Signal Processing by Vestibular Nuclei Neurons Is Dependent on the Current Behavioral Goal

KATHLEEN E. CULLEN, JEFFERSON E. ROY, AND PIERRE A. SYLVESTRE

Aerospace Medical Research Unit, Department of Physiology, McGill University, Montreal, Quebec, Canada

ABSTRACT: The vestibular sensory apparatus and associated vestibular nuclei are generally thought to encode angular head velocity during our daily activities. However, in addition to direct inputs from vestibular afferents, the vestibular nuclei receive substantial projections from cortical, cerebellar, and other brainstem structures. Given this diversity of inputs, the question arises: How are the responses of vestibular nuclei neurons to head velocity modified by these additional inputs during naturally occurring behaviors? Here we have focused on the signal processing done by two specific classes of neurons in the vestibular nuclei: (1) position-vestibular-pause (PVP) neurons that mediate the vestibulo-ocular reflex (VOR), and (2) vestibular-only (VO) neurons that are thought to mediate, at least in part, the vestibulo-collic reflex (VCR).

We first characterized neuronal responses to passive rotation in the head-restrained condition, and then released the head to record the discharges of the same neurons during self-generated head movements. VOR interneurons (i.e., PVP neurons) faithfully transmitted head velocity signals when the animal stabilized its gaze, regardless of whether the head motion was actively or passively generated; their responses were attenuated only when the monkey's behavioral goal was to redirect its axis of gaze relative to space. In contrast, VCR interneurons (i.e., VO neurons) faithfully transmitted head velocity signals during passive head motion, but their responses were greatly (and similarly) attenuated during all behaviors (i.e., gaze shifts, gaze pursuit, gaze stabilization) during which the monkey's behavioral goal was to move its head relative to the body. To characterize the mechanism(s) that underlie this differential processing, we tested neurons during passive rotation of the head relative to the body, as well as during a task in which a monkey actively "drove" both its head and body together in space. We conclude that neither passive activation of neck proprioceptors nor knowledge of self-generated head-in-space motion directly mediate the observed reductions in head-velocity-related modulation. Instead, we propose that the VOR and VCR pathways use efference copies of oculomotor and neck movement commands, respectively, for the differential processing of vestibular information.

KEYWORDS: Vestibular; Gaze; Head-free; Voluntary; Oculomotor; Neck

Address for correspondence: Dr. Kathleen E. Cullen, Aerospace Medical Research Unit, Department of Physiology, McGill University, 3655 Drummond Street, Room 1220, Montreal, Quebec, Canada, H3G 1Y6.

cullen@med.mcgill.ca

INTRODUCTION

The activity of vestibular nuclei neurons has been well characterized in the head-restrained monkey during eye movements and passive whole-body rotation. Several distinct classes of neurons exist within the vestibular nuclei and neighboring nucleus prepositus hypoglossi.[1–10] Of these, two classes of neurons are thought to play an important role in generating vestibular reflexes: (1) position-vestibular-pause (PVP) neurons mediate the vestibulo-ocular reflex (VOR[2,9,11]) and (2) vestibular-only (VO) neurons mediate the vestibulo-collic reflex (VCR[12,13]).

The VOR is classically described as a reflex that produces a compensatory eye movement of equal and opposite amplitude to the movement of the head. The most direct pathway that mediates the VOR consists of only three neurons (vestibular afferents, to interneurons in the vestibular nuclei, to extraocular motoneurons[14]). PVP neurons constitute most of the intermediate leg of this pathway. The simplicity of this three-neuron arc is reflected in the fast response time of the VOR; compensatory eye movements lag head movements by only 7–10 ms in the primate.[15–17] The VOR effectively stabilizes the visual axis in space, and therefore the visual world on the retina for the wide range of head motions that are generated during our daily activities such as walking and running.[18–19] However, under natural conditions where the head is not restrained, a combination of eye and head movements (i.e., a gaze shift) is commonly used to rapidly redirect the visual axis to a new target in space (in humans[20–25] and monkeys[26–32]). During gaze shifts, the eye movements produced by the VOR would be counterproductive; the VOR would produce an eye movement command in the direction opposite to that of the intended shift of gaze. Indeed, there is substantial evidence which argues that the VOR is not fully functional during gaze shifts. A series of behavioral experiments in which the head was mechanically perturbed have suggested that the VOR is completely suppressed during large gaze shifts[22–23,32–34] and is significantly attenuated during smaller gaze shifts.[23,30,35] Furthermore, we have recently shown that a reduction in the vestibular sensitivity of PVP neurons provides a neural correlate for the on-line suppression of the VOR during gaze shifts.[36–38]

In addition to its crucial role in stabilizing the eye relative to space via the VOR, the vestibular system also coordinates postural reflexes that are critical for maintaining head and body posture during our daily activities. The vestibulo-collic reflex (VCR) functions to stabilize the head relative to space, by generating a neck motor command to move the *head* in the direction opposite to the current head-in-space velocity. However, as was the case for the VOR, this reflex can be counterproductive during certain behaviors. For example, during active head-on-body motion (gaze shifts and gaze pursuit), the head movement command produced by the VCR would be in the direction opposite to that of the planned head motion. The VCR pathway is thought to be mediated, at least in part, by VO neurons, a distinct population of vestibular nuclei neurons. These neurons receive direct monosynaptic projections from vestibular nerve afferents and in turn project to the cervical spinal cord.[12–13,39–40] Recent studies have shown that the head-velocity signals carried by VO neurons during gaze shifts are dramatically attenuated compared to those evoked by passive whole-body rotations.[41–43] This finding suggests that the head-velocity signals carried by the VCR pathway are attenuated during active head-on-body motion.

The goal of the present study was to determine which mechanism(s) contribute to reducing the head-velocity sensitivities of PVP and VO neurons during voluntary gaze shifts. To address this question, we first investigated whether inputs from neck proprioceptors mediate, at least in part, the observed reduction in neuronal modulation. We then investigated whether the head velocity signals encoded by vestibular nuclei neurons were systematically attenuated during all voluntary motion of the head in space, or alternatively whether they were modulated as a result of the differences in the animal's behavioral goal during gaze shifts and passive whole-body rotation. We conclude that neither the passive activation of neck proprioceptive inputs nor the monkey's knowledge of its self-generated head motion directly mediates the differential processing of vestibular information at the level of the vestibular nucleus. Rather, we argue that the VOR and VCR pathways utilize efference copies of oculomotor and neck movement commands, respectively, for behaviorally dependent processing of vestibular information.

MATERIALS AND METHODS

Surgical Procedures

Three monkeys (*Macaca mulatta*) were prepared for chronic extracellular recording. All experimental protocols were approved by the McGill University Animal Care Committee and complied with the guidelines of the Canadian Council on Animal Care. The surgical preparation was similar to that previously described elsewhere.[44] Briefly, in a sterile surgical procedure, a stainless steel post, used to restrain the animal's head, and a stainless steel recording chamber were attached to the head using dental acrylic and cortical screws. In the same procedure, an 18–19 mm in diameter eye coil (three loops of Teflon-coated stainless steel wire) was implanted in the right eye behind the conjunctiva to allow the measurement of eye position.[45] Animals were given two weeks to recover from the surgery before any experiments were performed.

Experimental Paradigms

During experiments, the monkey was comfortably seated in a primate chair that was fixed to the suprastructure of a vestibular turntable. Extracellular single-unit activity was recorded using enamel-insulated tungsten microelectrodes (7–10 MΩ impedance, Frederick-Haer) as has been described elsewhere.[44] Gaze and head positions were measured using the magnetic search coil technique.

The activity of neurons was initially recorded with the monkey in the head-restrained condition during voluntary eye movements and passive whole-body rotation. Neuronal responses were recorded during eye movements made to track a target that was (1) stepped between horizontal positions over a range of ±30 deg and (2) moved sinusoidally (0.5 Hz, 80 deg/s peak velocity) in the horizontal plane. Neuronal sensitivities to head velocity were tested by passively rotating monkeys about an earth vertical axis in the dark (pWBR; 0.5 Hz, 80 deg/s peak velocity), and while the monkeys canceled their VOR by fixating a target that moved with the vestibular turntable (pWBRc). Target velocity, turntable motion, on-line data displays, and data acquisition were controlled by a UNIX-based real-time data acquisition system (REX[46]).

After a neuron was fully characterized in the head-restrained condition, the monkey's head was slowly and carefully released. Once released, the monkey was free to rotate its head through the natural range of motion in the yaw (horizontal), pitch (vertical), and roll (torsional) axes. Neuronal responses to voluntary head movements were characterized during combined eye-head gaze shifts (15 to 65 deg in amplitude) and combined eye-head gaze pursuit of a sinusoidally moving target (0.5 Hz, 80 deg/s peak velocity). Neuronal sensitivities to passive activation of neck proprioceptive inputs were characterized by passively rotating the head on a stationary body, and by passively rotating the body under an earth stationary head. In the latter paradigm, the torque generated by the animal against the head restraint was simultaneously measured (Sensotec Inc.). In some experiments, rapid perturbations were applied to the head during gaze shifts using a torque motor (Animatics Inc.).

Analysis of Neuronal Discharges

A multiple regression analysis was used to characterize each unit's discharge dynamics. For VO neurons, the resting discharge (bias, spikes/s), head velocity sensitivity ([spikes/s]/[degree/s]), and the phase shift relative to head velocity were first estimated during passive whole-body rotations. For PVP neurons, an additional eye position sensitivity ([spikes/s]/[degrees]) was estimated during smooth pursuit and fixation, and an eye velocity sensitivity ([spikes/s]/[degree/s]) was estimated during smooth pursuit. These coefficients were then utilized to predict the neuronal discharges during other paradigms (referred to as pWBR model). Parameter estimates were also obtained during all paradigms using similar model structures. Details of this analysis have been described elsewhere.[38,43]

To confirm that isolation of the same neuron was maintained before and after the head-restrained–unrestrained transition, resting discharge rates were compared. In addition, the pWBRc paradigm was repeated for the majority of neurons following head release to verify that each neuron's sensitivity to passive whole-body rotation remained comparable to that observed during the initial head-restrained characterization.

RESULTS

PVP and VO neurons are known to receive direct monosynaptic projections from vestibular nerve afferents.[2,9,41] To date, both cell types have been well characterized in head-restrained monkeys. PVP neurons (1) are modulated in response to ipsilateral head-in-space motion during passive whole-body rotation, (2) are sensitive to contralaterally directed eye position and velocity during head-restrained ocular fixation and smooth pursuit, and (3) cease firing during contralaterally directed saccades and vestibular quick phases. VO neurons are modulated in response to head-in-space motion during passive whole-body rotation and are insensitive to eye movements. In the present study, we first characterized neurons during standard head-restrained paradigms (saccades, ocular fixation at different orbital positions, smooth pursuit, pWBR, and pWBRc) to classify them as either PVP or VO neurons.

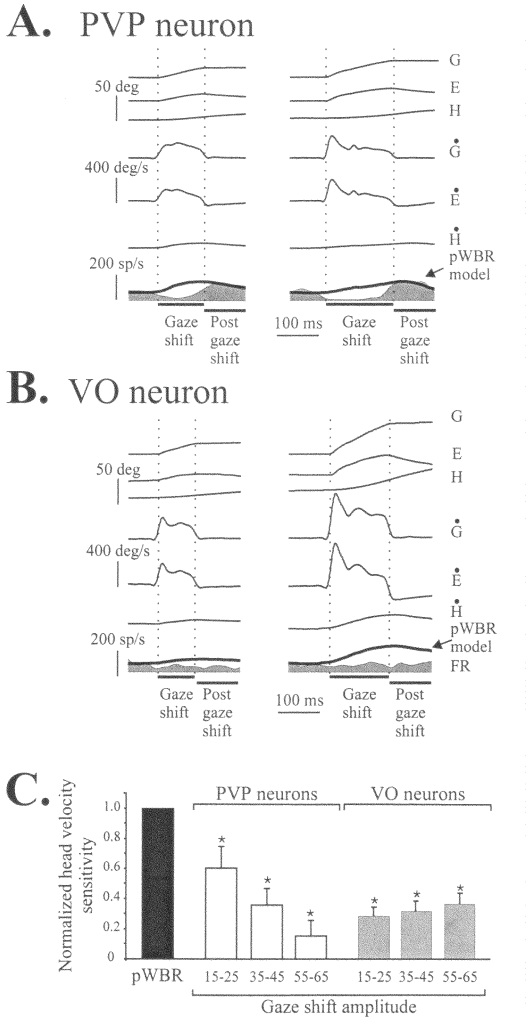

FIGURE 1. Voluntary eye-head gaze shifts: (**A**) The activity of this typical PVP neuron was significantly attenuated during gaze shifts. (**B**) The activity of the example VO neuron was also significantly attenuated during combined eye-head gaze shifts. For each cell in **A** and **B**, the activity predicted by the neuron's modulation during passive whole-body rotation is superimposed on the firing rate (pWBR model; *thick trace*). (**C**) During gaze shifts, the average head velocity sensitivity across PVP neurons (*open columns*) was significantly smaller than that estimated during passive whole-body rotations (*black column*; $^{*}p < 0.05$), and decreased with increasing gaze shift amplitude. During gaze shifts, the average head velocity sensitivity across VO neurons was similarly and significantly attenuated for all gaze shift amplitudes (*gray shaded columns*). Error bars show SEM. *Dotted vertical lines* indicate the onset and offset of gaze shifts based on a ±20 deg/s criterion. Traces directed upwards are in the ipsilateral direction. Abbreviations: G, E, and H: gaze (= E + H), eye and head positions; $\dot{G}$, $\dot{E}$, and $\dot{H}$: gaze, eye-in-head and head-in-space velocities; FR: firing rate.

Active Head-on-Body Motion: Gaze Shifts

The discharge of each neuron was then characterized during combined eye-head gaze shifts. To do this, the monkey's head was released from its restraint, allowing rotation through the natural range of motion in all three axes. The waveform of each neuron's activity was carefully monitored to ensure that the cell remained undamaged and well isolated. FIGURE 1 shows examples of neuronal discharges during voluntary eye-head gaze shifts for an example PVP neuron (FIG. 1A) and VO neuron (FIG. 1B). These two neurons were typical in that they were poorly modulated in response to voluntary head motion during large (55–65 deg) as well as small (25–35 deg) gaze shifts. A model *prediction* based on each neuron's head motion sensitivity during passive whole-body rotation, and also on eye motion for PVP neurons (see METHODS), consistently overestimated the neuronal discharges during combined eye-head gaze shifts (FIG. 1A and B: pWBR model, thick traces). In order to quantify this observation, we determined the best *estimate* of each neuron's head velocity sensitivity during gaze shifts. The head-velocity signal carried by PVP neurons was reduced in an amplitude-dependent manner (FIG. 1C: open bars), whereas the attenuation of VO neuron modulation was constant across all amplitudes of gaze shifts (FIG. 1C: gray bars). These findings are consistent with the results of previous studies of PVP[38] and VO[41–43] neurons.

In addition to direct projections from the vestibular nerve, the vestibular nuclei receive inputs from neck proprioceptors,[40,47–48] cortical structures (reviewed in ref. 49), cerebellar structures (reviewed in ref. 50), and other brainstem structures (re-

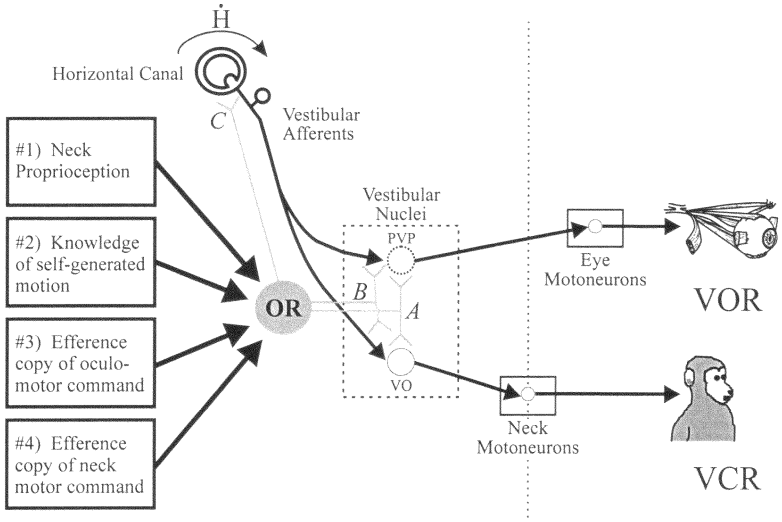

FIGURE 2. Possible mechanisms for the reduced head velocity sensitivities of vestibular neurons during gaze shifts. Inputs from the neck proprioceptors (#1), cognitive representations of the monkey's knowledge of self-generated movement (#2), and/or efference copies from the oculomotor (#3) and neck (#4) premotor circuitries could modulate PVP and VO neurons discharges either ***(A)*** postsynaptically at the vestibular neuron level, ***(B)*** presynaptically at the vestibular neuron level, and/or ***(C)*** at the level of the vestibular sensory apparatus.

viewed in ref. 51). Accordingly, several possible mechanisms could be used to attenuate the responses of PVP and VO neurons to voluntary head-on-body motion at the level of the vestibular nuclei (FIG. 2, sites A or B) or the vestibular afferents (FIG. 2, site C). For example, a neuron's response to active head-on-body motion could be attenuated by (#1) inhibitory inputs from neck proprioceptors, (#2) the monkey's knowledge of its self-generated head motion, or (#3, #4) an efference copy of the motor behavior (i.e., an eye and/or neck motor command) that is generated**.** In order to distinguish between these three possibilities we carried out the series of experiments described below.

Are Neck Afferent Inputs the Source of the Vestibular Suppression?

Passive rotation of the head relative to the body modulates vestibular nuclei neuron activity in decerebrate animals via activation of neck proprioceptors (reviewed in ref. 52). It is conceivable that in alert monkeys neck afferent inputs contribute, at least in part, to the suppression of PVP and VO neuron responses during gaze shifts (FIG. 1*)*. To address this possibility, we rapidly rotated the animal's head on its body such that the passively elicited head velocities were comparable to those generated during large amplitude voluntary gaze shifts. During this paradigm, neuronal firing rates were well predicted by a model based on the neuron's response to passive whole-body rotation (pWBR model: FIG. 3A and B, for PVP and VO neurons, respectively). For both populations of neurons, the estimated head velocity sensitivities during passive head-on-body rotations were similar to those measured during passive whole-body rotations ($p > 0.6$). Indeed, when the response of each neuron to the passive head motion was subtracted from its overall discharge, the residual modulation was found to be negligible, indicating that the passive activation of the neck muscle spindles did not alter the sensitivity of PVP and VO neurons to head-in-space motion.

To further characterize the neck inputs on these neurons, we used a second paradigm in which the monkey's head was held stationary relative to the earth and its body was rotated beneath it. Only periods during which the animal generated minimal voluntary neck activation (see METHODS) were included in the analysis. The example neurons shown are representative of our sample in that they were unresponsive to passive rotation of the body under the head (FIG. 4A and B, for PVP and VO neurons, respectively). The neurons' activities were well described by their spontaneous discharge rates (thick traces superimposed on firing rates) and poorly predicted by a model which would be consistent with neck afferent inputs suppressing vestibular responses during voluntary combined eye-head gaze shifts (thin traces superimposed on firing rates). For our sample of neurons, neck rotation sensitivities estimated during this paradigm were negligible, and thus did not significantly contribute to the reduction in neuronal sensitivities to head motion that was observed during gaze shifts.

Are Neuronal Responses Attenuated during All Planned Movements of the Head-in-Space?

To determine whether vestibular neurons demonstrate attenuation during all self-generated motion of the head in space, we characterized the neuronal activity of PVP and VO neurons during *voluntary* head motion that did not involve activation of the

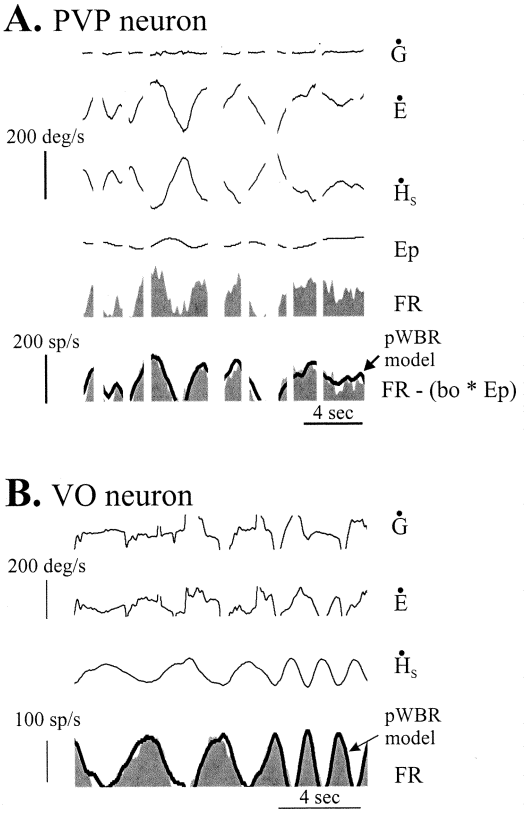

FIGURE 3. Passive rotations of the head on a stationary body: ***(A)*** The activity of this typical PVP neuron could be predicted based on the neuron's response to passive whole-body rotation. The firing rate was corrected for the eye position sensitivity of the neuron (bo * Ep) prior to fitting. (**B**) During the same paradigm, the activity of this typical VO neuron could also be accurately described using the passive whole-body rotation model.

neck musculature. FIGURE 5 shows examples of neuronal activity during a task in which the monkey controlled the velocity and direction of the vestibular turntable: head-restrained monkeys "drove" their own body motion by rotating a steering wheel connected to the motor controller of the vestibular turntable. Each monkey was well trained in this task, and could accurately align its head/body position with a target that moved on the screen facing the animal. Thus, the trajectory of the head motion was the result of a goal-directed action taken by the monkey. Both PVP (FIG. 5A) and VO (FIG. 5B) neurons were strongly modulated by the resultant voluntary head-in-space motion. Moreover, each neuron's activity was well predicted by a model based on its modulation during passive whole-body rotation (FIG. 5A and B; pWBR model, thick trace). Thus, the monkey's knowledge of its self-generated head motion did not reduce the head velocity sensitivity of vestibular nuclei neurons.

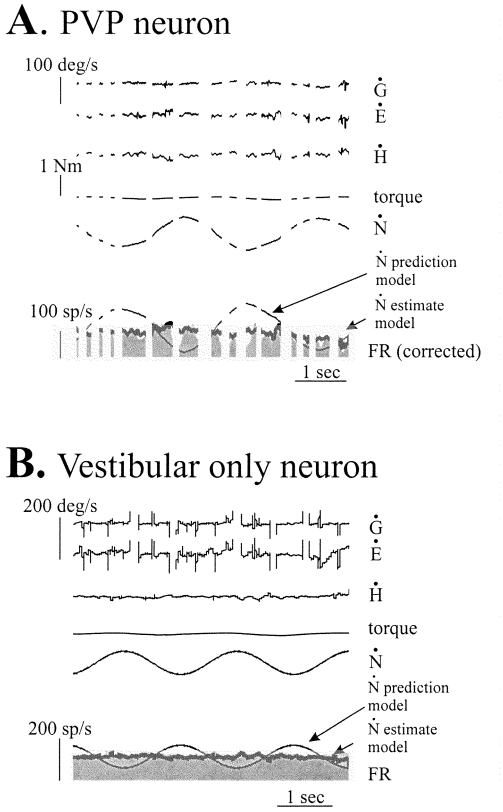

FIGURE 4. Passive rotations of the body under a stationary head. **(A)** The example PVP neuron was not modulated when the monkey's body was passively rotated beneath its stationary head. Accordingly, the neuronal discharge was not well predicted by a neck velocity-based model (neck prediction; see text). Note that minimal torque was generated during this paradigm. **(B)** Similarly, the example VO neuron was not modulated during this paradigm, and thus its activity was not well described by the neck prediction model.

Are Neuronal Responses Attenuated during All Active Head-on-Body Movements?

To determine whether each neuron demonstrated similar attenuation for different voluntary behaviors during which the monkey moved its head relative to its body, neuronal responses were recorded during (1) active head motion made during gaze stabilization and (2) gaze pursuit. During the 10–80 ms interval that immediately followed a gaze shift, the monkey's head was still moving on its neck, but its gaze was stable (interval labeled "post gaze shift" in FIG. 1A and B). FIGURE 6A illustrates the head velocity sensitivities for our sample of PVP (open columns) and VO (gray shaded columns) neurons during this interval. For PVP neurons, little attenuation was observed for either large or small amplitude gaze shifts. Thus, the head-velocity

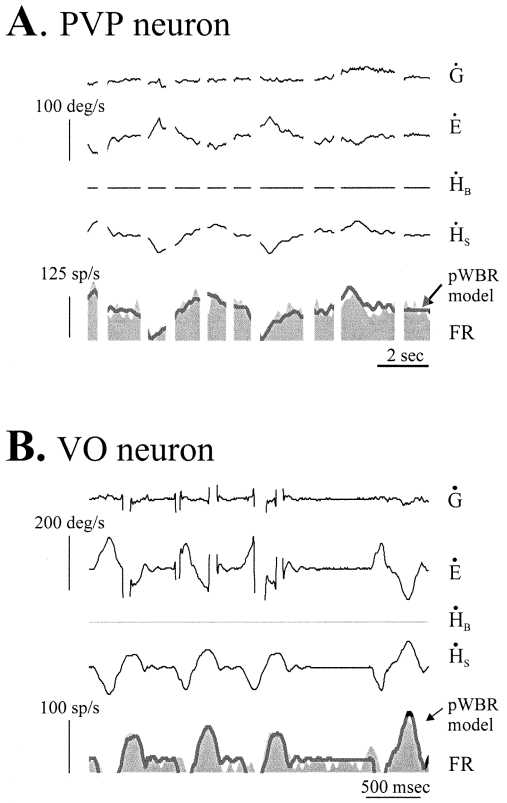

FIGURE 5. Voluntary motion of the head-and-body together in space. ***(A)*** The example PVP neuron was typical in that its response was well predicted by the passive whole-body rotation model when head-restrained monkeys reoriented their bodies and heads in space by manually controlling a steering wheel to rotate the vestibular turntable. ***(B)*** During the same paradigm, the activity of this typical VO neuron could also be accurately described using the passive whole-body rotation model. $\dot{H}_B$: head-on-body velocity.

information carried by PVP neurons was attenuated only *during* the gaze shift; once gaze was stabilized, neuronal responses to head velocity were comparable to those seen during passive whole-body rotation (compare open columns in FIGS. 1C and 6A). In contrast, the head-velocity information carried by VO neurons was significantly reduced in the post gaze shift interval and comparable to that seen during the gaze shift itself (compare gray columns in FIGS. 1C and 6A).

FIGURE 6B and C show the activity of example PVP and VO neurons, respectively, during combined eye-head gaze pursuit. Both classes of neurons were less modulated in response to head motion during gaze pursuit than to head motion during passive whole-body rotation. This is illustrated for the example neurons, where a model prediction based on the neurons' behavior during passive whole-body rotation

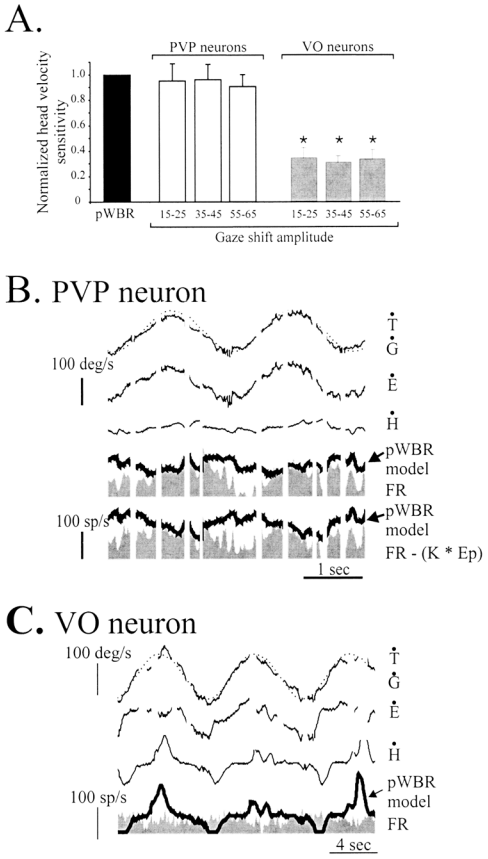

FIGURE 6. Voluntary head-on-body motion during the post gaze shift interval and voluntary combined eye-head gaze pursuit. (**A**) The head sensitivity of PVP neurons was not significantly attenuated immediately following gaze shifts (*white bars*). In contrast, VO neuron discharges were attenuated in this same interval, for all gaze shift amplitudes (gray filled bars). (**B**) The example PVP neuron's response to self-generated head motion during gaze pursuit was reduced compared to that predicted by the neuron's sensitivity to passive whole-body rotation. (**C**) The head-velocity-related modulation of the example VO neuron was greatly attenuated during combined eye-head gaze pursuit. $\dot{T}$: Target velocity.

(pWBR) is superimposed on the firing rate profiles (thick traces). The pWBR model consistently overestimated the neuron's modulation during gaze pursuit. The estimated head-velocity-related modulation of PVP neurons showed less attenuation during gaze pursuit (mean attenuation = ~30%) than during gaze shifts. However, head-velocity-related modulation of VO neurons was similarly attenuated (mean attenuation = ~65%) during all voluntary behaviors in which the monkey moved its head relative to its body (i.e., gaze shifts, active head motion made during gaze stabilization, and gaze pursuit).

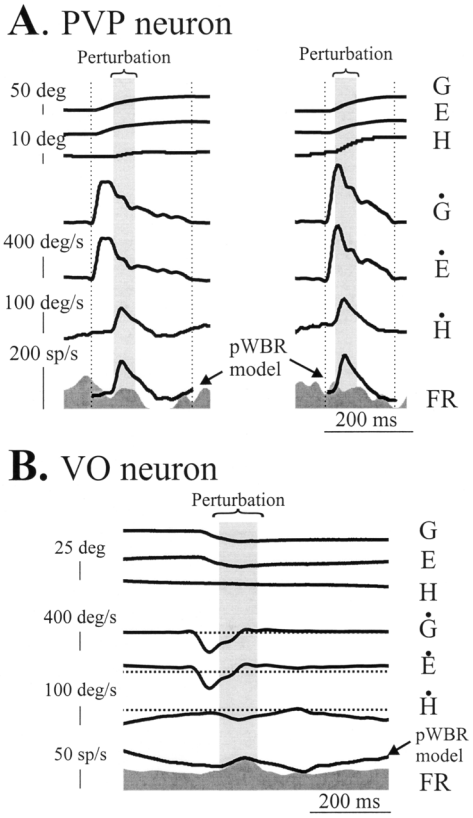

FIGURE 7. Transient mechanical perturbations of the head applied during combined eye-head gaze shifts. (**A**) When a transient high-frequency mechanical perturbation was applied to the head during an ongoing gaze shift (*gray shaded box*), the response of the example PVP neuron was greatly attenuated from that expected based on its sensitivity to passive head velocity during head-restrained whole-body rotation. (**B**) In contrast, the example VO neuron faithfully encoded the passive component of head velocity in this paradigm.

Are Vestibular Neurons Responsive to Head Perturbations Applied during Active Head Motion?

The implications of the above results can perhaps be best appreciated by examining the differences in the responses of the two cell types to externally applied perturbations *during* active head movements. We designed an experiment in which we applied a rapid perturbation of the head on the body using a small torque motor while the monkey was generating a gaze shift. As is illustrated in FIGURE 7A, the head velocity sensitivity of PVP neurons was reduced in response to both the passively applied and actively generated head motion during such gaze shifts. Thus, the sensitivity to all head motion, regardless of its source, was reduced when the monkey

was shifting its gaze. In contrast, as is illustrated for the example neuron in FIGURE 7B, VO neurons remained selectively sensitive to the passive component of the head motion during gaze shifts, and their robust response to the passively applied perturbation could be predicted by the neuron's sensitivity to passive whole-body rotation. Thus for VO neurons, only the neuronal response to the self-generated head-on-body motion was reduced.

DISCUSSION

Suppression of VOR Pathways Depends on the Gaze Goal

The attenuation that we observe for PVP neurons during *gaze shifts* can be accounted for by known brainstem mechanisms (FIG. 8). We have previously shown that burst neurons (BNs) in the paramedian pontine reticular formation carry head as well as eye velocity signals during gaze shifts (BN panel, thick model fit[53]). BNs are known to project directly to neurons in the vestibular nuclei that are activated during contralateral head rotation (type II[54]). These type II neurons in turn send inhibitory projections to type I PVP neurons, which were the topic of the present study.[55] Examples of the discharge patterns of BNs and type I PVP neurons during gaze shifts are illustrated within dotted boxes. We propose that the eye and head velocity signals carried by BNs could account, via type II VN/PH neurons, for the attenuation of PVP neurons head sensitivity during gaze shifts (PVP panel, thick model fit; see ref. 38). We also propose that during *combined eye-head gaze pursuit*, the mechanism underlying the attenuation in PVP neurons modulation is likely to involve a similar interaction between the direct VOR pathway and the premotor circuitry that drive smooth pursuit eye movements (not shown).

During gaze shifts, the head velocity sensitivity of PVP neurons is greatly attenuated but not completely suppressed (FIG. 1C). This finding indicates that PVP neurons carry a residual head-related signal to the extraocular motoneurons during gaze shifts. However, this signal is not seen at the level of single motoneurons; we have shown in a series of studies on extraocular motoneurons during head-restrained eye movements and combined eye-head gaze shifts that neuronal responses remained correlated to eye motion at all times.[56–57] Thus, the residual signals carried by PVP neurons during gaze shifts must be offset at the level of the extraocular motoneurons (indicated by the "?" in FIG. 8). It is likely that the head movement-related signals carried by burst neurons during gaze shifts, which are known to project directly to the extraocular motoneurons, function to offset the residual head velocity input carried by the VOR pathway.[53]

Suppression of VCR Pathways Depends on the Head Goal

Earlier studies have demonstrated that VO neurons, in squirrel monkey, differentially encode head motion during passive rotation versus the active head movements that are generated during gaze shifts.[13,41,58] We found that VO neuron responses were attenuated by, on average, 63% during gaze shifts in rhesus monkey;[43] a finding that is consistent with these previous studies. Given that VO neurons demonstrated no sensitivity to neck activation during passive rotation of the head on body, we

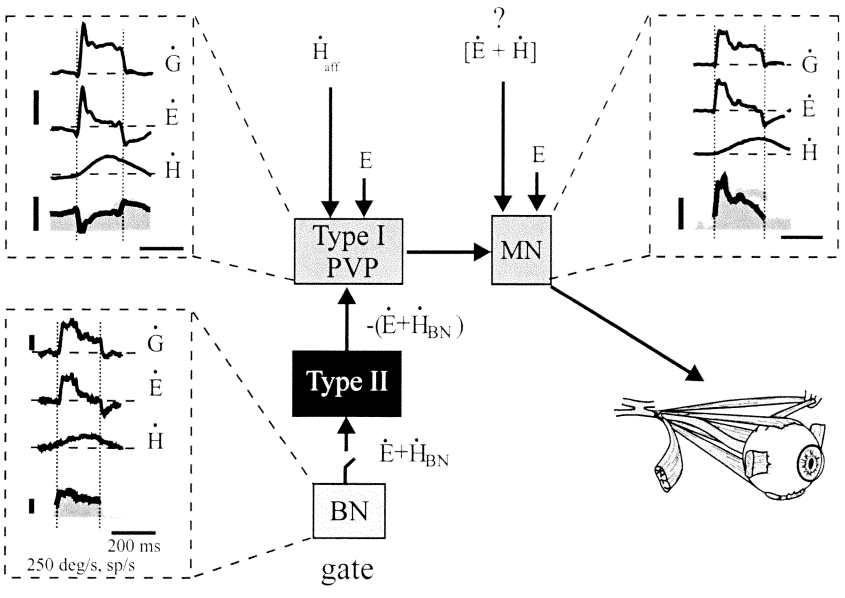

FIGURE 8. Brainstem mechanism for the attenuation of PVP neurons during gaze shifts. Type I PVP neurons (present study) receive a strong monosynaptic connection from the ipsilateral vestibular afferents ($\dot{H}_{aff}$) and, in turn, project directly to extraocular motoneurons (MNs). During steady fixation and slow eye movements, PVP neurons also carry an eye position signal (E) which is provided by the intrinsic properties of these vestibular neurons and/or their interconnections with the nucleus prepositus hypoglossi and cerebellum. During saccades, vestibular quick phases and gaze shifts, brainstem burst neurons (BNs) become active as denoted by the "gate," and provide an inhibitory input ($-[\dot{E} + \dot{H}_{BN}]$) to type I PVP neurons via type II vestibular and/or prepositus hypoglossi neurons. We propose that the residual head velocity signal carried by type I PVP neurons is then offset at the level of individual abducens motoneurons by BNs (see ?). The activity of a typical BN, a type I PVP neuron, and an abducens motoneuron are depicted in the dotted boxes.

conclude that direct inputs from neck proprioceptors do not account for the attenuated responses during gaze shifts. Moreover, we found that VO neurons reliably encoded head velocity during self-generated head motion when the head and body moved together in space, and we were thus able to rule out the possibility that attenuation was mediated by a signal that reflected the monkey's knowledge that it will move or is moving its head relative to space. Finally, we showed that VO neurons demonstrate comparable attenuation during active head-on-body movements made when the premotor saccadic burst generator is not active—immediately following gaze shifts (where gaze was stable but the head was still in motion) and during gaze pursuit.

Thus, attenuation of head-velocity signals encoded by VO neurons was selective to active head-on-body movements and was comparable for all movements generated by activation of the neck musculature regardless of whether the animal was sta-

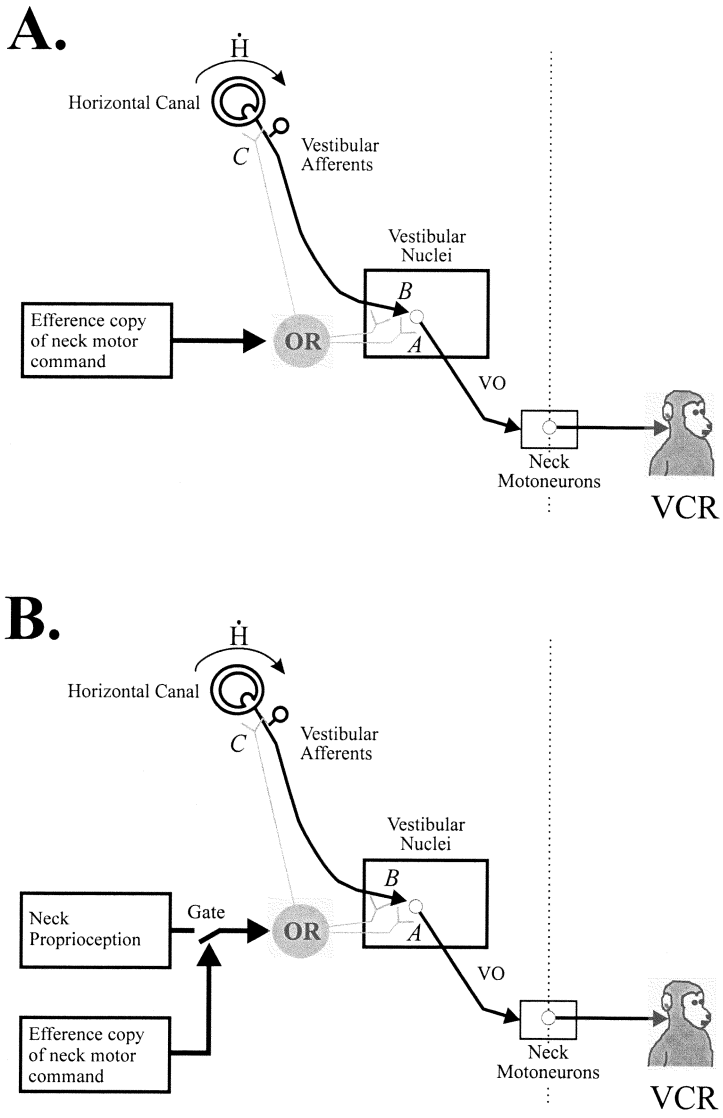

FIGURE 9. Brainstem mechanism for the attenuation of VO neurons during gaze shifts. (**A**) An efferent copy of the neck motor command (voluntary $\dot{H}_B$) is subtracted from the vestibular afferents signal ($\dot{H}_S$) at the level of either (*A*) the semicircular canals, (*B*) presynaptic to the VO neurons, and/or (*C*) at the VO neuron itself. Neither neck proprioceptive information alone nor an internal representation of head-in-space motion mediates the differential processing of self-generated head-on-body motion. (**B**) Alternatively, an efferent copy of the neck motor command (voluntary $\dot{H}_B$) could be utilized to "gate in" neck proprioceptive inputs during active head-on-body movements.

bilizing its gaze or redirecting its gaze to a new point in space. We hypothesize that a copy of the motor command to the neck motoneurons (a neck motor efference signal) is used to attenuate the head velocity sensitivity of VO neurons during voluntary head-on-body movements. This effect could be mediated by a direct efference copy of the neck motor command input to VO neurons (FIG. 9A), or alternatively by a neck efference copy signal that would influence the activity of VO neurons by selectively "*gating in*" inhibitory neck proprioceptive signals (FIG. 9B).

Summary of Goal-dependent Modulation of Vestibular Nuclei Neurons

We have shown that the VOR and VCR pathways process vestibular signals differently depending on the animal's current behavioral goal. It is particularly apparent from our analysis of neuronal responses to passive head perturbations during active head movements (FIG. 7) that PVP neurons faithfully encode head velocity only when the animal is stabilizing its gaze, whereas VO neurons faithfully encode head velocity during all head motion that is *not* generated via voluntary activation of the neck musculature. We propose that the VOR and VCR pathways use efference copies of oculomotor and neck movement commands, respectively, for this selective processing of vestibular information (FIG. 2, mechanisms #3 and #4, respectively). Given that (1) the VOR functions to stabilize gaze in space by producing compensatory eye movements of opposite direction to that of the head, and (2) the VCR functions to stabilize the head in space via activation of the neck musculature, we conclude that the behaviorally dependent modulation of the VOR and VCR pathways that we observed is appropriate to suppress oculomotor and head movement commands which are counterproductive to the animal's *current behavioral goal.*

ACKNOWLEDGMENTS

This study was supported by the CIHR, the NSERC, and the FRSQ.

REFERENCES

1. CHUBB, M.C., A.F. FUCHS & C.A. SCUDDER. 1984. Neuron activity in monkey vestibular nuclei during vertical vestibular stimulation and eye movements. J. Neurophysiol. **52:** 724–742.
2. CULLEN, K.E. & R.A. MCCREA. 1993. Firing behavior of brain stem neurons during voluntary cancellation of the horizontal vestibulo-ocular reflex. I. Secondary vestibular neurons. J. Neurophysiol. **70:** 828–843.
3. CULLEN, K.E., C. CHEN-HUANG & R.A. MCCREA. 1993. Firing behavior of brainstem neurons during voluntary cancellation of the horizontal vestibulo-ocular reflex. II. Eye-movement related neurons. J. Neurophysiol. **70:** 844–856.
4. FUCHS, A.F. & J. KIMM. 1975. Unit activity in vestibular nucleus of the alert monkey during horizontal angular acceleration and eye movement. J. Neurophysiol. **38:** 1140–1161.
5. KELLER, E.L. & P. DANIELS. 1975. Oculomotor related interaction of vestibular and visual stimulation in vestibular nucleus cells in the alert monkey. Exp. Neurol. **46:** 187–198.
6. LISBERGER, S.G. & F.A. MILES. 1980. Role of the primate vestibular nucleus in long-term adaptive plasticity of the vestibulo-ocular reflex. J. Neurophysiol. **43:** 1725–1745.

7. MCFARLAND, J.L. & A.F. FUCHS. 1992. Discharge patterns of nucleus prepositus hypoglossi and adjacent vestibular nucleus during horizontal eye movement in behaving macaques. J. Neurophysiol. **41:** 319–332.
8. MILES, F.A. 1974. Single unit firing patterns in the vestibular nuclei related to voluntary eye movements and passive body rotation in conscious monkeys. Brain Res. **71:** 215–224.
9. SCUDDER, C.A. & A.F. FUCHS. 1992. Physiological and behavioural identification of vestibular nucleus neurons mediating the horizontal vestibuloocular reflex in trained rhesus monkeys. J. Neurophysiol. **68:** 244–264.
10. TOMLINSON, R.D. & D.A. ROBINSON. 1984. Signals in vestibular nucleus mediating vertical eye movements in the monkey. J. Neurophysiol. **51:** 1121–1136.
11. MCCREA, R.A., E.M. STRASSMAN & S.M. HIGHSTEIN. 1987. Anatomical and physiological characteristics of vestibular neurons mediating the horizontal vestibulo-ocular reflex of the squirrel monkey. J. Comp. Neurol. **264:** 547–570.
12. BOYLE, R. 1993. Activity of medial vestibulospinal tract cells during rotation and ocular movement in the alert squirrel monkey. J. Neurophysiol. **70:** 2176–2180.
13. BOYLE, R., T. BELTON & R.A. MCCREA. 1996. Responses of identified vestibulospinal neurons to voluntary eye and head movements in the squirrel monkey. Ann. N.Y. Acad. Sci. **781:** 244–263.
14. LORENTE DE NO', R. 1933. Vestibular-ocular reflex arc. Arch. Neurol. Psychiatry **30:** 245–291.
15. CULLEN, K.E., T. BELTON & R.A. MCCREA. 1991. A non-visual mechanism for voluntary cancellation of the vestibulo-ocular reflex. Exp. Brain Res. **83:** 237–252.
16. LISBERGER, S.G. & T.A. PAVELKO. 1986. Vestibular signals carried by pathways subserving plasticity of the vestibulo-ocular reflex in monkeys. J. Neurosci. **6:** 346–354.
17. MINOR, L.B., R.A. CLENDANIEL & D.M. LASKER. 1998. High-frequency dynamics of the horizontal VOR in squirrel monkeys. I. Responses in normal monkeys and following lens-induced adaptation. Soc. Neurosci. Abstr. **24:** 1659.
18. GROSSMAN, G.E., R.J. LEIGH, L.A. ABEL, *et al*. 1988. Frequency and velocity of rotational head perturbations during locomotion. Exp. Brain Res. **70:** 470–476.
19. GROSSMAN, G.E., R.J. LEIGH, E.N. BRUCE, *et al*. 1989. Performance of human vestibuloocular reflex during locomotion. J. Neurophysiol. **62:** 264–271.
20. ANDRÉ-DESHAYS, C., A. BERTHOZ & M. REVEL. 1988. Eye-head coupling in humans. I. Simultaneous recording of isolated motor units in dorsal neck muscles and horizontal eye movements. Exp. Brain Res. **69:** 399–406.
21. BARNES, G.R. 1979. Vestibulo-ocular function during co-ordinated head and eye movements to acquire visual targets. J. Physiol. **287:** 127–147.
22. GUITTON, D. & M. VOLLE. 1987. Gaze control in humans: eye-head coordination during orienting movements to targets within and beyond the oculomotor range. J. Neurophysiol. **58:** 427–459.
23. PÉLISSON, D., C. PRABLANC & C. URQUIZAR. 1988. Vestibulo-ocular reflex inhibition and gaze saccade control characteristics during eye-head orientation in humans. J. Neurophysiol. **59:** 997–1013.
24. ZANGEMEISTER, W.H. & L. STARK. 1982a. Gaze latency: variable interactions of head and eye latency. Exp. Neurol. **75:** 389–406.
25. ZANGEMEISTER, W.H. & L. STARK. 1982b. Types of gaze movement: variable interactions of eye and head movements. Exp. Neurol. **77:** 563–577.
26. BIZZI, E., R.E. KALIL & V. TAGLIASCO. 1971. Eye-head coordination in monkeys: evidence for centrally patterned organization. Science **173:** 452–454.
27. DICHGANS, J., E. BIZZI, P. MORASSO & V. TAGLIASCO. 1973. Mechanisms underlying recovery of eye-head coordination following bilateral labyrinthectomy in monkeys. Exp. Brain Res. **18:** 548–562.
28. LANMAN, J., E. BIZZI & J. ALLUM. 1978. The coordination of eye and head movement during smooth pursuit. Brain Res. **153:** 39–53.
29. MORASSO, P., E. BIZZI & J. DICHGANS. 1973. Adjustment of saccade characteristics during head movements. Exp. Brain Res. **16:** 492–500.
30. TOMLINSON, R.D. 1990. Combined eye-head gaze shifts in the primate. III. Contributions to the accuracy of gaze saccades. J. Neurophysiol. **64:** 1873–1891.

31. TOMLINSON, R.D. & P.S. BAHRA. 1986a. Combined eye-head gaze shifts in the primate. I. Metrics. J. Neurophysiol. **56:** 1542–1557.
32. TOMLINSON, R.D. & P.S. BAHRA. 1986b. Combined eye-head gaze shifts in the primate. II. Interactions between saccades and the vestibulo-ocular reflex. J. Neurophysiol. **56:** 1558–1570.
33. FULLER, J.H., H. MALDONADO & J. SCHLAG. 1983. Vestibular-oculomotor interaction in cat eye-head movements. Exp. Brain Res. **271:** 241–250.
34. LAURUTIS, V.P. & D.A. ROBINSON. 1986. The vestibulo-ocular reflex during human saccadic eye movements. J. Physiol. **373:** 209–233.
35. TABAK, S., J.B.J. SMEETS & H. COLLEWIJN. 1996. Modulation of the human vestibuloocular reflex during saccades: probing by high-frequency oscillation and torque pulses of the head. J. Neurophysiol. **76:** 3249–3263.
36. CULLEN, K.E. & J.E. ROY. 1998. Modulation of vestibular neuron activity: active versus passive head movements. Barany Society's Symposium Satellite Meeting: The contributions of the oculo-motor and skeleto-motor systems to perceptual functions. Freiburg, Germany.
37. ROY, J.E. & K.E. CULLEN. 1997. Relationships between vestibular neuron spike trains and the dynamics of voluntary gaze shifts in the rhesus monkey. Soc. Neurosci. Abstr. **23:** 295.
38. ROY, J.E. & K.E. CULLEN. 1998. A neural correlate for vestibulo-ocular reflex suppression during voluntary eye-head gaze shifts. Nature Neurosci. **1:** 404–410.
39. GDOWSKI, G.T. & R.A. MCCREA. 1999. Integration of vestibular and head movement signals in the vestibular nuclei during whole-body rotation. J. Neurophysiol. **81:** 436–449.
40. WILSON, V.J., Y. YAMAGATA, B.J. YATES, *et al*. 1990. Response of vestibular neurons to head rotations in vertical planes. III. Response of vestibulocollic neurons to vestibular and neck stimulation. J. Neurophysiol. **64:** 1695–1703.
41. MCCREA, R.A., G.T. GDOWSKI, R. BOYLE & T. BELTON. 1999. Firing behavior of vestibular neurons during active and passive head movements: vestibulo-spinal and other non-eye-movement related neurons. J. Neurophysiol. **82:** 416–428.
42. ROY, J.E. & K. E. CULLEN. 1999. Differential processing of head velocity signals in the vestibular nuclei: voluntary head/neck versus head/space motion. Soc. Neurosci. Abstr. **25:** 265.
43. ROY, J.E. & K.E. CULLEN. 2001. Selective processing of vestibular reafference during self-generated head motion. J. Neurosci. **21:** 2131–2142.
44. SYLVESTRE, P.A. & K.E. CULLEN. 1999. Quantitative analysis of abducens neuron discharge dynamics during saccadic and slow eye movements. J. Neurophysiol. **82:** 2616–2632.
45. FUCHS, A.F. & D.A. ROBINSON. 1966. A method for measuring horizontal and vertical eye movements in the monkey. J. Physiol. (Lond.) **191:** 609–631.
46. HAYS, A.V., B.J. RICHMOND & L.M. OPTICAN. 1982. A UNIX-based multiple process system for real-time data acquisition and control. WESCOM Conf. Proc. **2:** 1–10.
47. ANASTASOPOULOS, D. & T. MERGNER. 1982. Canal-neck interaction in vestibular nuclear neurons of the cats. Exp. Brain Res. **46:** 269–280.
48. BOYLE, R. & O. POMPEIANO. 1981. Responses of vestibulospinal neurons to sinusoidal rotation of the neck. J. Neurophysiol. **44:** 633–649.
49. FUKUSHIMA, K. 1997. Corticovestibular interactions: anatomy, electrophysiology, and functional considerations. Exp. Brain Res. **117:** 1–16.
50. VOOGD, J., M. GERRITS & J.H. RUIGROK. 1996. Organization of the vestibulocerebellum. Ann. N.Y. Acad. Sci. **781:** 553–579.
51. HIGHSTEIN, S.M. & R.A. MCCREA. 1988. The anatomy of the vestibular nuclei. *In* Neuroanatomy of the Oculomotor System. J.A. Büttner-Ennever, Ed.: 177–202. Elsevier Science. New York.
52. WILSON, V.J. 1991. Vestibulospinal and neck reflexes: interaction in the vestibular nuclei. Arch. Ital. Biol. **129:** 43–52.
53. CULLEN, K.E. & D. GUITTON. 1997. Analysis of primate IBN spike trains using system identification techniques. I. Relationship to eye movement dynamics during head-fixed saccades. J. Neurophysiol. **78:** 3259–3282.

54. SASAKI, S. & H. SHIMAZU. 1981. Reticulovestibular organization participating in generation of horizontal fast eye movement. Ann. N. Y. Acad. Sci. **374:** 130–145.
55. SHIMAZU, H. & W. PRECHT. 1966. Inhibition of central vestibular neurons from the contralateral labyrinth and its mediating pathway. J. Neurophysiol. **29:** 467–492.
56. CULLEN, K.E., H.L. GALIANA & P.A. SYLVESTRE. 2000. Comparing Extraocular motoneuron discharges during head-restrained saccades and head-unrestrained gaze shifts. J. Neurophysiol. **83:** 630–637.
57. SYLVESTRE, P.A., J.E. ROY & K.E. CULLEN. 2001. Do extraocular motoneurons encode head velocity during head-restrained versus head-unrestrained saccadic and smooth pursuit movements? Ann. N. Y. Acad. Sci. **942:** this volume.
58. MCCREA, R.A., C. CHEN-HUANG, T. BELTON & G.T. GDOWSKI. 1996. Behavior contingent processing of vestibular sensory signals in the vestibular nuclei. Ann. N. Y. Acad. Sci. **781:** 292–303.