Journal of Neurophysiology
Articles in PresS. J Neurophysiol (March 22, 2006). doi:10.1152/jn.01320.2005

FINAL ACCEPTED VERSION JN-01320-2005.R2

Head Movements Evoked by Electrical Stimulation in the Frontal Eye Field of the Monkey: Evidence for Independent Eye and Head Control

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Running Title: Independent eye and head control in FEF

Keywords: Frontal eye field; Head movement; Eye movement; Gaze shift; Microstimulation; Cortex

Words in Abstract: 249
Total pages of text: 29
Tables: 1
Figures: 11

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ABSTRACT

When the head is free to move, electrical stimulation in the frontal eye field (FEF) evokes eye and head movements. However, it is unclear whether FEF stimulation-evoked head movements contribute to shifting the line of sight, like visually guided coordinated eye-head gaze shifts. Here we investigated this issue by systematically varying initial eye (IEP) and head (IHP) positions at stimulation onset. Despite the large variability of IEP and IHP and the extent of stimulation-evoked gaze amplitudes, gaze displacement was entirely accounted for by eye (re head) displacement. Overall, the majority (3/4) of stimulation-evoked gaze shifts consisted of eye-alone movements, in which head movements were below the detection threshold. When head movements did occur, they often started late (re gaze shift onset) and coincided with rapid eye deceleration, resulting in little change in the ensuing gaze amplitudes. These head movements often reached their peak velocities over 100 ms following the end of gaze shifts, indicating that the head velocity profile was temporally dissociated from the gaze drive. Interestingly, head movements were sometimes evoked by FEF stimulation in the absence of gaze shifts, particularly when IEP was deviated contralaterally (re the stimulated side) at stimulation onset. Furthermore, head movements evoked by FEF stimulation resembled a subset of head movements occurring during visually guided gaze shifts. These unique head movements minimized the eye deviation from the center of the orbit and contributed little to gaze shifts. The results suggest that head motor control may be independent from eye control in the FEF.

INTRODUCTION

The frontal eye field (FEF) extends from the caudal to the anterior end of the arcuate gyrus (Bruce et al. 1985; Schall et al. 1995). Past studies have shown that this region is associated with the initiation of eye movements (Bizzi and Schiller 1970; Bruce et al. 1985; Dias and Segraves 1999; Goldberg et al. 1986; Keating and Gooley 1988; Robinson and Fuchs 1969; Schall 2002; Schiller et al. 1979; Smith 1949; Sommer and Tehovnik 1997; Tehovnik et al. 2000; van der Steen et al. 1986). Whether the FEF participates in generating head movements is not clear. In an early anecdotal observation, Levinsohn (1909, described in Smith 1949) reported that stimulation in the dorsomedial frontal cortex, i.e. the supplementary eye field (SEF) as identified today, evoked head movements that often preceded eye movements. In contrast, this was not observed in the lateral oculomotor region, i.e. the FEF as identified today. Levinsohn noted this unique characteristic as the major difference between dorsomedial and lateral oculomotor regions of the frontal cortex, i.e. the SEF and the FEF.

Past studies have revealed some seemingly conflicting findings regarding whether the FEF is involved in the control of head movements (Bizzi and Schiller 1970; van der Steen et al. 1986). Van der Steen et al. (1986) conducted a unilateral FEF lesion study in head-unrestrained monkeys and found that the lesioned monkeys were reluctant to track objects in the contralateral visual field. When the monkeys did track visual targets, the monkeys moved their heads more often than their eyes. When gaze shifts occurred, the accompanying head amplitudes were atypically large and eye (re head) amplitudes were small. At gaze completion, the eye was often counter-rotated rapidly to near the center of the orbit, unlike its pre-lesion behavior. These findings were interpreted by the authors as indicating that FEF lesions led to selective *eye* movement deficits.

Bizzi and Schiller (1970) recorded the neuronal activity in the FEF of head-unrestrained

monkeys. They found that, in agreement with the role of FEF in eye movement control, FEF neurons discharged in association with eye movements. However, they also found an unusual type of neuron that discharged *exclusively* during head movements. Even though the exact characteristics and anatomical connectivity of FEF *head* neurons have not been identified, the presence of the head movement-related discharge in FEF neurons remains an enigma in the understanding of FEF function (cf. Knight and Fuchs 2001; cat FEF: Guitton and Mandl 1978).

Recent development of experimental techniques in head-unrestrained monkeys has made it possible for investigators to revisit the issues of motor control in head-unrestrained conditions (Chen and Walton 2005; Collins and Barnes 1999; Corneil et al. 2002; Cullen et al. 2004; Crawford and Guitton 1997; Freedman and Sparks 1997; Gandhi and Sparks 2001; Goffart et al. 1998; Goossens and van Opstal 1997; Guitton et al. 2003; Isa and Sasaki 2002; Martinez-Trujillo et al. 2003; Peterson 2004; Phillips et al. 1995; Stahl 2001; Sparks et al. 2001; Waitzman et al. 2002). A recent study (Tu and Keating 2000) reported that FEF stimulation evoked both eye and head movements. The authors noted that, at low current intensity (25 μA), FEF stimulation evoked eye movements. When the stimulation intensity was increased to 200-300 μA, stimulation evoked gaze shifts accompanied by head movements. However, these head movements were too small (4.3° ± 0.4° in Tu and Keating 2000) to contribute significantly to gaze shifts. These findings raise new questions regarding the exact role of head movements evoked by FEF stimulation.

The present study addressed the following questions. First, does FEF stimulation evoke head movements? If so, do stimulation-evoked head movements contribute to shifting the line of sight (i.e. gaze)? In other words, is the FEF involved in *gaze* (*eye* plus *head*) feedback control? *Gaze feedback hypothesis* has been postulated to account for the head involvement in large orienting gaze shifts (Guitton et al. 1990, 2003; Laurutis and Robinson 1986). The hypothesis

states that the gaze error (difference between *current* and *desired* gaze displacements) signal drives both eye and head movements, such that the range of gaze displacement is extended beyond the range accomplished by eye (re head) displacement alone. This explanation accounts for the fact that large visually guided gaze shifts (e.g. gaze amplitude ≥ 20°) usually recruit significant contribution of the head (Freedman and Sparks 1997; Fuller 1992; Galiana and Guitton 1992; Guitton et al. 1990, 2003; Laurutis and Robinson 1986; Tomlinson and Bahra 1986). On the other hand, according to this hypothesis, there exists a temporal coupling between head and gaze velocities. As the gaze error diminishes by *the end of gaze shifts*, the drive to move the head will diminish and head velocity will begin to decrease (Guitton et al. 1990, 2003; Matsuo et al. 2004). Therefore the head should reach its peak velocity *prior to*, as opposed to hundreds of ms following, the end of gaze shifts. The present stimulation study provided an opportunity to evaluate these predictions in the FEF.

Note that *head contribution to gaze shifts* is limited to the head displacement between gaze shift onset and gaze shift offset, during which the vestibuloocular reflex (VOR) is suppressed in order for the eyes and head to move in the same direction (Cullen et al. 2004; Guitton et al. 1990). The total *head displacement* additionally includes the head movement which may occur *prior to* the onset of gaze shift (VOR gain ≈ 1) and the head movement which often lasts beyond the end of gaze shift (VOR gain ≈ 1) (Bizzi et al. 1971; Chen and Walton 2005; Corneil et al. 2002; Freedman and Sparks 1997; Guitton et al. 1990; Tomlinson and Bahra 1986). Both monkeys used in the present study had previously participated in a SEF study (Chen and Walton 2005), in which stimulation evoked significant contribution of the head to gaze shifts. It is pertinent to know whether differential motor control mechanisms exist in the two eye fields of the *same* monkeys under the *same* task controls.

Second, does FEF stimulation evoke head movements independent of gaze shifts? Recent studies have shown that low current stimulation in the superior colliculus (Corneil et al. 2002; Pelisson et al. 2001) or stimulation at contralateral eye positions in the SEF evoked head movements in the absence of gaze shifts (Chen and Walton 2005). In addition, stimulation-evoked *postgaze-shift* head movements (i.e., the head displacements between gaze shift offset and head offset) in the SEF facilitated re-centering the eyes in the orbits (Chen and Walton 2005). It is pertinent to know under what circumstances FEF stimulation evokes head-alone movements and whether stimulation-evoked postgaze-shift head movements minimized the eye deviation from the center of the orbit (Sparks et al. 2001).

It has been shown that initial eye (IEP) and head (IHP) positions are pertinent variables that determine the metrics of head movements (Chen and Walton 2005; Delreux et al. 1991; Freedman and Sparks 1997; Goossens and van Opstal 1997; Phillips et al. 1995; Tomlinson and Bahra 1986; Volle and Guitton 1993). In this study, IEP and IHP were systematically varied for the sake of assessing FEF stimulation-evoked head movements. We found that FEF stimulation indeed evoked head movements in addition to eye movements; however, the head movements contributed little to shifting the line of sight. The findings agree with early studies and suggest that head motor control may be independent from eye control in the FEF.

METHODS

Subject and experimental procedures. Two juvenile rhesus monkeys (*Macaca mulatta*, 5-7 kg) served as subjects. They were implanted with a chamber (angled 15° from the midsagittal plane) and head-posts. The details of the surgical implants, chairing setups, and neurophysiological procedures have been described previously (Chen and Walton 2005). All surgical and experimental

procedures conformed to the guidelines for the Care and Use of Animals of National Institutes of Health and the Institutional Animal Care and Use Committee.

Eye and head positions were tracked using the search coil technique (Fuchs and Robinson 1966; Judge et al. 1980). A 42" cubic coil and a phase-angle detection system (CNC Engineering Inc.) were used to measure horizontal and vertical position signals of gaze (eye re space) and head coils, sampled at 500 Hz. During recording, a lightweight microlaser (Edmund Scientific Inc. #M52263) was mounted on the monkey's head to provide the visual feedback of head positions. The signals of gaze and head coils were calibrated under conventional, head-fixed conditions based on the alignment of gaze and head coil signals with the visual targets of known positions. Eye (re head) positions were computed off line by mathematically converting horizontal and vertical *gaze* coil signals to unit vectors, rotated with respect to *head* vectors in Fick coordinates. Movement amplitude was computed following vector rotations. Data were acquired using a Pentium microcomputer running in-house data acquisition software.

Standard microelectrodes (Frederic Haer, Inc.) were used to penetrate dura, record neuronal signals, and deliver electrical stimulation (for details, see Chen et al. 2001). Neural signals were band-pass (500 – 5 kHz) filtered using a differential BAK amplifier. Microstimulation was carried out using a stimulator (Grass S88) and an optical isolation unit (Grass PSIU6). The stimulation trains consisted of 0.2-ms, monopolar, cathodal pulses. Typical stimulation was 80 μA (range: 50 - 150 μA), 200 Hz (range: 100 - 200 Hz), and 300 ms (range: 300 - 500 ms). Prolonged stimulation ensured that the movements of interest (i.e. head movements) were *not* truncated prematurely (for review, see Freedman et al. 1996; Graziano et al. 2002). When necessary, stimulation of different parameters was explored. Since the threshold of stimulation-evoked *head* movements in the FEF was not known, we typically applied stimulation of 2-3X the threshold current (i.e., the current that

evoked movements in 50% of the trials) for eliciting *eye* movements. It was difficult to monitor the actual current delivered through the high-impedance electrodes (0.5 – 1.2 MΩ measured in saline at 1 kHz). All of the current intensity reported here was taken from the face value of the stimulator.

Behavioral paradigms and microstimulation. Visual targets were presented on a tangent screen with 49 x 41 tri-state (red, green, yellow) light-emitting diodes (LEDs). The LEDs were equally spaced at 2 inch intervals in both horizontal and vertical dimensions. The LED board was placed 72 cm (28.5 inches) from the monkeys. The room was dimly lit with a 5W light bulb behind the LED board.

The monkeys were trained in a visually guided gaze shift task that permitted independent control of gaze and head positions (Fig. 1A). The behavioral task consisted of two phases: an initial eye/head alignment-and-dissociation phase and a subsequent visually guided gaze shift phase. The initial phase began with monkeys sitting in head forward positions, aligning the microlaser beam with a visual target (red LED). Later, a second (green) target was illuminated, and the monkeys deviated their eyes to the target while maintaining a stable head position. The green target was usually displayed in ≤ 27° steps horizontally or vertically with respect to the initial red target (e.g., Fig. 1C). 600-800 ms following the onset of the green target, all targets and the microlaser were extinguished for 400-500 ms. The same red and green targets and microlaser beam were re-illuminated briefly (500-700 ms) and then re-extinguished.

The visually guided gaze shift phase began 400 - 600 ms following the end of the first phase (Fig. 1A). A yellow target was illuminated at a randomly chosen location. Juice reward was contingent upon monkeys making a gaze shift to the yellow target. Note that the location of the yellow targets was spatially (up-down and left-right) balanced and selected at random in order to minimize any directional bias of movements. Likewise, the red and green targets mentioned in the

initial task phase were spatially balanced and selected at random.

In the control trials (Fig. 1A), gaze and head positions were constrained under close-loop real-time control within a 5°- and 10°-radius "window," respectively, around the designated targets. If either gaze or head stepped outside of the window during the designated periods, the trial was aborted.

In ~50% of the trials within a block, electrical microstimulation trials (Fig. 1B) were carried out. Stimulation trials began with the initial eye-head alignment-dissociation task just like that in the control trials. The electrical stimulation phase began with stimulation 200 ms following the extinction of both visual targets and microlaser. The entire stimulation phase was conducted in darkness without constraint over the eye or head positions. Approximately 800-1400 ms following the end of stimulation, the visually guided gaze shift phase began. Reward was contingent upon the monkey making a gaze shift to a visual (yellow) target, as in the control trials.

Figure 1C illustrates schematic examples of head, gaze, and eye positions independently controlled in "EHD (eye-head dissociation)" and "EHA (eye-head alignment)" trials. In the EHD example trial, the eyes were oriented in upper-right direction, while the head remained centered with respect to the body. In the EHA example trials, the head was oriented leftward with respect to the body, while the eyes remained centered in the orbit.

In some large-saccade sites, we carried out *nontask-mode* stimulation, in which the stimulation train was delivered during the inter-trial interval (duration: 500 - 1500 ms). Nontask-mode stimulation trials were 50% interleaved with task-mode stimulation trials. Unlike the latter, there was no visual target or microlaser illuminated in the former. There was no IEP or IHP constraint throughout the nontask-mode stimulation trials.

Care was taken to exclude the data obtained in stimulating the white matter from the

analyses. The electrodes were always advanced deep, and the border between gray and white matter was identified based on the overall diminished unit discharge. Once the electrode was confirmed to have reached the white matter, the electrodes were then slowly withdrawn. Stimulation was carried out > 100 μm away from the border of the white and gray matters. Because it was impossible to know whether a given electrode penetration was parallel, orthogonal, or oblique with respect to the cortical surface, we considered the stimulation depth separated by 500 μm as *different* sites. The evoked movements in different sites were analyzed separately.

Data analyses. Data analyses were performed using an in-house program on a Windows platform. Movement onset and offset were determined based on the velocity criteria (gaze: 80 °/s for horizontal and vertical onsets and 60 °/s for horizontal and vertical offsets; head: 6 °/s for both horizontal and vertical onset and offset). For details of the offline threshold-filter computation, see Chen and Walton (2005). Movements were displayed 100 ms before and 800 ms following stimulation onset, and measurements were taken strictly based on the velocity criteria. Any movement detected before stimulation onset was removed from further analysis. Throughout this paper, only stimulation-evoked gaze shifts and head movements with onset latency ≤ 300 ms were included in the analysis. The criterion of minimal onset latency for gaze shifts and head movements was 20 and 50 ms, respectively.

Staircase small-saccade (< 10°) gaze shifts were occasionally encountered. These trials were excluded from further analysis. Statistical analyses were performed using Statistica (Statsoft Co.). Throughout this paper, the data are described and plotted as mean ± S.D..

At the end of the experiments, the monkeys were sacrificed with an overdose of pentobarbital and the brains were removed for histological examination. Stainless-steel pins were inserted in known coordinates during perfusion in order to facilitate coordinate reconstruction.

RESULTS

A total of 132 (M1: 111, M2: 21) stimulation sites (56 penetrations; M1: 49, M2: 7) were studied in the left FEF of two head-unrestrained monkeys. The low-threshold saccadic sites in the FEF were identified based on stimulation-evoked staircase saccades and smooth pursuit from the caudal end of the arcuate sulcus (Bruce et al. 1985; Fukushima et al. 2000; MacAvoy et al. 1991; Russo and Bruce 1993; Tehovnik et al. 2000). This study was aimed at large-saccade sites in the FEF, as large-amplitude gaze shifts were likely to recruit significant head movements (Guitton et al. 1990; Sparks et al. 2001; Tomlinson and Bahra 1986).

In one of the monkeys, the FEF was meticulously mapped along the rostral-caudal dimension (Fig. 2A). Consistent with the notion that the FEF is topographically organized as a saccadic amplitude map, we found that large saccades were evoked in the rostral sites and small saccades and smooth pursuits were evoked in the caudal sites (Bruce et al. 1985; Fukushima et al. 2000; MacAvoy et al. 1991). Stimulation-evoked gaze shift sites stretched ~10 mm rostro-medially from the small-saccade and smooth pursuit sites. We exhausted the mapping up to 2 mm anterior from the most rostral large-saccade sites of the FEF. There was no evidence of site-specific head movement clustering in the FEF.

Figure 2B illustrates example traces of the stimulation-evoked horizontal gaze (Gh), eye (Eh, re head), and head (Hh) positions and velocities of a staircase, small-saccade (caudal) site in the FEF. These short-latency staircase saccades were evoked by prolonged stimulation (500 ms). The peaks of horizontal gaze and eye velocity traces were truncated to facilitate the display of horizontal head velocity profiles. During the gaze shift (Fig. 2B, shaded region), horizontal gaze and eye velocity traces completely overlapped, while horizontal head velocity remained near baseline. The result, in agreement with past studies, confirmed that small gaze shifts (Gh

amplitude= 4.8° in Fig. 2B) often do *not* recruit a significant contribution of the head.

Figure 2C illustrates example traces of the stimulation-evoked movements in a large-saccade site of the FEF. Two main features can be noted. First, following gaze shift onset, the head position trace deviated from its baseline slowly. It was impossible to detect head movement onset based on visual inspection of the head position trace. Second, during the gaze shift, the horizontal gaze position almost completely overlapped the horizontal eye (re head) position. Approximately 15 ms before gaze completion, the head started to move above the velocity threshold. Note the eye movement decelerated rapidly toward the end of the gaze shift; hence, the head movement contributed little to the resultant gaze displacement.

The head movement reached its peak velocity (45 °/sec) ~110 ms following the end of gaze shifts. The gaze position following gaze shifts was stable, i.e. the eye counter rotated in the orbit approximately by same velocity as the head (VOR gain ≈ 1). Both examples illustrated in Figure 2 (B and C) were obtained when IEP was centered in the orbit and IHP was centered with respect to the body.

Our results indicate that the characteristics of stimulation-evoked movements varied depending upon IEP and IHP at stimulation onset. Particularly, "*eye alone,*" "*eye and head,*" and (occasionally) "*head-alone*" movements could be evoked by FEF stimulation at a given large-saccade site. This point will be elaborated below.

Kinematics of stimulation-evoked gaze shifts and head movements

Figure 3 plots the relationship between movement amplitudes and velocities of the stimulation-evoked gaze shifts (A and B) and head movements (C and D) in the FEF. For the sake of data comparison between task conditions, gaze shifts were separated into EHD (left) and EHA

(middle) trials (see METHODS). In EHD trials, IEP at stimulation onset ranged -28: 28° horizontally and -25: 28° vertically. In EHA trials, IHP at stimulation onset ranged -32: 32° horizontally and -12: 28° vertically. All stimulation trials of both monkeys were pooled in the analysis. Several kinematic characteristics can be noted.

First, the range of horizontal and vertical gaze amplitudes varied widely during EHD (n = 2,973) and EHA (n = 1,703) trials (Fig. 3A). In contrast, head movements varied over a smaller range (n = 1,203; Fig. 3C). The average horizontal head amplitude was 4.3 ± 2.9°, while the average vertical head amplitude was 1.0 ± 1.9° (slope = 0.07; r = 0.21, $P < 0.001$).

Second, unlike the peak velocity of horizontal *gaze shifts* which could be as high as 1000 °/sec (Fig. 3B), the peak velocity of horizontal *head movements* never exceeded 100 °/sec. The peak velocity of horizontal head movements was linearly correlated with horizontal head amplitude (slope = 3.57; r = 0.89; $P < 0.01$), as has been reported for the head movements occurring during visually guided gaze shifts (Freedman and Sparks 1997; Guitton et al. 1990).

Third, like stimulation-evoked gaze shifts that were primarily contralateral, the vast majority (98.4%; 1,184/1,203) of stimulation-evoked head movements was directed contralaterally with respect to the stimulated side. The remaining had small (-1.7 ± 0.9°) head movements in the ipsilateral direction.

Finally, less than 1/4 (23% [694/2,973] in EHD trials and 23% [396/1,703] in EHA trials) of stimulation-evoked gaze shifts were accompanied by head movements. In most of the trials, *eye-alone* movements were observed, i.e., head movements were below the velocity threshold (see METHODS).

Eye alone movements. The range of horizontal gaze amplitudes varied significantly as a function of eye position, 0.8: 49° (23 ± 8°; n = 1,154), 0.1: 43° (11 ± 7°; n = 900), and 0.1: 20° (4 ±

3°; n = 212) for IEPi (IEPh ipsilateral to the stimulated side), IEPo (IEPh centered in the orbit), and IEPc (IEPh contralateral to the stimulated side) conditions, respectively. The range of vertical gaze amplitudes was –39: 47° (19 ± 14°), -20: 53° (13 ± 8°), and –14: 39° (8 ± 7°) for IEPi, IEPo, and IEPc conditions, respectively. The orbital effect resembles that observed under head-unrestrained conditions (Russo and Bruce 1993).

Effects of varying horizontal IEP

Figure 4 illustrates the movement traces showing the effects of varying horizontal IEP (IEPh) on horizontal head and gaze velocities following electrical stimulation in a FEF site. The trials were grouped by IEPh conditions. Five traces (two of high peak velocities, two of low peak velocities, and one of medium peak velocity) were selected to represent horizontal head and gaze velocity profiles for each IEPh condition. In these trials, IHP remained centered with respect to the body (the range of horizontal and vertical IHP: -8: 8°). Only IEPh was systematically varied. The range of IEPh was -28: -15°, -10: 10°, and 15: 28° in IEPi, IEPo, and IEPc conditions, respectively.

Three main features of movement timing and dynamics can be noted in Figure 4. First, the likelihood for FEF stimulation to evoke head movements varied depending on horizontal IEP. In IEPi condition (Fig. 4, left), head movements were *not* detectable even though the current intensity was increased up to 150 μA (lower-left). In contrast, in IEPo (Fig. 4, middle) and IEPc conditions (Fig. 4, right), stimulation did evoke head movements in ~1/3 of the trials. Second, when stimulation did evoke head movements, head movement onset often lagged behind gaze shift onset. Third, head velocities often did not reach their peaks until after gaze shifts were completed. The velocity profile of the *late* head movements can be best appreciated in IEPc trials.

To quantify the effect of varying horizontal IEP on eye and head contributions to gaze

shifts, *eye-and-head* movements were selected for further analyses (Fig. 5; Table 1). Overall, eye-and-head movements represented <5%, 21%, and 32% of the stimulation-evoked gaze-shift trials in IEPi (n = 1,214), IEPo (n = 1,149) and IEPc (n = 552) conditions, respectively. That is, the probability of evoking head movements in FEF stimulation increased as horizontal IEP was deviated in the contralateral direction (i.e. the direction of the stimulation-evoked gaze shifts).

Figure 5E illustrates the results of eye and head contributions to gaze shifts. Regardless of the variability of horizontal and vertical IEPs, eye (re head) amplitudes were linearly correlated with gaze (Gh) amplitudes (Figs. 5E and F). That is, horizontal and vertical amplitudes of eye (re head) movements totally accounted for horizontal (Fig. 5E) and vertical (Fig. 5F) amplitudes of gaze shifts, respectively. Horizontal (Fig. 5E) and vertical (Fig. 5F) contribution of the head to gaze shifts was negligible.

Effects of varying horizontal IHP

Figure 6 illustrates the movement traces showing the effect of horizontal IHP (IHPh) on the horizontal head and gaze velocities in a large-saccade site of the FEF. In these experiments, IEP remained within ± 8° centered in the orbit, and IHP was systematically varied. These trials were grouped by IHPh (IHPi [ipsilateral IHPh; range: -32: -20°], IHPo [IHPh centered; range: -10: 10°], and IHPc [contralateral IHPh; range: 20: 32°]) conditions. Five traces (two of high peak velocities, two of low peak velocities, and one of medium peak velocity) were selected to represent the horizontal head and gaze velocity profiles of each IHP group.

Four major features of movement kinematics can be noted in Figure 6. First, in IHPc condition (Fig. 6, right), the head was already significantly deviated in the direction of stimulation-evoked movements; hence, the stimulation failed to evoke any detectable head movement. Second,

head movements were mostly evoked when the head was centered relative to the body (IHPo [Fig. 6, middle] or deviated toward the stimulated side (IHPi [Fig. 6, left]). Horizontal head velocities often did not rise above the velocity detection threshold until near the end of gaze shifts (arrowheads). This result resembled those observed in EHD trials (Fig. 4). Third, head movement velocity remained relatively low (≤ 25 °/sec) near the end of gaze shifts. The apparent dissociation between head velocities and gaze velocities can be appreciated during two staircase gaze shifts (∇; Fig. 6). In both examples, the horizontal gaze displacements was ≥ 50° (≥ 30° and ≥ 20° for the first and second gaze shifts, respective). Note that despite the fact that the head was in motion and thus could easily accelerate, head velocity profile was *not* altered during the second stimulation-evoked gaze shift. Finally, head movements often reached their peak velocities >> 50 ms following gaze offset (Fig. 6, left and middle).

Figure 7 quantifies the effects of varying IHP on the stimulation-evoked movements of all trials (n = 1,694) of all sites (n = 26; M1= 19, M2= 7). The probability for FEF stimulation to evoke eye-and-head movements was 58%, 21%, and 10% for IHPi (n = 106), IHPo (n = 1,528), and IHPc (n = 60) conditions, respectively (Table 1). The horizontal amplitude of gaze shifts in 90% of these trials was less than 26°. Horizontal gaze displacement was totally accounted for by horizontal eye displacement (Fig. 7C, □). Head contribution to horizontal (Fig. 7C, gray *) and vertical (data not plotted) gaze shifts was negligible.

Nontask-mode stimulation

Nontask-mode stimulation was conducted in 12 large-saccade sites (M1= 7; M2= 5) in the FEF (see METHODS; Fig. 7). In these trials (n = 444), the range of IHP at stimulation onset was –31: 32°. At this IHP range, the range of horizontal IEP was –21: 26° in the orbit.

Half (51%; n = 227/444) of these were *eye-alone* movements, the remaining were *eye-and-head* movements. In the latter movements, the maximal horizontal gaze amplitude was 31° (Fig. 7D), whereas the maximal horizontal head amplitude was 16° (Fig. 7E; Table 1). However, given comparable metrics, head contribution to stimulation-evoked horizontal gaze shifts remained negligible (Fig. 7F, bottom, +). Horizontal gaze displacement was entirely accounted for by horizontal eye displacement (Fig. 7F, bottom, □).

Visually guided gaze shifts

Figure 8 illustrates the metrics of visually guided *eye-and head* movements (n = 2,931; M1: 1,557, M2: 1,374). These visually guided movements were obtained following the yellow target in the control and stimulation trials (see METHODS). There were three major differences in the eye-head coordination between visually guided and stimulation-evoked movements.

First, for visually guided gaze shifts, horizontal head amplitudes were a monotonic function of horizontal gaze amplitudes (e.g. Freedman and Sparks 1997; Phillips et al. 1995; cat: Guitton et al. 1990). When horizontal gaze shifts were 25-35° in IEPo condition, the average horizontal amplitude of the head was 17 ± 8° (n = 301; Fig. 8A, top). In contrast, given comparable horizontal gaze amplitudes, the average horizontal amplitude of FEF stimulation-evoked head movements was only 5 ± 3° (n = 60). The difference was highly significant ($F = 130$, $P < 0.001$).

Second, for visually guided gaze shifts, small, but significant vertical head movements were often observed. For example, when the vertical amplitude of gaze shifts was 25-35° in IEPo condition, the average vertical amplitude of the head was 11 ± 8° (n = 401, Fig. 8B, top). In contrast, given comparable vertical gaze amplitudes, the average vertical amplitude of FEF stimulation-evoked head movements was only 1.3 ± 1.2° (n = 20). The difference was significant (F

= 34, P < 0.001).

Third, head contribution to visually guided horizontal gaze shifts was a function of horizontal gaze amplitudes and horizontal IEP in the orbit (Fig. 8A, bottom). For example, when the horizontal amplitude of gaze shifts was 50° in IEPo condition, the contribution of the head was as large as 13°. In contrast, we never observed FEF stimulation-evoked gaze shifts as large as 50° in horizontal amplitude in IEPo condition. When horizontal amplitude of visually guided gaze shifts was 25-35° in IEPo condition, the average contribution of the head was 4 ± 2° (n = 301; Fig. 8A, bottom). In contrast, given comparable horizontal gaze amplitude, the average head contribution to FEF stimulation-evoked gaze shifts was only 0.6 ± 0.5° (n = 60). The difference was highly significant (F = 139, P < 0.001).

Timing difference between head movement onset and gaze shift onset

Head movement onset varied systematically as a function of horizontal IEP (Fig. 9A) and IHP (Fig. 9B), whereas gaze shift onset remained consistent across EHD and EHA trials. There was a significant correlation between head movement onset and IEPh (Fig. 9A) or IHPh (Fig. 9B). There was no significant correlation between gaze shift onset and IEPh (Fig. 9A) or IHPh (Fig. 9B).

Figure 9C illustrates the relative onset of eye and head movements between stimulation-evoked and visually guided *eye-and-head* movements. The vast majority of the trials (98% [681/651] in EHD trials, 99% [404/410] in EHA trials, and 95% [202/213] in nontask-mode stimulation trials**)** exhibited positive values, i.e., head movement onset lagged behind gaze shift onset. On average, head movement onset lagged gaze shift onset by 86 ± 58 ms, 88 ± 53 ms, and 57 ± 49 ms in EHD, EHA, and nontask-mode stimulation trials, respectively. Head contribution to

horizontal gaze shifts was negligible regardless of the latency difference between head and gaze shift onsets (EHD trials: slope = 0.00; r = 0.51; EHA trials: slope = –0.01; r = 0.60; nontask-mode trials: slope = -0.01; r = 0.54).

Peak velocity latencies of head movements

Figure 10 quantifies the latency difference between gaze shift offset and the peak velocities of head movements. Only the trials of head amplitude ≥ 2° were selected for analysis. Over 90% of stimulation trials (98% [567/576] in EHD trials and 97% [300/311] in EHA trials) exhibited positive values (Figs. 10A and B; H ≥ 2, □). This indicates that the vast majority of head movements reached their peak velocities *following* gaze completion. The average peak velocity of head movements of all stimulation (EHD and EHA) trials combined was 136 ± 91 ms, and the *mode* of the distribution fell on the 121-130-ms bin.

One may wonder whether head movements of relatively large amplitudes might reach their peak velocities near the end of gaze shifts. Figures 10A and B (■) plots the distributions when only the stimulation-evoked head movements of ≥ 5° were considered. The average peak velocity of head movements of all stimulation (EHD and EHA) trials combined was 150 ± 102 ms, and the distribution peak fell on the same 121-130-ms bin. In other words, regardless of whether the head movements were small or large, the distribution exhibited peaks at comparable latencies.

The next question is under what circumstances do visually guided gaze shifts recruit head movements similar to those observed by FEF stimulation. We analyzed the visually guided movements with comparable horizontal gaze amplitudes (≤ 42°) and total head amplitude (≥ 2°) (Fig. 10C. □). The average peak head velocity latency of these visually guided movements was 69 ± 85 ms (n = 2,631), which was significantly different from that evoked by FEF stimulation (t = 14;

$P < 0.001$).

Further analysis indicates that different subsets of visually guided gaze shifts recruited head movements of different peak velocity latencies. When the horizontal contribution of the head was ≥ 2° (Fig. 10C; ■), the average latency of the peak head velocity (re gaze offset) was 24 ± 45 ms (n = 1,192). When the horizontal contribution of the head was ≤ 1° (Fig. 10C, ▒), the average latency of the peak head velocity was 129 ± 96 ms (n = 781). The difference between the two distributions was highly significant ($t = 33$; $P < 0.001$). The latter distribution was *not* significantly different from that of stimulation-evoked eye-head movements ($t = 1.5$; $P > 0.10$).

Postgaze–shift head displacement

Horizontal postgaze-shift head displacement (Hpgh) was defined as the head displacement between gaze completion and when the head stopped moving. Hpgh was positively correlated with horizontal eye position at gaze offset in EHD and EHA trials (Fig. 11). The data of the two trial types overlapped each other (ANCOVA, homogeneity-slope model; $F = 3$, $P > .07$). However, compared to visually guided gaze shifts, FEF stimulation-evoked head movements were smaller. When the eye position following gaze completion was approximately 20°, the average Hpgh in visually guided movements was ~10°, whereas the average FEF stimulation-evoked Hpgh was significantly smaller (~4°). Overall, there was a significant difference between FEF stimulation-evoked Hpgh and visually guided Hpgh (ANCOVA, homogeneity-slope model, $F = 810$, $P < 0.001$).

Head alone movements. FEF stimulation sometimes evoked head movements in the absence of gaze shifts (e.g. the fourth IEPc trial in Fig. 4). Nearly all (99%; 308/311) of these head-alone movements were obtained in IEPc condition; the average horizontal amplitude of the

head was 5 ± 2° (range: 2: 18°). The remaining movements (2 trials at IEPh ≈ 0° and 1 trial at IEPh ≈ 13°) had a relatively smaller horizontal amplitude of the head (2.4 ± 0.2°) compared to those obtained in IEPc condition. The displacement of *head-alone* movements as a function of eye position at head movement onset (●) is superimposed on Figure 11. It can be noted that, when eye positions were >10° contralateral to the stimulated side, the data points of head-alone movements fell on top of those of EHD and EHA trials. Compared to visually guided gaze shifts, head-alone movements contributed less to minimizing the eye deviation from the center of the orbit (ANCOVA, homogeneity-slope model; $F = 578$, $P < 0.001$).

DISCUSSION

The present study provides several lines of evidence indicating that FEF stimulation-evoked head movements contributed little to shifting the line of sight. First, despite the large variability of IEP and IHP and the extent of stimulation-evoked gaze amplitudes, gaze displacement was entirely accounted for by eye (re head) displacement. The majority (3/4) of stimulation-evoked gaze shifts consisted of eye-alone movements, in which head movements were below the detection threshold. When head movements did occur during stimulation-evoked gaze shifts, head movement onset often lagged gaze shift onset and coincided with rapid eye deceleration. This resulted in little change in the ensuing gaze amplitudes. Second, head velocities were temporally dissociated from gaze velocities. Unlike visually guided coordinated eye-head gaze shifts in which head movements often reached their peak velocities near the end of gaze shifts, FEF stimulation-evoked head movements often reached their peak velocities > 100 ms following the end of gaze shifts. Third, head movements were evoked by FEF stimulation regardless of the occurrence of gaze shifts. When IEP was deviated in the direction contralateral to the stimulated side, approximately 1/3 of

stimulation-evoked head movements occurred in the absence of gaze shifts. Finally, postgaze-shift head displacement was positively correlated with the eye position in the orbit, suggesting that these *late* head movements did contribute to minimizing the eye deviation from the center of the orbit. This process did *not* involve a change of gaze. Some alternative interpretations of these findings are discussed below.

One may argue that some forms of task-associated movement suppression (or promotion) were involved in the findings of the present study. Specifically, the demands in this study for controlling initial eye and head positions might have contributed to the apparent *late* onset of stimulation-evoked head movements. This possibility is unlikely for several reasons. First, comparable results were observed in nontask-mode as well as task-mode stimulation trials. In the former task, there was no feasible promotion or suppression of a given type of movement, yet the stimulation-evoked gaze shifts recruited negligible contribution of the head. Second, FEF stimulation was conducted in darkness, 200 ms following the extinction of visual targets. This procedure minimized the influence of visual fixation (Goldberg et al. 1986; Tehovnik and Slocum 2000). Third, the reward was *not* contingent upon any movements during or following stimulation. Rather, the reward was contingent upon the visually guided gaze shifts at the end of the trials (see METHODS). Fourth, the direction of stimulation-evoked head movements was not random but primarily contralateral with respect to the stimulated side, suggesting that these head movements were likely evoked by stimulation as opposed to initiated volitionally. Fifth, significant contribution of the head was observed during visually guided gaze shifts (Fig. 8), indicating that the animals were capable of performing coordinated eye-head movements. Finally, stimulation-evoked head movements in the FEF were dramatically different from those in the SEF, in which stimulation-evoked gaze shifts recruited significant contribution of the head (Chen and Walton

2005). These results were obtained in the *same* animals under the *same* task demands. Therefore, it seems that the lack of head contribution to stimulation-evoked gaze shifts was unique for the FEF.

The metrics of FEF stimulation-evoked head movements in this study were in general agreement with the recent study of Tu and Keating (2000). First, low current stimulation in the FEF evoked primarily eye-alone movements. High current stimulation evoked gaze shifts accompanied by head movements that were otherwise undetectable (200-300 μA at 250 Hz in Tu and Keating 2000; ≤ 150 μA at 200 Hz in this study). Second, head movement onset often lagged behind gaze shift onset (Fig. 2 in Tu and Keating 2000; Fig. 9). Third, the average *horizontal* amplitude of stimulation-evoked head movements was modest (4.3° ± 0.4° in Tu and Keating 2000; 4.3° ± 2.9° in this study). Fourth, these head movements contributed little to shifting the line of sight (Fig. 2 in Tu and Keating 2000; Figs. 2, 5, 7, and 9; Table 1). However, note that *head contribution to gaze shifts* and *head amplitude* were described inter-changeably in Tu and Keating (2000); hence, they concluded that head contribution (*amplitude* in their measurement) was significant in the report (cf. Scudder et al. 2002).

Head movements and the role of FEF in orienting gaze shifts

Gaze feedback hypothesis has been proposed to account for the head involvement in large orienting gaze shifts (Guitton et al. 1990, 2003; Laurutis and Robinson 1986). The hypothesis states that a *gaze* motor command provides the drive to move the eyes and head, such that the range of gaze displacement is extended beyond the range accomplished by eye (re head) displacement alone (Freedman and Sparks 1997; Fuller 1992; Guitton et al. 1990, 2003; Laurutis and Robinson 1986; Tomlinson and Bahra 1986). As the FEF is anatomically located upstream from most of the oculomotor structures, the question then is whether the FEF issues a gaze motor command that

coordinates eye and head movements, which are presumably controlled independently at the brainstem level. Interestingly, based on the following observations, this possibility appears not supported. First, FEF stimulation-evoked gaze shifts did *not* recruit significant contribution of the head, albeit stimulation-evoked gaze shifts were 20-42° in horizontal amplitude (horizontal IEP centered in the orbit). In contrast, visually guided gaze shifts with comparable gaze displacements always recruit significant contribution of the head (e.g. Freedman and Sparks 1997; Fig. 8). Second, head velocities appeared dissociated from the occurrence of gaze shifts (e.g. stimulation-evoked large staircase gaze shifts in Fig. 6). Unlike the typical visually guided coordinated gaze shifts, stimulation-evoked head movements did *not* accelerate rapidly during gaze shifts (Figs. 2, 4, 6). Third, visually guided *coordinated* eye-head gaze shifts often begin to *decelerate* by the end of gaze shifts, whereas FEF stimulation-evoked head movements did *not* (c.f. Guitton et al. 1990, 2003). Instead, the head often continued to *accelerate* and reached its peak velocity > 100 ms following gaze offset (Figs. 10A and B). That is, the head velocity profile was temporally dissociated from the presumed gaze drive. The results all point to the same conclusion: FEF stimulation-evoked head movements were *not* driven by the *gaze drive signal*. It seems that the FEF neither generated a gaze motor command nor coordinated eye and head movements. Note head movements with long peak velocity latencies have been shown *embedded* in some natural, visually guided gaze shifts (Phillips et al. 1995). Our analysis indicates that this unique type of head movements contributed little to shifting to the line of sight (Fig. 10C, ▒).

The notion of head motor control independent from eye control in the FEF is consistent with the findings of past studies. It has been found that some FEF neurons discharged exclusively during head movements (Bizzi and Schiller 1970). A recent brief report indicated that the motor-burst discharge of some FEF neurons lasted beyond the end of gaze shifts; the duration of the motor

burst was positively correlated with the duration of head movements (Knight and Fuchs 2001). These studies suggest that the FEF neuronal discharge encodes some forms of head motor commands that are dissociated from the neural processes that generate gaze shifts.

If the head motor control is indeed independent from the eye control in the FEF, one would predict that under some circumstances FEF stimulation may evoke head movements in the absence of gaze shifts. This prediction was indeed observed. *Head-alone* movements were evoked by FEF stimulation, particularly when IEP was deviated 27° contralaterally at stimulation onset. It is possible that the independent head control mechanism in the FEF offers the flexibility for better coordinating eye and head movements (Bizzi et al. 1971; Chen and Walton 2005; Goossens and van Opstal 1997; Morasso et al. 1973; Phillips et al., 1995; van der Steen et al. 1986). This assertion needs to be verified in the future study.

One may wonder the exact role of the FEF in the control of head movements. Recent studies have shown that SEF stimulation-evoked head movements facilitated re-centering the eyes in the orbits (Chen and Walton 2005; Sparks et al. 2001). Our findings indicate that FEF stimulation-evoked postgaze-shift head displacements were positively correlated with eye positions, suggesting that these head movements may contribute to minimizing the eye deviation from the center of the orbit (Fig. 11). However, stimulation-evoked postgaze-shift head displacements were relatively small in the FEF, as compared to those evoked by SEF stimulation or visually guided gaze shifts. It seems that the FEF may play a role, but is unlikely the main source, in re-centering the eyes in the orbits. This issue remains speculation.

Comparison with the SEF

A recent stimulation study indicates that the SEF contained mechanisms of head control

independent from those of gaze control (Chen and Walton 2005). Interestingly, this study also suggests that the FEF contained independent eye and head control mechanisms. However, SEF stimulation evoked significant contribution of the head to gaze shifts (Chen and Walton 2005; Martinez-Trujillo et al. 2003), whereas FEF stimulation evoked little contribution of the head to gaze shifts (Tu and Keating 2000; this study). It appears that some fundamental differences exist in the head control mechanisms between FEF and SEF.

Based on our stimulation studies, the differences in the control of eye and head movements between FEF and SEF are enormous (Chen and Walton, 2005; this study). First, < 1/3 (29%) of SEF stimulation trials evoked eye-alone movements. In contrast, the majority (75%) of FEF stimulation trials did so. Second, when initial eye positions were deviated in the *ipsilateral* direction, nearly all (97%) of SEF stimulation trials consisted of *eye-and-head* movements. However, under comparable IEPi condition, <5% of FEF stimulation trials consisted of eye-and-head movements; nearly all (95%) were *eye-alone* movements. Third, when initial eye positions were deviated in the contralateral direction, nearly all (93%) of SEF stimulation-evoked movements were *head-alone* movements. While under comparable IEPc conditions, only approximately 1/3 (308/1,072) of FEF-stimulation-evoked head movements occurred in the absence of gaze shifts. Fourth, in the SEF, ~40% of stimulation-evoked head movements exhibited a peak velocity latency ≤ 50 ms following gaze offset (unpublished observation, L. L. Chen and M. M. G. Walton). In contrast, in the FEF, only 18% of such trials did so (Fig. 10). Fifth, ~1/3 (35%) of SEF stimulation-evoked eye-and-head movements were *early-head* movements in which head movement onset preceded gaze shift onset, whereas merely 5% of these existed in the FEF (Fig. 9; Levinsohn 1909 [described in Smith 1949]). Sixth, SEF stimulation-evoked gaze shifts often evoked significant contribution of the head, whereas FEF stimulation-evoked gaze shifts recruited

negligible contribution of the head (Figs. 5 and 7; Table 1). Finally, SEF stimulation evoked significant head contribution to postgaze-shift eye centering, similar to that observed in visually guided gaze shifts. However, a smaller effect was found in the FEF (Fig. 11).

The question then is whether there exist neuronal discharge characteristics in the FEF and SEF that account for their differences in eye and head control. At this point, our knowledge toward this end is very limited. Both FEF and SEF are extensively connected with other cortical and subcortical areas that are implicated for oculomotor functions (Huerta et al. 1986; Leichnetz et al. 1984; Shook et al. 1990; Stanton et al. 1993; Tehovnik et al. 2000). It has been shown that FEF neurons have strong visual and motor sensitivities associated with oculomotor metrics (Bruce et al. 1985; Chen and Wise 1995a; Dias and Segraves 1999; Huerta et al. 1986; Schall 2002; Schlag and Schlag-Rey 1987). In contrast, SEF neurons and those in neighboring cortices are most sensitive to the context in which movements were executed, e.g. self paced vs. visually guided or conditional visuomotor association vs. spatial attention (Amador et al. 2000; Chen and Wise 1995b, 1996; Fujii et al. 2002; Stuphorn et al. 2000; Tanji 1994; Wise et al. 1997). All of these studies were conducted in head-restrained conditions. Little is known regarding how different types of motor neurons in the FEF and SEF would respond when the head is free to move. Future studies in head-unrestrained conditions hold the promise to elaborate the function of these eye fields.

Since FEF/SEF stimulation evoked non-volitional movements that disengaged the animals' active fixation (or stabilization) of gaze and head, one may wonder whether the animals developed strategies to impede stimulation-evoked movements. Specifically, did the training of active fixation (*in the absence of visual stimuli*) induce short-term or long-term cortical neural plasticity that led to differential outcomes in the stimulation-evoked movements in the FEF and SEF? This cognitive control issue is out of the scope of the present study. Nonetheless, the following observations do

not seem to support this possibility. First, our finding of negligible contribution of the head to FEF stimulation-evoked gaze shifts agreed with the study of Tu and Keating (2000), which did *not* train monkeys to actively maintain stable head positions. Hence, the training did *not* seem to alter the metrics of stimulation-evoked head movements. Second, the results of nontask-mode stimulation, although drastically different between FEF and SEF, were consistent with those obtained in task-mode stimulation in either the SEF (Chen and Walton 2005) or the FEF (this study). This indicates that the effect of active fixation, if any, did not cross-contaminate our observations. Therefore these observations suggest: 1) FEF and SEF differed primarily in their predisposed functions and/or 2) cognitive variables, if any, might influence the movement metrics that were *not* included in our analyses. Note that cognitive control biases stimulation-evoked movements has been demonstrated under carefully controlled circumstances (e.g. Gold and Shadlen 2000; Tehovnik and Slocum 2004). Adequate manipulation of the relevant variables is needed to elucidate the cognitive control mechanisms.

Comparison with the superior colliculus

It has been shown that electrical stimulation in the superior colliculus evoked *constant* gaze shifts independent of horizontal IEP (Freedman et al. 1996). This finding has been taken as a critical piece of evidence suggesting that the superior colliculus encodes gaze (eye plus head) displacement (Freedman et al. 1996; cf. May and Porter 1992). Since the superior colliculus is reciprocally connected with the FEF, one may wonder whether the FEF also encodes constant gaze displacement. Interestingly, this possibility was *never* observed any stimulation site in the FEF. FEF stimulation-evoked gaze amplitudes varied dramatically depending upon eye positions in the orbits (Figs. 5A and B), similar to the orbital effect observed under head-restrained conditions

(Russo and Bruce 1993; Tehovnik et al. 2000). It seems that some fundamental differences exist in the read-out of the electrically-evoked commands between the FEF and the superior colliculus.

At least two major lines of evidence suggest that *eye* and *head* motor control in the FEF are different from that in the superior colliculus. First, when the head is free to move, the site-specific maximal gaze displacement (70-80°) evoked by collicular stimulation is dramatically extended beyond the oculomotor range (Freedman et al. 1996; Segraves and Goldberg 1992; cat: Pare et al. 1994). This was not observed in FEF stimulation (Fig. 2A). FEF stimulation-evoked gaze shifts pushed the eyes as far as their orbital limits (≤ 42° in *horizontal* amplitude, horizontal IEP centered in the orbit; Table 1) with little contribution of the head. In other words, the gaze map in the FEF remains within the oculomotor range whether or not the head is free to move (Bruce et al. 1985; Russo and Bruce 1993; Fig. 2A). It is of interest that this finding is consistent with the previous lesion study in head-free monkeys, in which FEF lesion led to selective eye deficits (van der Steen et al. 1986). The results suggest that the FEF indeed encodes eye (re head) movements.

Second, head-alone movements were evoked by *subthreshold* (below the threshold for evoking eye saccades) current stimulation in the superior colliculus (Corneil et al. 2002; Pelisson et al. 2001). Also, high frequency (≥ 500 Hz) stimulation in the superior colliculus evoked the site-specific maximal gaze shifts, whereas low frequency (e.g. ≤ 250 Hz) stimulation tended to truncate or attenuate the amplitude of the evoked movements (Freedman et al. 1996). In contrast, *suprathreshold* current stimulation was required in the FEF (and SEF) to evoke detectable head movements (Chen and Walton 2005; Tu and Keating 2000; this study). Also, low frequency (≤ 200 Hz) stimulation in the FEF/SEF evoked the site-specific maximal gaze shifts (or head movements), whereas high frequency (400-800 Hz) stimulation tended to attenuate the amplitude of the evoked movements (Chen and Walton 2005; L.L. Chen and D.L. Sparks, unpublished observation). This

implies that different coding schemes for eye and head movements may exist between the FEF/SEF and the superior colliculus.

That high current was needed to evoke detectable head movements in the FEF and SEF is of particular interest. To our knowledge, there is no known *head*-gating mechanism existing in the frontal cortex or downstream that accounts for these findings. Future studies are needed to verify such a possibility. In addition, large current spread recruits larger population of neurons, suggesting that the head motor commands encoded in the FEF and SEF may be distributed widely across neuronal populations. The exact nature of head motor control in the FEF deserves to be elucidated in the future.

ACKNOWLEDGEMENTS

The author thanks H Samuel for designing the primate chair and microlaser fixture, K Pearson and J Li for programming support, M Correa for help with peak-fit analysis, D Sparks for support, and C Langford for editorial assistance. The author thanks L Goffart, C Kaneko, and D Sparks for comments on an earlier version of the manuscript and anonymous reviewers for constructive comments. Supported by grants EY13444 and DC06429.

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Table 1. Average (mean ± S.D.; °) and data range (minimum: maximum; °) of gaze amplitude (horizontal: Gh; vertical: Gv), head amplitude (horizontal: Hh; vertical: Hv), and head contribution to gaze shifts (horizontal: HcGh; vertical: HcGv) under eye-head dissociation (EHD), eye-head alignment (EHA), and nontask-mode stimulation conditions. Data included the stimulation-evoked *eye-and-head* movements only.

		EHD			EHA			Nontask
		IEPi	IEPo	IEPc	IHPi	IHPo	IHPc	
Gh	Mean	36 ± 10	19 ± 8	6 ± 4	21 ± 6	21 ± 8	19 ± 8	16 ± 5
	Range	18 : 55	0.2: 42	0.1: 21	8 : 36	0.2 : 42	6 : 27	4 : 31
Gv	Mean	16 ± 22	14 ± 10	8 ± 7	11 ± 9	12 ± 11	9 ± 2	11 ± 7
	Range	-37: 54	-40 : 35	-36 : 38	-7 : 28	-40 : 37	6 : 12	-20 : 25
Hh	Mean	3.3 ± 2.4	3.6 ± 2.6	5.3 ± 2.9	4.7 ± 4.1	4.4 ± 3.2	1.7 ± 1.8	5.1 ± 3.6
	Range	0.2 : 11	0.1 : 16	1 : 16	0.1 : 15	0.1 : 16	0.1 : 5	0.1 : 16
Hv	Mean	0.4 ± 2.3	0.9 ± 1.4	1.6 ± 1.9	0.1 ± 0.9	0.4 ± 0.6	0.7 ± 1.2	1.3 ± 1.9
	Range	-6 : 7	-5 : 6	-4 : 9	-1 : 3	-16 : 6	0 : 3	-3 : 10
HcGh	Mean	0.4 ± 0.3			0.5 ± 0.4			0.6 ± 0.7
	Range	-0.4 : 2.9			0.0 : 2.9			-0.2 : 4.4
HcGv	Mean	0.1 ± 0.2			0.1 ± 0.3			0.1 ± 0.4
	Range	-1.2 : 1.1			-1.9 : 1.1			-1.1 : 0.9
N		55	246	340	61	317	6	217
% of Total		4.5%	21%	32%	58%	21%	10%	49%

FIGURE LEGENDS

Figure 1. Onsets and offsets of visual targets ("Red," "Green," and "Yellow") and microlaser ("laser") in the control (**A**) and stimulation (**B**) trials. The shaded panels in **A** and **B** indicate the initial eye/head (E/H) alignment-dissociation phases of the task; the open panels, visually guided gaze shift phases. Note that stimulation (**B**) was delivered 200 ms following the extinction of all visual targets and microlaser; these visual sources remained extinguished throughout the rest of the task. Re-illuminating the visual targets in control trials (**A)** ensured that the animals were motivated to maintain their *current* eye and head positions rather than anticipating and executing volitional or anticipatory movements. **C**: Schematics illustrating horizontal and vertical head (Hh and Hv), gaze (Gh and Gv), and eye (re head; Eh and Ev) positions at stimulation onset, separated for EHD (eye-head dissociation) and EHA (eye-head alignment) trials. The symbol ● marks a particular example of gaze, head, and eye positions out of possible combinations (○).

Figure 2. Penetration sites in the FEF of monkey M1 (**A**, top) and the distribution of the amplitudes of stimulation-evoked gaze shifts assorted according to the penetration sites (**A**, bottom). Ar: arcuate sulcus; Ce: central sulcus; Pr: principal sulcus. The symbols (**A**, bottom) are plotted in proportion to the number of trials for the given gaze amplitude range (□: total gaze amplitude (G) ≥ 20°, n = 45; ○: G ≥ 10° but < 20°, n = 76; Δ: G ≥ 5° but < 10°, n = 41). The trials included in the plot were obtained when IHP was centered with respect to the body and horizontal IEP (IEPh) was centered in the orbits. Crosses (x) indicate the sites in which stimulation-evoked gaze amplitudes were < 5°; these data were excluded from this study. Smooth pursuit sites are

marked by "S." Horizontal ticks (-) mark the sites in which stimulation (150 μA) failed to evoke gaze shifts. The vertical dashed line indicates the coordinate approximately in line with the caudal end of the arcuate sulcus. **B** and **C**: Horizontal position and velocity traces of stimulation-evoked gaze (G; light gray), eye (re head; E; gray), and head (H; black) movements in a small-saccade site (**B**) and a large-saccade site (**C**) in the left FEFs. Both cases were obtained when IEPh was centered in the orbits (range: -3: 3°) and IHP was centered with respect to the body (range: -4: 4°). Upward deflection indicates contralateral (rightward) movement, whereas downward deflection indicates ipsilateral (leftward) movement. The peaks of gaze and eye velocities are truncated in the plots. The shaded regions mark the gaze shifts of concern. Horizontal bars indicate the duration of stimulation, 500 ms (top) and 300 ms (below). Arrowhead and arrow in **C** indicate head movement onset and offset, respectively. Stimulation in Site **B** (M1): 80 μA and 200 Hz. Stimulation in Site **C** (M2): 100 μA and 200 Hz.

Figure 3. Amplitude and velocity of the stimulation-evoked gaze shifts and head movements in the FEF. **A**: Range of horizontal (Gh, abscissa) and vertical (Gv, ordinate) gaze amplitudes in EHD (left) and EHA (right) trials. **B**: Peak velocity of horizontal gaze shift as a function of horizontal gaze amplitude in EHD and EHA trials. Only the trials in which gaze shift onset latencies were ≤ 300 ms were included in the analysis. Central line of box plots indicates the median; each side of the box indicates either 25% or 75% of the total; whiskers at both ends indicate 1% and 99% of the total. In EHD trials, the middle 98% range (1 - 99% in the box plot) was 0.6: 44° and -14: 39° for horizontal and vertical gaze amplitudes, respectively. In EHA trials, the middle 98 % range was 1.1: 33° and -12: 34° for horizontal and vertical gaze amplitudes, respectively. **C:** Range of horizontal (Hh, abscissa) and vertical (Hv, ordinate) head amplitudes. The middle 98% range was

0.2: 13° and -4: 6° for horizontal and vertical head amplitudes, respectively. Only the trials in which horizontal head onset latencies were ≤ 300 ms were included in the analysis. Data were pooled from EHD and EHA trials. Positive values indicate rightward (contralateral) or upward movements. **D:** Peak velocity of horizontal head movements as a function of horizontal head amplitudes. The middle 98% range of horizontal peak head velocity was 11: 72 °/sec (30 ± 11 °/sec).

Figure 4. Effects of varying horizontal IEP on the stimulation-evoked horizontal gaze (gray; peak truncated) and head (black) velocities in a large-saccade site of the FEF (M1). Data are separated for IEPi (range: -28: -15°, left panels), IEPo (range: -10: 10°; middle panels), and IEPc (range: 15: 28°, right panels) conditions. In all conditions, IHP remained centered with respect to the body at stimulation onset. Shaded regions indicate the duration of stimulation. Arrowhead and arrow indicate head movement onset and offset, respectively. The threshold current for evoking eye movements was ~35 μA. The average horizontal gaze amplitude was 27 ± 4° (n = 28), 19 ± 4° (n = 26), and 8 ± 2° (n = 21) in IEPi, IEPo, and IEPc conditions, respectively.

Figure 5. Effects of horizontal IEP. Top: Position traces depicting the measurement of head contribution (horizontal: HcGh; vertical: HcGv) to stimulation-evoked gaze shifts in a FEF site. **A** and **B**: Distributions of stimulation-evoked horizontal (**A**) and vertical (**B**) gaze amplitudes. Data included both *eye-alone* and *eye-and-head* movements, separated for IEPc (■), IEPo (▒), and IEPi (□) conditions. The average horizontal amplitude of gaze shifts was 24 ± 9° (range: 0.8: 55°; n = 1,214), 13 ± 8° (range: 0.1: 43°; n = 1,149), and 5 ± 4° (range: 0.1: 21°; n = 552) for IEPi, IEPo, and IEPc conditions, respectively (**A**). The average vertical amplitude of gaze shifts was 18 ± 14°

(range: -39: 42°; n = 1,034) and 25 ± 11° (range: -0.8: 54°; n = 180) for monkeys M1 and M2, respectively (**B**). Gray bars represent overlapped distributions. **C-F**: Data included only *eye-and-head* movements. The data in **C** and **D** were separated for IEPc (Δ), IEPo (*), and IEPi (□) conditions, whereas the data in **D** and **F** were separated for M1 (gray +) and M2 (Δ). **C** and **D**: Horizontal (Hh; **C**) and vertical (Hv; **D**) head amplitudes as a function of stimulation-evoked horizontal gaze and vertical gaze amplitudes, respectively. The average vertical amplitude (Hv) of head movements was 0.8 ± 1.4° and -0.1 ± 3.3° for monkeys M1 and M2, respectively. **E** and **F**: Horizontal (Eh; **E**) and vertical (Ev, **F**) eye amplitude and head contribution to stimulation-evoked horizontal (**E**) and vertical (**F**) gaze shifts as a function of horizontal and vertical gaze amplitudes, respectively. The slope of linear regression is 0.99 ($r = 0.998$, $F = 111{,}457$, $P < 0.001$; **E**) for *horizontal* eye amplitude as a function of *horizontal* gaze amplitude and 0.99 for *vertical* eye amplitude as a function of *vertical* gaze amplitude ($r = 0.99$, $F = 10{,}009{,}831$, $P < 0.001$**; F**).

Figure 6. Effects of varying horizontal IHP on the stimulation-evoked horizontal gaze (gray; peaks truncated) and head (black) velocities in a large-saccade site in the left FEF (M2). Data are separated for IHPi (range: -32: -20°; left), IHPo (range: -10: 10°; middle), and IHPc (range: 20: 32°, right panels) conditions. In all conditions, IEP remained centered in the orbit at stimulation onset. Arrowhead and arrow indicate head movement onset and offset, respectively. Stimulation: 100 μA, 200 Hz, and 300 ms. The threshold current for evoking saccades was ~50 μA. Note the lack of re-acceleration of the head in the two staircase gaze shifts (marked by ∇). In these cases, the head velocities were *not* altered by either onset or offset of the second gaze shifts, suggesting a temporal dissociation between head velocity and gaze velocity. The average horizontal amplitude of gaze shifts was 24 ± 3° (range: 20: 29°; n = 10), 27 ± 2° (range: 24: 30°; n

= 10), and 19 ± 2° (range: 16: 21°; n = 10) for IHPi, IHPo, and IHPc conditions, respectively. The average vertical amplitude of gaze shifts was 5 ± 3°. The average horizontal head amplitude was 10 ± 3° (range: 7: 15°) and 9 ± 3° (range: 3: 16°) for IHPi and IHPo conditions, respectively. The average peak head velocity was 52 ± 12° (range: 37: 70°) and 50 ± 15° (range: 23: 94°) for IHPi and IHPo conditions, respectively. There was no significant difference between IHPi and IHPo conditions in either horizontal head amplitude ($t = 0.9$, $P > 0.34$) or peak horizontal head velocity ($t = 0.4$, $P > 0.70$).

Figure 7. Effects of horizontal IHP (**A-C**) and nontask-mode stimulation (**D-F**). **A** and **D**: Distributions of stimulation-evoked horizontal gaze amplitudes. The data in **A** included *eye-alone* and *eye-and-head* movements, separated for IHPc (■), IHPo (□), and IHPi (▒) conditions. The data in **B-F** included *eye-and-head* movements only. **B** and **E:** Horizontal head amplitude as a function of horizontal gaze amplitude. **C** and **F**: Horizontal eye amplitude and head contribution to horizontal gaze shifts (HcGh) as a function of horizontal gaze amplitude. The slope of linear regression of horizontal eye amplitude as a function of horizontal gaze amplitude is 0.98 ($r = 0.998$, $F = 105{,}461$, $P < .001$) and 0.97 (slope = 0.97; $r = 0.99$, $F = 15{,}823$, $P < 0.001$) for EHA and nontask-mode trials, respectively.

Figure 8. Head amplitude (**A** and **B**, top) and head contribution to visually guided gaze shifts (**A** and **B**, bottom). **A**: Horizontal head amplitude (top) and head contribution to horizontal gaze shifts (HcGh; bottom) as a function of horizontal gaze amplitude. Data are separated for IEPc (Δ), IEPo (*), and IEPi (□) conditions. **B**: Vertical head amplitude (top) and head contribution to vertical gaze shifts (HcGv; bottom) as a function of vertical gaze amplitude. Data were obtained

from visually guided gaze shifts in the control and stimulation trials of the same monkeys (e.g. Fig. 1A; see METHODS). Data are separated for IEPu (upward IEP, range: 11: 30°; □), IEPo (range: -10: 10°; *), and IEPd (downward IEP, range: -30 : -11°; ○) conditions. All data were rectified according to the direction (left vs. right or up vs. down) of gaze shifts; positive values indicate the directions of the movements.

Figure 9. The onset latency of stimulation-evoked head movements (Δ and ---) and gaze shifts (○ and —) as a function of horizontal initial eye (IEPh, **A**) and head (IHPh, **B**) positions. Positive values in the abscissa indicate contralateral (rightward) directions with respect to the stimulated sides (left FEFs). In EHD trials (**A**), the average latency for gaze shift onset was 91 ± 50 ms (median= 78; range: 20: 300; n = 2,947), whereas the average latency for head movement onset was 179 ± 61 ms (median = 184; range: 52: 300; n = 1,039). The correlation between head movement onset and IEPh was -0.23 ($F = 56$, $P < 0.001$), whereas that between gaze shift onset and IEPh was -0.01 ($F = 0.2$, $P > 0.66$). In EHA trials (**B**), the average latency for gaze shift onset was 81 ± 48 ms (median= 70; range: 20: 298; n = 1,694), whereas the average latency for head movement onset was 178 ± 60 ms (median= 182; range: 54: 300; n = 761). The correlation between head movement onset and IHPh was -0.20 ($F = 33$, $P < 0.001$), whereas that between gaze shift onset and IHPh was -0.04 ($F = 2.4$, $P > 0.12$). **C:** The distribution histogram (top) of the latency difference between head movement onset and gaze shift onset and scattergram (bottom) for head contribution to stimulation-evoked horizontal gaze shifts (HcGh) as a function of the latency difference between head and gaze shift onsets in EHD (□) and EHA (■) trials. Overlapped bins are marked by ▒. Only *eye-and-head* movements were included in the analysis. Movements in EHD and EHA trials were comparable in amplitudes (Table 1).

Figure 10. Distributions of the peak velocity latencies of head movements (re gaze offset) in EHD (**A**), EHA (**B**), and visually guided (**C**) trials. **A** and **B:** Stimulation-evoked movements separated for total head amplitude ≥ 2° (□) and ≥ 5° (■). The average peak velocity latency of head movements (H ≥ 2, □) was 142 ± 89 ms (n = 576) and 124 ± 95 ms (n = 311) for EHD and EHA trials, respectively. **C:** Visually guided gaze shifts (□), separated for ≥ 2° (■) or ≤ 1° (▒) head contribution to horizontal gaze shifts (HcGh). Only the visually guided gaze with the metrics (horizontal gaze amplitude (≤ 42°) and total head amplitude (≥ 2°)) comparable to the EHD and EHA trials were included in the analysis.

Figure 11. Horizontal postgaze-shift head displacement (Hpgh) as a function of horizontal eye position (EPh; re head) at gaze offset in EHD (Δ), EHA (□), head-alone movement (●), and visually guided (○) trials. Only the trials with ≥ 2° of head movements were included in the analysis. The shaded region indicates the data range for visually guided trials. Note that head-alone data are plotted as horizontal head amplitude (ordinate) as a function of the horizontal eye position at head movement onset (abscissa). The slopes of linear regression for Hpgh as a function of horizontal eye position at gaze offset was 0.14, 0.19, and 0.36 for EHD ($r = 0.48$, $F = 157$, $P < 0.001$), EHA ($r = 0.48$, $F = 113$, $P < 0.001$), and visually guided ($r = 0.49$, $F = 899$, $P < 0.001$) trials.

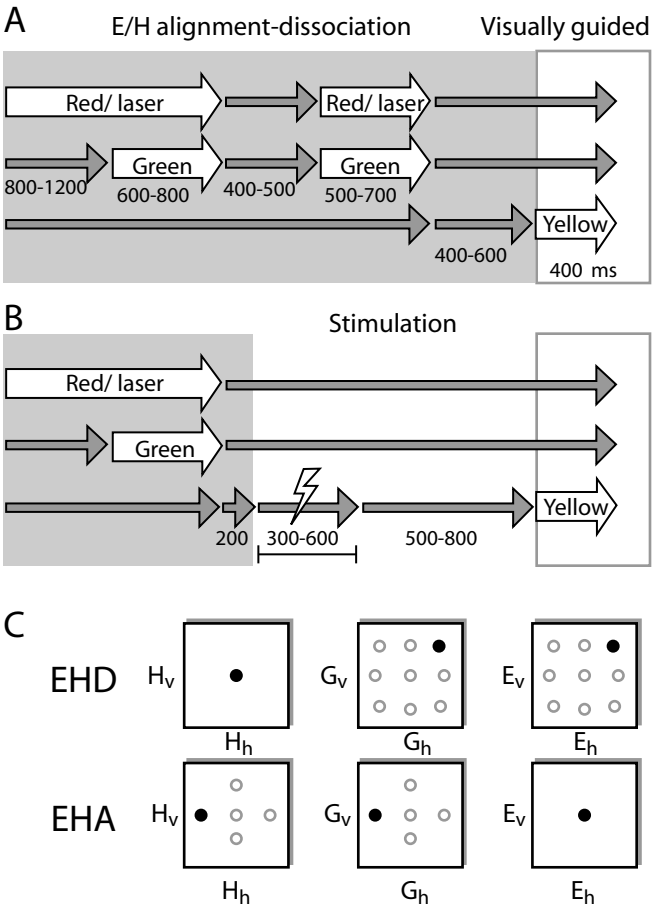
A
E/H alignment-dissociation
Visually guided
Red/ laser
Red/ laser
Green
Green
800-1200
600-800
400-500
500-700
Yellow
400-600
400 ms
B
Stimulation
Red/ laser
Green
Yellow
200
300-600
500-800
C
EHD
EHA
Hv
Gv
Ev
Hh
Gh
Eh

FIGURE 1

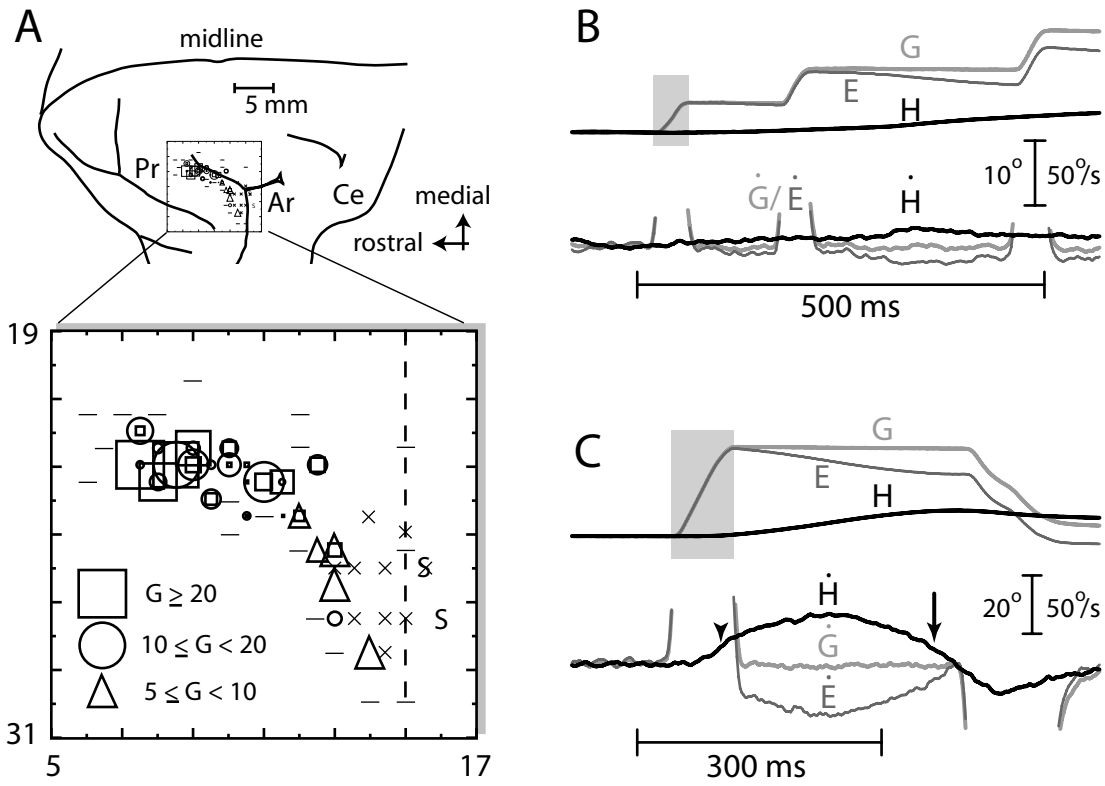

FIGURE 2

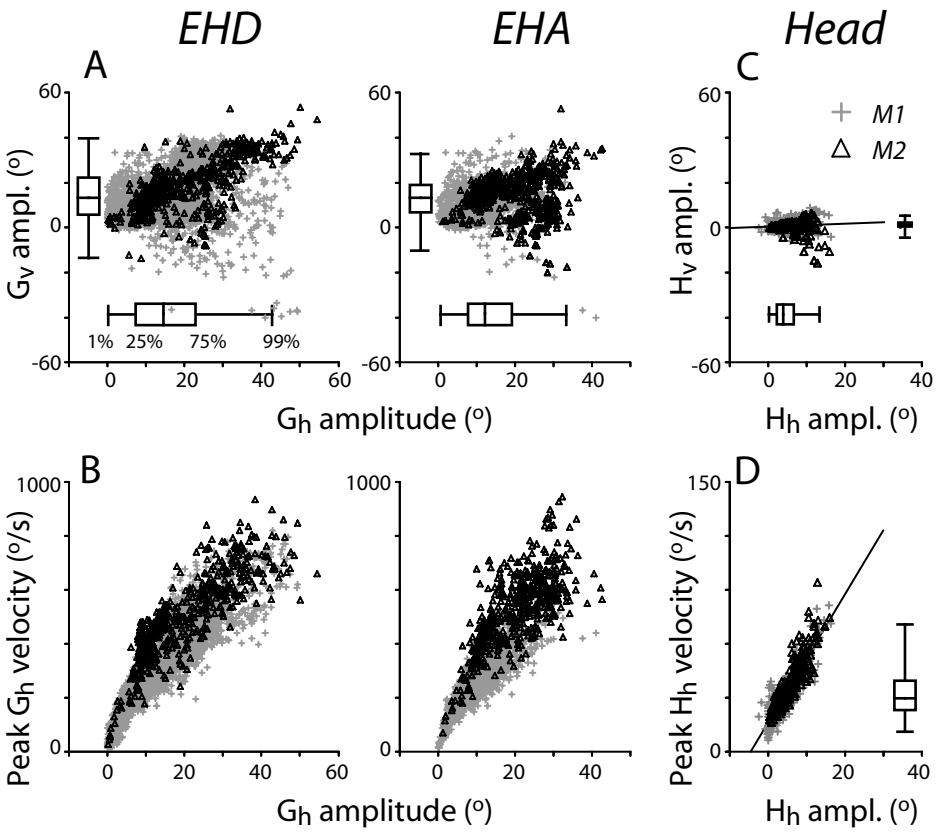

FIGURE 3

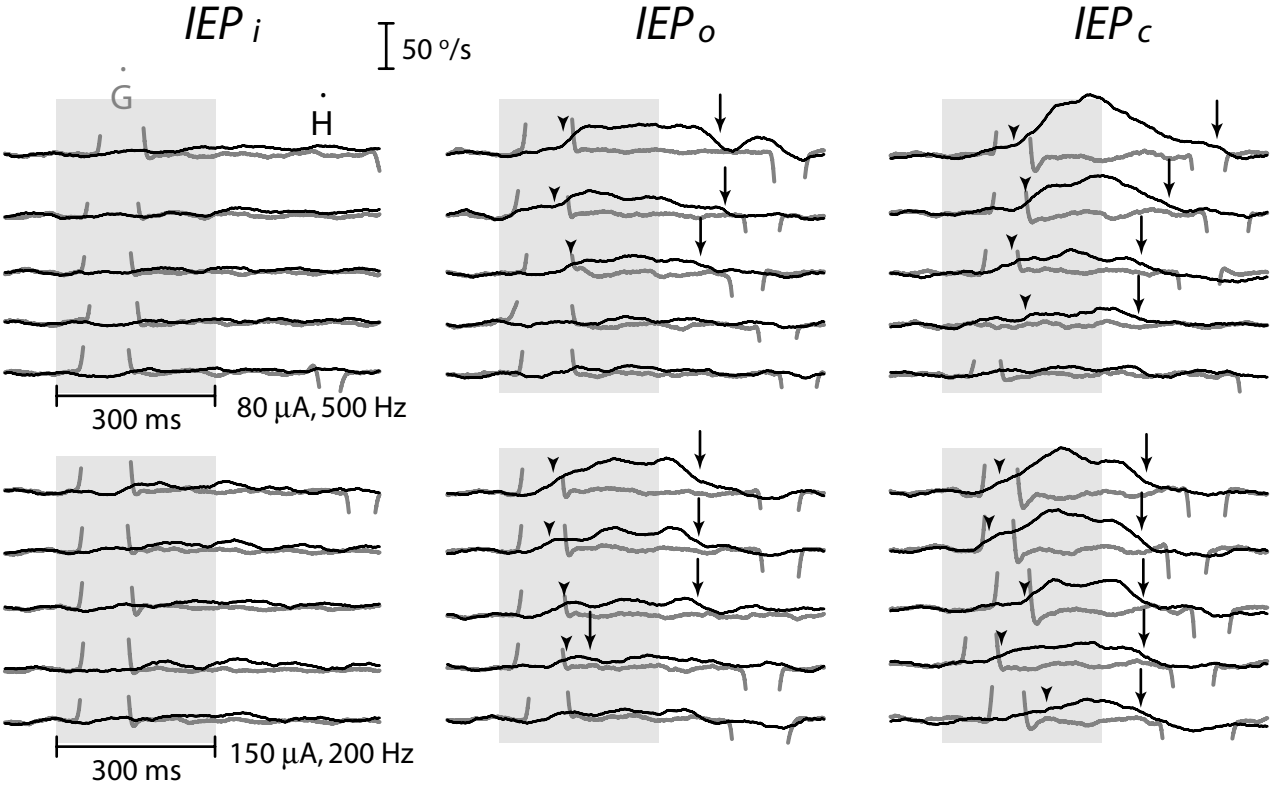

FIGURE 4

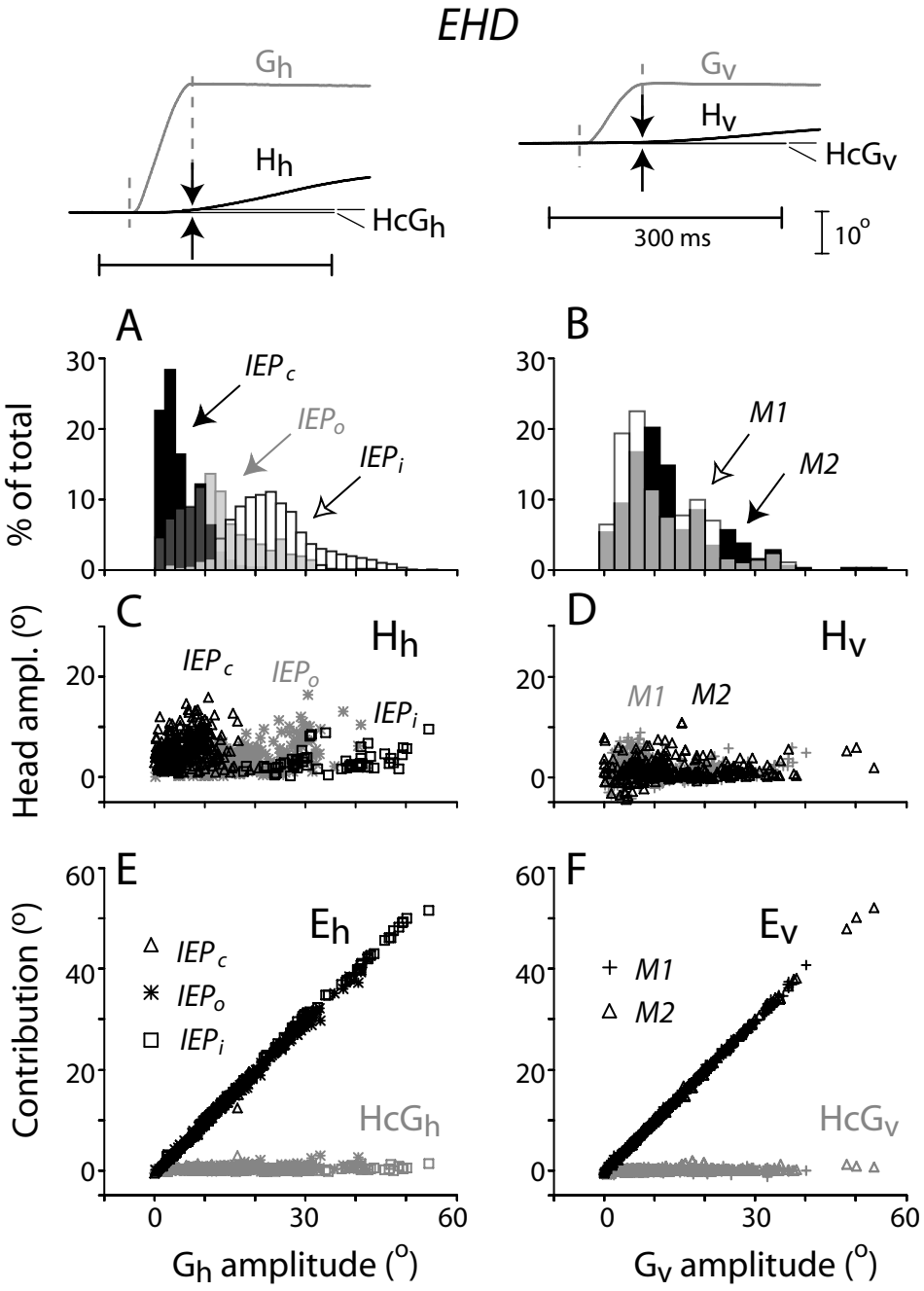

FIGURE 5

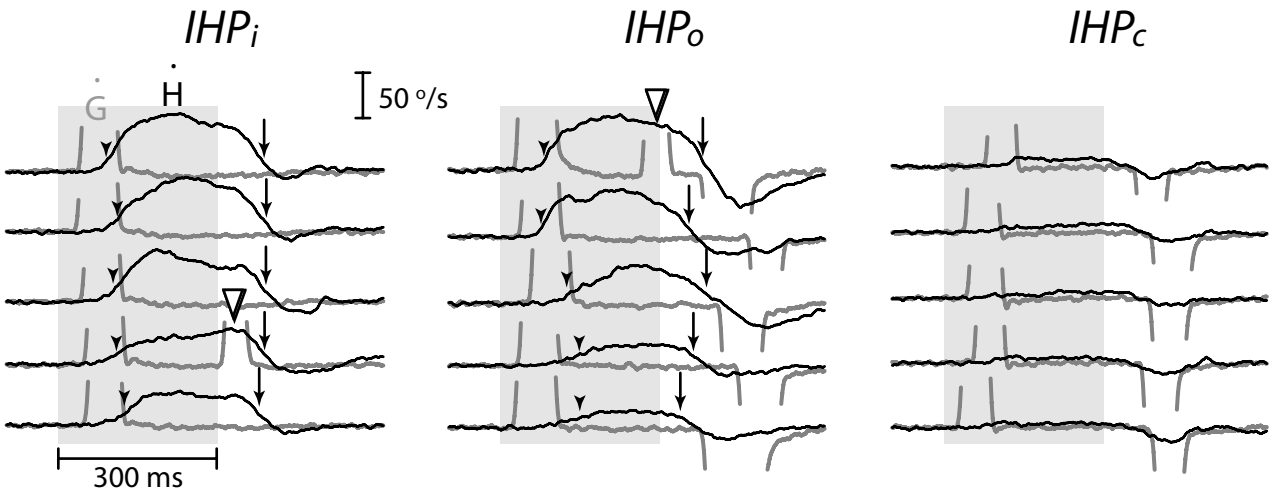

FIGURE 6

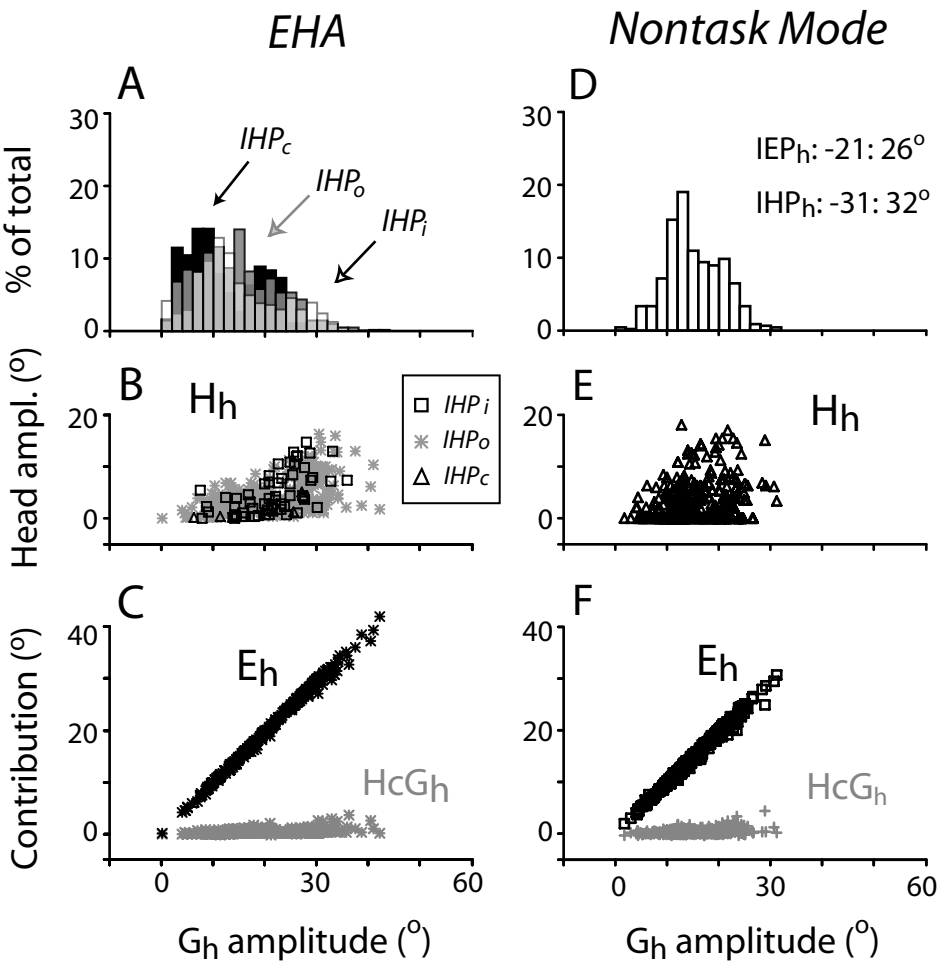

FIGURE 7

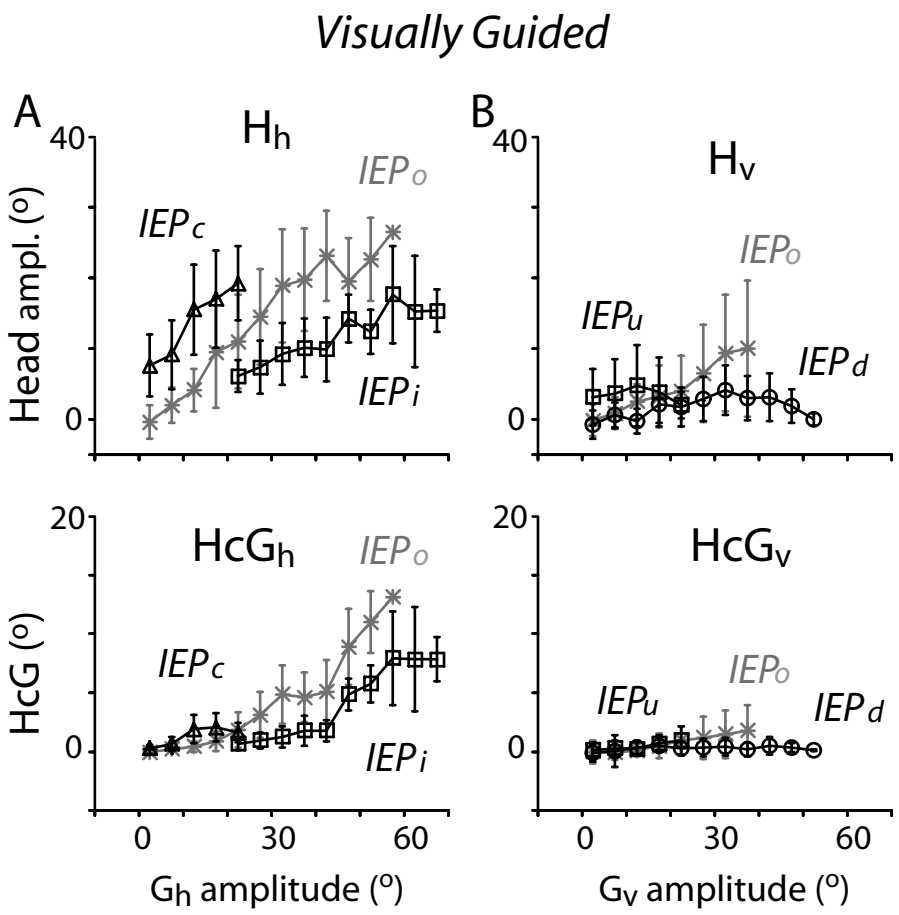

FIGURE 8

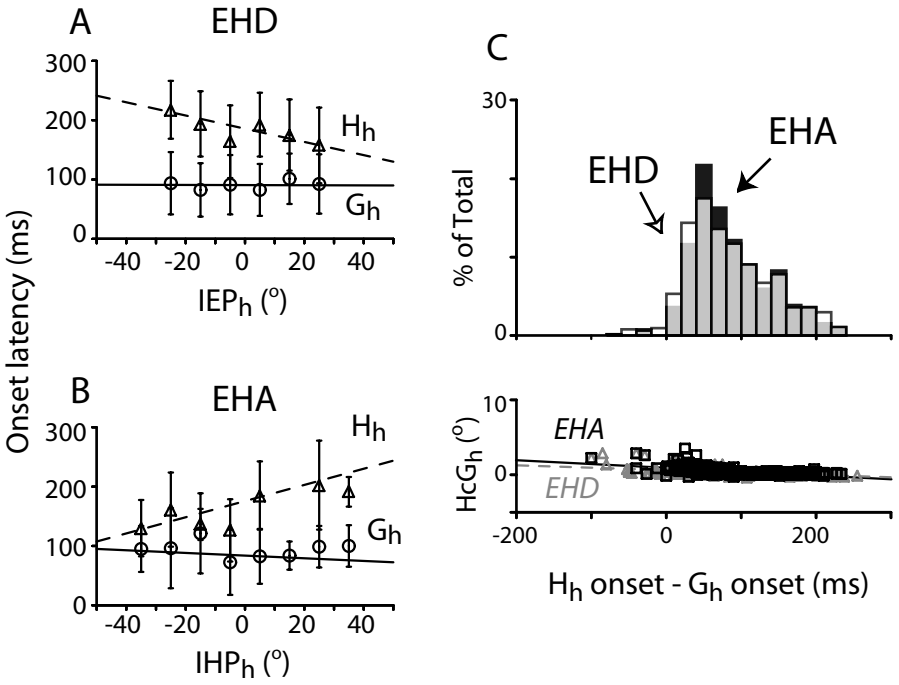

FIGURE 9

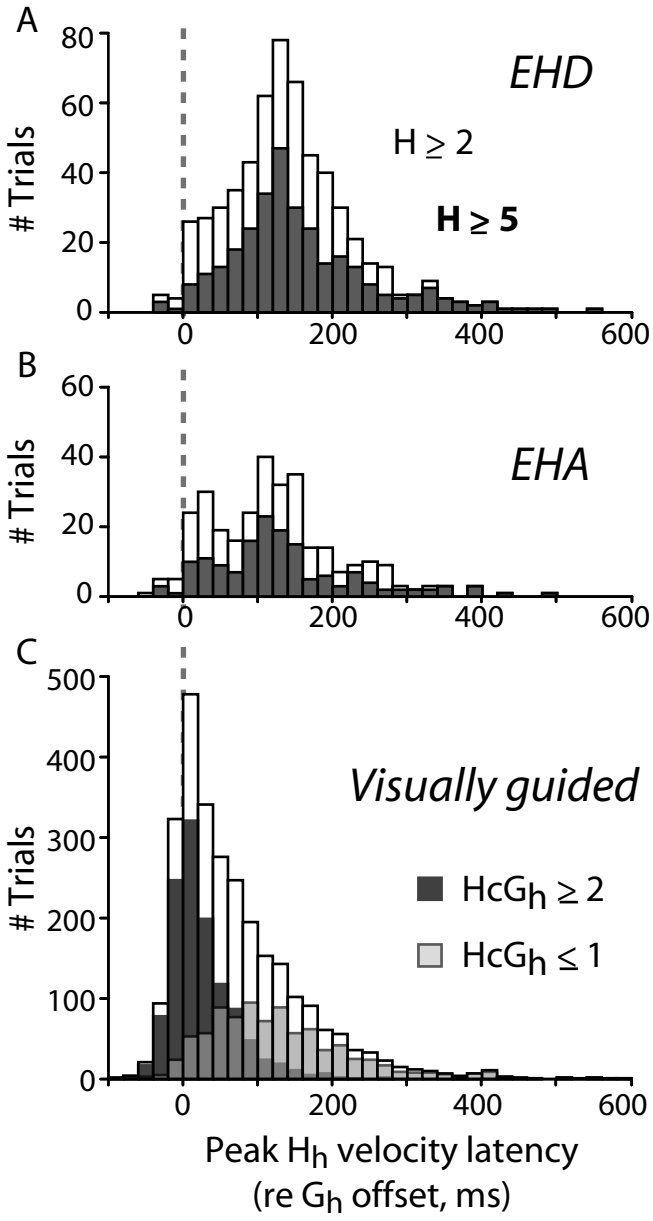

FIGURE 10

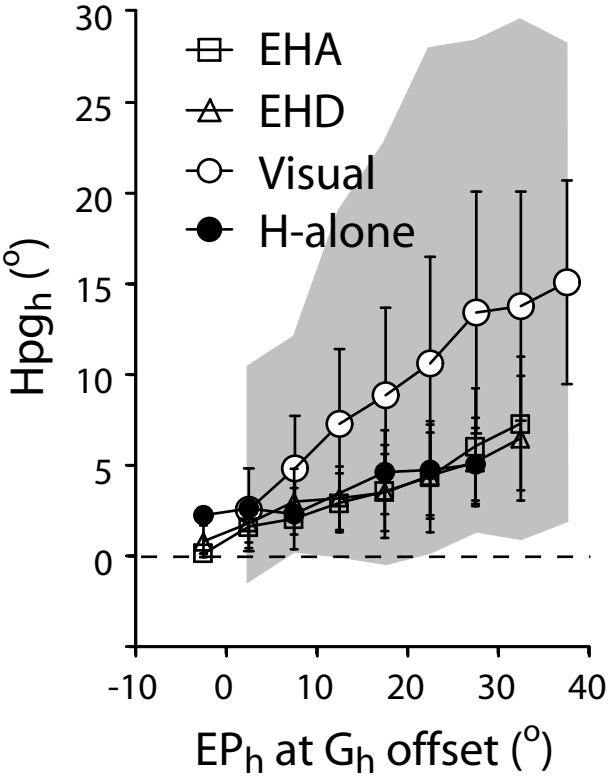

FIGURE 11