (Chen 2006; Knight and Fuchs 2007), whereas those from the SC do not (Freedman et al. 1996). We speculate that the magnitude of neck EMG accompanying isometric gaze shifts is comparatively less when evoked from the FEF versus the SC. This difference may relate to the greater degree of topography in the SC. Adjacent FEF stimulation sites can evoke gaze shifts with very different directions (Bruce et al. 1985). Assuming the cephalomotor command evoked from either structure reflects an average of all sites stimulated (Lee et al. 1988), the greater heterogeneity of vector sizes and directions from the FEF would yield a damped cephalomotor command compared with the more homogenous population evoked from the SC.

Our findings are consistent with a topographically organized projection from the FEF to the SC (Komatsu and Suzuki 1985; Segraves and Goldberg 1987; Sommer and Wurtz 2000; Stanton et al. 1988). The facilitation latencies evoked from the FEF (16.5 ± 6.9 ms on contra-OCI) is ~3 ms longer than that evoked from the SC (13.4 ± 4.5 ms on contra-OCI; reported in Corneil et al. 2002a), consistent with ~2 ms required for axonal conduction between the FEF and SC (Everling and Munoz 2000; Segraves and Goldberg 1987; Sommer and Wurtz 1998) and a further 1 ms for synaptic processing. We cannot rule out the contribution of FEF efferent pathways that bypass the SC and access the brain stem more directly [e.g., the nucleus reticularis pontis caudalis (Huerta et al. 1986), which projects to the cervical spinal cord (Robinson et al. 1994)]. Frontal projections to the pontomedullary reticular formation housing reticulospinal neurons seem stronger in the cat, but may exist in the monkey (see Isa and Sasaki 2002 for review).

Comparison to our previous work in the SC (Corneil et al. 2002a,b) is facilitated by using the same gap paradigm (a direct comparison of recruitment magnitudes is not possible because different monkeys were used). Neural correlates of fixation
disengagement exist in the both the FEF and SC (Dias and Bruce 1994; Dorris and Munoz 1995), and gaze shifts from both structures are evoked more commonly or at lower currents when visual fixation is disengaged (Goldberg et al. 1986; Marrocco 1978; Opris et al. 2001; Paré et al. 1994; Sparks and Mays 1983; Tehovnik et al. 1999). Although neck EMG remains constant during the gap interval, the magnitude of neck EMG evoked by short-duration SC stimulation increases during the gap interval, mirroring the progressive disengagement of visual fixation (Corneil et al. 2007). Had we not used a gap interval, we speculate that the evoked neck EMG magnitudes would have been lower, but we have no reason to believe that the state of visual fixation would have influenced the gaze and head movement systems differentially. The very short neck EMG response latencies suggest that the evoked FEF activity is relayed directly to the brain stem, leaving little opportunity for voluntary modulation of the neck EMG response (recall, however, that the level of neck EMG before stimulation, which is under voluntary control, would influence both muscle recruitment and movement kinematics).

Finally, we found that evoked gaze shifts were larger when the head was unrestrained but that the magnitude of the eye movement did not systematically differ with head restraint (Fig. 3, E–G). This preliminary finding suggests that head-restrained eye movements are the eye movement components generated when the head is restrained, paralleling reports from the SC (Freedman et al. 1996; Paré et al. 1994). A stronger conclusion about the nature of eye movements evoked from the FEF awaits a more systematic examination across a variety of initial eye positions and head restraint.

Comparison to natural orienting head movements

A coarse comparison of amplitude-matched evoked versus volitional gaze shifts showed that evoked neck EMG reached far greater levels of activity regardless of head restraint and also displayed more oscillatory activity time-locked to stimulation onset (Fig. 6). These findings resemble those made from the SC; the unnatural appearance of neck EMG evoked from the SC has been considered elsewhere (Corneil et al. 2002b). Head movements evoked from the FEF or SC likely resemble natural head movements because of the head’s substantial inertia (Winters 1988; Zangemeister et al. 1981), despite substantial differences in the underlying neuromuscular commands.

Finally, although we observed rapid recruitment of a head turning synergy, extensor muscle recruitment occurred at longer and more variable latencies (Figs. 13 and 14). We speculate that unilateral FEF activation imposed by stimulation differs from the bilateral distribution of FEF activity accompanying volitional vertical gaze shifts (Bruce et al. 1985). Bilateral FEF stimulation, which can evoke vertical gaze shifts (Brucher 1966a), may elicit more rapid and consistent recruitment of the extensor musculature.

Is a postural or perceptual mechanism responsible for the evoked movements?

In the Introduction, we described four mechanisms that could account for head movements generated after FEF stimulation. The percept and postural mechanisms surmise that head movements are evoked indirectly by FEF stimulation, caused by either an elicited percept or an eccentric orbital position. Both mechanisms should now be rejected as the ultimate cause of head motion evoked from the FEF. The development of a percept presumably requires additional processing in sensory cortices, yet observed neck EMG response latencies approached the minimal conduction time from the FEF to the motor periphery. Neither mechanism explains why neck EMG and head movements should appear on trials without gaze shifts. (For the percept mechanism: if a percept is elicited, why program only a head movement? For the postural mechanism: why generate a head movement that increases the amount of orbital deviation?) Finally, both mechanisms predict that evoked neck EMG should resemble that accompanying a volitional gaze shift, because the evoked movements are programmed responses to either a percept or orbital deviation; neither mechanism is consistent with the distinct patterns of evoked neck EMG.

Although we can discount the percept mechanism as the cause of eye and head motion, a percept may well follow FEF stimulation (and neck muscle contraction may itself induce a percept). Chen and Tehovnik (2007) have recently reviewed the generation of phosphenes after stimulation of the visual cortex. Extensive projections interconnect the visual and frontal cortices (Bullier et al. 1996; Schall et al. 1995), and these projections presumably underlie the modulation of activity within extrastriate visual areas after FEF stimulation (Moore and Armstrong 2003). Although FEF stimulation elicits very rapid recruitment of the neck musculature consistent with a motor command, simultaneous activation of FEF projections to sensory cortices may inextricably produce accompanying percepts.

In this regard, we disagree with the contention of Chen and Tehovnik (2007) that supra-gaze threshold currents are necessary to study head motion; if anything, the direct and indirect spread inherent to larger stimulation currents and prolonged stimulation durations (McIlwain 1982; Stoney et al. 1968) complicates the interpretation of behavioral responses. At least in the SC and the FEF, recording neck EMGs permits insights into the neural programming of head movements at low currents (≤50 μA), even with the head restrained. The comparative biomechanics of the head means that the lack of head motion (either during or after a gaze shift) does not infer the absence of a cephalomotor command, nor the temporal uncoupling of eye and head motor programs.

The combination of stimulation and neck EMG is transferable to brain areas upstream from the FEF and SC and could establish the chronometry of the cephalomotor command, paralleling the assessment of signal timing across the visual system (Pouget et al. 2005; Schmolesky et al. 1998). Combining stimulation with neck EMGs could also help discern whether stimulation in other brain areas evokes sensory percepts or motor programs. It is possible that stimulation in areas projecting either directly or indirectly to the FEF (e.g., V1, middle temporal and medial superior temporal visual areas, and the inferotemporal cortex) will elicit neck EMG response latencies that are only slightly longer than after FEF stimulation, resemble the evoked patterns of neck EMG reported here, and be relatively immune from task demands, consistent with recruitment of the shortest path to the motor periphery. Alter-
natively, if stimulation in these areas induces percepts that influence subsequent behaviors, as traditionally assumed (Bradley et al. 2005; Ditterich et al. 2003; Murphey and Maunsell 2007; Nichols and Newsome 2002; Tehovnik et al. 2005), neck EMGs should develop much later, resemble volitional recruitment patterns, and change with the task at hand (e.g., in the case of V1 stimulation, neck EMGs should be associated with a saccade if the animal is trained to look to a phosphene, but absent if the animal is trained to maintain fixation).

Does FEF stimulation issue a gaze command or separate eye and head commands?

We now consider the two remaining mechanisms, which suggest that FEF stimulation evokes movements directly through projections to the oculomotor system. The salient difference between these mechanisms is whether FEF stimulation produces separate eye or head commands or a gaze command that is decomposed into eye and head commands downstream from the FEF. The weight of evidence presented in this paper supports the latter mechanism. Although our results do not completely rule out a separate channels mechanism, they necessitate modifications that are hard to reconcile with oculomotor physiology. First, because neck EMG is evoked from almost all FEF stimulation sites, the area of tissue activated by 50 μA of stimulation current would have to spread to both "eye-only" and "head-only" channels. Hence, the intermingling of any "eye-only" and "head-only" channels, if they do exist, must be less than the spread of activity at 50 μA (estimated at a radius of 200 μm; Stoney et al. 1968). "Head-only" channels would also be far more numerous than previously realized and interspersed throughout the entire FEF, making it improbable that previous studies activated "eye-only" channels selectively. Second, the intermingled "eye-only" and "head-only" channels would have to be organized topographically to explain the correlations between neck EMG parameters and gaze shift magnitude. Third, if the influence of the FEF is relayed through the SC (as for saccades; Hanes and Wurtz 2001), the separately encoded channels in the FEF would have to merge into a gaze command at the SC before being decomposed again into eye and head commands downstream from the SC (see Freedman et al. 1996 for the shortcomings of the separate channels hypothesis in explaining movements evoked from the SC). Although these modifications are not impossible, it is more parsimonious to conclude that a FEF gaze command is relayed through the SC.

Some FEF and SC neurons specifically encode head movements independent of gaze shifts (Bizzi and Schiller 1970; Walton et al. 2007). Could such neurons correspond to the "head-only" channel of the separate channels mechanism? We view this as unlikely. In both structures, head-only neurons are relatively infrequent (~25% in the SC; 15% in the FEF) and intermingled with more numerous saccade-related neurons. Arborizations from functionally identified saccade-related SC neurons terminate in the vicinity of spinal-projecting populations (see Isa and Sasaki 2002 and Scudder et al. 2002 for review), and preliminary evidence shows that low-frequency activity emitted by some SC saccade-related neurons selectively engages a head turning synergy before gaze shifts (Rezvani and Corneil 2006). Thus it is difficult to conceive that
FEF or SC stimulation activates head-only neurons selectively and that such neurons constitute the sole cephalomotor drive after stimulation.

Differences in timing of evoked cephalomotor and oculomotor responses

The cephalomotor command preceded the onset of oculomotor responses by \( \sim 20 \) ms. This finding implies that FEF stimulation recruits head premotor elements that are not subjected to the same control as gaze shifts (a similar conclusion follows from neck EMG responses on those trials without gaze shifts). Consider, for example, the sequence of events occurring on an average trial, with the neck EMG response beginning 17 ms after FEF stimulation onset, and the evoked gaze shift beginning another 17 ms later. Previous findings permit a number of estimations regarding the timing of recruitment of the eye and head premotor elements (Fig. 15; to be conservative, we will tend to overestimate the delays in the oculomotor circuit and underestimate the delays in the cephalomotor circuit). For example, we can surmise that \( \geq 2 \) ms are required for the conduction of action potentials along the axons of neck muscle motoneurons and the synaptic delay at the associated neuromuscular junction. Additionally, we can surmise that an additional 2 ms (more if a polysynaptic pathway is involved) are required from the activation of pontomedullary reticulospinal cells to the recruitment of neck muscle motoneurons. Thus activation of various head premotor cells occurs on average \( \sim 13 \) ms after FEF stimulation.

On the oculomotor side, the delay between the activation of extraocular motoneurons and the onset of eye motion is \( \sim 8.5 \) ms (Fuchs and Luschei 1970). These extraocular motoneurons are driven by burst neurons (BNs) of the saccadic burst generator, residing within the paramedian pontine reticular formation (PPRF) for horizontal saccades. A number of studies estimate that PPRF activation, which is synchronous with cessation of activity of omnipause neurons (OPNs), precedes saccade onset by \( \sim 11 \) ms (see Scudder et al. 2002 for review). This value is equally valid for saccades evoked by SC stimulation (Paul and Gnadt 2006). We therefore estimate that activation of the brain stem burst neurons occurs on average 23 ms after FEF stimulation.

These estimates imply that activation of head premotor elements precedes activation of the brain stem burst generation by \( \geq 10 \) ms. If we assume that SC activation begins \( \sim 3 \) ms after the onset of FEF stimulation, the primary reason for the timing differences in recruitment of eye and head premotor elements is the time required to silence the OPNs and activate the brain stem burst neurons. Supporting this, if the FEF or SC is stimulated during a saccade (when the OPNs are already inactive and the burst generator engaged), the consequences of stimulation are seen much sooner, within as little as 10 ms of stimulation onset in the SC or FEF (Marrocco 1978; Miyashita and Hikosaka 1996; Munoz et al. 1991; Slag-Rey et al. 1989). In this case, the durations of the cascades of polysynaptic events in the eye and head premotor pathways are approximately equal.

In conclusion, FEF stimulation recruits neck muscles before gaze shifts. The patterning and timing of such recruitment, and the similarities of that evoked from the SC, supports a role for the FEF in eye-head gaze shifts and implies that the FEF influences are relayed through the SC. Regardless of the functional pathways mediating this recruitment, the situation of the FEF at the interface between executive control centers within the prefrontal cortex and more dedicated motor circuits in the brain stem makes the FEF a logical place to examine how top-down signals sculpt the contextual flexibility of eye and head contributions to isometric gaze shifts.

ACKNOWLEDGMENTS

We thank Dr. S. Everling, B. Chapman, S. Hyder, S. Rezvani, and S. Stevenson for comments on earlier versions of the manuscript; two anonymous reviewers for constructive criticism; T. Admans for outstanding contributions to animal husbandry; and S. Rezvani for help in data collection.

REFERENCES


