


Vestibular Contributions to Primate Neck Postural Muscle Activity during Natural Motion

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To maintain stable posture of the head and body during our everyday activities, the brain integrates information across multiple sensory systems. Here, we examined how the primate vestibular system, independently and in combination with visual sensory input, contributes to the sensorimotor control of head posture across the range of dynamic motion experienced during daily life. We recorded activity of single motor units in the splenius capitis and sternocleidomastoid muscles in rhesus monkeys during yaw rotations spanning the physiological range of self-motion (up to 20 Hz) in darkness. Splenius capitis motor unit responses continued to increase with frequency up to 16 Hz in normal animals, and were strikingly absent following bilateral peripheral vestibular loss. To determine whether visual information modulated these vestibular-driven neck muscle responses, we experimentally controlled the correspondence between visual and vestibular cues of self-motion. Surprisingly, visual information did not influence motor unit responses in normal animals, nor did it substitute for absent vestibular feedback following bilateral peripheral vestibular loss. A comparison of muscle activity evoked by broadband versus sinusoidal head motion further revealed that low-frequency responses were attenuated when low- and high-frequency self-motion were experienced concurrently. Finally, we found that vestibular-evoked responses were enhanced by increased autonomic arousal, quantified via pupil size. Together, our findings directly establish the vestibular system's contribution to the sensorimotor control of head posture across the dynamic motion range experienced during everyday activities, as well as how vestibular, visual, and autonomic inputs are integrated for postural control.

Key words: motor unit; natural motion; neck muscle; postural control; vestibular; vestibulocollic

Significance Statement

Our sensory systems enable us to maintain control of our posture and balance as we move through the world. Notably, the vestibular system senses motion of the head and sends motor commands, via vestibulospinal pathways, to axial and limb muscles to stabilize posture. By recording the activity of single motor units, here we show, for the first time, that the vestibular system contributes to the sensorimotor control of head posture across the dynamic motion range experienced during everyday activities. Our results further establish how vestibular, autonomic, and visual inputs are integrated for postural control. This information is essential for understanding both the mechanisms underlying the control of posture and balance, and the impact of the loss of sensory function.

Introduction

The ability to maintain posture and balance during our everyday activities requires the integration of multiple sensory and motor signals. In this context, the vestibular organs provide essential information about motion of the head in space, which is rapidly transmitted via central vestibular pathways to drive compensatory

vestibulospinal reflexes that help stabilize head and body posture (Roy and Cullen, 2001; Cullen and Roy, 2004; Brooks and Cullen, 2013). To date, however, the vestibular system's contributions to the control of posture during natural motion experienced in daily life, both independently and in combination with other sensory cues, are not well understood.

In this context, the pathways responsible for stabilizing the head relative to space constitute an excellent model to understand the vestibular system's contribution to postural control. First, the central brainstem and cerebellar vestibular circuits that mediate compensatory neck muscle responses have been well characterized in primates (Roy and Cullen, 2001; Cullen and Roy, 2004; Brooks and Cullen, 2013; Zobeiri and Cullen, 2022). Second, relative to the complex biomechanics of the appendicular system, the biomechanics of head-on-body motion in the yaw plane are relatively simple because the majority of movement

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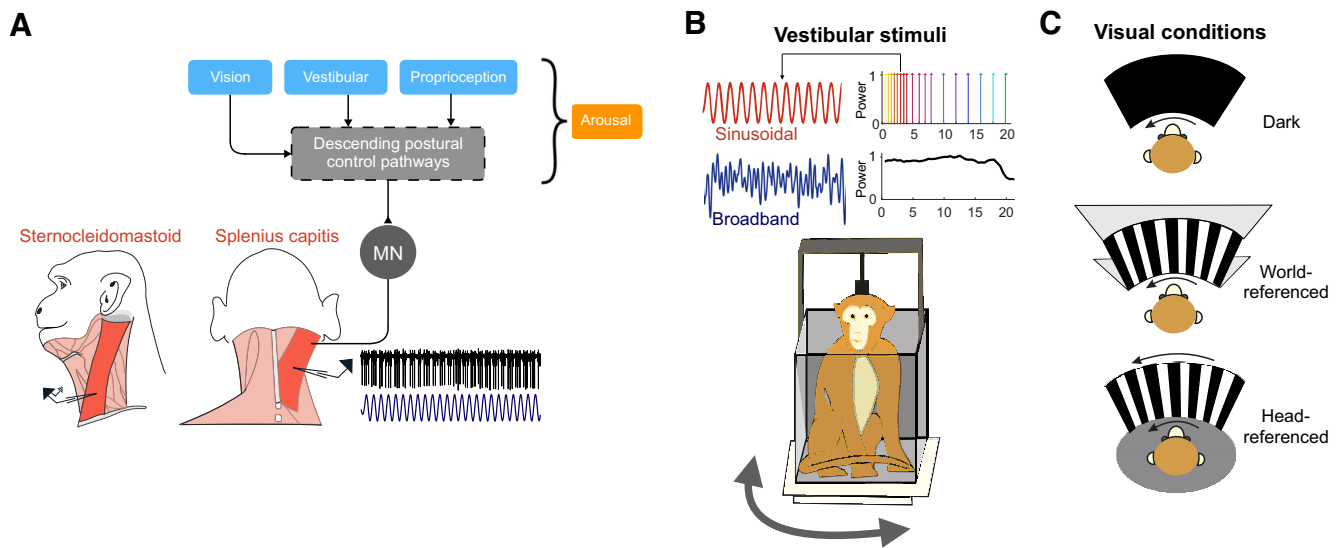


Figure 1. Experimental paradigm to study descending postural control pathways. **A**, Illustration of the different descending postural control pathways that can contribute to neck motor unit activity. **B**, Schematic of our vestibular stimulation protocol where we applied sinusoidal and broadband yaw angular motion containing frequencies up to 20 Hz to head-fixed monkeys. **C**, The conditions used to manipulate visual feedback to assess visual-vestibular integration for postural control during sinusoidal motion.

occurs around a single pivot joint (atlantoaxial). Finally, two particularly strong muscles that contribute to stabilizing the head in the yaw plane are accessible for recording in primates (sternocleidomastoid [SCM] and splenius capitis [SPL]) (Corneil et al., 2001; Blouin et al., 2007).

During everyday activities, primates experience vestibular input with frequency content approaching 20 Hz (humans: Grossman et al., 1988; Pozzo et al., 1990; Carriot et al., 2014; monkeys: Armand and Minor, 2001; Carriot et al., 2017). Yet, to date, head motion responses to vestibular stimulation have only been studied at relatively low frequencies (<4 Hz) for rotations (monkeys: Reynolds and Gdowski, 2008; humans: Guitton et al., 1986; Keshner and Peterson, 1995). Likewise, prior studies that examined neck muscle activity during rotations only probed this lower-frequency range in cats (Berthoz and Anderson, 1971; Ezure and Sasaki, 1978; Bilotto et al., 1982; Vidal et al., 1982; Goldberg and Peterson, 1986). Based on these neck muscle recordings, Peng et al. (1996, 1999) developed a model of human head postural control in which the vestibular contribution (vestibulocollic reflex [VCR]) was assumed to have high-pass tuning. Importantly, however, these predictions have never been experimentally validated. Consequently, to date, the vestibular system's contribution to head stabilization across a bandwidth corresponding to the self-motion experienced in everyday life remains unknown. Furthermore, how the vestibular system works in combination with visual sensory cues for the control of posture remains an open question.

Accordingly, to directly address these questions regarding the vestibular system's contribution to postural control, we recorded the activity of single neck motor units in alert rhesus macaques during whole-body rotations up to 20 Hz. Response gains in motor units increased with frequency up to 16 Hz in normal animals and remained significant at higher frequencies. In contrast, responses were negligible across this entire frequency range after bilateral peripheral vestibular loss. When vestibular information is less reliable, it is possible that inputs from other modalities (e.g., visual and proprioceptive) can be upweighted to substitute (Sadeghi et al., 2010, 2011, 2012). Surprisingly, we found the presence of visual cues neither altered postural muscle activity in normal animals, nor substituted for absent vestibular feedback

following vestibular loss. Furthermore, during more complex head motion, motor unit gains for low-frequency motion were attenuated when experienced concurrently with high-frequency motion. Finally, given that the autonomic system is well situated to play a crucial role in modulating postural reflexes (Balaban, 2004), we examined the influence of arousal, quantified by pupil size. We found a significant enhancement of neck muscle responses during a heightened state of arousal. Together, our findings reveal that the vestibular system provides an essential contribution to neck postural muscle activity across the range of dynamic motion experienced during everyday life.

Materials and Methods

Four rhesus monkeys (*Macaca mulatta*), 2 male and 2 female, were prepared for surgery for a head implant used to fixate the head using aseptic surgical techniques. A titanium post used to immobilize the head was attached to the skull using titanium screws and dental acrylic. Bilateral vestibular loss (BVL) was induced in 1 female monkey (Monkey G). Briefly, gentamicin treatment was delivered via intratympanic injection in the right ear, and the left labyrinth was surgically disrupted, together resulting in a horizontal vestibular ocular reflex (VOR) gain <0.1 measured at 2 Hz (Mitchell et al., 2013). Each monkey was given a minimum of 2 weeks to recover from the surgery before experiments began. All surgery and experimental procedures were approved by the Johns Hopkins Animal Care and Use Committee, which is accredited by the Association for the Assessment and Accreditation of Laboratory and Animal Care. Three monkeys (Monkeys C, D, and G) were involved in experiments examining vestibular and visual contributions to neck postural muscle responses, and 2 monkeys (Monkeys D and J) were involved in experiments probing the influence of autonomic arousal (see Experimental design and statistical analyses below).

Neck motor unit recordings. Motor unit activity was recorded from the right SPL and left SCM muscles using custom-made fine-wire electrodes (Stablohm 800A; California Fine Wire) (see Fig. 1A). When active, both muscles contribute to rotating the head to the right. Electrodes were made by tightly winding a pair of stainless-steel wires together and removing ~1 mm of shielding from the end of one wire. Electrodes were steam sterilized and inserted through a hypodermic needle under ultrasound guidance (SonoSite MicroMaxx) into the SPL approximately at the level of C3 and the superficial proximal third of SCM. We confirmed activity in these muscles during attempted head yaw movements made while the monkey was head-fixed. The ground

was connected to a metal chamber in the head implant or surface electrode placed on the mastoid process. EMG signals were amplified ($\times 2000$), band-pass analog filtered (30–10,000 Hz) (NeuroLog system, Digitimer), and digitized at 30 kHz on a Cerebus Neural Signal Processor (Blackrock Microsystems). We inserted one electrode in each muscle (SPL and SCM) during a total of 16 experimental to examine vestibular contributions to posture.

Experimental design and statistical analyses. During experiments, monkeys were seated in a primate chair that was mounted on top of a vestibular turntable with their heads stabilized with respect to the chair. Natural vestibular stimulation was applied by rotating the vestibular turntable in the yaw plane. Our experimental approach, focused on SPL and SCM motor unit responses to yaw rotations, builds on existing neurophysiological and modeling literature, which is most advanced for yaw axis vestibular stimulation (for review, see Goldberg and Cullen, 2011). Rotational head velocity signals were measured with a head-mounted MEMS sensor and digitized at 1000 Hz. First, we applied sinusoidal rotations at a velocity of 40°/s to each monkey in the dark at 18 frequencies from 0.5 to 20 Hz (0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 5, 6, 7, 8, 10, 12, 14, 16, 18, and 20 Hz), with 30 cycles delivered at each frequency (see Fig. 1B).

Next, to examine multisensory integration of visual and vestibular feedback in normal animals, muscle responses to sinusoidal motion in the dark were compared with those recorded in two visual conditions: world-referenced and head-referenced visual surrounds (see Fig. 1C). In both conditions, the monkey viewed an identical patterned visual scene of black vertical lines spaced 10° apart on a white backdrop. In the world-referenced visual condition, the visual scene remained stationary relative to the world, thereby providing complimentary visual cues about self-motion that were congruent with vestibular information. In the head-referenced visual condition, the visual scene rotated with the monkey, thereby providing visual information that conflicted with vestibular self-motion information (i.e., visual input indicating no self-motion).

Additionally, we examined the effect of visual stimulation that was out of plane, namely, visual stimulation in the roll and pitch axes, rather than yaw axis. To do this, we applied roll or pitch visual motion by projecting dots on the unpatterned visual surround (Optotest, TechnoConcept, 40°/s) while monkeys experienced concurrent yaw sinusoidal motion. Roll axis visual stimulation was applied both in counterclockwise (CCW) and clockwise (CW) directions, and pitch axis visual stimulation was applied in both upward and downward directions. In addition, we recorded muscle activity in a condition during which the same dots were projected on the surround but remained stationary during corresponding yaw rotations. Finally, to assess whether visual information could substitute for the loss of vestibular feedback during self-motion, we examined muscle responses after BVL in the world-referenced surround condition.

In addition to the sinusoidal stimuli testing described above, we applied broadband noise stimulation (flat power from 0 to 20 Hz, root-mean-square velocity = 20°/s, two 1 min trials; see Fig. 1B), and response gains were compared with those recorded during single sine waves. Finally, to examine the modulation due to arousal level, we used a positively-valenced social paradigm and measured pupil size under isoluminant conditions as an index of autonomic arousal (Varazzani et al., 2015; Joshi et al., 2016). Pupil size as well as horizontal and vertical eye position data were recorded using video-oculography with a frame rate of 200 Hz (FLIR Firefly S, Teledyne FLIR). First, in Monkey D, we applied three 1 min trials of broadband noise motion at baseline and after placing Monkey J in her presence. We then applied these stimuli to Monkey J while Monkey G was in his presence and then at baseline. This experiment was repeated twice for each pair, and we focused our recordings on the right SPL muscle only. In each case, both monkeys displayed behavior indicating a friendly interaction (e.g., lip smacking) as well as an increase in pupil size when in the presence of the other monkey.

To first determine frequencies where single neck motor units exhibited activity that was significantly correlated with motion stimuli, we estimated coherence between angular velocity (with the convention that ipsilateral, i.e., rightward, motion is positive), and neck EMG (Rosenberg et al., 1989; Halliday et al., 1995). We primarily examined single motor unit spike times (discriminated using a custom MATLAB program) since spike times have a high temporal resolution and the resulting signal is extracted

from the background noise. However, we also examined multiunit activity (rectified EMG, bandpass filtered from 100 to 10,000 Hz with a fourth-order dual-pass Butterworth filter) to validate whether multiunit recordings can be used to examine muscle responses to stimuli applied in this study. For each motion paradigm, velocity signals were first low-pass filtered using a fourth-order dual-pass Butterworth filter with cutoff frequencies of $2n + 1$, where n is the highest frequency in the stimulus. All signals were resampled to 1024 Hz and concatenated across trials for the healthy monkeys and BVL monkey and analyzed with a frequency resolution of 0.5 Hz (2 s segments). For sinusoidal vestibular stimulation, we analyzed data precisely at the 18 frequencies delivered; for broadband noise stimulation, we considered all data points between 0.5 and 20 Hz (in 0.5 Hz increments). Coherence (R_{xl}^2) was calculated at each frequency (λ) as follows:

$$|R_{xl}(\lambda)|^2 = \frac{|f_{xl}(\lambda)|^2}{f_{xx}(\lambda)f_{ll}(\lambda)}$$

where f_{xl} is the cross-spectrum and f_{xx} and f_{ll} are the autospectra of the velocity and motor unit activity (spike times or rectified EMG) (Halliday et al., 1995). At frequencies where neck muscle activity showed significant (beyond 99% confidence intervals (CIs), see Experimental design and statistical analyses) coherence with velocity, we examined the gain and phase of the response (Rosenberg et al., 1989). Gain at each frequency was estimated as the absolute value of the cross-spectrum divided by the power spectrum of the velocity signal at the same frequency; and for comparisons between broadband noise and sinusoidal stimulation, values were normalized to the maximum gain under each condition.

For comparison with previous research, we implemented the VCR transfer function of the neuromechanical model developed by Peng et al. (1996) using MATLAB Simulink. To facilitate comparisons with our results, gain from the neuromechanical model was normalized to gain at 16 Hz; and both gain and phase data are plotted with respect to angular velocity.

To assess whether the linear relationship between rotation velocity and motor unit activity (spike times or rectified EMG) was significant at each frequency, we constructed 99% confidence intervals (CIs) for coherence (positive limit) based on the number of segments and assumed independence between the two signals (Halliday et al., 1995). We extracted and analyzed gain and phase values only at frequencies where there was significant coherence. In the resulting phase–frequency relationship during sinusoidal stimulation, we noted that there appeared to be separate regions that displayed different phase slopes. Thus, to more precisely determine where the inflection point occurred, we found the two linear regressions that, when fit to the phase–frequency relationship, produced the highest variance accounted for.

To examine differences in gain and phase between the different visual stimulation conditions and autonomic arousal states, we constructed bootstrapped 95% CIs by resampling (with replacement) and pooling data from all motor units discriminated under each condition. Resampling was repeated 10,000 times to determine point-wise CIs with positive and negative limits, and differences were considered significant in nonoverlapping regions. To compare coherence between autonomic arousal states, we performed a χ^2 difference of coherence (DOC) test (Amjad et al., 1997).

From the video-oculography data, we calculated pupil diameter during each trial of broadband noise stimulation over periods where the eye was relatively centered in the orbit (within $\pm 10^\circ$ from center in both vertical and horizontal directions), and compared diameter between the two autonomic arousal states using paired-samples t tests.

Results

The aim of the current study was to establish how the vestibular system, independently and in concert with other inputs (Fig. 1A), contributes to the sensorimotor control of head posture at frequencies spanning the range naturally experienced during everyday activities. First, to understand the vestibular system's contribution to the activation of neck muscles, we recorded the spike activity of SPL and

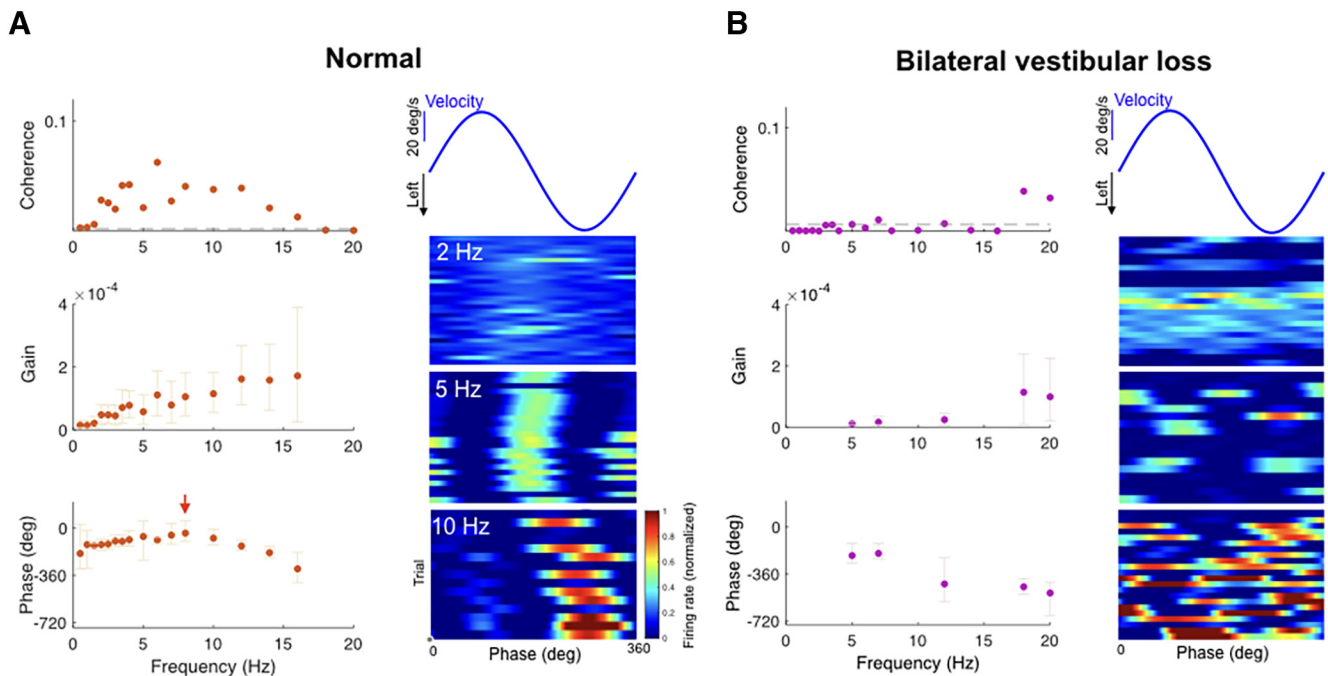


Figure 2. Neck motor units show vestibular-evoked responses across the dynamic range of natural motion. **A**, SPL motor unit responses to sinusoidal vestibular stimulation in normal monkeys ($N = 26$ motor units) in the dark. Dashed lines indicate 99% CIs for coherence between rotation velocity and motor unit spike times. Gain (spikes/m/s) and phase lag (deg) of motor unit responses relative to velocity are demonstrated at frequencies with significant coherence. Error bars indicate 95% CIs. Red arrow (at 8 Hz) indicates where the transition occurs between two different phase slopes. The modulation in motor unit firing rate in response to 3 sine wave frequencies (2, 5, and 10 Hz) is shown for one example neuron. **B**, SPL ($N = 6$ motor units) responses to the same sinusoidal stimulation after BVL.

SCM motor units in normal animals during sinusoidal rotations up to 20 Hz (Fig. 1B). Next, we compared these responses to those evoked after bilateral peripheral vestibular loss. We then performed a systematic series of experiments to determine how the addition of visual information influences the control of head posture during self-motion (Fig. 1C). In addition, we compared muscle activity evoked by broadband head motion to that evoked by single sine waves to assess whether neck muscles are activated in a linear manner. Finally, we investigated the influence of autonomic arousal, quantified by pupil size, on neck postural muscle responses to motion.

The vestibular system contributes to neck postural muscle activity across the range of natural motion

To understand the contributions of the vestibular system to postural control, we first examined neck motor unit activity during whole-body yaw rotations spanning the range of natural self-motion (i.e., up to 20 Hz) (Carriot et al., 2014, 2017) in normal animals. Our results showed compensatory neck postural muscle responses to motion were significant across the natural frequency range, with gain increasing as a function of frequency up to 16 Hz. Figure 2A (left) shows coherence, gain, and phase for our population of single SPL motor units during sinusoidal motion applied in darkness, where we were able to decompose 26 motor units. Figure 2A (right) shows heat plots of the response of a typical example SPL motor unit to sinusoidal whole-body rotation at three sample frequencies. Notably, leftward angular rotation evoked an increase in motor unit activity in the right SPL, consistent with the generation of a compensatory postural response to stabilize the head in space. Over our population, single SPL motor units showed significant coherence ($>99\%$ CIs) with angular velocity from 0.5 to 16 Hz in darkness (Fig. 2A), with gain increasing with frequency. The phase of the response demonstrated two

regions with a transition point located at 8 Hz (Fig. 2A, red arrow). Below 8 Hz, phase was $\sim 160^\circ$, indicating that contralateral (leftward) velocity was associated with increased activation of right SPL motor units; while at higher frequencies, phase showed a linearly increasing lag with frequency.

Next, to determine the vestibular system's contribution to the activation of neck musculature, we examined motor unit activity after bilateral peripheral vestibular loss during the same yaw rotation stimulation in darkness. Figure 2B (left) shows coherence, gain, and phase for the population of recorded single SPL motor units following vestibular loss. Figure 2B (right) shows heat plots for a typical example SPL motor unit's response for the same three frequencies shown in Figure 2A. Comparison of Figure 2A and 2B reveals that, in contrast to the robust modulation described above in normal animals, motor unit modulation was strikingly absent following BVL. This finding suggests that sensory input from the vestibular system is largely responsible for driving the neck motor unit responses that we observed in normal animals.

Visual inputs do not enhance neck muscle activation in normal animals nor substituted for peripheral vestibular loss

During our daily activities, the vestibular and visual systems are often activated in concert. Accordingly, we also examined whether and how visual information about self-motion is integrated with vestibular feedback for postural control. Visually-driven activation of neck muscles is relatively slow (beginning at 55 ms) (Corneil et al., 2004) compared with vestibular driven activation (beginning at 8 ms) (Colebatch et al., 1994). Thus, one possibility is that the addition of visual cues during self-motion would preferentially enhance neck motor unit responses for lower frequencies over which the visual system could contribute to the sensorimotor control of stability (<1.5 Hz) (Keshner and Peterson, 1995). In contrast,

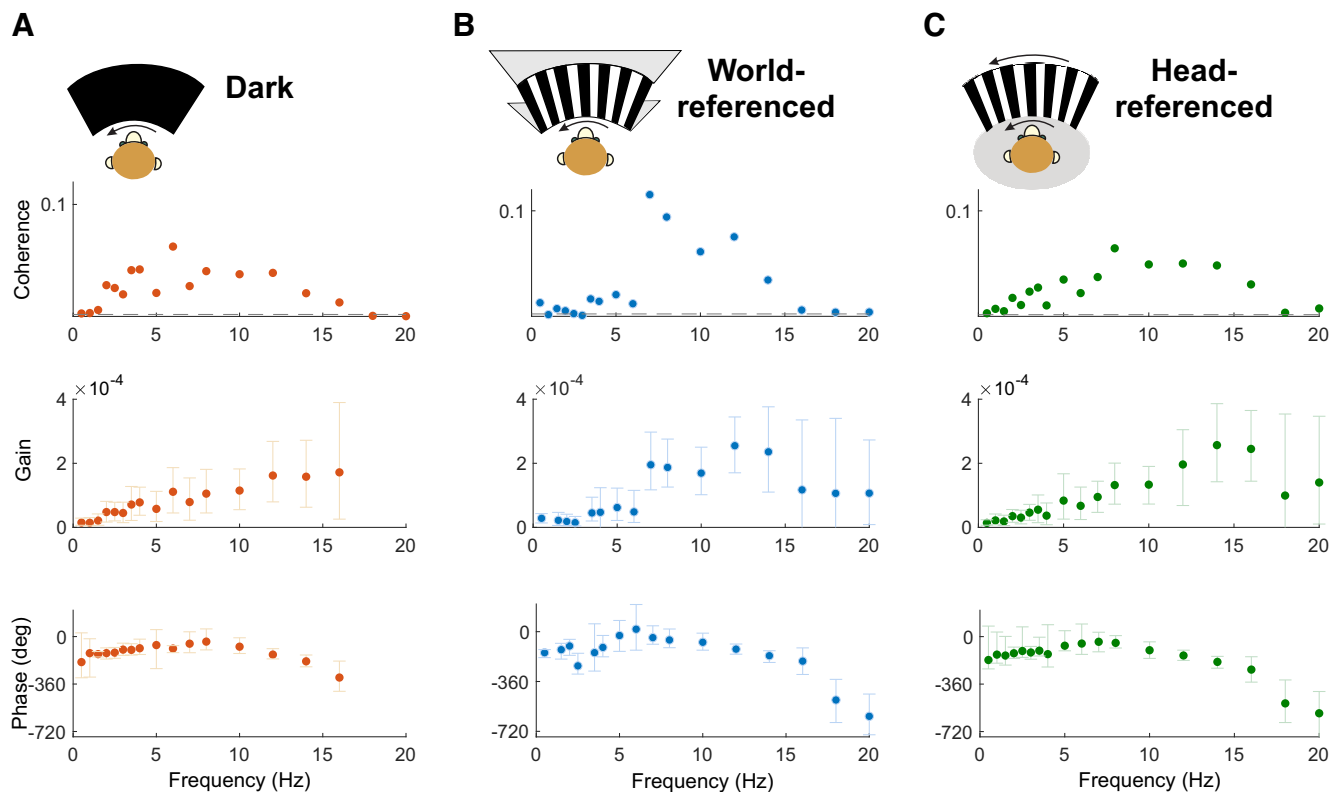


Figure 3. Visual cues do not affect vestibular-evoked postural responses. SPL motor unit responses to sinusoidal vestibular stimulation in healthy monkeys under three different visual conditions: **A**, complete darkness ($N = 26$ motor units); **B**, world-referenced visual surround ($N = 18$ motor units); **C**, head-referenced visual surround ($N = 26$ motor units). Dashed lines indicate 99% CIs for coherence. Gain (spikes/m/s) and phase (deg) data are demonstrated at frequencies with significant coherence. Error bars indicate 95% CIs.

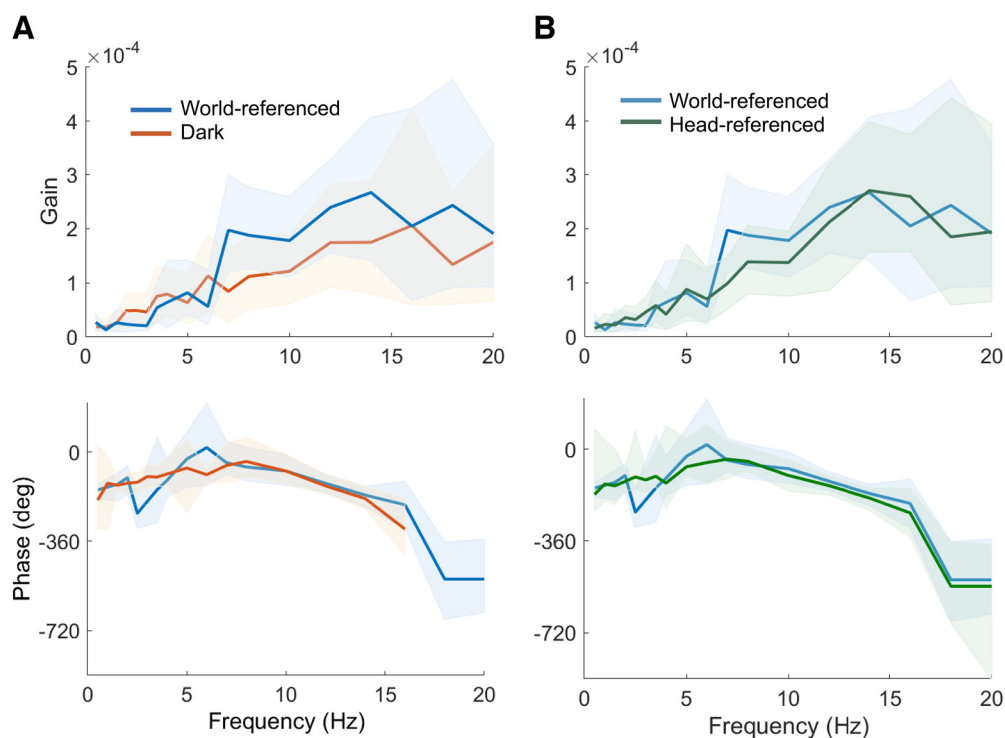


Figure 4. Motor unit response gains and phases are similar across visual conditions. **A**, Comparison of motor unit response gain (spikes/m/s) and phase (deg) between the world-referenced surround ($N = 18$ motor units) and dark ($N = 26$ motor units) conditions. **B**, Comparison between the world-referenced and head-referenced ($N = 26$ motor units) visual conditions. Shaded areas represent 95% CIs.

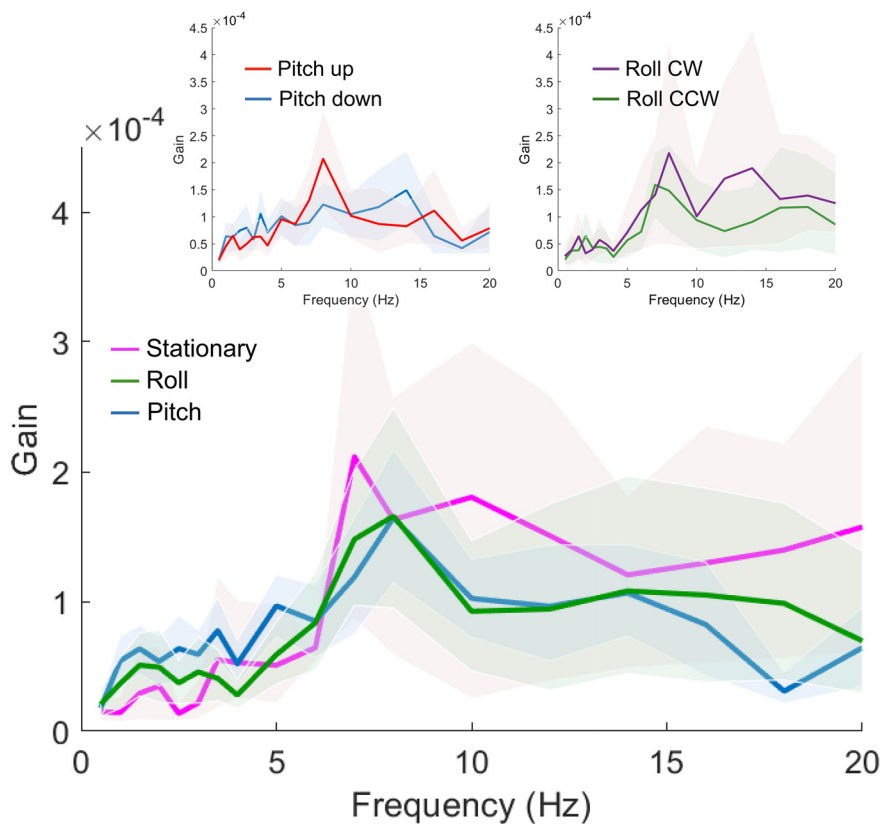


Figure 5. Out of plane visual stimulation does not influence vestibular postural reflexes. SPL motor unit responses to sinusoidal vestibular stimulation with a stationary visual scene of dots compared with roll and pitch downward visual motion stimulation. Insets, Comparisons between pitch upward ($N = 18$ motor units) versus downward ($N = 17$ motor units), and roll CCW ($N = 16$ motor units) versus CW ($N = 14$ motor units).

at higher frequencies, the pathway delays of the visual system would make visually-driven responses too delayed to contribute. To directly test whether this was the case, normal monkeys were centered in a patterned visual surround that remained stationary relative to the world (i.e., world-referenced). We then rotated the monkey to simultaneously activate the vestibular and visual systems so that the information provided by both sensory systems was congruent (i.e., both accurately signaled to the monkey that they were moving relative to the world). In this condition, we were able to decompose 18 motor units and found that overall, in contrast to this proposal, motor unit responses (coherence, gain, and phase) appeared similar in the dark (Fig. 3A) versus world-referenced condition (Fig. 3B).

To further investigate whether the visual system contributes to postural responses at lower frequencies, we recorded motor unit activity during a second combined visual-vestibular stimulation condition. As shown in Figure 3C, the monkey was again centered in a patterned visual surround, but in this condition the visual surround moved with the head (i.e., head-referenced), and thus provided visual information of no motion that conflicted with vestibular afferent feedback of sinusoidal motion relative to the world. If the visual system provides an important contribution to pathways involved in postural stability, then incongruent feedback from the visual system might be expected to preferentially dampen motor unit responses at lower frequencies. However, we found this was not the case; instead, in our population of 26 decomposed motor units, responses were again similar in the head-referenced (Fig. 3C) relative to world-referenced and dark conditions (Fig. 3A,B).

To specifically examine the effect of vision, we next directly compared the gain and phase of the responses evoked in our two visual conditions. Figure 4 shows the average gain and phase curves of neck postural muscle activity for the congruent (world-referenced) and conflicting (head-referenced) visual-vestibular stimulation conditions, respectively. The average gain and phase curves evoked in darkness are superimposed on the world-referenced condition to facilitate comparison with the vestibular-only stimulation condition. Overall, the comparison of response gains and phases revealed no significant difference (CIs overlapping) between the vestibular only (dark) and congruent visual-vestibular (world-referenced) conditions (Fig. 4A). Furthermore, response gains and phases were comparable across both conflicting and congruent visual-vestibular stimulation conditions (Fig. 4B). Thus, visual inputs did not influence the dynamics of neck postural muscle activity evoked by vestibular pathways in normal animals over the physiologically relevant frequency range of head movements.

We then investigated whether visual stimulation that is out of the plane of concurrent vestibular stimulation alters neck motor unit activity during yaw rotations across the same frequency range. To test this, we applied visual stimulation in either the pitch or roll axes (see Materials and Methods) while monkeys experienced yaw sinusoidal motion. Figure 5 shows motor unit gain across conditions. Comparison of motor unit gains in the upward versus downward pitch conditions revealed no significant differences (Fig. 5, left inset). Likewise, no significant differences were seen in the CCW versus CW roll conditions (Fig. 5, right inset). We then pooled motor units across the two directions of pitch and roll, and compared motor unit gains with those evoked by the same yaw vestibular stimulation without visual motion and again found no significant differences between conditions. Together, our results indicate that neither yaw axis nor out of the plane visual stimulation altered vestibular postural reflexes.

After vestibular loss, extravestibular signals have been shown to substitute for absent vestibular input in pathways that mediate gaze and postural stability (Sadeghi et al., 2010, 2011, 2012). Accordingly, we asked whether extravestibular visual information might influence compensatory postural responses following complete bilateral peripheral vestibular loss to help substitute for lack of vestibular afferent feedback. Surprisingly, however, our results showed that this was also not the case. When visual information was provided to the monkey with BVL (world-referenced surround), neck motor unit responses remained minimal (Fig. 6). This result indicates that visual information indeed did not substitute to stabilize the head in space when normal vestibular input was absent. Thus, together, our results provide evidence that visual inputs do not make a major contribution to postural neck muscle activity in normal animals, nor are they upweighted to provide improvements in postural stability over a physiologically relevant frequency range.

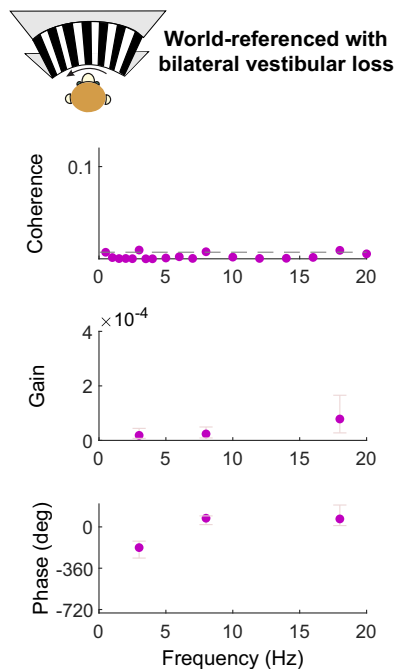


Figure 6. Visual cues do not substitute for absent vestibular feedback following bilateral peripheral vestibular loss. SPL motor unit responses ($N = 6$ motor units) to sinusoidal vestibular stimulation with a world-referenced visual surround (i.e., with accurate visual cues of self-motion) after BVL. Dashed lines indicate 99% CIs for coherence between rotation velocity and motor unit spike times. Error bars indicate 95% CIs.

following vestibular loss. We further consider these results in relation to studies of patients with vestibular hypofunction in the Discussion.

Complex motion evokes nonlinear responses in neck motor units

During everyday life, the motion experienced by the head is typically more complex than pure sinusoidal motion comprised of a single frequency. Furthermore, neurons in central vestibular pathways that mediate postural responses to passive vestibular stimulation have been shown to respond nonlinearly to broadband motion (Massot et al., 2012). Thus, it is essential to examine the mechanisms by which the vestibular system contributes to postural control during more complex motion characteristic of that experienced during everyday activities (Carriot et al., 2014, 2017). To assess whether head motion activates neck muscles in a linear manner, we applied broadband whole-body rotations containing frequencies from 0 to 20 Hz to normal animals. We found that single motor units had significant coherence ($>99\%$ CIs) with angular velocity only at higher frequencies (9–18 Hz) (Fig. 7A). The coherence for each recorded motor unit is demonstrated in heat plots. Comparison of normalized gain between broadband versus sinusoidal (overlaid) stimulation revealed that, although gain peaked at a similar frequency for both types of stimuli, at the lower frequencies, gain was attenuated during broadband relative to sinusoidal stimulation. Overall, gain from 9 to 10.5 Hz was reduced by $\sim 50\%$ when low-frequency motion was experienced concurrently with high-frequency head motion. Interestingly, a similar suppression of low-frequency responses in the presence of high-frequency input has previously been observed at the level of the central vestibular neurons that mediate vestibulospinal pathways (Massot et al., 2012). In contrast, the phase of the response to broadband noise (slope = $38^\circ/\text{Hz}$)

and sinusoidal (slope = $35^\circ/\text{Hz}$) were comparable for both broadband and sinusoidal stimulation. For completeness, we also recorded motor unit responses to broadband noise stimulation after BVL (Fig. 7B). As was observed above for single sine wave stimulation, motor unit modulation was minimal across the entire tested frequency range. We did observe small responses (i.e., weak but significant coherence and low gain) at the highest frequencies.

As reviewed above, Peng et al. (1996) previously developed a neuromechanical model of human head postural control in which the vestibular contribution (VCR) was estimated from data collected at frequencies of ≤ 4 Hz in cats. To compare our results to this prediction, we superimposed the gains and phases predicted by the Peng et al. (1996) neuromechanical model (Fig. 7, left, black lines) on our experimentally measured values. Notably, model values were only consistent with our experimentally measured VCR gains and phases at lower frequencies. As frequency increased, however, measured and predicted values diverged markedly. In contrast to measured values, model gains continued to increase >16 Hz and phase plateaued. Thus, while our experimental values at low frequencies were similar to those modeled from data in cats, our findings suggest the responses to high-frequency vestibular stimulation cannot be accurately predicted based lower-frequency responses alone.

Finally, since single motor units serve as the gold standard for examining motor output, we also contrasted responses in rectified EMG. We found that response dynamics were similar between single motor units and rectified EMG in the normal animals (Fig. 8, left), and again minimal responses were observed after BVL (Fig. 8, right). Furthermore, during our paradigms, SPL motor units often demonstrated consistent background activity, whereas SCM motor units were rarely active, likely because this muscle has a higher threshold and is primarily recruited at more extreme ranges of motion (Corneil et al., 2001). For this reason, we focused our analyses on SPL motor units, which is a complementary target to SCM for clinical assessments of cervical vestibular evoked myogenic potentials (VEMPs) (Camp et al., 2017; Mohammed Ali et al., 2019). Overall, we were able to record motor units in SCM that were active during voluntary contractions in 10 recording sessions in the normal animals, yet they were rarely active for more than brief periods during passive rotations. Nevertheless, we obtained data from two SCM motor units during broadband noise stimulation paradigms (Fig. 9). In these units, the response gains increased with frequency, and phase showed a linear increase in lag >8 Hz, thus demonstrating a similar pattern to that described above for SPL motor units.

Heightened autonomic arousal enhances vestibular-evoked neck postural muscle responses

To date, studies investigating the dynamics of neck postural muscle responses to self-motion have not explored the influence of arousal. Since the vestibular system is known to have connections with the autonomic system, we hypothesized that autonomic state would have an influence on neck postural muscle responses. To address this question, we used a social paradigm (see Materials and Methods), in which testing was done before and after introducing a novel monkey to the experimental room, within the view of the subject monkey. Arousal was then quantified by measuring the change in the subject monkey's pupil size.

We first confirmed that our social paradigm resulted in pupil dilation compared with control conditions (all p values < 0.01).

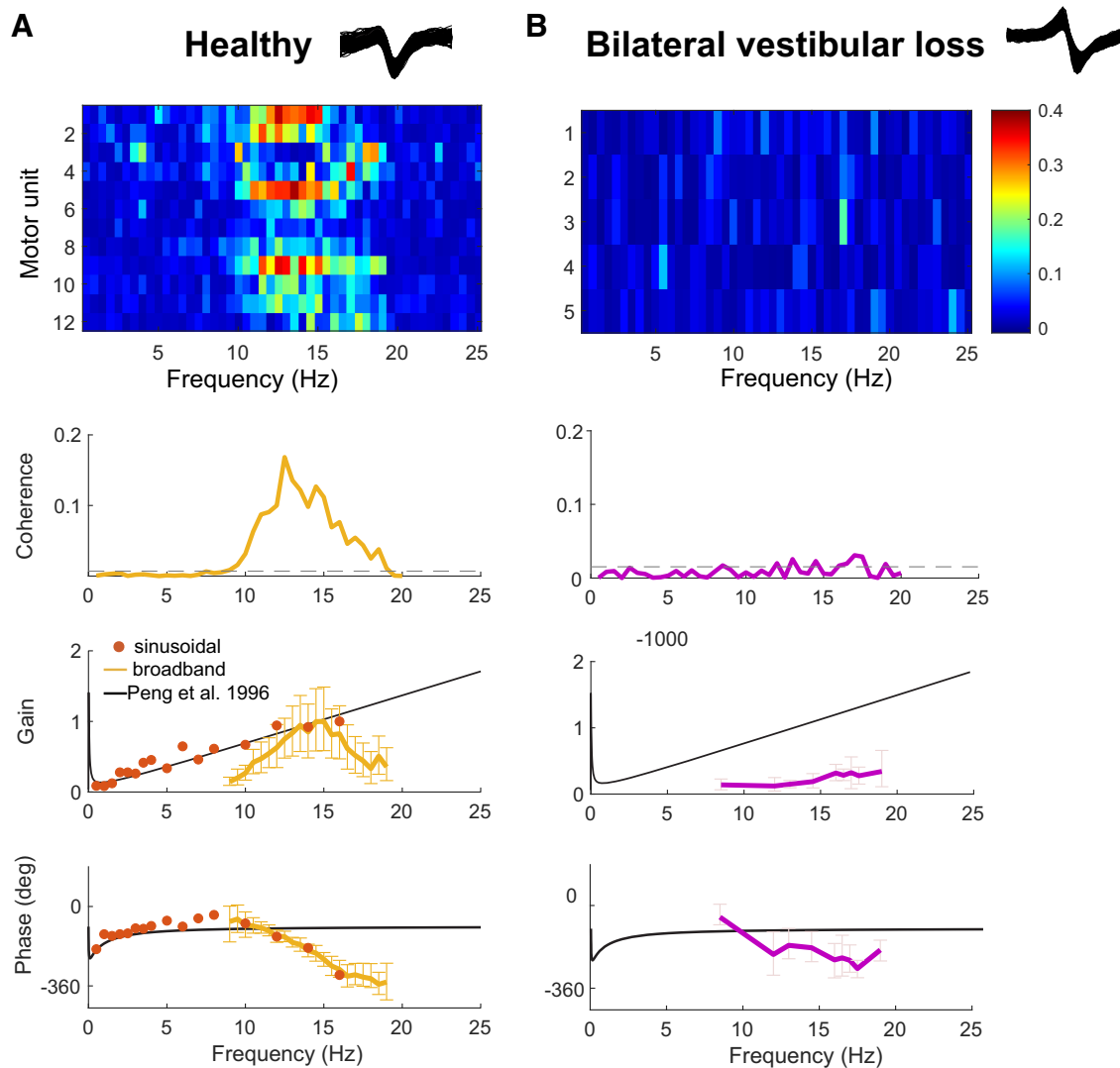


Figure 7. Neck motor units show nonlinear responses during complex motion, and responses at high frequencies differ markedly from previous model predictions. **A**, SPL motor unit responses to broadband (0–20 Hz white noise) vestibular stimulation in normal monkeys ($N = 12$ motor units). Dashed lines indicate 99% CIs for coherence between rotation velocity and motor unit spike times. Gain (normalized to maximum) and phase (deg) data are demonstrated at frequencies that exhibit significant coherence. Error bars indicate 95% CIs. For comparison, the superimposed dots represent gain for motor units in response to sinusoidal stimulation from Figure 2A. Black lines indicate the predicted VCR gain and phase from the neuromechanical model developed by Peng et al. (1996). **B**, SPL motor unit responses ($N = 5$ motor units) to the same broadband vestibular stimulation after BVL.

We then examined the change in neck postural muscle responses in the heightened arousal versus control conditions. Consistent with our hypothesis, we found that neck motor unit responses were significantly enhanced during the increased autonomic arousal compared with control conditions (Fig. 10A). To further investigate differences between conditions, we directly compared coherence, gain, and phase using a pooled DOC and bootstrapped CIs (Fig. 10B). The χ^2 pooled DOC test revealed that coherence was higher in the increased arousal condition at frequencies ~ 10 – 16 Hz. Similarly, gain was significantly higher ~ 13 Hz (95% CIs nonoverlapping). Phase, however, was similar between conditions, with means and CIs overlapping. Together, these findings indicate that arousal enhanced the postural control pathways from the vestibular system to neck motor units, without influencing pathway delays.

Discussion

Our central finding is that the vestibular system contributes to the sensorimotor control of head posture across the

dynamic range of motion experienced during everyday activities. Specifically, by recording the activity of single neck motor units in alert monkeys, we provide direct evidence that vestibular-evoked motor unit responses are significant for rotations up to 20 Hz. Furthermore, visual information neither augmented the activation of neck motor units in normal animals nor substituted for absent vestibular feedback following peripheral loss. Using broadband stimulation, we further demonstrated that motor unit gain for low-frequency motion was attenuated when experienced concurrently with high-frequency motion. Finally, we found that increased autonomic arousal led to a significant enhancement in motor unit responses. Together, our findings systematically disambiguate the contribution of the vestibular system to postural stability across an ethological range of natural motion, as well as reveal the influences of multisensory and autonomic inputs.

Vestibular feedback contributes to neck postural muscle activity across the range of motion experienced during daily life

In the present study, we systematically established, for the first time, the vestibular system's contribution to head stabilization

across a broad bandwidth corresponding to the self-motion experienced in everyday life (up to 20 Hz) (Carriot et al., 2014, 2017). Prior investigations of VCR-evoked neck muscle activity focused on the cat model and only applied stimulation at lower frequencies (<4 Hz) (for review, see Goldberg and Cullen, 2011). Peng et al. (1996, 1999) then used these experimental findings to estimate the VCR's contribution to human head compensation in a neuromechanical model. At these lower stimulation frequencies, our findings from primate SPL neck motor units match the model predictions of Peng et al. (1996, 1999). At higher frequencies, however, our data markedly differ (Fig. 7). In contrast to the increase in gain and flat phase predicted by the Peng et al. (1996, 1999) model, motor unit gains decrease beyond 16 Hz and phase lags increase beyond 8 Hz. Interestingly, artificial activation of the peripheral vestibular system via galvanic vestibular stimulation (Kwan et al., 2019; Forbes et al., 2020) evokes similar dynamics in human SPL (Forbes et al., 2013). Future studies that record from additional neck muscles that contribute to head stabilization (e.g., obliques capitis, rectus capitis posterior) (Corneil et al., 2001), as well as establish robust measures of biomechanical properties, such as viscosity and stiffness, will ultimately be required to develop a physiologically complete neuromechanical VCR model.

Our finding that motor unit gain increases with frequency is further consistent with the known response dynamics within the VCR pathways (for review, see Cullen, 2012). Primary vestibular afferents from semicircular canals show increasing gain with frequency over the bandwidth of 0–20 Hz (Sadeghi et al., 2007; Massot et al., 2012). This high-pass tuning is particularly prominent for irregular afferents, which show steeper gain increases compared with their more regular counterparts (Carriot et al., 2014). Interestingly, irregular afferents send stronger projections to the subclass of vestibular nuclei neurons that mediate the VCR (vestibular-only [VO] cells), whereas regular afferents provide a stronger contribution to visual stability via the VOR pathways (for review, see Cullen, 2019). These central VO neurons, like irregular canal afferents, demonstrate increasing gain with frequency up to 20 Hz (Massot et al., 2011, 2012).

Visual-vestibular contributions to the sensorimotor control of head posture

Here we show that neck motor unit responses to yaw motion were nearly absent following complete peripheral vestibular loss. Correspondingly, patients with bilateral vestibular hypofunction display impaired head stabilization in response to translational perturbations applied while seated (Keshner, 2003) and standing (Shupert and Horak, 1996). This leads to the question: How do central postural pathways adapt to peripheral vestibular loss? There is evidence from both behavioral (Haran and Keshner, 2008; Peterka et al., 2011) and neurophysiological (Sadeghi et al., 2010, 2011, 2012) studies that, when vestibular information is less reliable, inputs from other modalities (e.g., visual and proprioceptive) can be upweighted to substitute.

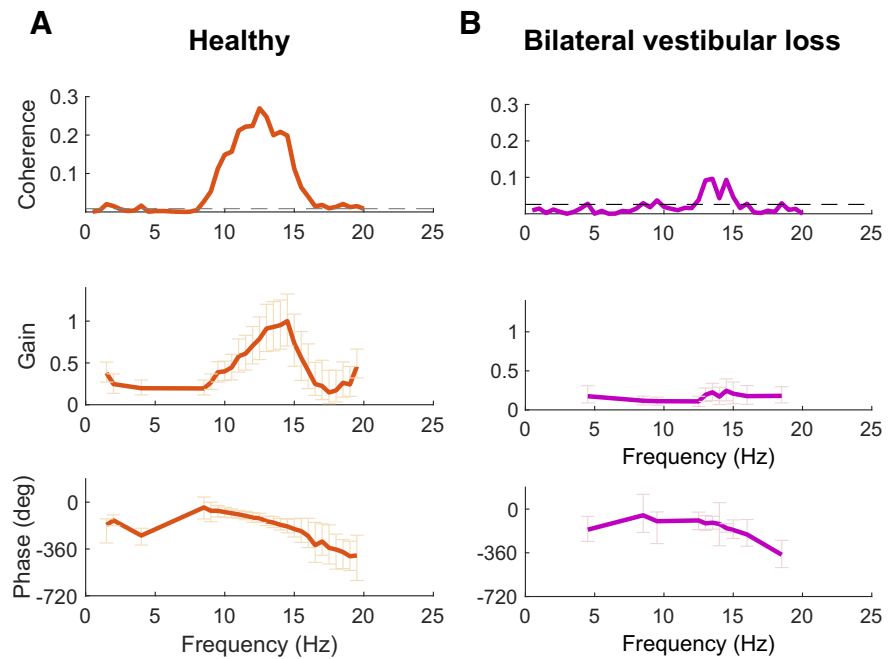


Figure 8. Multiunit muscle activity demonstrates similar responses to single motor units. SPL rectified EMG responses to broadband noise (0–20 Hz) vestibular stimulation in healthy (**A**, $N = 15$ trials) and BVL (**B**, $N = 6$ trials) monkeys. Dashed lines indicate 99% CIs for coherence. Gain (spikes/m/s) and phase (deg) data are demonstrated at frequencies with significant coherence. Error bars indicate 95% CIs.

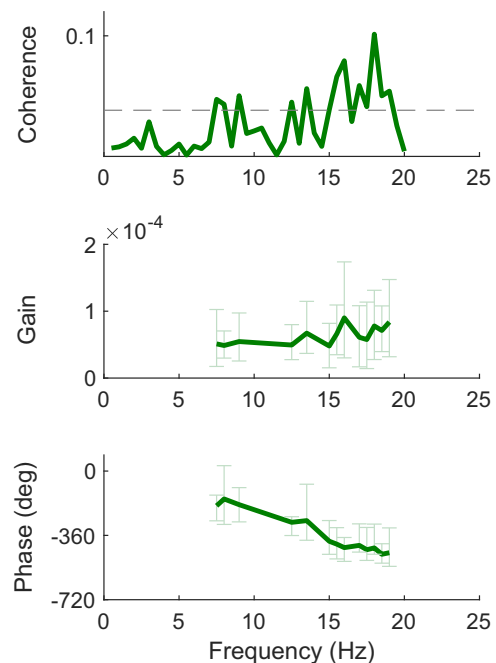


Figure 9. SCM motor units demonstrate increasing response gain across the range of natural self-motion. SCM single motor unit ($N = 2$ motor units) responses to broadband noise (0–20 Hz) vestibular stimulation in a normal monkey. Dashed lines indicate 99% CIs for coherence. Gain (spikes/m/s) and phase (deg) data are demonstrated at frequencies with significant coherence. Error bars indicate 95% CIs.

Therefore, we were surprised to find that visual input did not augment neck muscle responses, even after vestibular loss. Prior work in humans has shown that visual feedback can augment the ability to stabilize the head at frequencies <1.5 Hz (Guittion et al., 1986; Keshner and Peterson, 1995), although this is likely

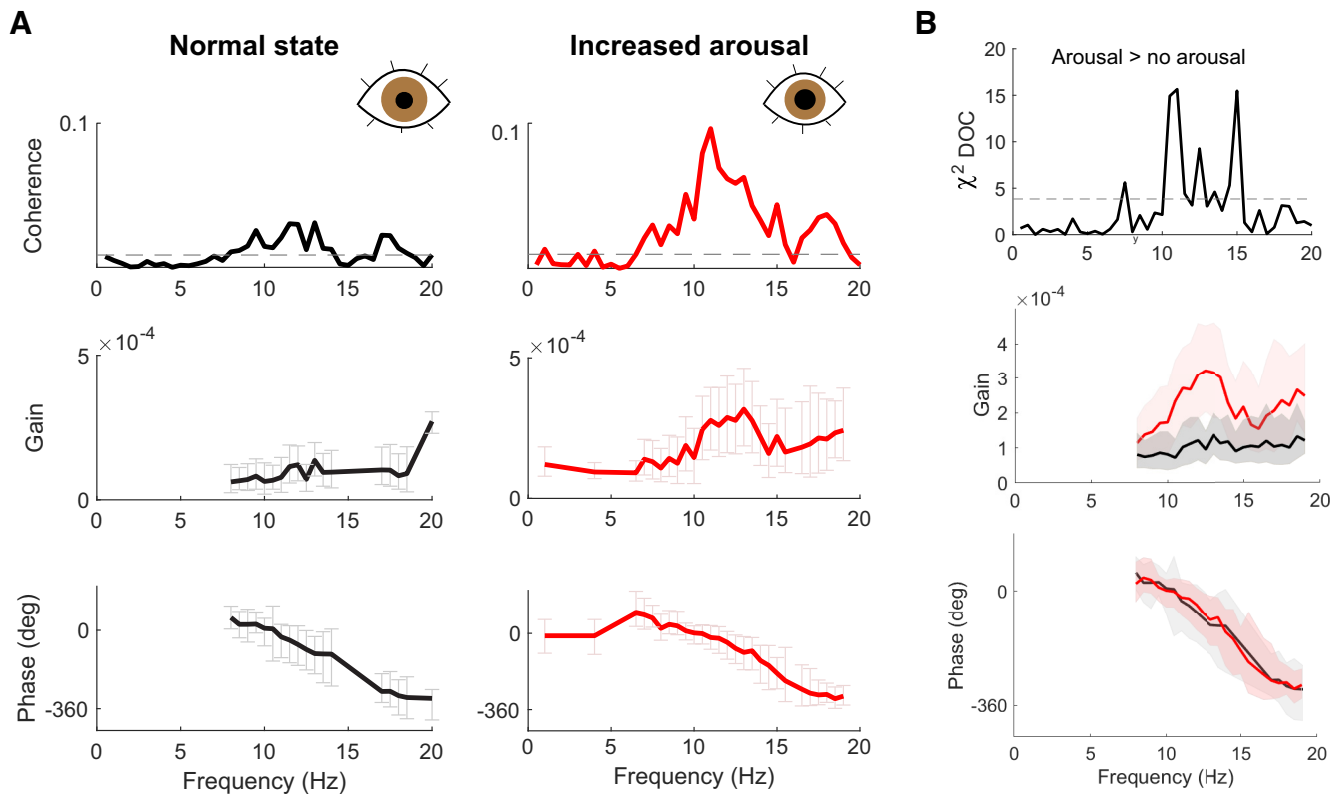


Figure 10. Autonomic arousal enhances neck motor unit responses during natural self-motion. **A**, SPL motor unit responses to broadband noise (0–20 Hz) vestibular stimulation under normal conditions (left, $N = 6$ motor units) and increased autonomic arousal (right, $N = 6$ motor units). Dashed lines indicate 99% CIs for coherence between rotation velocity and motor unit spike times. Gain and phase data are demonstrated at frequencies that exhibit significant coherence. **B**, Comparisons of coherence, gain, and phase between arousal states. Dashed line indicates the significance level for the χ^2 test. Shaded areas represent 95% CIs.

through long-latency voluntary pathways. In our present study, it may have been difficult to detect any influence of vision on the VCR at these lower frequencies because of the low gain of motor unit responses. It is also possible that visual inputs have a more prominent influence in dimensions that signal a change in center of mass relative to base-of-support position, such as horizontal linear translations. For example, it has been reported that visual motion in the pitch and roll planes has a stronger influence on standing postural control relative to yaw (Luo et al., 2018). Future studies focused on translational stimulation as well as pitch/roll rotations will be required to fully understand how visual signals alter neck postural responses during the multidimensional head motion naturally experienced (Carriot et al., 2014, 2017).

Last, recent studies have shown that the loss of vestibular input to central pathways significantly alters the natural statistical structure of head motion in human subjects (Zobeiri et al., 2021a,b). It thus follows that this change in statistics will impact the sensory input experienced by other systems (e.g., visual and proprioceptive) and subsequently could constrain the brain's ability to substitute or compensate for vestibular loss using other inputs. The integration of visual with vestibular information has been well studied in higher-order cortical areas, including posterior parietal cortex (Chen et al., 2011a,b; Marigold and Drew, 2011; Avila et al., 2019), an area that both contributes to the perception of self-motion and spatial orientation, and accesses spinal motoneurons via several descending pathways (Potocanac and Duysens, 2017). Future studies will be required to understand how neurons integrate the multidimensional visual-vestibular stimulation experienced during natural activities to provide robust

postural responses as well as our perception of spatial orientation and self-motion.

Autonomic arousal influences vestibular postural control pathways

Given that the autonomic system is strongly interconnected with the vestibular system (Balaban, 2004), we also investigated the influence of arousal on vestibular-evoked neck postural muscle responses. We used pupil diameter as a proxy for autonomic arousal; pupil diameter is strongly related to locus coeruleus activity in primates (Varazzani et al., 2015; Joshi et al., 2016), a structure that has widespread neuromodulatory effects that can influence motor responses (Maness et al., 2022). We found that both coherence and gain were significantly enhanced during heightened arousal ~ 10 –16 Hz. The observed influence at higher frequencies suggests preferential enhancement of the VCR for more dynamic self-motion. In this context, it is interesting that arousal also preferentially influences postural sway at higher frequencies (Zaback et al., 2019). The observed increase in coherence specifically suggests that the autonomic system has an influence on pathways mediating this response (Mildren et al., 2020). Thus, our present findings provide a neural correlate for reports in prior human behavioral studies that vestibular-evoked postural responses are enhanced when autonomic arousal is increased by postural threat (Horslen et al., 2014). Arousal likewise enhances vestibular evoked myogenic potentials, which are also mediated by VCR pathways (Naranjo et al., 2015), as well as the gain of another essential vestibular motor reflex, namely, the VOR. For example, both psychostimulants as well as tasks that increase arousal enhance VOR gain (Kasper et al., 1992; Yardley

et al., 1995). Together, our findings reveal at the motor unit level the important role of the autonomic system in modulating descending postural control pathways in alert animals.

Neck motor unit responses to low-frequency self-motion are attenuated when experienced concurrently with higher frequencies

During daily life, we rarely encounter motion that is comprised of a single frequency. In light of this, we applied broadband noise motion and found that, relative to sinusoidal stimuli, motor units had nonsignificant coherence and attenuated gain at low frequencies. Our present finding that neural responses to low-frequency head motion are attenuated when experienced concurrently with high-frequency motion is consistent with properties of primate central VO neurons (Massot et al., 2012), which comprise the first central stage of the VCR pathway. We speculate that the low-frequency suppression imparts some functional advantages. While motion experienced during everyday activities contains frequencies approaching 20 Hz, the majority of power is <10 Hz. Thus, biasing motor responses to high-frequency stimuli may serve to enhance the ability to respond to unexpected transient events experienced simultaneously during sustained lower-frequency motion. For instance, in a scenario where one is standing while riding the metro, it is essential to generate compensatory postural reflexes in response to unexpected sudden stops or other transient motion. Future experiments will be needed to investigate how the response selectivity of populations of motor units shapes postural responses to ensure stability to such self-motion stimulation.

Diversity statement

Recent work has identified a bias in citation practices in science whereby papers from women and other minority scholars are under-cited relative to the number of such papers in the field. To assess the diversity in citations in our current paper, we obtained the predicted gender and racial/ethnic category of the first and last authors (<https://github.com/dalejn/cleanBib>). After excluding self-citations of the first and last authors, our references contain 15.91% woman(first)/woman(last), 12.15% man/woman, 15.91% woman/man, and 56.03% man/man. Our references contain 7.59% author of color (first)/author of color(last), 15.98% white author/author of color, 23.86% author of color/white author, and 52.56% white author/white author. This method is limited in that the data used to make the predictions may not, in every case, be indicative of gender or racial/ethnic identity, and it cannot account for intersex, non-binary, or transgender people, as well as Indigenous and mixed-race authors.

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