Recruitment of a Head-Turning Synergy by Low-Frequency Activity in the Primate Superior Colliculus

Sam Rezvani1,2 and Brian D. Corneil1,2,3

1Canadian Institutes of Health Research Group in Action and Perception, 2Department of Physiology and Pharmacology, and 3Department of Psychology, University of Western Ontario, London, Ontario, Canada

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Rezvani S, Corneil BD. Recruitment of a head-turning synergy by low-frequency activity in the primate superior colliculus. J Neurophysiol 100: 397–411, 2008. First published May 21, 2008; doi:10.1152/jn.90223.2008. Low-frequency activity within the oculomotor system helps bridge sensation and action. Given ocular stability, low-frequency activity sustained by some neurons within the intermediate and deep superior colliculus (dSC) is assumed to be separated from motor output. However, the dSC is an orienting structure and the influence of low-frequency dSC activity at other effectors remains untested. We studied this by simultaneously recording activity from saccade-related dSC neurons and electromyographic (EMG) activity from neck muscles that turn the head. Monkeys performed a gap-saccade paradigm with varying levels of reward expectancy. Despite head restraint and even for relatively small target eccentricities (≤10°), increasing reward expectancy for a given target increased the level of low-frequency activity on dSC neurons encoding saccades to the rewarded target and increased the recruitment of a neck muscle synergy that would turn the head toward the target. The magnitude of neck muscle recruitment correlated positively on a trial-by-trial basis with the level of low-frequency dSC activity, and such correlations were optimized when neck muscle activity was shifted about 20 ms later to account for delays in the tecto-reticulo-spinal pathway. Further, dSC activity discriminated about the side of target presentation approximately 11 ms earlier than neck EMG activity. Considered alongside neck EMG responses evoked causally by SC stimulation, our results are consistent with low-frequency dSC activity recruiting a head-turning synergy. Our results support a brain stem burst generator via a brief high-frequency (≥100 Hz) series of action potentials (Sparks 1978). These neurons may also emit more persistent trains of action potentials at a lower frequency (≤100 Hz; elsewhere termed “buildup” or “preparatory”) that are not necessarily associated with saccades (Glimcher and Sparks 1992; Mays and Sparks 1980; Mohler and Wurtz 1976; Munoz and Wurtz 1995; Sparks et al. 1976). Low-frequency dSC activity does not influence eye motion because the brain stem burst generator is inhibited tonically by brain stem omnipause neurons (OPNs; Munoz et al. 2000).

Saccade-related dSC neurons project to brain stem premotor circuits controlling eye and head movements (Grantyn and Berthoz 1985; Isa and Sasaki 2002; Moschovakis et al. 1996; Rodgers et al. 2006; Scudder et al. 1996). It is widely believed that the OPN-mediated inhibition of eye premotor circuits is not present on head premotor circuits (Corneil et al. 2002b; Galiana and Guitton 1992; Gandhi and Sparks 2007; Phillips et al. 1999). These observations led us to hypothesize that low-frequency dSC activity recruits a head-turning synergy. A demonstration that low-frequency dSC activity engages the motor periphery would be important, in that such activity has traditionally been linked to high-level processes assumed to be divorced from overt motor output, such as target or saccade selection, attentional allocation, motor preparation, decision making, and representations of reward variables (see DISCUSSION).

The precise role for the dSC in head movement control remains an open question. Stimulation studies have demonstrated that low-current or short-duration dSC stimulation can engage cephalomotor circuits independent of gaze shifts (Corneil et al. 2002a,b, 2007; Pélisson et al. 2001), consistent with the concept of selective OPN gating of gaze shifts. Such selective gating is also consistent with observations of transient visual bursts of neck muscle recruitment following visual target presentation (Corneil et al. 2004) and with our more recent observation that such visual bursts of neck muscle recruitment are modulated by reflexive allocation of covert attention (Corneil et al. 2008). In each of these latter studies, the patterning of neck muscle recruitment displayed a remarkable similarity to known patterns of activity on saccade-related dSC neurons.

However, other results have suggested a more nuanced role for the dSC in head movement control, particularly in relation to the potential contribution of sources other than dSC saccade-related neurons. For example, chemical inactivation of the dSC in head-unrestrained primates produces pronounced gaze-shifting deficits (increased reaction times, lower peak velocities) without imparting similar effects on accompanying head move-
ments (Walton et al. 2008), consistent with the contribution of nontectal sources to head orienting. Furthermore, by training primates to make head movements without gaze shifts, Walton and colleagues (2007) were able to identify a previously unrecorded population of dSC neurons active during head-only movements. Such putative head-related neurons are intermingled with dSC saccade-related neurons and, although they do not appear to be organized in the topographic fashion expected from dSC stimulation studies (more caudal dSC stimulation elicits larger neck muscle responses and head movements), these neurons may underlie some of the cephalomotor drive originating from the dSC.

Together, these observations motivated us to directly assess whether low-frequency dSC activity displayed by some saccade-related neurons engages cephalomotor output. To answer this question, we recorded both dSC activity and electromyographic (EMG) activity from neck muscles known to turn the head while monkeys performed a head-restrained saccade task. Neck EMG recordings provide a resolved measure of the neural drive to the head in a variety of behavioral and stimulation protocols, even when the head is restrained (Corneil et al. 2007, 2008; Elsley et al. 2007). The selected oculomotor task (Fig. 1) uses an asymmetric reward schedule to manipulate the reward expectancy associated with saccades made into or opposite to the recorded dSC neuron’s movement field. A similar paradigm reliably modulated neural activity in the caudate nucleus (Lauwereyns et al. 2002) and proves to be an efficient way to manipulate low-frequency dSC activity. Using this task, we find that the level of dSC low-frequency activity is correlated with the recruitment of a head-turning synergy, even on a trial-by-trial basis and for relatively small amplitude gaze shifts (∼10°) not typically associated with head motion.

Portions of this manuscript previously appeared in abstract form (Rezvani and Corneil 2006).

METHODS

Subjects and physiological procedures

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

Each animal underwent two surgeries to enable chronic recording of gaze position, extracellular recording within the dSC, and recording of dorsal neck EMG activity via chronically implanted bipolar electrodes. Details of these surgeries were previously provided (Elsley et al. 2007). Herein, we focus on the EMG activity recorded from the obliquus capitis inferior (OCI) and rectus capitis posterior major (RCP maj) muscles (Fig. 1A) because these muscles are known to constitute the core of the horizontal head-turning synergy (Corneil et al. 2001, 2002a; Elsley et al. 2007). We focused on muscles involved in horizontal head movements because the head contributes more to horizontal versus vertical gaze shifts (Freedman 2005; Freedman and Sparks 1997a) and to ease comparison with our previous microstimulation results (Corneil et al. 2002a, 2007), where stimulation was applied unilaterally. During these experiments, the monkeys were placed in a primate chair (Crist Instruments) that constrained trunk rotation and permitted head restraint. The dSC recordings in this study were performed with the head restrained, which was necessary to standardize the position of the head relative to the body, since this is known to influence neck EMG (Corneil et al. 2001).

Experimental procedures

During the experimental sessions, the monkeys were placed within the center of a 3-ft³ coil system (CNC Engineering). The monkeys faced an array of 49 tricolor light-emitting diodes (LEDs, MV5437; Fairchild Semiconductors) arranged in a radial fashion surrounding a central LED. LEDs were positioned at visual angles that corresponded in a two-dimensional polar coordinate system to six radial eccentricities (5, 10, 15, 20, 27, and 35°) and eight radial angles (0, 45, 90, 135, 180, 225, 270, and 315°; 0° = rightward, and 90° = upward). All aspects of the experiment were controlled at 1,000 Hz by customized real-time LabVIEW programs interfacing with the hardware through a PXI controller (National Instruments). Single-neuron activity was recorded via tungsten microelectrodes (0.5–2 MΩ at 1 kHz; FHC, Bowdoin, ME) lowered through 23-gauge guide tubes secured within a Delrin grid (Crist Instruments). Neural activity was amplified,
filtered, and stored for off-line sorting via a Plexon MAP system (Plexon, Dallas, TX). Isolated action potential waveforms that surpassed a user-defined threshold were stored at 40 kHz; detected extracellular action potentials were recorded at 1 kHz.

Behavioral paradigms

During each experimental session, subjects first made saccades from the central LED to targets presented at various locations on the LED board, while we searched for dSC neurons with task-related activity (i.e., a neuron with visual- or motor-related activity). The preferred vector of an isolated neuron was defined as the target location associated with the most vigorous activity for target-directed saccades. Once we identified the preferred vector for an isolated neuron, the subject performed sequential blocks of a gap-saccade task with differing levels of reward expectancy within each block (Fig. 1B). Regardless of reward expectancy, the basic paradigm required the subject to fixate a central fixation point (FP) within a computer-controlled window (3° radius) for an interval chosen from 750, 875, 1,000, 1,125, or 1,250 ms. The FP was then extinguished and the subject had to maintain central fixation within the window for 200 ms prior to the illumination of a peripheral target. The subject then had 800 ms to look to the peripheral target; a liquid reward was delivered if the animal maintained fixation within a 3–5° radius window around the target (this window was enlarged for more peripheral targets). Within a block of trials, the peripheral target could be presented at one of two locations. These locations were selected to either coincide with the preferred vector of the dSC neuron being recorded or be located at the diametrically opposite location. The selection of which target would be presented on a given trial was pseudorandomized so that the subject could not predict the sequence of target presentation. Because we recorded from both dSCs in all subjects, we will refer to target presentation as either lying within the movement field of the isolated neuron or opposite of the movement field of the isolated neuron.

For each neuron, we ran three different blocks of the gap-saccade task; within each block the amount of reward delivered for targets presented within or outside of the movement field varied (Fig. 1B). In the first block, termed the Equal-Reward Block, the same magnitude of reward was provided for correct saccades either into or opposite the movement field (the solenoid controlling reward delivery was opened for 150 ms for both target locations; delivering ~0.07 ml per correct trial). In the second block, termed the High-Reward Block, a greater amount of liquid reward was provided for correct saccades to the target within the movement field [the solenoid was opened for 250 ms for targets in the movement field (~0.115 ml per trial) and for 50 ms (~0.025 ml per trial) for targets opposite to the movement field]. In the third block, termed the Low-Reward Block, the reward expectancies were reversed so that a greater amount of liquid reward was provided for correct saccades to the target location opposite to the movement field. We collected a minimum of 50 trials from the equal-reward block and 100 trials from both the high-reward and low-reward blocks.

Data analysis and neuronal classification

The activity of isolated dSC neurons was recorded simultaneously with neck muscle activity. Details concerning the processing of the EMG signals have been provided elsewhere (Elsley et al. 2007); briefly the analog EMG signals were amplified and filtered (head-stage: ×20 gain, bandwidth: 20 Hz to 17 kHz; preamplifier ×50 gain, bandwidth 100 Hz to 4 kHz; Plexon) and digitized at 10 kHz. Off-line, EMG signals were notch filtered to remove 60 Hz, rectified, and integrated into 1-ms bins (Bak and Loeb 1979). These off-line steps attenuated peak-to-peak amplitudes by approximately threefold. The activity of dSC neurons were quantified by convolving each spike train with a postsynaptic activation function with a rise time of 1 ms and a decay time of 20 ms (Hanes et al. 1995). We confirmed that the same qualitative results were observed if we convolved neural activity with a Gaussian function (σ = 10 ms) or counted the number of action potentials.

As mentioned earlier, our on-line search criteria were to simply isolate neurons with task-related activity. Off-line, we first classified neurons as having visual and/or motor-related activity based on their discharge profile during the equal-reward block (this simplified classification since many express saccades were generated in the high-reward block). Neurons with visual activity had to display a distinct series of action potentials at a time-locked latency approximately 40–60 ms following target presentation in the preferred direction. Neurons were classified as having motor-related activity if they displayed a peak in neural activity around the time of saccades directed in the preferred direction (~±20 ms around saccade onset).

Off-line, we further screened neurons to identify those with low-frequency activity during the gap interval. To be included in our analysis, dSC neurons had to display a motor-related peak in activity >100 Hz for saccades into the neuron’s response field in the equal-reward block and, moreover, had to display a significant increase of low-frequency activity during the gap interval in at least one of three different reward blocks. These criteria are similar to those used previously (Dorris and Munoz 1998) and, although an increase in low-frequency activity is one of the criteria of build-up neurons described by Munoz and Wurtz (1995), we made no attempt to characterize neurons based on the other criteria such as neuronal movement fields (e.g., open vs. closed) or activity at saccade end (e.g., clipped, partially clipped, or unclipped). An increase in low-frequency activity was assessed by comparing the convolved activity at the end of the fixation period (in the 10 ms preceding FP disappearance) to the interval immediately preceding the arrival of target-relation information (25 to 35 ms after target onset; Wilcoxon signed-rank test, P < 0.05). We assessed the timing of the arrival of target-relation information into the dSC by performing a time-series receiver-operating characteristic (ROC) analysis on the subset of isolated dSC neurons that had a transient burst of activity time-locked to target presentation in the neuron’s movement field (69 neurons fulfilled this criterion; many, but not all, of these neurons also displayed low-frequency and/or motor-related activity). On average, the activity of these neurons diverged 51 ± 13 ms (mean ± SD) following target presentation either into or opposite to the neuron’s response field (median: 49, range: 39–74 ms, n = 69). Thus we are confident that the 25- to 35-ms interval we selected sampled dSC activity at the end of the gap interval without contamination by transient responses related to target presentation.

Computer algorithms were used to determine the beginning and end of saccades using a velocity criterion (30°/s). These marks were later verified by an experimenter and corrected if necessary within a customized graphical user interface written in Matlab (The MathWorks). This interface permitted the experimenter to inspect all trials, discarding trials with aberrant saccade sequences or neck EMG activity (e.g., associated with chewing the sipper tube). Trials with saccadic reaction times (SRTs) <60 ms of target presentation were rejected as being anticipatory. Fewer than 3% of trials were discarded.

Following this trial-by-trial inspection, customized Matlab programs extracted a number of parameters (e.g., level of neck EMG activity, SRTs) to investigate how these parameters varied across the differing reward expectancies. For the block-by-block analysis, we first had to determine how quickly the subjects adjusted to the new-reward schedule. To do this, we examined the SRTs for trials at the start of a new block and compared these SRTs to the average SRT from the last 10 trials within the block. Across our sample, subjects generated SRTs characteristic of the last trials of the block by the third trial (Fig. 2), consistent with previous reports on how rapidly monkeys adjust to an altered reward schedule (Lauwereyns et al. 2002). To be conservative, for the block-by-block analysis presented in the first part of the results, we discarded the first three trials of every block for all monkeys.
Influence of reward expectancy on low-frequency dSC activity and SRT

Increasing reward expectancy for movements into a neuron’s movement field led to marked increases in the neuron’s low-frequency activity prior to target onset and decreases in SRTs. Despite head restraint, increasing reward expectancy also led to the recruitment of a head-turning synergy that would turn the head toward the highly rewarded targets. To demonstrate these dependencies with reward expectancy, we first show data from a representative neuron that was recorded from the right dSC and discharged most vigorously for large leftward saccades (Fig. 3). During the equal-reward block (Fig. 3A), this neuron discharged a high-frequency (>100 Hz) series of action potentials that commenced about 70 ms after leftward target presentation and peaked around the time of leftward saccade initiation. Such high-frequency activity was absent following rightward target presentation. Another feature of this neuron is that it started to discharge at a gradually increasing level of low-frequency (<100 Hz) activity near the end of the gap interval, reaching a level of about 20–25 Hz regardless of target direction (* in Fig. 3A) just before the arrival of visual information in the dSC (~60 ms after target presentation).
After this, neural activity increased sharply following leftward target presentation and gradually decreased following rightward target presentation. It is important to recall that the subject could not anticipate the side of target presentation during the gap interval, even though FP disappearance provides a warning cue about impending target presentation. This pattern of low- and high-frequency levels of activity is consistent with previous reports of buildup (Munoz and Wurtz 1995) or prelude (Mohler and Wurtz 1976) activity from the dSC. In this block, both rightward and leftward saccades were usually generated at SRTs <150 ms.

The same neuron displayed a somewhat different profile of activity during the high-reward block (Fig. 3B). Compared with the equal-reward block, the low-frequency activity emitted by this neuron began to increase earlier during the gap interval, reaching substantially higher levels of low-frequency activity (~75 Hz just after target presentation) regardless of target direction (* in Fig. 3B). Following (leftward) target presentation into the neuron’s movement field, this neuron emitted a high-frequency period of activity that peaked with leftward saccades; because leftward SRTs were much shorter in the high- versus equal-reward blocks, the peak in high-frequency activity occurred earlier after target onset in the high-reward block. About 100 ms after (rightward) target presentation opposite to the neuron’s movement field, the level of low-frequency activity gradually began to diminish, prior to the generation of rightward saccades at considerably prolonged SRTs.

In the low-reward block, the neuron displayed no low-frequency activity during the gap interval (Fig. 3C). Following (leftward) target presentation into the neuron’s movement field, the neuron discharged a few spikes at a fixed latency and then continued to discharge at relatively low levels of activity up until a higher level of activity that accompanied the generation of leftward saccades at very long SRTs. In contrast, the neuron did not discharge following (rightward) target presentation opposite to the neuron’s movement field and remained silent prior to the generation of rightward saccades at very short SRTs.

Influence of reward expectancy on neck EMG

Despite head restraint, the neck EMG activity recorded during this reward series fluctuated with reward expectancy. In Fig. 4, we represent the activity recorded from two bilateral pairs of neck muscles (OCI and RCP maj) across the three reward expectancy blocks (data from the same experimental session as shown in Fig. 3). In this figure, the presumed function of a muscle is referenced to the side of the neural recording; thus left-OCI is termed an agonist muscle [recall that dSC stimulation recruits the OCI and RCP maj muscles contralateral to the side of stimulation (Corneil et al. 2002a)]. During the equal-reward block, the greatest amount of EMG activity (>=500 μV) is observed on leftward (agonist) muscles around the time of leftward saccades into the movement field, and on rightward (antagonist) muscles around the time of rightward saccades opposite to the movement field (e.g., top two subplots in Fig. 4Aii; bottom two subplots in Fig. 4Aii). During the gap interval, there are occasionally modest levels of neck EMG that precede the arrival of visual information at the level of the dSC or at the neck (Corneil et al. 2004); such “presensory” EMG activity is most easily seen on L-OCI prior to rightward gaze shifts as it is dissociated from movement-related EMG activity (top two subplots in Fig. 4Aii). In the equal-reward block, such presensory EMG activity was relatively rare and did not occur on every trial.

In the high-reward block, we observed an augmented amount of activity on the agonist muscles (Fig. 4B). Both L-OCI and L-RCP maj reached greater levels (~1 mV) of activity immediately following leftward saccades (top two subplots of Fig. 4Bi) compared with the equal-reward block. Further, both L-OCI and L-RCP maj displayed a much greater level of presensory activity, which began to increase during the latter portion of the gap interval. This presensory activity is most obvious on trials where the animal ultimately generated rightward saccades away from the movement field (top two subplots of Fig. 4Bii), peaking at about 250 μV around 75 ms after rightward target presentation. In contrast, the antagonist muscles displayed negligible amounts of presensory activity and increased in activity only around the time of rightward saccades generated at prolonged SRTs (bottom two subplots of Fig. 4Bii).

These patterns of EMG activity were reversed in the low-reward block (Fig. 4C): the antagonist muscles R-OCI and R-RCP maj peaked in activity shortly after very short latency rightward saccades and also displayed a far greater level of presensory activity during the gap interval (recall these muscles would be “agonists” to unrecorded dSC neurons opposite to the side of recording). In contrast, presensory EMG activity was negligible on the agonist muscles contralateral to the side of dSC recording.

Quantification of low-frequency dSC activity and neck EMG across reward expectancy

In Fig. 5A, we display the mean spike density and mean EMG waveforms from the representative example, focusing on how these waveforms change during the gap and immediate posttarget interval. Because the animal cannot anticipate the side of impending target presentation, we have pooled data for both rightward and leftward targets for this figure (recall that this interval precedes the arrival of visual information into the dSC). One important feature to appreciate from Fig. 5A is how the changes in the mean EMG activity from the agonist OCI and RCP maj muscles parallel the changes in the spike density waveform of the recorded dSC neuron. During all blocks of reward expectancy, the neural and agonist EMG waveforms appeared very similar: both measures exhibited minimal to moderate levels of activity during the low- and equal-reward blocks, respectively, and both measures increased considerably during the high-reward block along a similar time course. In contrast, the antagonist EMG waveforms displayed the opposite patterns across reward expectancy, presumably since such antagonist EMG activity is related to unrecorded neurons in the opposite dSC.

To quantify how low-frequency dSC activity and neck EMG varied with reward expectancy, we focused on an interval 25–35 ms after target presentation (shaded columns in Fig. 5A). This interval precedes the arrival of visual information in the dSC reported previously (Bell et al. 2006; Wurtz and Goldberg 1972); moreover, we confirmed this interval also precedes the visual response latencies we encountered (see METHODS). During this period, neural activity recorded from the dSC and
EMG activity from the contralateral agonist muscles increased with increasing reward expectancy, whereas EMG activity from the ipsilateral antagonist muscles decreased with increasing reward expectancy (Fig. 5B). All of the modulations with reward expectancy were highly significant (all five ANOVAs, \( P < 0.001 \)), as were all post hoc tests (\( P < 0.05 \)).

We performed this quantitative analysis during the period 25–35 ms following target presentation for all 55 neurons that met our criteria and for the EMG activity and SRTs recorded during these sessions (Fig. 6A shows the neural and muscle data averaged across all experimental sessions). Manipulations of reward expectancy exerted highly significant effects on each of these measures (for all repeated-measures ANOVAs, \( P \ll 10^{-5} \)); both neural activity and contralateral neck EMG activity increased with increasing reward expectancy (Fig. 6, B–D, empty bars). SRTs displayed the opposite trend, being shorter when the saccade was made to a target associated with a relatively high reward (Fig. 6E). Interestingly, over half of our
population of neurons (30/55) did not display a significant increase in activity during the gap interval of the equal-reward block [meeting some criteria of burst neurons (Munoz and Wurtz 1995)], but did so during the gap interval of the high-reward block [meeting some criteria of buildup neurons (Munoz and Wurtz 1995)]. This observation mirrors previous results that the functional classification of dSC neurons is not inviolate (Basso and Wurtz 1997; Dorris and Munoz 1998; Paré and Munoz 2001), but can vary depending on behavioral context.

We analyzed how the changes in EMG activity, dSC activity, and SRT across reward expectancy scaled with target eccentricity, since stimulation in more caudal dSC locations evokes progressively larger neck EMG responses (Corneil et al. 2002a). Given this topography, we predicted that greater levels of presensory EMG activity would be present for more eccentric targets (recall target eccentricities ranged from 5 to 27°) because more eccentric targets require larger gaze shifts and concomitantly larger head movements if the head were unrestrained. Consistent with this, the magnitude of presensory EMG activity on both OCI and RCP maj when recorded from the same side as the high-reward target increased linearly for progressively more eccentric targets (one-way ANOVA of EMG activity across target eccentricity, followed by linear trend analysis; $P < 0.001$ as were all post hoc tests at $P < 0.05$)

We also investigated the mean level of neural activity and neck EMG activity early (100–200 ms) after the monkey’s eyes landed in the fixation window (Fig. 6, B–D, filled bars). During this
interval, which preceded the start of the gap interval by ≥500 ms, the mean level of neural activity was not influenced by reward expectancy (repeated-measures ANOVA, $P_{\text{FDR}} = 0.39$), but the level of EMG activity recorded from OCI and RCP maj increased significantly with increasing levels of reward expectancy (both $P_{\text{FDR}} < 10^{-5}$). Both muscles also displayed greater levels of activity early in the fixation interval for more eccentric target locations (both $P_{\text{FDR}} < 0.05$). Thus early in the fixation interval, reward expectancy exerted an influence on neck muscle activity but not dSC activity. This result suggests the presence of a nontectal influence on neck EMG activity.

Finally, we also examined the influence of reward expectancy on initial eye position. If the extraocular eye muscles were being recruited in a manner similar to neck muscles, one could expect that initial eye position at the time of fixation point offset or target presentation would be biased in the direction of the more highly rewarded target. Across our population, we saw no evidence for initial eye position to be biased systematically toward the highly rewarded target (relative to initial eye position on the equal-reward blocks, the eye was biased 0.2° leftward when the leftward target was associated with higher reward and 0.02° leftward when the rightward target was associated with higher reward).

**Correlation between dSC activity and neck EMG**

Having established that variations in reward expectancy influenced low-frequency dSC activity, SRT, and the level of neck EMG across blocks of trials, we next investigated whether there are significant trial-by-trial correlations between these parameters. Previous research demonstrated a significant negative correlation between low-frequency dSC activity and SRT on a trial-by-trial basis in a variety of paradigms (Dorris and Munoz 1998; Fecteau et al. 2004; Ikeda and Hikosaka 2007); our experimental hypothesis predicts that low-frequency dSC activity should be positively correlated with the level of presensory neck EMG activity.

To investigate these correlations, we pooled the data recorded from a single neuron across all three variations in reward magnitude and plotted the mean level of low-frequency dSC activity in the interval 25–35 ms after target onset versus either SRT (Fig. 7A for our representative neuron) or the level of presensory neck EMG activity during the same interval (Fig. 7B; note we summed the EMG activity across contralateral OCI and RCP maj). Consistent with previous reports, we observed a significant trial-by-trial negative correlation between low-frequency dSC activity and the ensuing SRT across...
significant positive correlation to be associated with a greater level of neck EMG activity in the high- vs. equal-reward blocks.

Although we pooled data across all reward blocks to perform the above-cited correlations, a close inspection of Fig. 7B shows that a given level of neural activity (e.g., 15 Hz) tended to be associated with a greater level of neck EMG activity in the high-reward block versus the equal-reward block. To investigate this, we calculated a Reward Sensitivity Index (RSI) for neck EMG in the following manner. First, we correlated firing for neurons in the equal-reward block; equivalent results followed by a linear trend analysis (one-way ANOVA of Pearson’s $r$ across target eccentricity ($P = 0.01$), followed by a linear trend analysis ($P < 10^{-5}$)). In contrast, the $r$-values for the correlations between dSC activity and ensuing SRT did not vary linearly across target eccentricity (one-way ANOVA, $P = 0.06$; no linear trend).

We also investigated whether the correlations between dSC activity and either SRT or neck EMG activity scaled with target eccentricity. For example, the correlation between dSC and neck EMG activity should be stronger for more eccentric targets associated with larger head movements, given the known topography of the colliculo-cephalomotor drive (Cornell et al. 2002a). Consistent with this, the $r$-values of the correlation between dSC activity and neck EMG increased linearly for progressively more eccentric targets (one-way ANOVA of Pearson’s $r$ across target eccentricity ($P = 0.01$), followed by a linear trend analysis ($P < 10^{-5}$)). In contrast, the $r$-values for the correlations between dSC activity and ensuing SRT did not vary linearly across target eccentricity (one-way ANOVA, $P = 0.06$; no linear trend).

Although we pooled data across all reward blocks to perform the above-cited correlations, a close inspection of Fig. 7B shows that a given level of neural activity (e.g., 15 Hz) tended to be associated with a greater level of neck EMG activity in the high-reward block versus the equal-reward block. To investigate this, we calculated a Reward Sensitivity Index (RSI) for neck EMG in the following manner. First, we correlated neck EMG and neural activity separately for the equal- and high-reward blocks; such RSI outliers had negligible neural activity. C and D: histograms of Pearson’s $r$-values across the sample of 55 neurons for correlations between dSC activity and SRT (C) or dSC activity and neck EMG activity (D). Both distributions lay significantly displaced from zero (C; mean ± SD, $r = -0.32 ± 0.20$; t-test vs. zero, $P < 10^{-5}$; D; mean ± SD, $r = 0.31 ± 0.23$; t-test vs. zero, $P < 10^{-5}$). E and F: frequency histograms of reward sensitivity indices for SRT (E) and neck EMG (F), expressing the change in the measured parameter associated with a given level of neural activity in the high- vs. equal-reward blocks.

### Figure 7

- **A** and **B**: Trial-by-trial correlations between low-frequency dSC activity vs. SRT (A) and presensory neck EMG activity (B). A and B show data from the present data set, pooled across all 3 reward expectancy blocks. The level of presensory neck EMG was obtained by summing the activity recorded from contra-OCI and contra-RCP maj, since both muscles are known to contribute to head turns. For the correlation in A, Pearson’s $r = -0.77$, $P < 10^{-5}$, $n = 75$. For the correlation in B, $r = 0.86$, $P < 10^{-5}$, $n = 218$. There are many more points in B compared with A for 2 reasons. First, data for the correlation in B could come from trials where the target appeared either into or opposite to the movement field. Second, for the correlation in A, we discarded trials from the low-reward block where the SRT was >4SDs away from the mean SRT on equal- and high-reward blocks; such RSI outliers had negligible neural activity. C and D: histograms of Pearson’s $r$-values across the sample of 55 neurons for correlations between dSC activity and SRT (C) or dSC activity and neck EMG activity (D). Both distributions lay significantly displaced from zero (C; mean ± SD, $r = -0.32 ± 0.20$; t-test vs. zero, $P < 10^{-5}$; D; mean ± SD, $r = 0.31 ± 0.23$; t-test vs. zero, $P < 10^{-5}$). E and F: frequency histograms of reward sensitivity indices for SRT (E) and neck EMG (F), expressing the change in the measured parameter associated with a given level of neural activity in the high- vs. equal-reward blocks.
are obtained if other values are chosen; we did not extend this analysis to the low-reward block since only eight neurons had a significant positive correlation in the low-reward block.) This yields an estimate of the neck EMG activity associated with 15 Hz of activity in both the equal- and high-reward blocks. With these values, we then calculated the RSI for each neuron as

$$RSI = \frac{\text{Estimated value}_{\text{high}} - \text{estimated value}_{\text{equal}}}{\text{Estimated value}_{\text{high}} + \text{estimated value}_{\text{equal}}}$$

RSIs for the 31 neurons for which this analysis was performed for the correlation between neural activity and neck EMG are shown in Fig. 7F. The majority of these indices were >0, meaning that greater levels of neck EMG were observed for a given level of neural activity in the high-reward block (mean ± SD = 0.45 ± 0.43, t-test vs. zero, $P < 10^{-5}$).

We performed an analogous analysis for SRT (Fig. 7E). The majority of the SRT indices were <0, meaning that shorter SRTs were correlated with a given level of neural activity in the high-reward block ($n = 22$, mean ± SD = -0.10 ± 0.07, t-test vs. zero $P < 10^{-5}$).

**Optimal time shift for correlation between dSC activity and neck EMG**

The preceding analyses correlated low-frequency dSC activity and neck EMG activity within a 10-ms window spanning from 25 to 35 ms after target presentation. This analysis does not take into consideration any time delay between a change in dSC activity and any corresponding change in neck EMG activity; although the precise number of synapses between dSC neuron and neck muscle motoneurons in the primate is unknown, our previous work demonstrated that contra-OCI and contra-RCP maj are activated about 13 ms after dSC stimulation (Corneil et al. 2002a). We therefore investigated whether the correlation between low-frequency dSC activity and neck EMG activity improved as the window within which neck EMG activity was integrated shifted later in time to account for the efferent delay (Fig. 8A; note we also shifted the neck EMG activity window earlier in time for comparison).

The thick solid line in Fig. 8B shows the results of this correlation analysis, repeated for all neurons within our sample across shifts in the neck EMG activity window from -30 to +30 ms (in 1-ms increments, relative to the +25- to +35-ms window over which dSC activity was measured. Note in Fig. 8B that the mean r-value for a 0-ms shift is 0.31; this is the mean of the distribution shown in Fig. 7D. The mean r-values decrease progressively as the EMG window is shifted back in time and increase as the EMG window is shifted forward in time, reaching a peak value when dSC activity is correlated to neck EMG activity recorded 20 ms later. Following this peak, the mean r-values decrease suddenly because larger forward shifts in time begin to encompass the visual burst of neck EMG following target onset. Although this increase in the r-value is relatively modest, the time of the peak r-value (20 ms) is consistent with our experimental hypothesis, in that it approximates the conduction time along the tecto-reticulo-spinal projection (see DISCUSSION).

In Fig. 8B, the time course of the r-value is compared with the results from a bootstrap analysis (thin line, with dashed lines tracing the “stderr”), which randomly reshuffled the trial-by-trial neck EMG versus dSC activity within each of three reward blocks for each cell (100 iterations per block per cell). This bootstrap analysis gives an estimate of the degree of correlation inherent to the two monotonically rising signals separate from the trial-by-trial dependencies. These curves were significantly different at all time points (paired t-test at each point, corrected for multiple comparisons, $P < 10^{-5}$).

**Comparison of discrimination of side of target presentation by low-frequency dSC activity and neck EMG activity**

A potential problem with the preceding time-shift analysis is that both dSC and neck EMG signals increase monotonically following target onset. Thus the increase in the population r-value may simply be the result of shifting the neck EMG window to consider intervals with greater activity, and thus a greater signal-to-noise ratio, with the timing of the peak being
dictated by the intrusion of the visual burst of neck EMG. Because these concerns qualify our conclusions regarding the optimal time shift between dSC and neck EMG activity, we sought an additional analysis that could provide insights into the relative timing of dSC and neck EMG activity and, accordingly, analyzed the comparative timing of dSC and neck EMG signals related to target presentation.

Of the 55 neurons satisfying our inclusion criteria 31 also displayed visually related activity by emitting a brief discharge of action potentials following the presentation of a contralateral visual stimulus. Because these neurons were recorded simultaneously with neck EMG activity, we can ask which of dSC or neck EMG activity indicates side of target presentation first. We analyzed this aspect of our data by using a time-series ROC analysis on both dSC and neck EMG activity, with data segregated by the side of target presentation (for further details see Corneil et al. 2004; we term this time the discrimination time). An example of this ROC analysis for simultaneously recorded dSC and neck EMG activity is shown in Fig. 9A using the representative data shown in Figs. 3 and 4. For this example, dSC activity discriminated about the side of target presentation 7 ms before neck EMG activity (50 vs. 57 ms after target presentation, respectively). Across our sample, the discrimination time for dSC activity was almost always (30/31) less than the discrimination time for neck EMG activity, with dSC activity discriminating the side of target presentation on average 11.4 ± 8.5 ms (range: −2 to 38 ms) earlier than neck EMG activity (Fig. 9B; paired t-test; P < 10−5; dSC activity: 47.4 ± 4.2 ms, median 46 ms, range: 39–58 ms; EMG activity: 58.4 ± 6.7 ms, median 56 ms, range: 49–77 ms). Thus across our sample of simultaneously recorded dSC and neck EMG activity, activity that depended on the side of target presentation appeared approximately 11 ms earlier in dSC compared with neck EMG activity.

**Head-unrestrained behavior**

In two of our three monkeys, we ran head-unrestrained experiments without dSC recordings. Although a detailed analysis of these results will be presented in a future report, we present here an exemplar data set to show some of the consequences of neck muscle recruitment during this task on head position and movement. Briefly, we observed qualitatively similar profiles of neck EMG regardless of head restraint, with the level of neck EMG in the pretarget period increasing on the muscle ipsilateral to the side of the high anticipated reward (Fig. 10, A and B). Consistent with the head-restrained results, the reaction times for both gaze-shift and head-movement initiation varied inversely with the amount of anticipated reward (Fig. 10C). In our task, head-movement reaction times tended to be less than gaze-shift reaction times; this is in part because the minimal saccadic reaction time of 60 ms (see METHODS) was not applied to head movements, since we did not constrain head position. In fact, we frequently observed anticipatory head movements toward the highly rewarded target, even though gaze remained stable due to the vestibulo-ocular reflex. We have previously reported such “head-only movements” in a variety of behavioral and stimulation protocols (Corneil and Elsley 2005; Corneil and Munoz 1999; Corneil et al. 2002b; Elsley et al. 2007). Such head-only movements occurred most often in the direction of the highly rewarded target (Fig. 10D). Finally, on a block-by-block basis, we observed that the initial position in the fixation interval (i.e., prior to the disappearance of the fixation point) of the head was biased toward the highly rewarded target (Fig. 10E). This position bias confounds customary measures of eye–head
coordination, such as how much the head moves during a gaze shift. Our future report will present a more detailed analysis of the profiles of eye–head coordination in this task.

**DISCUSSION**

Our results demonstrate that increases in low-frequency dSC activity correlate with the recruitment of a head-turning synergy. Such recruitment persisted despite head restraint but scaled with target eccentricity, consistent with the generation of a larger head turn if the head was unrestrained. We observed strong similarities between low-frequency dSC activity and neck EMG activity both across differing blocks of reward expectancy and from trial to trial. These relationships mirrored an inverse relationship between dSC activity and the ensuing saccade reaction time. The optimal correlation between dSC and neck EMG activity was not recorded with the head unrestrained. The experimental task was exactly the same and, in this example, potential targets were placed either 35° to the right or left. The profiles of neck EMG activity in the pretarget period resembled those recorded with the head restrained, with neck EMG increasing on those muscles ipsilateral to the more highly rewarded target (A, B). C: the reaction times of both gaze (solid line) and head (dashed line) movements varied inversely with reward expectancy (for B–E, the high-reward blocks have been collapsed across target direction). D: the monkey also generated a greater number of anticipatory head movements toward the highly rewarded location, even though the subsequent gaze shift was directed in the opposite direction. We have termed these sequences “head-only movements,” for consistency with previous work. E: during the fixation interval, we also observed a bias in the initial position of the head toward the side of the highly rewarded target. All of the relationships shown in B–E were highly significant (ANOVA; P < 10⁻⁵).

**Recruitment of a head-turning synergy as a sequela of low-frequency dSC activity**

Two observations support a role for the dSC activity in the intermediate stages of sensorimotor transformations. First, low-frequency levels of dSC activity correlate with a variety of high-level processes such as target or saccade selection, attentional allocation, motor preparation, decision making, and representations of reward variables (Basso and Wurtz 1997; Dorris and Munoz 1998; Dorris et al. 2007; Fecteau et al. 2004; Glimcher and Sparks 1992; Horwitz and Newsome 1999; Ignashchenkova et al. 2002a; Ikeda and Hikosaka 2003; Krauzlis and Dill 2002; McPeek and Keller 2002). Second, subsaccadic stimulation (in terms of either current or frequency) of the dSC influences...
behavior in a manner consistent with modulations of such high-level processes (Carello and Krauzlis 2004; Cavanaugh and Wurtz 2004; Horwitz et al. 2004; Muller et al. 2005). We speculate that unrecorded changes in neck muscle activity would have accompanied many of these experiments; this supposition is supported by our recent work demonstrating neck muscle recruitment associated with reflexive covert orienting during a saccadic cueing task (Cornel et al. 2008). Further, low-current dSC stimulation recruits a head-turning synergy without or prior to gaze shifts (Cornel et al. 2002a,b; Pélisson et al. 2001) and very short duration dSC stimulation elicits neck muscle responses that covary with degree of motor preparation (Cornel et al. 2007). There is no anatomical evidence to date for separate populations of primate dSC efferent neurons that could permit selective communication with upstream cortical areas (e.g., via projection through the thalamus or pulvinar) without communicating with downstream eye and head premotor centers (Moschovakis et al. 1988a,b). Indeed, the functional signals sent along one ascending efferent pathway to the medial dorsal nucleus of the thalamus represent all of the signals within the dSC in a delayed-saccade task (Sommer and Wurtz 2004), as do the signals conveyed downstream via the predorsal bundle (Rodgers et al. 2006). Thus we speculate that any process that increases low-frequency dSC activity will recruit the head premotor circuitry; we will subsequently return to the significance of this supposition.

If low-frequency dSC activity is conveyed to downstream premotor targets, then the brain stem omnipause neurons (OPNs) assume a crucial role in preventing low-frequency dSC activity from engaging the brain stem burst generator. OPN activity remains constant during a 200-ms gap interval, despite increasing levels of low-frequency dSC activity (Everling et al. 1998; Munoz et al. 2000), presumably sustaining inhibition of the brain stem burst generator. The biomechanics of eye motion are such that very small changes in extraocular muscle force can move the eyes (Goldberg et al. 1998; Sparks and Gandhi 2003), yet we observed no bias in initial eye position and we did not expect changes in motor preparation and head muscle recruitment during a saccadic cueing task (Corneil et al. 2008).

To date, no study in head-unrestrained primates has systematically examined low-frequency activity. The work of Freedman and Sparks (1997b) demonstrated that the motor-related burst of dSC activity encoded the desired gaze shift, regardless of the contributions of the eye and head. More recently, Walton et al. (2007) reported a new functional class of dSC neurons that increase their activity during head movements that either do or do not accompany a gaze shift. Such putative head-related neurons are distinct from the saccade-related neurons recorded in this study: they are not topographically organized throughout the dSC and discharge very modestly or not at all during gaze shifts composed solely of eye movements. We likely selected against head-related cells given our use of head restraint and our requirement for movement-related activity in excess of 100 Hz. Future studies will be required to determine the role of putative head-related neurons in cephalomotor and oculomotor control.

The optimal correlation between low-frequency dSC and neck EMG activity occurs when the latter is shifted 20 ms later in time. This 20-ms value is longer than the 13-ms facilitation latencies for OCI and RCP maj following dSC stimulation (Corneil et al. 2002a) and is also longer than the 11-ms difference between the time that dSC or neck EMG activity signals the side of target presentation. The shorter stimulation-evoked facilitation latency (13 ms) and shorter differences in discrimination time (11 ms) likely attest to faster temporal summation due to a higher stimulation frequency (300 Hz) or following visual target presentation, compared with the mean level of low-frequency activity observed in the high-reward block (~30 Hz; Fig. 6B). Consistent with this, the latencies of evoked saccades decrease with increasing stimulation frequency (Stanford et al. 1996).

Expectation of reward, allocation of attention, or motor preparation?

The influence of reward-related variables is ubiquitous throughout the oculomotor system (Glimcher 2003; Sugrue et al. 2005), but it is not always easy to dissociate reward from attention and motor preparation (Maunsell 2004; Roesch and Olson 2007). Increasing reward expectancy in a memory-guided saccade task increases both dSC activity (Ikeda and Hikosaka 2003, 2007) and neck muscle activity (Roesch and Olson 2003, 2005). Although our results extend these findings to an immediate response paradigm, they also demonstrate the difficulty in ascribing a particular function to an area based on correlated neural activity. Our task directly manipulated reward expectancy, but changes in both SRT and neck EMG attest to accompanying changes in motor preparation and motor recruitment prior to the arrival of target-related information in the dSC. One can be certain of function at the motor periphery: neck muscle motoneuron activity signals motor output, regardless of correlations with other high-level signals.

In our opinion, what a neuron does depends in part on where the signal is sent; given neuronal branching it is perhaps not surprising that a neuron can seem to have multiple functions. For example, saccade-related dSC activity plays a motor role by engaging the saccadic burst generator, but is also implicated in remapping visual space in the frontal cortex via ascending projections through the thalamus (Sommer and Wurtz 2006). Similar lines of reasoning can ascribe to low-frequency dSC activity a motor preparatory role by virtue of projections to the saccadic burst generator (such as changes in SRT), a motor recruitment role by virtue of projections to the cephalomotor system (such as changes in neck EMG), and various high-level roles (e.g., attention, reward representations) by virtue of ascending projections to the cortex.

How closely does neck EMG reflect dSC activity?

Our recent report (Corneil et al. 2008) demonstrated that neck muscle recruitment during reflexive covert orienting resembled dSC activity (Dorris et al. 2002; Fecteau et al. 2004). The current report extends these results by simultaneously recording dSC and neck EMG activity, permitting trial-by-trial analyses. Although our results are consistent with dSC activity recruiting a head-turning synergy, it is important to emphasize that neck EMG activity need not only reflect activity carried along the tecto-reticulo-spinal pathway. Indeed, we observed a number of instances where neck EMG activity did not simply follow dSC activity.
First, it is important to acknowledge that neck muscle motoneurons are the final common path for a number of descending systems. The presence of a nontectal influence on neck EMG is apparent in the early fixation interval, wherein the recruitment of a head-turning synergy but not low-frequency dSC activity scales with reward expectancy (Fig. 6, filled bars). The source of this reward-dependent recruitment remains to be determined, but it is plausible that it could stem from cortical areas signaling aspects of task set (Coe et al. 2002). Such nontectal sources may be similar to those mediating head turns despite dSC inactivation (Walton et al. 2008). Another nontectal source influencing neck EMG is apparent following saccade offset. Neck EMG activity remained high consequent to the eccentric orbital position, presumably due to reticolospinal neurons that discharge proportionally to orbital eye position (Grantyn and Berthoz 1987), even though dSC activity diminished (Figs. 3 and 4).

Second, another difference between dSC and neck EMG activity is how they scaled with target eccentricity. Although the magnitude of low-frequency dSC activity did not scale with target eccentricity, progressively larger target eccentricities led to larger and more robust neck EMG responses, consistent with the topography of the colliculo-cephalomotor drive (Corneil et al. 2002a). Consequently, the relationship between dSC and neck EMG activity is stronger for more eccentric target locations.

Third, we speculate that neck EMG best reflects the differential activity across both dSCs. Two observations support this qualification. First, neck EMG did not increase during the gap interval of the equal-reward block, even though the activity of many low-frequency dSC neurons increases in this interval (see also Corneil et al. 2004, 2007). However, in the equal-reward block, low-frequency dSC activity increases in both dSCs, in that targets associated with equivalent reward expectancies can appear in one of two potential locations. The introduction of differing reward expectancies leads to differing levels of low-frequency dSC activity across both dSCs, ultimately leading to the recruitment of a head-turning synergy favoring the highly rewarded target. Second, the same level of dSC activity was correlated with a higher level of neck EMG in the high- versus equal-reward block (Fig. 7F), presumably because of the negligible level of low-frequency activity in the opposite dSC in the high-reward block. We have previously speculated that mutually inhibitory projections within downstream head premotor circuits implement the comparison of activity across both dSCs (Corneil et al. 2007), in a manner analogous to proposed computation of differences in spike rates elsewhere in the brain (Gold and Shadlen 2002). Neck EMG activity best reflects differential dSC activity, regardless of whether such differential activity is introduced via stimulation (Corneil et al. 2002a, 2007), sensory events (Corneil et al. 2004), or cognitive processes, as shown here and elsewhere (Corneil et al. 2008).

Together, our observations demonstrate that aspects of dSC activity can be reflected in the recruitment of a head-turning synergy. However, the relationship between these two variables is not one to one, given that our results demonstrate that changes in neck EMG most closely follow dSC activity during the gap and peritarget intervals of the high-reward block. Future studies combining neck EMG recordings with more complex mappings between sensory events, cognitive variables, and motor actions are required to further investigate the relationships between low-frequency dSC activity and cephalomotor output.

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