

BEHAVIORAL NEUROSCIENCE

Neuromuscular recruitment related to stimulus presentation and task instruction during the anti-saccade task

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Abstract

The contextual control of movement requires the transformation of sensory information into appropriate actions, guided by task-appropriate rules. Previous conceptualizations of the sensorimotor transformations underlying anti-saccades (look away from a stimulus) have suggested that stimulus location is first registered and subsequently transformed into its mirror location before being relayed to the motor periphery. Here, by recording neck muscle activity in monkeys performing anti-saccades, we demonstrate that stimulus presentation induces a transient recruitment of the neck muscle synergy used to turn the head in the wrong direction, even though subjects subsequently looked away from the stimulus correctly. Such stimulus-driven aspects of recruitment developed essentially at reflexive latencies (~60–70 ms after stimulus presentation), and persisted at modest eccentricities regardless of head-restraint. Prior to stimulus presentation, neck muscle activity also reflected whether the animals were preparing for an anti-saccade or a pro-saccade (look toward a stimulus). Neck muscle activity prior to erroneous anti-saccades also resembled that observed prior to pro-saccades. These results emphasize a parallel nature to the sensorimotor transformations underlying the anti-saccade task, suggesting that the top-down and bottom-up processes engaged in this task influence the motor periphery. The bottom-up aspects of neck muscle recruitment also fit within the context of recent results from the limb-movement literature, showing that stimulus-driven activation of muscle synergies may be a generalizing strategy in inertial-laden systems.

Introduction

The anti-saccade task, which requires subjects to look to the diametrically opposite location of a peripheral visual stimulus, has become an important paradigm for studying the contextual control of movement (Hallett, 1978; Munoz & Everling, 2004). This task involves a form of stimulus–response incompatibility, as subjects must suppress the tendency to look to the peripheral stimulus and transform stimulus location into a motor command for a saccade in the opposite direction. A number of clinical populations are deficient in this task (Guitton *et al.*, 1985; Gaymard *et al.*, 1998; Vidailhet *et al.*, 1999; Crawford *et al.*, 2002), consistent with the importance of the frontal lobes in contextual control of movement. The availability of a non-human primate model of this task (Amador *et al.*, 1998; Bell *et al.*, 2000) has enabled investigations of underlying neural processing throughout the neuraxis (Schlag-Rey *et al.*, 1997; Everling *et al.*, 1999; Everling & Munoz, 2000; Olson & Gettner, 2002; Sato & Schall, 2003; Johnston & Everling, 2006). Such investigations have revealed how ‘bottom-up’ signals related to stimulus presentation are integrated with ‘top-down’ signals conveying task instruction into an appropriate motor command.

Presentation of a visual stimulus initiates a cascade of short-latency visual responses in striate and extrastriate cortices, and in numerous oculomotor areas in parietal cortex, frontal cortex, and the brainstem (Wurtz *et al.*, 1980; Bruce & Goldberg, 1985; Colby *et al.*, 1996; Schmolesky *et al.*, 1998; Bisley *et al.*, 2004; Pouget *et al.*, 2005; Bell *et al.*, 2006; Kirchner *et al.*, 2009). This visual-grasp reflex (Hess *et al.*, 1946) culminates in consistently short-latency, time-locked recruitment of neck (Corneil *et al.*, 2004, 2008) and limb muscles (Pruszynski *et al.*, 2010). It is thought that these visual responses on neck or limb muscles may be due to selective gating of descending commands from the superior colliculus, permitting recruitment of head or limb motor circuits without necessitating gaze shifts.

These results suggest that stimulus presentation induces a reflexive series of neural events culminating in motor recruitment. The goal of this manuscript is to examine neck muscle activity in an anti-saccade task, with one objective being to answer whether stimulus presentation leads to a reflexive visual response on the neck muscles that turn the head in the wrong direction. Such a finding would suggest that the bottom-up processes engaged by stimulus presentation induce an erroneous manifestation in the motor periphery, even when gaze is ultimately moved in the correct direction. A second objective investigates whether neck muscle activity displays any dependency with top-down task instruction prior to stimulus onset and, if so, whether such activity is predictive of ensuing task performance. Addressing these objectives will provide additional insights into the

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oculomotor circuits mediating contextual control in a task widely used as an exemplar for stimulus–response incompatibility.

Sections of this manuscript have previously been presented in abstract form (Chapman & Corneil, 2007).

Materials and methods

Subjects and surgical procedures

Two male rhesus macaque monkeys (*Macaca mulatta*, monkeys *je* and *gr*) weighing approximately 6 and 5.5 kg, respectively, performed this experiment. Each animal underwent two surgeries as described elsewhere (Elsley *et al.*, 2007). In the first surgery, a head post and scleral search coil were implanted and anchored into an acrylic implant to permit head-restraint and the monitoring of eye position, respectively (Judge *et al.*, 1980). In the second surgery, bipolar hook electrodes were implanted bilaterally in five neck muscles that are involved in orienting the head both horizontally and vertically. We focus on obliquus capitis inferior and rectus capitis posterior major (OCI and RCP; Fig. 1A), which are small suboccipital muscles that form the core of the ipsilateral head-turning synergy in the monkey (Lestienne *et al.*, 1995; Corneil *et al.*, 2001). All experiments were conducted in accordance with the Canadian Council on Animal Care policy as well as protocol issued by the Animal Use Subcommittee of the University of Western Ontario Council on Animal Care.

Training and behavioral paradigm

Prior to electromyographic (EMG) recordings, monkeys were placed in a customized primate chair (Crist Instruments, Hagerstown, MD, USA) designed to either completely restrain the head from any movement or allow complete motility of the head. Each monkey wore

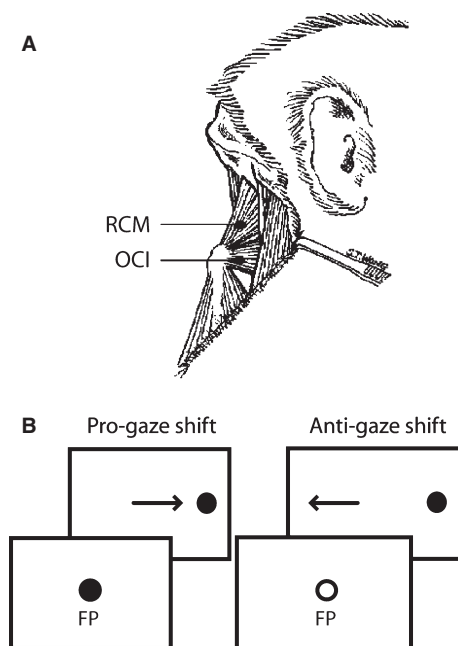


FIG. 1. (A) Line-drawing of the deeper muscles of the dorsal neck, highlighting some of the suboccipital muscles involved in ipsilateral head turns. Obliquus capitis inferior (OCI) spans from the middle of the C2 vertebrae to the outside of the C1 vertebrae. Rectus capitis posterior major (RCP) spans from the middle of the C2 vertebrae to the skull. (B) Schematic of the anti-saccade task. The color of a central fixation point (FP) signified the type of trial (red = pro-saccade; green = anti-saccade).

a customized jacket (Lomir Biomedical, QC) that could be attached to the primate chair and restricted trunk rotation to a maximum of 10° in any direction. The monkeys were then placed into a dark, sound-attenuated room, and placed within the center of a 3-ft³ coil system (CNC Engineering, Seattle, WA, USA) 24 inches in front of an array of horizontal tri-colored (red, green or orange) equiluminant LEDs. Both monkeys learned the anti-saccade task (Fig. 1B) with the head restrained. To learn the anti-saccade task, a red and green stimulus was presented on opposite sides of a green central fixation point (FP), and monkeys learned to look to the stimulus that matched the color of the FP. The intensity of the peripheral green stimulus was gradually reduced on green FP trials until it was completely extinguished so that monkeys were making anti-saccades by looking away from the red stimulus.

Once the monkeys were proficient at the task with the head restrained, we released the head to collect head-unrestrained anti-saccade data. All head-unrestrained trials began with the extinguishing of a diffuse background white light that was presented to prevent dark adaptation. A red or green FP was presented directly in front of the monkey. The monkeys were required to look at the FP within 1000 ms and hold gaze within a computer-controlled window (radius = 5°) for a period of 450 (monkey *je*) or 600 (monkey *gr*) ms. A red or green FP instructed the monkeys to generate a pro-saccade or anti-saccade, respectively, in response to stimulus onset. The stimulus was presented randomly to the left or the right of the FP, and the monkeys had to direct gaze either toward or away from this stimulus within 1000 ms. The monkeys had to maintain stable fixation within a window around the goal location for 600 ms (on anti-saccade trial, a stimulus was presented at the goal location halfway through this interval to reinforce the task). A 1000-ms inter-trial interval was presented between trials. A block consisted of ~ 200 trials of intermixed pro- and anti-saccade trials presented with an equal probability. Within a block, peripheral stimuli were placed at a fixed horizontal eccentricity; across blocks, stimulus location was varied amongst 15, 20, 27, 35, 45 and 60° . We collected a total of ~ 800 trials (400 pro-saccade and 400 anti-saccade trials) at each eccentricity. A customized LABVIEW program controlled the experiment in real-time at a rate of 1 kHz through a PXI box (National Instruments) and implemented sub-blocks of 20 trials (five pseudo-randomized trials of each unique trial and direction combination) to ensure that the monkeys were making pro- and anti-saccades during each block. A liquid reward was administered at the end of each correct trial through a sipper tube that was attached to the head post. The sipper tube did not interfere with either head movements or viewing of the stimuli. We also collected data from monkey *je* with the head restrained, with stimulus eccentricity varying amongst 10, 15, 20, 27 and 35° across blocks.

Data collection and processing

Head rotations were measured via a second coil secured to the head post in the frontal plane. Horizontal gaze (eye-in-space) and head movements were filtered, amplified and digitized at a rate of 10 kHz onto a MAP box (Plexon, Dallas, TX, USA). Off-line, coil signals were down-sampled by a factor of 10–1 kHz. Monkeys were monitored throughout the experiment by investigators via infrared cameras positioned outside the monkey's line of sight. The protocol for processing EMG signals has been described elsewhere (Elsley *et al.*, 2007); briefly, the processing of the EMG signals commenced at a headstage plugged directly onto the EMG connector embedded within the acrylic implant. This headstage performed differential amplification of the EMG signals ($20 \times$ gain) and filtering (bandwidth, 20–17 kHz). A flexible ribbon cable linked the headstage to the Plexon preamplifier,

which contained a signal processing board customized for EMG recordings (50 × gain; bandwidth, 100–4 kHz). EMG signals were notch filtered to remove 60-Hz noise, rectified and integrated into 1-ms bins, using a rationale described previously (Bak & Loeb, 1979). These steps (particularly the rectification of the EMG signal) attenuated the digitized peak-to-peak voltages by a factor of ~3.

Offline analysis was conducted via customized MATLAB (The Mathworks, Nantick, MA, USA) programs. We designed an interface permitting an analyst to inspect all trials and discard trials if, for example, there were aberrant patterns of gaze movements or excessive background EMG activity across the recorded muscles (e.g. if the animal was shifting position). This program also automatically detected the beginning and end of gaze shifts and head movements using velocity crossing thresholds of 30 or 10 deg/s, respectively. Anticipatory movements (< 60 ms from stimulus presentation) and movements that showed a lack of attention (> 600 ms from stimulus presentation) were excluded from analysis (< 5% of movements were removed with these criteria). Customized MATLAB programs extracted aspects of behavioral performance and analysed muscle recruitment. The rationale and details of these methodologies are provided below.

Data analysis

Customized MATLAB programs extracted aspects of behavioral performance and analysed muscle recruitment. A key part of our analysis is to examine when the recruitment of a given muscle differed depending on whether a stimulus was presented to the left or right. Accordingly, we adopted a time-series receiver operating characteristic (ROC) analysis, as described previously (Corneil *et al.*, 2004). Briefly, for every time point spanning from 100 ms before stimulus presentation to 300 ms after, we calculated the area under the ROC curve. This metric is based on the comparative distribution of EMG activity from all trials at that time point, segregated by whether the stimulus appeared ipsilateral or contralateral to the muscle under consideration. The metric expresses the probability that an ideal observer could correctly distinguish the side of stimulus presentation based solely on such EMG activity. A value of 0.5 indicates that the observer would perform at chance, whereas a value of 0.0 or 1.0 indicates perfect performance. We use such time-series ROC plots to define the 'discrimination time', which was defined as the time at which the ROC metric exceeded a value of 0.6 for five of eight consecutive points. The value of 0.6 was chosen as the threshold as this exceeds the 95% confidence interval determined by the distribution of ROC values in the 100 ms preceding stimulus presentation. In practice, modifications in either the threshold value or the number of points required to exceed this value had only a minor influence on discrimination time, as the ROC metric typically increased sharply around the time of the visual response on neck muscles.

Results

We collected a total of > 9600 trials from two monkeys with the head unrestrained, and > 3600 trials from monkey *je* with the head restrained. Previous work (Corneil *et al.*, 2004, 2008) has shown that visual responses on neck muscles are present regardless of head-restraint, and we compared the data collected from monkey *je* across head-restraint to confirm that the same holds true for the anti-saccade task. Our analyses of movement timing, kinematics or EMG activity revealed no effect of the side of the stimulus; hence, we pooled all data across stimulus direction. Our convention is to refer to anti-saccades with respect to the movement's landing point; therefore, a leftward

anti-saccade is one that moves gaze away from a stimulus appearing on the right.

In the following sections, we first analyse the behavior of our two monkeys in the head-unrestrained anti-saccade task to establish similarities with the previous head-restrained literature. We then quantify the bottom-up, stimulus-driven aspect of neck muscle recruitment (the visual response on neck muscles), comparing its timing and magnitude across pro- and anti-saccade trials. Third, we analyse the influence of the top-down instruction to prepare for a pro- or anti-saccade on neck muscle activity, focusing on the fixation period prior to stimulus presentation. We also examine whether such activity differs prior to correct or erroneous anti-saccades. We conclude with a close examination of head movement kinematics, demonstrating that stimulus presentation in the anti-saccade task induces a very subtle stimulus-direction movement that falls well below head movement detection criteria.

Behavioral assessment of head-unrestrained anti-saccades

Both monkeys became very proficient at the anti-saccade task with performance > 75% at all eccentricities, but they displayed slightly different patterns of behavior (Table 1). Monkey *je* initiated gaze saccades and head movements ~40 ms earlier on pro- vs. anti-saccade trials, whereas monkey *gr* initiated movements at approximately equal reaction times (RTs) regardless of trial type. Although this result may seem surprising, monkey *gr* had substantially longer RTs than monkey *je* (paired *t*-test of mean RT for pro- and anti-saccades across eccentricity, $t_{11} = 5.51$, $P = 10^{-4}$), and others have reported shorter RTs on anti-saccade trials in some monkeys (Amador *et al.*, 1998; Johnston & Everling, 2006). In terms of peak velocity, both monkeys generated slower gaze saccades and head movements on anti-saccade trials for the larger stimulus eccentricities (e.g. $\geq 30^\circ$), consistent with the absence of a visual target at the goal location (Edelman *et al.*, 2006). In general, these patterns resemble those described in previous reports of anti-saccade behavior in head-restrained monkeys (Amador *et al.*, 1998; Bell *et al.*, 2000) and head-unrestrained humans (Chapman & Corneil, 2008). Monkey *je* also performed the anti-saccade task with the head restrained, and generated anti-saccades at longer RTs and slower peak velocities compared with pro-saccades (Table 1).

We also analysed the propensity for both monkeys to produce 'head-only' errors toward the stimulus on anti-saccade trials. Head-only errors, which are generally between 3 and 7° in amplitude and can reach peak velocities of over 50 deg/s, have been observed in a variety of paradigms featuring competitive environments or changing experimental contexts (Ron & Berthoz, 1991; Corneil & Munoz, 1999; Pélissier *et al.*, 2001; Corneil & Elsley, 2005). Such sequences consist of an orienting head movement toward a stimulus and a compensatory vestibulo-ocular reflex movement of the eye-in-head to maintain gaze stability. Consistent with results in humans (Chapman & Corneil, 2008), both monkeys produced negligible numbers of head-only movements (Table 1). However, as we will show in a later section, both monkeys produced a pattern of very subtle stimulus-directed head movements that were well below our detection criteria.

Neck muscle activity during head-unrestrained anti-saccades

We examined the recruitment of dorsal suboccipital muscles across trial type (pro- vs. anti-saccade) and stimulus eccentricity. We first show representative data recorded from the right-OCI muscle while monkey *je* made head-unrestrained pro- and anti-saccades to stimuli appearing 35° left or right (Fig. 2). Here, data are aligned to stimulus

TABLE 1. RTs, velocities and error rates for both monkeys in the head-unrestrained condition, and for monkey *je* in the head-restrained condition across all eccentricities

Monkey	Reaction time (ms)				Peak velocity (deg/s)				Error rates (%)	
	Gaze, pro-sac	Gaze, anti-sac	Head, pro-sac	Head, anti-sac	Gaze, pro-sac	Gaze, anti-sac	Head, pro-sac	Head, anti-sac	Anti-sac errors	Head-only
Unrestrained										
<i>gr</i> – 60°	304 ± 52	289 ± 52	241 ± 44	238 ± 49	864 ± 137	814 ± 139	410 ± 112	353 ± 117	22	1.4
<i>gr</i> – 45°	318 ± 55	301 ± 52	255 ± 56	247 ± 41	760 ± 125	693 ± 141	242 ± 44	204 ± 56	20	1.1
<i>gr</i> – 35°	299 ± 39	293 ± 58	231 ± 31	228 ± 49	934 ± 135	879 ± 138	220 ± 33	194 ± 44	14	1.3
<i>gr</i> – 27°	291 ± 48	287 ± 47	238 ± 39	235 ± 44	875 ± 119	770 ± 161	134 ± 22	130 ± 20	9	0.7
<i>gr</i> – 20°	265 ± 42	261 ± 41	222 ± 36	215 ± 35	836 ± 81	746 ± 148	129 ± 21	130 ± 22	7	1.0
<i>gr</i> – 15°	238 ± 36	245 ± 44	203 ± 36	189 ± 34	836 ± 104	875 ± 186	127 ± 21	176 ± 55	12	1.8
<i>je</i> – 60°	196 ± 53	232 ± 41	161 ± 33	186 ± 42	829 ± 107	775 ± 101	231 ± 27	217 ± 32	11	3.0
<i>je</i> – 45°	206 ± 45	245 ± 65	183 ± 43	198 ± 55	853 ± 111	802 ± 101	195 ± 35	193 ± 40	16	3.0
<i>je</i> – 35°	220 ± 41	254 ± 56	204 ± 37	210 ± 57	865 ± 88	780 ± 111	139 ± 22	145 ± 28	14	1.4
<i>je</i> – 27°	198 ± 33	239 ± 62	189 ± 33	197 ± 60	770 ± 58	684 ± 97	113 ± 11	125 ± 19	10	1.6
<i>je</i> – 20°	208 ± 43	248 ± 55	211 ± 42	209 ± 57	759 ± 55	684 ± 99	127 ± 31	114 ± 12	14	0.1
<i>je</i> – 15°	186 ± 41	259 ± 58	165 ± 39	184 ± 44	575 ± 59	521 ± 99	127 ± 32	132 ± 21	10	0.9
Restrained										
<i>je</i> – 35°	236 ± 57	241 ± 42	N/A	N/A	730 ± 66	598 ± 145	N/A	N/A	19	N/A
<i>je</i> – 27°	217 ± 55	221 ± 46	N/A	N/A	746 ± 79	597 ± 174	N/A	N/A	15	N/A
<i>je</i> – 20°	210 ± 45	236 ± 41	N/A	N/A	671 ± 46	531 ± 140	N/A	N/A	20	N/A
<i>je</i> – 15°	195 ± 45	226 ± 38	N/A	N/A	586 ± 42	475 ± 99	N/A	N/A	14	N/A
<i>je</i> – 10°	203 ± 51	256 ± 54	N/A	N/A	422 ± 38	362 ± 72	N/A	N/A	17	N/A

Standard deviations are presented with both RTs and velocities. Bold pairs (pro- vs. anti-) of measurements represent significant differences at $P < 0.05$.

onset, and segregated by trial type and the side of stimulus presentation (within each subplot, each row shows data from a different trial). Rightward stimulus presentation on pro-saccade trials elicited a transient increase in activity (~20 ms in duration) on the right-OCI muscle (i.e. stimulus ipsilateral to the muscle; Fig. 2A; solid rectangle in right panel), whereas leftward stimulus presentation elicited a mirroring suppression of EMG activity (Fig. 2A; dashed rectangle in left panel). Such lateralized recruitment began ~60–70 ms following stimulus onset, regardless of the ensuing RT, and was present on most if not all trials. Following this visual response, right-OCI displayed more prolonged changes in activity, increasing before rightward head movements and decreasing before leftward head movements. We observed a reciprocal profile of recruitment on left-OCI (data not shown in Fig. 2). Overall, the results from pro-saccade trials are consistent with our previous reports of visual responses on neck muscles (Corneil *et al.*, 2004, 2008).

The anti-saccade task provides an opportunity to investigate such visual responses in conditions involving stimulus–response incompatibility. Stimulus presentation in the anti-saccade task elicited the same initial pattern of neck muscle recruitment as in the pro-saccade task (Fig. 2B for right-OCI). Here, rightward (ipsilateral) stimulus presentation elicited a brief burst of recruitment ~60–70 ms later (Fig. 2B, solid rectangle in right panel), even though the ensuing gaze shift proceeded leftward. In contrast, a brief band of suppression followed leftward (contralateral) stimulus presentation (Fig. 2B, dashed rectangle in left panel). Thus, stimulus presentation in an anti-saccade task elicits a visual response on the ‘wrong’ neck muscles, relative to the goal of the task. Again, such recruitment was also present on most if not all trials. Shortly after this visual response, neck muscle activity resolved into a recruitment pattern consistent with movement direction; right-OCI activity decreased before leftward head motion, but increased before rightward head motion.

Figure 2C presents the recruitment of right-OCI when the monkey *je* made anti-saccade errors by looking incorrectly towards the stimulus on anti-saccade trials. Once again, stimulus presentation was followed by time-locked lateralization of right-OCI activity, increasing

or decreasing following rightward or leftward stimulus presentation, respectively. Following this visual response, right-OCI activity increased further for rightward head motion, and decreased for leftward head motion. Overall, the recruitment profile on anti-saccade errors resembled that observed on pro-saccade trials.

We consistently observed visual responses on neck muscles ipsilateral to stimulus presentation in both pro- and anti-saccade trials in both animals. Moreover, we also observed visual responses on neck muscles on most if not all trials even when the head was restrained, even at very modest stimulus eccentricities. Exemplar data are shown in Fig. 3 by displaying the recruitment of right-OCI in monkey *je* while head-restrained with stimuli placed at 35° (Fig. 3A) and at 10° (Fig. 3B). Note the similarity in the patterning of neck muscle activity shortly after stimulus presentation with the data obtained with the head-unrestrained shown in Fig. 2. The increases in neck muscle activity in the peri-saccadic interval and following saccade end are consistent with previous reports describing the tonic and phasic coupling of neck muscle activity with eye position (Lestienne *et al.*, 1984; André-Deshays *et al.*, 1991; Werner *et al.*, 1997). These results emphasize that the visual responses on neck muscles in an anti-saccade task persist both when the head is restrained, and at modest stimulus eccentricities similar to those used in behavioral and neuroimaging studies in both humans and monkeys (Amador *et al.*, 1998; Bell *et al.*, 2000; Koyama *et al.*, 2004).

Timing of visual response on neck muscles

To analyse the visual response on neck muscles, we employed a time-series ROC analysis (see Materials and methods). Our goal here is to determine when neck muscle activity discriminated the side of stimulus presentation (we term this the ‘discrimination time’; see Materials and methods). An example of this analysis is shown for the representative data recorded from right-OCI from monkey *je* (Fig. 4). To compare whether task instruction had any influence on discrimination time, we conducted separate time-series ROC analyses for data collected from pro- (Fig. 4A and B) and anti-saccade (Fig. 4C and D)

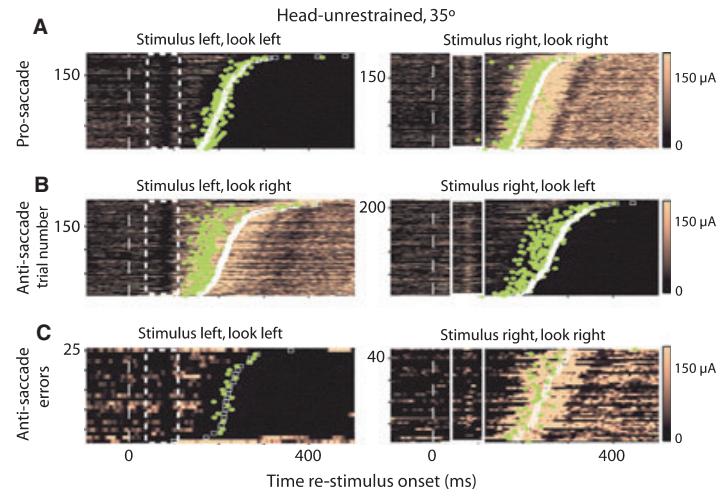


FIG. 2. Representative example of neck muscle recruitment on pro- and anti-saccade trials, showing the activity of right-OCI from monkey *je* while head-unrestrained with stimuli placed at 35°. Each subplot displays EMG activity aligned on stimulus presentation (white dashed line), segregated by trial type [pro-saccades (A), correctly performed anti-saccades (B), incorrectly performed anti-saccades (C)]. Left or right columns show data for stimuli presented to the left or right, respectively. Solid or dashed black rectangles denote changes in muscle recruitment aligned to stimulus onset. White squares represent gaze RT while triangles represent head RT. Data have been sorted by increasing gaze RT.

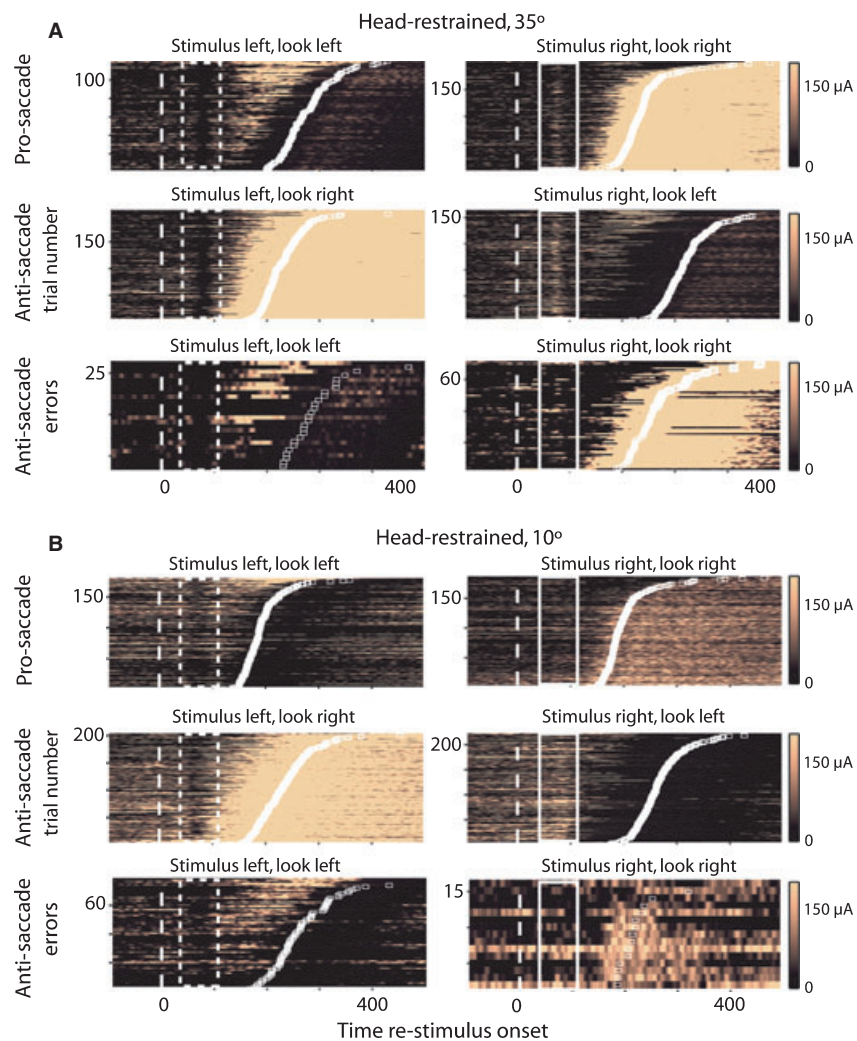


FIG. 3. Recruitment of right-OCI in monkey *je* (i.e. same muscle as in Fig. 2) while head-restrained with stimuli placed at either 35° (A) or 10° (B). Same format as Fig. 2.

trials. At each point in time, the ROC analysis derives a metric expressing the segregation of neck muscle activity depending on the side of stimulus presentation (a value of 0.5 indicates that neck muscle activity provides no information about the side of stimulus presentation, whereas values near 0.0 or 1.0 indicate that neck muscle activity is informative about the side of stimulus presentation). In Fig. 4A, we represent the recruitment of right-OCI aligned to stimulus presentation in a pro-saccade trial. Note how ipsilateral (rightward) or contralateral (leftward) stimulus presentation elicited a transient increase or decrease in activity about 60 ms later, respectively, followed by a more sustained increase or decrease in activity for rightward or leftward movements, respectively. The corresponding time-series ROC analysis for these data displayed a sharp but temporary increase in the area under the ROC curve to values exceeding 0.6 (Fig. 4B), followed by a more sustained increase in the ROC metric to values near 1.0. The discrimination time for the recruitment of right-OCI during pro-saccades was 64 ms (Fig. 4B).

We conducted a similar analysis on right-OCI data recorded on anti-saccade trials (Fig. 4C and D). Here, the increase or decrease in right-OCI activity following ipsilateral (rightward) or contralateral (leftward) stimulus presentation was short-lived, and was followed by a suppression or increase in activity for the leftward or rightward gaze shifts, respectively. Accordingly, the time-series ROC analysis of these data displayed a similarly transient increase in values about 0.6 before decreasing sharply to values below 0.1 for the remaining time (Fig. 4D; this decrease in the ROC metric occurs as rightward stimulus presentation is followed by leftward movements). The discrimination time derived from these data was 65 ms.

Thus, for our representative dataset, the discrimination times derived from right-OCI activity were very similar regardless of whether the monkey was performing pro- or anti-saccade trials. We repeated this analysis across our sample, deriving the discrimination times for pro- and anti-saccade trials separately for any muscle at any given stimulus eccentricity in each monkey (recall we implanted both OCI and RCP bilaterally in each monkey. We treated each recording as an independent sample. Hence, the discrimination times derived for right-OCI from monkey *je* with stimuli at 35° were kept separate from those derived for left-RCP in monkey *je* at 35°, and right-OCI from monkey *gr* at 20°). Across our sample, we observed no difference in the discrimination times on pro- vs. anti-saccade data (Fig. 5A; head-unrestrained pro-saccade discrimination times = 64.1 ± 7.7 ms; head-unrestrained anti-saccade discrimination times = 64.4 ± 9.6 ms; paired *t*-test, $t_{37} = -0.3$, $P = 0.7$). We also observed a strong correlation between these paired discrimination times, meaning that longer discrimination times from pro-saccade trials tended to occur with longer discrimination times derived from anti-saccade trials ($R = 0.86$, $P = 10^{-4}$; Fig. 5A). Further analysis of our sample also revealed differences between monkeys. On average, discrimination times were shorter for monkey *je* compared with monkey *gr* (monkey *je* discrimination time = 61.2 ± 7 ms; monkey *gr* discrimination times = 72.7 ± 5.7 ms, paired *t*-test, $t_{19} = -5.1$, $P = 10^{-4}$). Moreover, we observed slightly shorter discrimination times on anti- vs. pro-saccade trials for monkey *je* (60.5 ± 7.5 ms vs. 61.9 ± 6.9 ms, paired *t*-test, $t_{27} = 2.0$, $P = 0.04$), whereas slightly longer discrimination times were observed on anti- vs. pro-saccade trials for monkey *gr* (75.1 ± 6.4 vs. 70.3 ± 6.4 ms, paired *t*-test, $t_9 = -2.7$, $P = 0.02$).

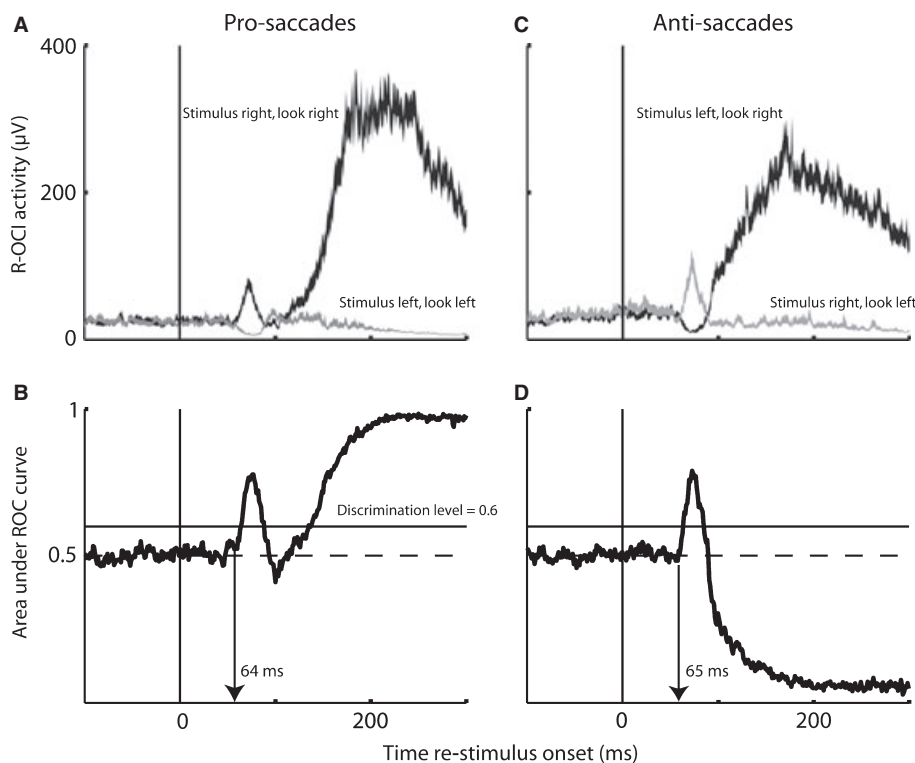


Fig. 4. Depiction of analysis for determining the timing of the visual response on neck muscles, using the representative data shown in Fig. 2. (A and C) Stimulus-aligned EMG activity for both pro- and anti-saccades, depending on whether the monkey had to look to the right (black profiles) or left (gray profiles). Contours span the extent of the average \pm the standard error of the mean. Note the divergence of these traces starting about 65 ms after stimulus onset. (B and D) Time-series receiver operating characteristic (ROC) analysis relative to stimulus onset, derived by computing the area under the ROC curve at each point in time. Note values fluctuate about 0.5 before and immediately after stimulus presentation, signifying that EMG activity did not provide any information about the side of stimulus presentation. ROC values subsequently increased to values > 0.7 before increasing prior to pro-saccades (B), and decreasing prior to anti-saccade (D). OCI, obliquus capitis inferior.

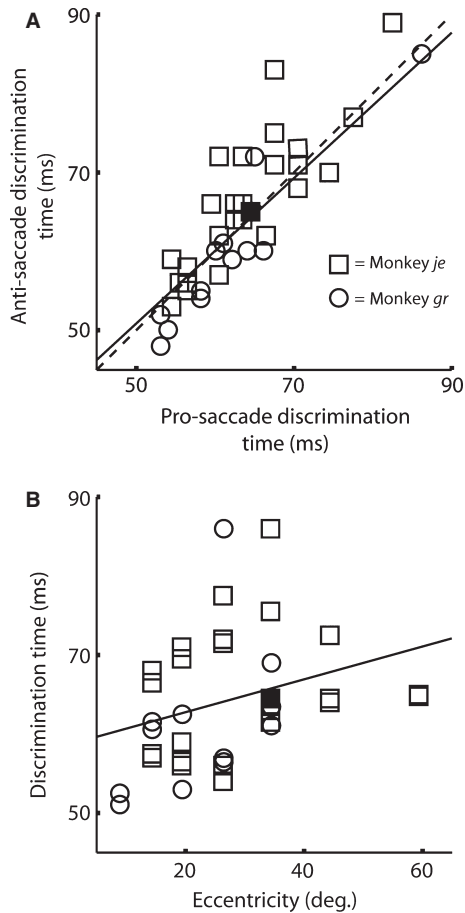


FIG. 5. (A) Scatterplot of pro- and anti-saccade discrimination times. Each point represents data taken from a unique combination of monkey (*je* or *gr*), muscle (OCI or RCM), side (left or right) and eccentricity. The solid line shows regression line and the dashed line shows the line of unity. (B) Plot of discrimination time (averaged across pro- and anti-saccades) as a function of stimulus eccentricity. The solid line shows the regression line. Solid squares in (A) and (B) show data derived from exemplar data shown in Figs 2 and 4.

In monkey *je* we observed no dependency of head-restraint on discrimination times (head-unrestrained discrimination times = 61.1 ± 9.4 ms; head-restrained discrimination times = 61.2 ± 4.9 ms; *t*-test, $t_{15} = -0.02$, $P = 0.98$).

Finally, we also examined how discrimination times varied with stimulus eccentricity. To do this, we averaged the discrimination time obtained for pro- and anti-saccade trials, and plotting this result as a function of stimulus eccentricity revealed a weakly increasing trend (Fig. 5B; $R = 0.3$, $P = 0.05$).

In summary, although there were small idiosyncratic differences in our two monkeys, stimulus presentation in both produced a short-latency (< 100 ms) visual response on neck muscles in both pro- and anti-saccade trials. This visual response depended only weakly on stimulus eccentricity, and in monkey *je* persisted regardless of head-restraint.

Comparative characteristics of visual response on neck muscles with trial type

We used the discrimination time to characterize and compare features of the visual response on neck muscles in pro- vs. anti-saccade trials. We measured the absolute magnitude of the visual response after the

discrimination time, the level of background EMG activity prior to the discrimination time, and the increase in the visual response above background (we term this the 'relative' magnitude of the visual response).

EMG voltages are not directly comparable across different muscles given the variation in the impedances of individual electrodes. Because of this, we analysed the characteristics of the visual responses by first calculating a unitless 'modulation index' as:

$$MI = (PRO - ANTI)/(PRO + ANTI)$$

Hence, MIs > 0 mean that a given measure was greater on pro-compared with anti-saccade trials. We calculated different MIs for the absolute magnitude of the visual response (Fig. 6A), the background activity prior to the visual response (Fig. 6B), and relative magnitude of the visual response above baseline (Fig. 6C). These analyses revealed different patterns of neck muscle recruitment in the two monkeys depending on the top-down instruction to prepare for a pro- or anti-saccade.

For example, the absolute magnitude of the visual response on neck muscles was greater for anti- vs. pro-saccade trials in monkey *je* (upper histogram, Fig. 6A; -0.11 ± 0.14 ; *t*-test vs. zero, $t_{27} = -3.2$, $P = 10^{-4}$), but was greater for pro- vs. anti-saccade trials in monkey *gr* (downward histogram, Fig. 6A; 0.13 ± 0.09 ; *t*-test vs. zero, $t_9 = 4.8$, $P = 10^{-4}$). A similar analysis of the background activity prior to the visual response revealed a significant skew to negative values for monkey *je*, but positive values for monkey *gr* (upper histogram, Fig. 6B; -0.14 ± 0.16 ; *t*-test vs. zero, $t_{27} = -4.8$, $P = 0.01$; downward histogram, 0.08 ± 0.11 ; *t*-test vs. zero, $t_9 = 2.2$, $P = 0.05$). These observations suggest that the differences between the absolute magnitude of the visual response on pro- vs. anti-saccades may be attributable to pre-existing differences in the background level of neck EMG. Consistent with this, we observed no significant difference in the relative magnitude of the visual burst in monkey *je* (upper histogram, Fig. 6C; -0.05 ± 0.27 ; *t*-test vs. zero, $t_{27} = -1.0$, $P = 0.3$), while the relative magnitude of the visual response was still skewed to positive values for monkey *gr* (downward histogram, Fig. 6C; 0.36 ± 0.2 ; *t*-test vs. zero, $t_9 = 5.8$, $P = 0.01$).

To summarize these results, monkey *je* adopted a profile of neck muscle recruitment where the level of background activity was selectively greater at the time of the visual response on anti-saccade trials, which led to a greater absolute magnitude of the visual response. In monkey *gr*, both the background level of neck muscle activity and the relative magnitude of the visual response were greater on pro-saccade trials.

In monkey *je*, we also compared the values of these parameters across head-restraint. The modulation indices show that the magnitude of EMG activity was larger on anti-saccade trials regardless of head-restraint (head-restrained = -0.2 ± 0.1 , *t*-test vs. zero, $t_{11} = -6.7$, $P = 0.001$; head-unrestrained = -0.04 ± 0.1 , *t*-test vs. zero, $t_{15} = -1.6$, $P = 0.1$). Background EMG activity values were skewed negatively regardless of head-restraint (head-restrained = -0.19 ± 0.1 , *t*-test vs. zero, $t_{11} = -6.4$, $P = 0.001$; head-unrestrained = -0.1 ± 0.1 , *t*-test vs. zero, $t_{15} = -2.3$, $P = 0.05$). Finally, the relative EMG magnitude was larger on anti-saccade trials when head-restrained, but larger on pro-saccade trials when head-unrestrained (head-restrained = -0.19 ± 0.2 , *t*-test vs. zero, $t_{11} = -2.4$, $P = 0.05$; head-unrestrained = 0.06 ± 0.2 , *t*-test vs. zero, $t_{15} = 1.1$, $P = 0.3$). These findings emphasize again that a qualitatively similar visual response on neck muscles is observed regardless of head-restraint.

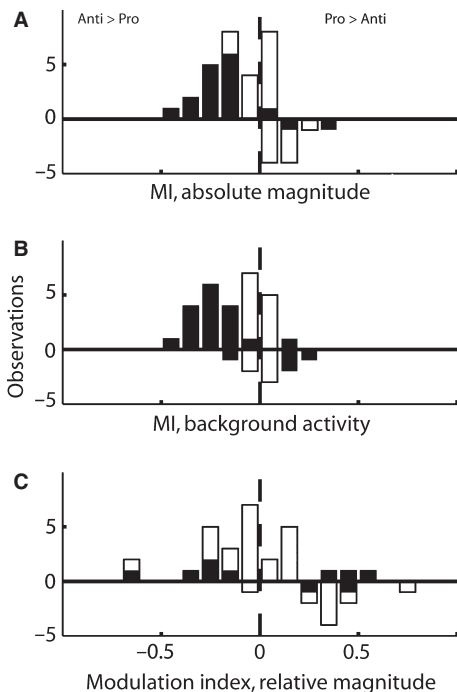


FIG. 6. Modulation indices (MIs) characterizing features of neck muscle activity either during or preceding the visual response on neck muscles. Modulation indices calculated as $([PRO - ANTI]/[PRO + ANTI])$, for either the absolute magnitude of the visual response (A), background EMG activity preceding the visual response (B), or relative magnitude of the visual response above background (C). MIs greater than zero signify occurrences when the parameter was greater on pro- vs. anti-saccade trials. Each observation is taken from a unique combination of monkey (*je* in upper histograms, *gr* in lower histograms), muscle (OCI or RCM), side (left or right) and eccentricity. The colored portions of the histograms represent occurrences where the distribution of the parameter differed significantly across pro- and anti-saccade trials.

Emergence of top-down influences on neck EMG activity before stimulus presentation

The preceding analyses suggest that each monkey adopted an idiosyncratic strategy that led to different comparative levels of background neck muscle activity with task instruction. We now examine the timeline of such task-dependent activity during the interval that the task instruction is available (conveyed by the color of the FP). Accordingly, we focused on neck EMG activity recorded during an interval spanning from the time that the monkey entered the fixation window to the time of stimulus presentation. By the end of this interval, the monkeys have consolidated the instruction to execute either a pro- or anti-saccade, but cannot predict the side of stimulus presentation or the direction of the appropriate saccade. The timeline for how the modulation index of background EMG activity changes during this interval is shown in Fig. 7 (recall different fixation intervals were used for the two monkeys). For this analysis we pooled the background MIs across all stimulus eccentricities and muscles from a given monkey, hence the contours in Fig. 7 represent how the upper and lower histograms from Fig. 6B change through time. For monkey *je*, the modulation index for background activity was centered near zero for the first ~ 350 ms of the fixation interval (signifying no differential background activity for pro- vs. anti-saccade trials), but then decreased to significantly negative values in the final ~ 150 ms preceding stimulus onset (signifying greater levels of recruitment prior to anti-saccades). In contrast, the modulation index of background activity observed from monkey *gr* attained significantly positive

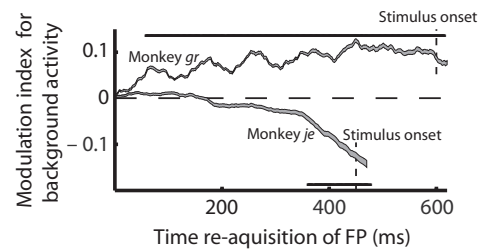


FIG. 7. Time course of the change in neck muscle activity on pro- and anti-saccade trials during the fixation interval prior to the visual response on neck muscles. Values denoted as a modulation index, calculated as in Fig. 6. The time course of how the modulation index differed for monkey *je* compared with monkey *gr*. We first calculated the time course of the modulation index for each monkey independently at each eccentricity, and then pooled across all eccentricities to derive the contours (which show the area subtended by the standard error of the mean). The solid horizontal lines represent the time points where the modulation index was significantly different from 0 at the $P < 0.05$ level. EMG, electromyogram.

values (signifying greater activity prior to pro-saccades) for most of the fixation interval.

Background neck muscle activity reflects performance on anti-saccade trials

Anti-saccade errors occur when the subject makes an inappropriate pro-saccade to the peripheral stimulus, and we wondered whether neck muscle activity was related in any way to ensuing task performance. In light of the differences in the background levels of neck EMG during the fixation interval noted above, we predicted that the level of background activity preceding anti-saccade errors should resemble that observed during pro-saccades. This is what we observed.

To show this result, we present the comparative levels of background activity recorded from the two monkeys during pro-saccades, correct anti-saccades and erroneous anti-saccades (Fig. 8). For this analysis, EMG activity was normalized relative to the background level of activity on pro-saccades immediately preceding the visual response, and then pooled across all muscles for a given monkey. For monkey *je*, note that the selective increase in neck EMG activity late in the fixation interval is observed only before correct anti-saccades. The profile of activity before erroneous anti-saccades is essentially indistinguishable from that recorded before pro-saccades. Similarly for monkey *gr*, the background neck EMG activity recorded prior to erroneous anti-saccades is very similar to that recorded prior to pro-saccades, with both being higher than the activity recorded prior to correct anti-saccades. Thus, despite the differences in the task-dependency of background activity in the two monkeys, a common observation in both monkeys is that the activity recorded prior to erroneous anti-saccades resembled that recorded prior to pro-saccades.

Subtle head movements in response to stimulus presentation

Although our monkeys rarely generated head-only errors toward the stimulus on individual anti-saccade trials, a very subtle head movement toward the stimulus emerged when we pooled data across all trials within our sample. This head movement tendency, which fell well below our detection criteria, is best revealed by comparing velocity traces for pro- and anti-saccades that carry gaze to the same location (see Fig. 9A–C for eye, head and gaze velocity traces from our exemplar data shown in Fig. 2). Recall from this example that the

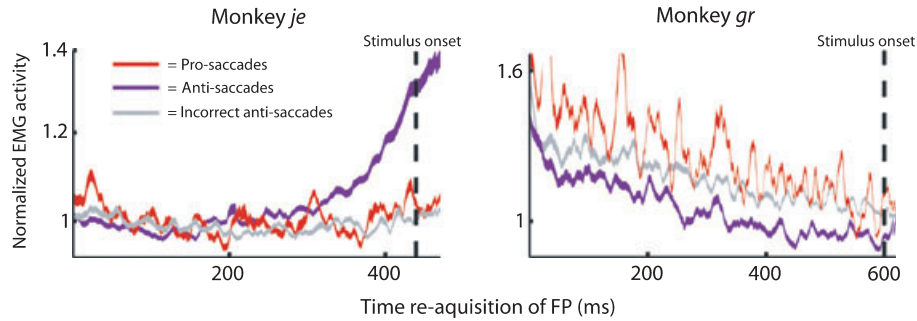


FIG. 8. Plot of normalized electromyogram (EMG) activity during the fixation interval, as a function of trial type and ensuing performance. Data were analysed separately for each monkey, and first normalized to EMG activity on pro-saccade trials immediately prior to the visual response on neck muscles, before being pooled across all eccentricities (and head-restraint for monkey *je*). Contours show area subtended by the standard error of the mean.

initial visual response on neck EMG was ipsilateral to stimulus presentation, and hence occurred on right or left muscles prior to rightward pro- or anti-saccades, respectively. A close analysis of head velocity (Fig. 9B) following stimulus onset revealed a very subtle rightward drift of the head on pro-saccade trials, and a mirroring leftward drift on anti-saccade trials. As such head movements were very slow (< 5 deg/s) and brief (< 100 ms), the overall amplitude of the movement ($< 0.5^\circ$) was far below our criteria for detecting head motion. Gaze (Fig. 9C) remained stable during such small head movements due to a compensatory movement of the eye in the opposite direction (Fig. 9A).

Although such movements were small and slow, their consistency enabled us to quantify when head velocities diverged on pro- vs. anti-saccade trials. As above, we employed a time-series ROC approach, hereby asking when head velocity relative to stimulus presentation discriminated between pro- and anti-saccade trials. In this example, ROC values fluctuated by about 0.5 prior to and immediately after stimulus presentation, and then increased to values > 0.6 about 90 ms after stimulus presentation (Fig. 9D). In this example, we defined the discrimination time as the time where the ROC value exceeded 0.6, which occurred 88 ms after stimulus presentation (recall from Figs 2 and 3 that the activity of right-OCI discriminated the side of stimulus presentation 64 ms later).

We repeated this analysis across both monkeys and all stimulus eccentricities, pooling the data across the side of stimulus presentation at each eccentricity. Across our sample, head velocity discrimination times averaged 96 ± 13 ms (range: 87–129 ms), and occurred at all stimulus eccentricities except for 15° for monkey *gr*. Head velocity discrimination times were significantly less for monkey *je* (89 ± 1 ms) compared with monkey *gr* (106 ± 15 ms, *t*-test, $t_9 = -2.88$, $P = 0.02$). Head movement discrimination times increased significantly with stimulus eccentricity in monkey *gr* ($r = 0.99$, $P = 0.001$), but not monkey *je* ($P = 0.12$). In both monkeys, the discrimination times for neck muscles led that for head velocity by ~ 20 ms (monkey *je* – 24 ± 6 ms; monkey *gr* – 21 ± 5 ms), consistent with a causal role for the visual response on neck muscles in this very small acceleration of the head.

Discussion

We recorded neck muscle activity while monkeys performed an anti-saccade task, and observed a transient expression of a head-turning synergy that emerged ~ 60 – 70 ms after stimulus presentation. Importantly, this recruited motor program favored a head turn in the wrong direction and occurred on virtually every trial, regardless of head-restraint and modest stimulus eccentricity. Despite idiosyncratic

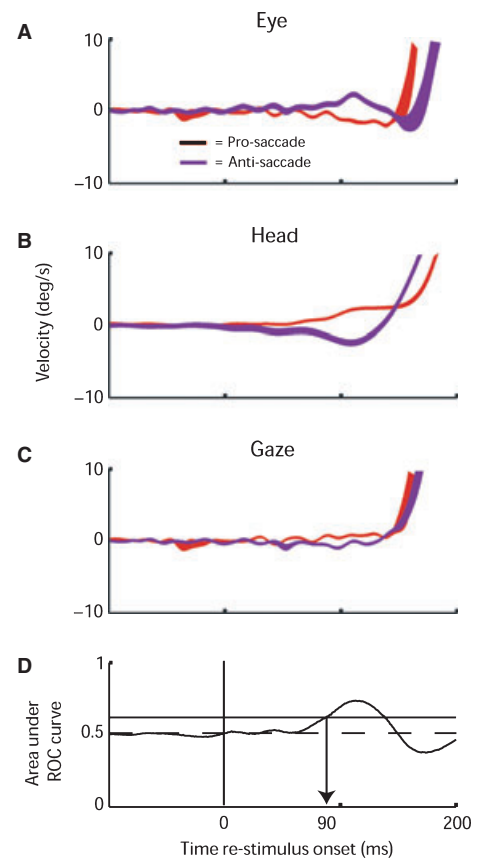


FIG. 9. Velocity traces in pro- and anti-saccade trials for eye (A), head (B) and gaze (C), derived from the same session in which the representative data shown in Fig. 2 were taken. Contours show the area subtended by the standard error of the mean. Trials requiring leftward gaze shifts were flipped prior to pooling. (D) Outcome of time-series receiver operating characteristic (ROC) analysis derived from head velocity traces, showing when head velocity differentiated between rightward and leftward-presented stimuli (same format as Fig. 4B).

differences in task-related activity, neck muscle activity in both monkeys on erroneous anti-saccade trials resembled that recorded during pro-saccade trials. Thus, aspects of neck muscle recruitment reflected bottom-up processes related to stimulus presentation and the top-down consolidation of task instruction. These results provide a new perspective on the circuits engaged during the anti-saccade task, emphasizing a much closer association with motor circuits than previously speculated.

Potential neural circuits mediating bottom-up and top-down aspects of neck muscle recruitment

First, we consider potential neural circuits that could mediate our results. Visual responses on neck muscles resembled those observed in visually guided (Corneil *et al.*, 2004) and inhibition-of-return (Corneil *et al.*, 2008) paradigms, appearing on muscles ipsilateral to the side of stimulus presentation. Although numerous areas in the oculomotor cortex respond to visual stimulus presentation (Schmolesky *et al.*, 1998; Bisley *et al.*, 2004), it is likely that the intermediate layers of the superior colliculus (iSC) relay such information to the cephalomotor system. iSC neurons display a time-locked response to contralateral stimulus presentation prior to correctly performed anti-saccades before the motor command develops in the other iSC (Everling *et al.*, 1999). Transient visual responses are observed in efferent iSC neurons contributing to the pre-dorsal bundle that projects to premotor head areas (Rodgers *et al.*, 2006). iSC neurons also discriminate the side of a visual stimulus ~10 ms before simultaneously recorded neck muscles (Rezvani & Corneil, 2008), consistent with the efferent lag from the iSC (Guitton *et al.*, 1980; Corneil *et al.*, 2002).

We can be confident that analogous visual responses are not developed on extraocular muscles. Momentary changes in the activity of extraocular motoneurons are sufficient to produce detectable eye motion (Sparks *et al.*, 2002), and the duration of the visual response on neck muscles was ~20 ms (equivalent to the duration of a 2–3° saccade). Any eye-in-head motion we did observe compensated for small motion of the head toward the stimulus. The presence or absence of transient visual responses on neck or extraocular muscles, respectively, attests to differences in premotor control. We and others have speculated that the selective influence of omni-pause neurons (OPNs) on eye but not head premotor centers enact such differential control (Galiana & Guitton, 1992; Corneil *et al.*, 2004; Gandhi & Sparks, 2007). We note that OPNs can also display a transient visual response ~60 ms following stimulus presentation (Everling *et al.*, 1998), presumably increasing OPN-mediated inhibition of the saccadic burst generator. In contrast, the neural circuit(s) mediating neck muscle activity that reflects task instruction likely does not involve the iSC. Rostrally located iSC neurons active during stable fixation display greater activity prior to anti-saccades (Everling *et al.*, 1999), resembling the task-related neck muscle activity seen in monkey *je*. However, the projection from the iSC to neck muscles is extremely weak or absent (Roucoux *et al.*, 1980; Corneil *et al.*, 2002; Hadjimitrakis *et al.*, 2007). In contrast, caudally located movement-related iSC neurons are more active prior to pro-saccades (Everling *et al.*, 1999), resembling the profile of neck muscle recruitment observed in monkey *gr*. However, neck muscle activity best reflects the differential distribution of activity in both iSCs (Rezvani & Corneil, 2008). Assuming that movement-related neurons in both iSCs increase equally prior to the presentation of the stimulus on pro-saccade trials, there should not be any increase in neck muscle recruitment.

Descending pathways taking origin from frontal cortices appear capable of relaying high-level signals to the motor periphery (Roesch & Olson, 2003). Activity in numerous frontal and associated thalamic areas differs when monkeys prepare for a pro- or an anti-saccade, frequently predicting task performance (Everling & Munoz, 2000; Amador *et al.*, 2004; Johnston & Everling, 2006; Johnston *et al.*, 2007; Kunimatsu & Tanaka, 2010). A diversity of studies employing multiple methodologies have implicated many of these areas in the control of orienting head movements in both humans and monkeys (Bizzi & Schiller, 1970; van der Steen *et al.*, 1986; Tu

& Keating, 2000; Martinez-Trujillo *et al.*, 2003; Petit & Beauchamp, 2003; Chen & Walton, 2005; Elsley *et al.*, 2007; Knight & Fuchs, 2007; Boulanger *et al.*, 2009; Tark & Curtis, 2009). Although circumstantial, it appears likely that some of these areas could mediate the aspects of neck muscle recruitment reflective of task instruction.

Blurring the sensorimotor transformation for anti-saccades

Performance in the anti-saccade task has been conceptualized as a race between two competing motor processes to threshold – a congruent process encoding a pro-saccade toward a stimulus, and an incongruent process encoding an anti-saccade in the opposite direction (Munoz & Everling, 2004; Kristjansson, 2007). Such models have proven useful in explaining performance in normal subjects and in a variety of clinical populations. Inherent to this conceptualization is a serial nature of processing, whereby the commitment to make either an erroneous pro-saccade or correct anti-saccade is relayed to the motor periphery only after the threshold has been exceeded. Such a discrete segregation between competition and motor execution does not extend to orienting head movements. Instead, the presence of neck muscle activity in response to stimulus onset and reflective of task consolidation suggests a more parallel nature to sensorimotor processing, integrating with the motor periphery.

The premotor mechanisms orienting the head are intimately associated with the oculomotor system. It is only downstream of the iSC that gaze shift programs are segregated into the component eye-in-head and head-on-body commands (Freedman *et al.*, 1996; Freedman & Sparks, 1997). Visual responses on neck muscles demonstrate that the oculomotor system delivers an orienting motor program to neck muscles essentially as soon as it is available, even while the competition between pro- and anti-saccades is ongoing. As mentioned above, the tecto-reticulo-spinal pathway is a likely candidate for relaying visual information onto the neck. What is not clear is which pathways carry the visual signal to the iSC prior to anti-saccades. On one hand, antidromic studies show that the frontal eye fields and lateral intraparietal area are likely candidates for relaying visual information to the iSC (Wurtz *et al.*, 2001). However, saccades evoked by stimulation in the frontal eye fields are not biased toward a visual stimulus before the generation of anti-saccades (Juan *et al.*, 2004), as would have been expected if the visual response within the frontal eye field interacted functionally with the iSC. Regardless of the precise pathway, it is clear that visual transients within the oculomotor system influence the motor periphery.

Biomechanical consequences of the visual response on neck muscles

The study of head-unrestrained anti-saccades provides an opportunity to investigate the biomechanical consequences of the visual response on neck muscles without confounds inherent in other paradigms. In the original report of visual responses of neck EMG (Corneil *et al.*, 2004), monkeys generated visually guided saccades, hence the transient visual response was followed by a larger and more sustained period of recruitment (i.e. Fig. 2A). Although small head movements toward a briefly-flashed cue were observed during an inhibition-of-return paradigm (Corneil *et al.*, 2008), the transient visual response to the cue was also followed by ~200 ms of tonic recruitment.

In contrast, the visual response on neck muscles during the anti-saccade task was not followed by more sustained levels of neck

muscle recruitment. As in humans (Chapman & Corneil, 2008), monkeys generated very few head-only errors, suggesting that the brief visual response of neck EMG did not result in head motion detectable on individual trials. However, thresholds for head movements are difficult to quantify (Chen & Walton, 2005), and detailed analytical methods are required to reveal subtle head movement tendencies across a sample of trials (Oommen & Stahl, 2005). A subtle influence of the visual response of neck EMG on head kinematics was revealed only after pooling head velocity traces across all pro- and anti-saccade trials (Fig. 9).

Summary

Our results suggest that the processes underlying task set and stimulus detection manifest in the cephalomotor periphery. When placed alongside results demonstrating neck muscle recruitment following sub-saccadic stimulation (Corneil *et al.*, 2010) or preparation (Rezvani & Corneil, 2008) within the oculomotor system, it becomes clear that stability of the gaze axis during covert processes cannot be used to infer the absence of motor recruitment. Recent results in the limb-movement literature have also supported the idea that presentation of stationary or moving visual stimuli can initiate reflexive recruitment of proximal limb muscles in cats, monkeys and humans (Schepens & Drew, 2003; Saijo *et al.*, 2005; Fautrelle *et al.*, 2010; Perfiliev *et al.*, 2010; Pruszynski *et al.*, 2010). Together, these results suggest that the earliest recruitment of the motor periphery following stimulus presentation arises not from a voluntary decision to initiate an action, but rather from activation of hard-wired circuits that target postural or proximal muscles. Such a strategy appears to generalize to multiple inertial-laden systems.

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Abbreviations

EMG, electromyogram; FP, fixation point; iSC, intermediate layers of the superior colliculus; OCI, obliquus capitis inferior; OPN, omni-pause neuron; RCP, rectus capitis posterior major; ROC, receiver operating characteristic; RT, reaction time.

References

- Amador, N., Schlag-Rey, M. & Schlag, J. (1998) Primate antisaccades. I. Behavioral characteristics. *J. Neurophysiol.*, **80**, 1775–1786.
- Amador, N., Schlag-Rey, M. & Schlag, J. (2004) Primate antisaccade. II. Supplementary eye field neuronal activity predicts correct performance. *J. Neurophysiol.*, **91**, 1672–1689.
- André-Deshays, C., Revel, M. & Berthoz, A. (1991) Eye-head coupling in humans. II. Phasic components. *Exp. Brain Res.*, **84**, 359–366.
- Bak, M.J. & Loeb, G.E. (1979) A pulsed integrator for EMG analysis. *Electroencephalogr. Clin. Neurophysiol.*, **47**, 738–741.
- Bell, A.H., Everling, S. & Munoz, D.P. (2000) Influence of stimulus eccentricity and direction on characteristics of pro- and antisaccades in non-human primates. *J. Neurophysiol.*, **84**, 2595–2604.
- Bell, A.H., Meredith, M.A., Van Opstal, A.J. & Munoz, D.P. (2006) Stimulus intensity modifies saccadic reaction time and visual response latency in the superior colliculus. *Exp. Brain Res.*, **174**, 53–59.
- Bisley, J.W., Krishna, B.S. & Goldberg, M.E. (2004) A rapid and precise on-response in posterior parietal cortex. *J. Neurosci.*, **24**, 1833–1838.
- Bizzi, E. & Schiller, P.H. (1970) Single unit activity in the frontal eye fields of unanesthetized monkeys during eye and head movement. *Exp. Brain Res.*, **10**, 150–158.
- Boulangier, M., Bergeron, A. & Guitton, D. (2009) Ipsilateral head and centring eye movements evoked from monkey premotor cortex. *Neuroreport*, **20**, 669–673.
- Bruce, C.J. & Goldberg, M.E. (1985) Primate frontal eye fields. I. Single neurons discharging before saccades. *J. Neurophysiol.*, **53**, 603–635.
- Chapman, B.B. & Corneil, B.D. (2007) Neuromuscular correlates of the sensorimotor transformation during an anti-gaze shift task. *Soc. Neurosci. Abstr.*, **33**, 178.13.
- Chapman, B.B. & Corneil, B.D. (2008) Properties of human eye-head gaze shifts in an anti-gaze shift task. *Vision Res.*, **48**, 538–548.
- Chen, L.L. & Walton, M.M. (2005) Head movement evoked by electrical stimulation in the supplementary eye field of the rhesus monkey. *J. Neurophysiol.*, **94**, 4502–4519.
- Colby, C.L., Duhamel, J.R. & Goldberg, M.E. (1996) Visual, presaccadic, and cognitive activation of single neurons in monkey lateral intraparietal area. *J. Neurophysiol.*, **76**, 2841–2852.
- Corneil, B.D. & Elsley, J.K. (2005) Countermanding eye-head gaze shifts in humans: marching orders are delivered to the head first. *J. Neurophysiol.*, **94**, 883–895.
- Corneil, B.D. & Munoz, D.P. (1999) Human eye-head gaze shifts in a distractor task. II. Reduced threshold for initiation of early head movements. *J. Neurophysiol.*, **82**, 1406–1421.
- Corneil, B.D., Olivier, E., Richmond, F.J., Loeb, G.E. & Munoz, D.P. (2001) Neck muscles in the rhesus monkey. II. Electromyographic patterns of activation underlying postures and movements. *J. Neurophysiol.*, **86**, 1729–1749.
- Corneil, B.D., Olivier, E. & Munoz, D.P. (2002) Neck muscle responses to stimulation of monkey superior colliculus. I. Topography and manipulation of stimulation parameters. *J. Neurophysiol.*, **88**, 1980–1999.
- Corneil, B.D., Olivier, E. & Munoz, D.P. (2004) Visual responses on neck muscles reveal selective gating that prevents express saccades. *Neuron*, **42**, 831–841.
- Corneil, B.D., Munoz, D.P., Chapman, B.B., Admans, T. & Cushing, S.L. (2008) Neuromuscular consequences of reflexive covert orienting. *Nat. Neurosci.*, **11**, 13–15.
- Corneil, B.D., Elsley, J.K., Nagy, B. & Cushing, S.L. (2010) Motor output evoked by sub-saccadic stimulation of primate frontal eye fields. *Proc. Natl. Acad. Sci. USA*, **107**, 6070–6075.
- Crawford, T.J., Bennett, D., Lekwuwa, G., Shaunak, S. & Deakin, J.F. (2002) Cognition and the inhibitory control of saccades in schizophrenia and Parkinson's disease. *Prog. Brain Res.*, **140**, 449–466.
- Edelman, J.A., Valenzuela, N. & Barton, J.J. (2006) Antisaccade velocity, but not latency, results from a lack of saccade visual guidance. *Vision Res.*, **46**, 1411–1421.
- Elsley, J.K., Nagy, B., Cushing, S.L. & Corneil, B.D. (2007) Widespread presaccadic recruitment of neck muscles by stimulation of the primate frontal eye fields. *J. Neurophysiol.*, **98**, 1333–1354.
- Everling, S. & Munoz, D.P. (2000) Neuronal correlates for preparatory set associated with pro-saccades and anti-saccades in the primate frontal eye field. *J. Neurosci.*, **20**, 387–400.
- Everling, S., Paré, M., Dorris, M.C. & Munoz, D.P. (1998) Comparison of the discharge characteristics of brain stem omnipause neurons and superior colliculus fixation neurons in monkey: implications for control of fixation and saccade behavior. *J. Neurophysiol.*, **79**, 511–528.
- Everling, S., Dorris, M.C., Klein, R.M. & Munoz, D.P. (1999) Role of primate superior colliculus in preparation and execution of anti-saccades and pro-saccades. *J. Neurosci.*, **19**, 2740–2754.
- Fautrelle, L., Prablanc, C., Berret, B., Ballay, Y. & Bonnetblanc, F. (2010) Pointing to double-step visual stimuli from a standing position: very short latency (express) corrections are observed in upper and lower limbs and may not require cortical involvement. *Neuroscience*, **169**, 697–705.
- Freedman, E.G. & Sparks, D.L. (1997) Activity of cells in the deeper layers of the superior colliculus of the rhesus monkey: evidence for a gaze displacement command. *J. Neurophysiol.*, **78**, 1669–1690.
- Freedman, E.G., Stanford, T.R. & Sparks, D.L. (1996) Combined eye-head gaze shifts produced by electrical stimulation of the superior colliculus in rhesus monkeys. *J. Neurophysiol.*, **76**, 927–952.
- Galiana, H.L. & Guitton, D. (1992) Central organization and modeling of eye-head coordination during orienting gaze shifts. *Ann. N. Y. Acad. Sci.*, **656**, 452–471.

- Gandhi, N.J. & Sparks, D.L. (2007) Dissociation of eye and head components of gaze shifts by stimulation of the omnipause neuron region. *J. Neurophysiol.*, **98**, 360–373.
- Gaymard, B., Rivaud, S., Cassarini, J.F., Dubard, T., Rancurel, G., Agid, Y. & Pierrot-Deseilligny, C. (1998) Effects of anterior cingulate cortex lesions on ocular saccades in humans. *Exp. Brain Res.*, **120**, 173–183.
- Guitton, D., Crommelinck, M. & Roucoux, A. (1980) Stimulation of the superior colliculus in the alert cat. I. Eye movements and neck EMG activity evoked when the head is restrained. *Exp. Brain Res.*, **39**, 63–73.
- Guitton, D., Buchtel, H.A. & Douglas, R.M. (1985) Frontal lobe lesions in man cause difficulties in suppressing reflexive glances and in generating goal-directed saccades. *Exp. Brain Res.*, **58**, 455–472.
- Hadjidimitrakis, K., Moschovakis, A.K., Dalezios, Y. & Grantyn, A. (2007) Eye position modulates the electromyographic responses of neck muscles to electrical stimulation of the superior colliculus in the alert cat. *Exp. Brain Res.*, **179**, 1–16.
- Hallett, P.E. (1978) Primary and secondary saccades to goals defined by instructions. *Vision Res.*, **18**, 1279–1296.
- Hess, W., Burgi, S. & Bucher, V. (1946) Motor function of tectal and tegmental area. *Monatsschr. Psychiatr. Neurol.*, **112**, 1–52.
- Johnston, K. & Everling, S. (2006) Monkey dorsolateral prefrontal cortex sends task-selective signals directly to the superior colliculus. *J. Neurosci.*, **26**, 12471–12478.
- Johnston, K., Levin, H.M., Koval, M.J. & Everling, S. (2007) Top-down control-signal dynamics in anterior cingulate and prefrontal cortex neurons following task switching. *Neuron*, **53**, 453–462.
- Juan, C.H., Shorter-Jacobi, S.M. & Schall, J.D. (2004) Dissociation of spatial attention and saccade preparation. *Proc. Natl. Acad. Sci. USA*, **101**, 15541–15544.
- Judge, S.J., Richmond, B.J. & Chu, F.C. (1980) Implantation of magnetic search coils for measurement of eye position: an improved method. *Vision Res.*, **20**, 535–538.
- Kirchner, H., Barbeau, E.J., Thorpe, S.J., Regis, J. & Liegeois-Chauvel, C. (2009) Ultra-rapid sensory responses in the human frontal eye field region. *J. Neurosci.*, **29**, 7599–7606.
- Knight, T.A. & Fuchs, A.F. (2007) Contribution of the frontal eye field to gaze shifts in the head-unrestrained monkey: effects of microstimulation. *J. Neurophysiol.*, **97**, 618–634.
- Koyama, M., Hasegawa, I., Osada, T., Adachi, Y., Nakahara, K. & Miyashita, Y. (2004) Functional magnetic resonance imaging of macaque monkeys performing visually guided saccade tasks: comparison of cortical eye fields with humans. *Neuron*, **41**, 795–807.
- Kristjansson, A. (2007) Saccade landing point selection and the competition account of pro- and antisaccade generation: the involvement of visual attention – a review. *Scand. J. Psychol.*, **48**, 97–113.
- Kunimatsu, J. & Tanaka, M. (2010) Roles of the primate motor thalamus in the generation of antisaccades. *J. Neurosci.*, **30**, 5108–5117.
- Lestienne, F., Vidal, P.P. & Berthoz, A. (1984) Gaze changing behaviour in head restrained monkey. *Exp. Brain Res.*, **53**, 349–356.
- Lestienne, F.G., Le Goff, B. & Liverneaux, P.A. (1995) Head movement trajectory in three-dimensional space during orienting behavior toward visual targets in rhesus monkeys. *Exp. Brain Res.*, **102**, 393–406.
- Martinez-Trujillo, J.C., Wang, H. & Crawford, J.D. (2003) Electrical stimulation of the supplementary eye fields in the head-free macaque evokes kinematically normal gaze shifts. *J. Neurophysiol.*, **89**, 2961–2974.
- Munoz, D.P. & Everling, S. (2004) Look away: the anti-saccade task and the voluntary control of eye movement. *Nat. Rev. Neurosci.*, **5**, 218–228.
- Olson, C.R. & Gettner, S.N. (2002) Neuronal activity related to rule and conflict in macaque supplementary eye field. *Physiol. Behav.*, **77**, 663–670.
- Oommen, B.S. & Stahl, J.S. (2005) Amplitudes of head movements during putative eye-only saccades. *Brain Res.*, **1065**, 68–78.
- Pélissier, D., Goffart, L., Guillaume, A., Catz, N. & Raboyeau, G. (2001) Early head movements elicited by visual stimuli or collicular electrical stimulation in the cat. *Vision Res.*, **41**, 3283–3294.
- Perfiliev, S.N., Isa, T., Johnels, B., Steg, G. & Wessberg, J. (2010) Reflexive limb selection and control of reach direction to moving targets in cats, monkeys and humans. *J. Neurophysiol.*, **104**, 2423–2432.
- Petit, L. & Beauchamp, M.S. (2003) Neural basis of visually guided head movements studied with fMRI. *J. Neurophysiol.*, **89**, 2516–2527.
- Pouget, P., Emeric, E.E., Stuphorn, V., Reis, K. & Schall, J.D. (2005) Chronometry of visual responses in frontal eye field, supplementary eye field, and anterior cingulate cortex. *J. Neurophysiol.*, **94**, 2086–2092.
- Pruszynski, J.A., King, G.L., Boisse, L., Scott, S.H., Flanagan, J.R. & Munoz, D.P. (2010) Stimulus-locked responses on human arm muscles reveal a rapid neural pathway linking visual input to arm motor output. *Eur. J. Neurosci.*, **32**, 1049–1057.
- Rezvani, S. & Corneil, B.D. (2008) Recruitment of a head-turning synergy by low-frequency activity in the primate superior colliculus. *J. Neurophysiol.*, **100**, 397–411.
- Rodgers, C.K., Munoz, D.P., Scott, S.H. & Paré, M. (2006) Discharge properties of monkey tectoreticular neurons. *J. Neurophysiol.*, **95**, 3502–3511.
- Roesch, M.R. & Olson, C.R. (2003) Impact of expected reward on neuronal activity in prefrontal cortex, frontal and supplementary eye fields and premotor cortex. *J. Neurophysiol.*, **90**, 1766–1789.
- Ron, S. & Berthoz, A. (1991) Eye and head coupled and dissociated movements during orientation to a double step visual target displacement. *Exp. Brain Res.*, **85**, 196–207.
- Roucoux, A., Guitton, D. & Crommelinck, M. (1980) Stimulation of the superior colliculus in the alert cat. II. Eye and head movements evoked when the head is unrestrained. *Exp. Brain Res.*, **39**, 75–85.
- Saijo, N., Murakami, I., Nishida, S. & Gomi, H. (2005) Large-field visual motion directly induces an involuntary rapid manual following response. *J. Neurosci.*, **25**, 4941–4951.
- Sato, T.R. & Schall, J.D. (2003) Effects of stimulus-response compatibility on neural selection in frontal eye field. *Neuron*, **38**, 637–648.
- Schepens, B. & Drew, T. (2003) Strategies for the integration of posture and movement during reaching in the cat. *J. Neurophysiol.*, **90**, 3066–3086.
- Schlag-Rey, M., Amador, N., Sanchez, H. & Schlag, J. (1997) Antisaccade performance predicted by neuronal activity in the supplementary eye field. *Nature*, **390**, 398–401.
- Schmolsky, M.T., Wang, Y., Hanes, D.P., Thompson, K.G., Leutgeb, S., Schall, J.D. & Leventhal, A.G. (1998) Signal timing across the macaque visual system. *J. Neurophysiol.*, **79**, 3272–3278.
- Sparks, D.L., Barton, E.J., Gandhi, N.J. & Nelson, J. (2002) Studies of the role of the paramedian pontine reticular formation in the control of head-restrained and head-unrestrained gaze shifts. *Ann. N. Y. Acad. Sci.*, **956**, 85–98.
- van der Steen, J., Russell, I.S. & James, G.O. (1986) Effects of unilateral frontal eye-field lesions on eye-head coordination in monkey. *J. Neurophysiol.*, **55**, 696–714.
- Tark, K.J. & Curtis, C.E. (2009) Persistent neural activity in the human frontal cortex when maintaining space that is off the map. *Nat. Neurosci.*, **12**, 1463–1468.
- Tu, T.A. & Keating, E.G. (2000) Electrical stimulation of the frontal eye field in a monkey produces combined eye and head movements. *J. Neurophysiol.*, **84**, 1103–1106.
- Vidailhet, M., Rivaud, S., Gouider-Khouja, N., Pillon, B., Gaymard, B., Agid, Y., Kennard, C. & Pierrot-Deseilligny, C. (1999) Saccades and antisaccades in parkinsonian syndromes. *Adv. Neurol.*, **80**, 377–382.
- Werner, W., Dannenberg, S. & Hoffmann, K.P. (1997) Arm-movement-related neurons in the primate superior colliculus and underlying reticular formation: comparison of neuronal activity with EMGs of muscles of the shoulder, arm and trunk during reaching. *Exp. Brain Res.*, **115**, 191–205.
- Wurtz, R.H., Richmond, B.J. & Judge, S.J. (1980) Vision during saccadic eye movements. III. Visual interactions in monkey superior colliculus. *J. Neurophysiol.*, **43**, 1168–1181.
- Wurtz, R.H., Sommer, M.A., Paré, M. & Ferraina, S. (2001) Signal transformations from cerebral cortex to superior colliculus for the generation of saccades. *Vision Res.*, **41**, 3399–3412.