

Vestibuloocular Reflex Signal Modulation During Voluntary and Passive Head Movements

JEFFERSON E. ROY AND KATHLEEN E. CULLEN

Aerospace Medical Research Unit, Department of Physiology, McGill University, Montreal, Quebec H3G 1Y6, Canada

Received 30 July 2001; accepted in final form 17 December 2001

Roy, Jefferson E. and Kathleen E. Cullen. Vestibuloocular reflex signal modulation during voluntary and passive head movements. *J Neurophysiol* 87: 2337–2357, 2002; 10.1152/jn.00625.2001. The vestibuloocular reflex (VOR) effectively stabilizes the visual world on the retina over the wide range of head movements generated during daily activities by producing an eye movement of equal and opposite amplitude to the motion of the head. Although an intact VOR is essential for stabilizing gaze during walking and running, it can be counterproductive during certain voluntary behaviors. For example, primates use rapid coordinated movements of the eyes and head (gaze shifts) to redirect the visual axis from one target of interest to another. During these self-generated head movements, a fully functional VOR would generate an eye-movement command in the direction opposite to that of the intended shift in gaze. Here, we have investigated how the VOR pathways process vestibular information across a wide range of behaviors in which head movements were either externally applied and/or self-generated and in which the gaze goal was systematically varied (i.e., stabilize vs. redirect). VOR interneurons [i.e., type I position-vestibular-pause (PVP) neurons] were characterized during head-restrained passive whole-body rotation, passive head-on-body rotation, active eye-head gaze shifts, active eye-head gaze pursuit, self-generated whole-body motion, and active head-on-body motion made while the monkey was passively rotated. We found that regardless of the stimulation condition, type I PVP neuron responses to head motion were comparable whenever the monkey stabilized its gaze. In contrast, whenever the monkey redirected its gaze, type I PVP neurons were significantly less responsive to head velocity. We also performed a comparable analysis of type II PVP neurons, which are likely to contribute indirectly to the VOR, and found that they generally behaved in a quantitatively similar manner. Thus our findings support the hypothesis that the activity of the VOR pathways is reduced “on-line” whenever the current behavioral goal is to redirect gaze. By characterizing neuronal responses during a variety of experimental conditions, we were also able to determine which inputs contribute to the differential processing of head-velocity information by PVP neurons. We show that neither neck proprioceptive inputs, an efference copy of neck motor commands nor the monkey’s knowledge of its self-motion influence the activity of PVP neurons *per se*. Rather we propose that efference copies of oculomotor/gaze commands are responsible for the behaviorally dependent modulation of PVP neurons (and by extension for modulation of the status of the VOR) during gaze redirection.

INTRODUCTION

The vestibular system is classically associated with detecting the motion of the *head-in-space* to generate the reflexes that are

crucial for our daily activities, such as stabilizing gaze (gaze = eye-in-head + head-in-space) via the vestibuloocular reflex (VOR) during walking and running (Grossman et al. 1988, 1989). During passive whole-body rotation in head-restrained animals, vestibular afferents originating in the semicircular canals encode the angular velocity of the head-in-space (Goldberg and Fernandez 1971). These vestibular afferents, in turn, project to second-order neurons within the vestibular nuclei, which encode angular head velocity during the compensatory eye movements generated by the VOR (Cullen and McCrea 1993; McCrea et al. 1987; Scudder and Fuchs 1992). However, in addition to input from the vestibular nerve, the vestibular nuclei receive projections from many structures that could influence their discharge. For example, neurons within oculomotor/gaze control pathways, such as the saccadic burst neurons in the paramedian pontine reticular formation, send direct projections to the vestibular nuclei (Sasaki and Shimazu 1981). Furthermore, neck muscle spindle afferents are known to influence the activity of vestibular nuclei neurons in decerebrate animals (Anastasopoulos and Mergner 1982; Boyle and Pompeiano 1981; Fuller 1988; Wilson et al. 1990) via a disynaptic pathway (Sato et al. 1997). Moreover, cortical areas, which have been implicated in more cognitive aspects of vestibular function including the perception of spatial orientation, the ability to navigate (in the absence of visual cues), and gaze control, project to the vestibular nuclei (for review, see Fukushima 1997). Thus given the convergence of multiple inputs to the vestibular nuclei, it is natural to ask how the signals carried by these inputs are integrated during our daily activities.

Here we have focused on the behavior of a distinct population of vestibular nuclei neurons termed position-vestibular-pause (PVP) neurons during horizontal head rotations. Type I PVP neurons are thought to constitute most of the intermediate leg of the direct VOR pathway; they receive a strong monosynaptic connection from the ipsilateral semicircular canal afferents and, in turn, project directly to the extraocular motoneurons (Cullen and McCrea 1993; McCrea et al. 1987; Scudder and Fuchs 1992). These neurons derive their name from the signals they carry during head-restrained oculomotor and vestibular paradigms: their firing rates increase when the eyes move to more contralaterally directed *positions*; during slow phase *vestibular* nystagmus, these neurons are sensitive to ipsilateral head rotations (i.e., a type I response); and their

Address for reprint requests: K. E. Cullen, Aerospace Medical Research Unit, 3655 Promenade Sir William Osler, Montreal, Quebec H3G 1Y6, Canada (E-mail: cullen@med.mcgill.ca).

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

discharges cease (*pause*) for ipsilaterally directed saccades and vestibular quick phases. Type II PVP neurons have oppositely directed eye- and head-motion sensitivities to those of type I PVP neurons, and their role in the processing of vestibular information is less well understood. Nevertheless, in general, they behave in a quantitatively similar manner to type I PVP neurons during head-restrained rotations and eye movements (Scudder and Fuchs 1992).

The first goal of this study was to address the general question of whether the PVP neuron responses to active and/or passive movements are modified in a manner that depends on the animal's current behavioral goal. For example, the response of PVP neurons might be selectively attenuated for gaze redirection versus stabilization, consistent with their role in mediating the VOR. Alternatively, it is also possible that PVP neurons might differentially encode head velocity during self-generated versus passively applied head-in-space rotations and/or during rotation of the head and body together in space versus rotation of the head relative to an earth-stationary body.

On the one hand, there is already much evidence to suggest that type I PVP neurons differentially encode head-velocity during gaze redirection versus gaze stabilization. First, while type I PVP neurons encode head velocity during the compensatory slow phase component of the VOR evoked by passive whole-body rotation, they pause or cease firing during vestibular quick phases where gaze is redirected (Cullen and McCrea 1993; Fuchs and Kimm 1975; Keller and Daniels 1975; Keller and Kamath 1975; Lisberger et al. 1994a,b; McConville et al. 1996; McCrea et al. 1987; Miles 1975; Roy and Cullen 1998; Scudder and Fuchs 1992; Tomlinson and Robinson 1984). Second, when gaze is voluntarily redirected using coordinated eye-head gaze shifts, the head-velocity signal carried by type I PVP neurons is significantly attenuated as compared with passive whole-body rotation (Cullen and McCrea 1993; McCrea et al. 1996; Roy and Cullen 1998) in an amplitude-dependent manner (Roy and Cullen 1998). Third, type I PVP neuron responses are attenuated by ~30% as compared with passive rotation in the dark when monkeys suppress their VOR (and therefore redirect their gaze to move with the head in space) during passive whole-body rotation by tracking a target that moves with the head (Cullen and McCrea 1993; McCrea et al. 1996; Roy and Cullen 1998; Scudder and Fuchs 1992).

On the other hand, whether PVP neurons differentially encode head-velocity during self-generated versus passively applied rotations of the head-in-space is less clear. It has been proposed that an enhanced sensitivity of the VOR pathways during active head movements might increase VOR responses in humans as compared with passive head motion when the goal is to stabilize gaze (Demer et al. 1993; Jell et al. 1988). However, this behavioral observation remains to be confirmed at the neural level. We have previously shown (Roy and Cullen 1998) that type I PVP neuron discharges in the rhesus monkey are similar during the VOR elicited by passive whole-body rotation and during the active head movements made in the time interval that immediately follows a gaze shift. In this interval, an ocular counter roll compensates for the residual active head motion such that the monkey's axis of gaze is stable relative to space. Gdowski and McCrea (1999) also reported that the majority of PVP neurons in squirrel monkeys encode head-in-space motion during simultaneous active and passive head motion. However, they emphasized that 35% of

the neurons were better related to the passive component of the motion than to the total head-in-space motion during this same paradigm. While this latter result is actually the opposite of what would be expected if the efficacy of the VOR was, in fact, enhanced during active head movements, its interpretation is limited given that the gaze goal of the monkeys was not reported.

The second goal of the present study was to determine the neural mechanism(s) that contribute to the differential processing of head-velocity information by PVP neurons. For example, during gaze shifts, there are several possible mechanisms that could modulate PVP neuron discharges. It is likely that inputs from the brain stem saccadic burst generator to the vestibular nuclei could function to suppress PVP neuron responses during voluntary combined eye-head gaze shifts (Roy and Cullen 1998). Specifically, burst neurons in the paramedian pontine reticular formation project to type II neurons in the vestibular nucleus (Sasaki and Shimazu 1981), which in turn send an inhibitory projection to type I PVP neurons (Nakao et al. 1982). This pathway almost certainly provides a powerful inhibitory drive to type I PVP neurons during rapid gaze shifts. It is also possible that inhibitory inputs from neck proprioceptors contribute to the attenuation of PVP neuron discharges. Studies in anesthetized animals have shown that the activation of neck proprioceptors can influence the activity of vestibular nuclei neurons (Anastasopoulos and Mergner 1982; Boyle and Pompeiano 1981; Fuller 1988; Wilson et al. 1990). Furthermore, McCrea and colleagues recently reported that most if not all secondary vestibular neurons (including type I PVP neurons) in squirrel monkey are sensitive to passive neck rotation (Gdowski and McCrea 1999, 2000; McCrea et al. 1996). Finally, a signal related to the voluntary head motion itself, such as an efferent copy of the motor command to the neck musculature (McCrea et al. 1996) or a cortically derived signal representing the monkey's self-generated head motion, could influence the responses of PVP neurons.

To determine how PVP neurons process head-velocity information across a wide variety of behaviors and to understand the mechanisms that underlie the observed differential processing, we devised a sequence of paradigms in which the gaze goal was systematically varied for externally applied and/or self-generated head movements. We first characterized the discharges of PVP neurons in the head-restrained condition during passive whole-body rotation when gaze was stable (VOR) and when gaze was redirected (VOR cancellation paradigm). The neuronal discharges were then recorded during different gaze control tasks while the monkey experienced passive rotations of its head-on-body, generated voluntary head-on-body movements to orient to novel targets or track a slowly moving target, was passively rotated while simultaneously generating active head movements, and voluntarily "drove" its head and body together relative to space. We found that, during active and/or passive head movements, type I PVP neurons robustly encoded head velocity whenever monkeys stabilized their gaze relative to space, and were similarly attenuated during gaze-redirection tasks. Furthermore, the responses of type II PVP neurons were quantitatively comparable to those of type I PVP neurons during most behavioral conditions. Our results support the hypothesis that an efference copy of the brain stem oculomotor/gaze commands to redirect the visual axis in space underlies the "on-line" reduction in VOR

pathway modulation when the VOR is functionally inappropriate.

METHODS

Three rhesus monkeys (*Macaca mulatta*) were prepared for chronic extracellular recording using aseptic surgical techniques. All experimental protocols were approved by the McGill University Animal Care Committee and were in compliance with the guidelines of the Canadian Council on Animal Care.

Surgical procedures

The surgical techniques were similar to those previously described by Roy and Cullen (2001). Briefly, an 18- to 19-mm-diam eye coil (3 loops of Teflon-coated stainless steel wire) was implanted in the right eye behind the conjunctiva. In addition, a dental acrylic implant was fastened to each animal's skull using stainless steel screws. The implant held in place a stainless steel post used to restrain the animal's head, and a stainless steel recording chamber that was positioned to access the medial vestibular nucleus (posterior and lateral angles of 30°). During the surgery isoflurane gas was utilized to initiate (2–3%) and maintain (0.8–1.5%) anesthesia. After the surgery, buprenorphine (0.01 mg/kg im) was utilized for postoperative analgesia, and monkeys were allowed to recover for 2 wk before commencing experimental sessions.

Data acquisition

At the onset of each experiment, the monkey sat comfortably in a primate chair, which was placed on a vestibular turntable. With the monkey initially head-restrained, extracellular single-unit activity was recorded using enamel-insulated tungsten microelectrodes (7–10 M Ω impedance, Frederick-Haer) as has been described elsewhere (Roy and Cullen 2001). The abducens nucleus, which was identified based on its stereotypical discharge patterns during eye movements (Cullen et al. 1993; Sylvestre and Cullen 1999), was located and used as a landmark to determine the location of the medial and lateral vestibular nuclei. Gaze and head position were measured using the magnetic search coil technique (Fuchs and Robinson 1966), and turntable velocity was measured using an angular velocity sensor (Watson). Unit activity, horizontal and vertical gaze and head positions, target position, and table velocity were recorded on DAT tape for later playback. Action potentials were discriminated during playback using a windowing circuit (BAK) that was manually set to generate a pulse coincident with the rising phase of each action potential. Gaze position, head position, target position, and table velocity signals were low-pass filtered at 250 Hz (8 pole Bessel filter) and sampled at 1,000 Hz.

Behavioral paradigms

Using juice as a reward, monkeys were trained to follow a target light (HeNe laser) that was projected, via a system of two galvanometer controlled mirrors, onto a cylindrical screen located 60 cm away from the monkey's head. Eye-motion sensitivities to saccades and ocular fixation were characterized by having the head-restrained monkey attend to a target that stepped between horizontal positions over a range of $\pm 30^\circ$. To determine neuronal eye-motion sensitivities during smooth pursuit, head-restrained monkeys tracked sinusoidal (0.5 Hz, 80°/s peak velocity) target motion in the horizontal plane. Head-velocity sensitivities to passive whole body rotation (0.5 Hz, 80°/s peak velocity) were tested by rotating monkeys about an earth vertical axis in the dark [passive whole-body rotation (pWBR)] and while they cancelled their VOR by fixating a target that moved with the vestibular turntable (pWBRC). Target and turntable motion, and

on-line data displays were controlled by a UNIX-based real-time data-acquisition system (REX) (Hayes et al. 1982).

After a neuron was fully characterized in the head-restrained condition, the monkey's head was slowly and carefully released to maintain isolation. Once released, the monkey was able to rotate its head through the natural range of motion in the yaw (horizontal), pitch (vertical), and roll (torsional) axes. The response of the same neuron was then recorded during the voluntary head movements made during combined eye-head gaze shifts (15–65° in amplitude) and during combined eye-head gaze pursuit of a sinusoidal target (0.5 Hz, 80°/s peak velocity). In addition, neuronal responses to combined passive and active head motion were recorded while head-unrestrained monkeys were passively rotated (0.5 Hz, 80°/s peak) and allowed to simultaneously generate voluntary head-on-body movements. A subset of neurons was tested during a "driving paradigm" in which the monkey moved its head and body together in space. During this paradigm, head-restrained monkeys manually manipulated a steering wheel to control the initiation of the movement as well as the rotational velocity of the turntable on which they were seated. The goal of the monkey was to align a chair mounted target with a moving laser target.

Finally, the influences of dynamic and static neck proprioceptive inputs on neural discharges were investigated. Two different paradigms were used to *dynamically* activate the neck afferents. First, the experimenter manually rotated the monkey's head to induce rapid motion of the head relative to a stationary body. Second, the monkey's head was held stationary relative to the earth while its body was passively rotated at 0.1, 0.2, 0.5, 1, 1.5, and 2 Hz at 20°/s peak velocity and 0.2, 0.5, 1, 1.5, and 2 Hz at 40°/s peak velocity. The gain of the cervicoocular reflex induced during the rotations was calculated as the resultant desaccaded eye velocity divided by the turntable velocity. To test for the influence of *static* neck afferent activation, the monkey's body was held at different static positions relative to its earth-stationary head, and the mean firing rate was calculated. During this testing, the torque produced by the monkey against the head-restraint was measured using a reaction torque transducer (Sensotec).

Analysis of neuron discharges

Before analysis, recorded gaze and head-position signals were digitally filtered at 125 Hz. Eye position was calculated from the difference between gaze and head-position signals. Gaze, eye, and head-position signals were digitally differentiated to produce velocity signals. The neural discharge was represented using a spike density function in which a Gaussian function was convolved with the spike train (SD of 5 ms for saccades and gaze shifts and 10 ms for remainder of the paradigms) (Cullen et al. 1996). Saccade and gaze shift onsets and offsets were defined using a $\pm 20^\circ$ /s gaze velocity criterion. Subsequent analysis was performed using custom algorithms (Matlab, Mathworks).

To quantify a neuron's response to eye movement, we analyzed periods of steady fixation to obtain a resting discharge (bias, sp/s) and an eye-position sensitivity [k_x , (sp/s)/°] and periods of saccade-free smooth pursuit to obtain a resting discharge (bias, sp/s), an eye-position sensitivity [k_{sp} , (sp/s)/°], and an eye-velocity sensitivity [r_{sp} , (sp/s)/(°/s)] using a multiple regression analysis (Roy and Cullen 1998). Spike trains were assessed to determine whether neurons paused or burst during saccades. In cases where neurons did burst, the resting discharge (bias, sp/s), eye position [k_{sac} , (sp/s)/°] and eye velocity [r_{sac} , (sp/s)/(°/s)] sensitivities were also estimated during saccades.

A least-squared regression analysis was then used to determine each neuron's phase shift relative to head velocity, resting discharge (bias, sp/s), and head velocity [g_{pWBR} , (sp/s)/°/s] during pWBR and pWBRC. Only unit data from periods of slow-phase vestibular nystagmus during pWBR or steady fixation during pWBRC that occurred between quick phases of vestibular nystagmus and/or saccades were

included in the analysis. A least-squared regression analysis was applied to neuronal discharges during active head-on-body motion, active head and body motion (driving paradigm), combined passive and active head motion, passive head-on-body rotations, and passive

body-under-head rotations. The models utilized for each condition are described in RESULTS. To quantify the ability of the linear regression analysis to model neuronal discharges, the variance-accounted-for (VAF) provided by each regression equation was determined. The VAF was computed as $\{1 - [\text{var}(\text{est} - \text{fr})/\text{var}(\text{fr})]\}$, where *est* represents the modeled firing rate (i.e., regression equation estimate) and *fr* represents the actual firing rate. Note that only data for which the firing rate was greater than zero were included in the optimization. Statistical significance was determined using paired Student's *t*-tests.

RESULTS

The firing behaviors of two distinct classes of vestibular nuclei neurons are presented in the following text. First, we describe the responses of type I PVP neurons during a sequence of paradigms in which the gaze goal was systematically varied and the head movements were externally applied and/or self-generated. We then describe the responses of type II PVP neurons whose head and eye-velocity sensitivities in the head-restrained condition were opposite to those of type I PVP neurons, during each of the same conditions.

Type I PVP neurons

HEAD-RESTRAINED CHARACTERIZATION. The type I PVP neuron illustrated in Fig. 1 is typical of our sample ($n = 24$) in that its firing rate increased for contralaterally directed eye positions during spontaneous eye movements (Fig. 1A, see *inset*), and its firing rate phase lagged contralaterally directed eye velocity and led contralaterally directed eye position during smooth pursuit (Fig. 1B). During pWBR (Fig. 1C) the neuron increased its firing rate in response to ipsilateral head motion (i.e., a type I response). In addition, each type I PVP neuron stopped firing or "paused" during ipsilaterally directed saccades and vestibular nystagmus quick phases (vertical arrows in Fig. 1, A and C). Thus the type I PVP neurons in our sample were comparable to those that have been described in previous reports (Cullen and McCrea 1993; Fuchs and Kimm 1975; Keller and Daniels 1975; Keller and Kamath 1975; Roy and Cullen 1998; Scudder and Fuchs 1992). We also utilized a second pWBR paradigm in which the monkey cancelled its VOR by fixating a head-centered visual target that moved with the vestibular turntable (pWBRc; Fig. 1D). This VOR cancellation paradigm has been used extensively to dissociate a neuron's vestibular

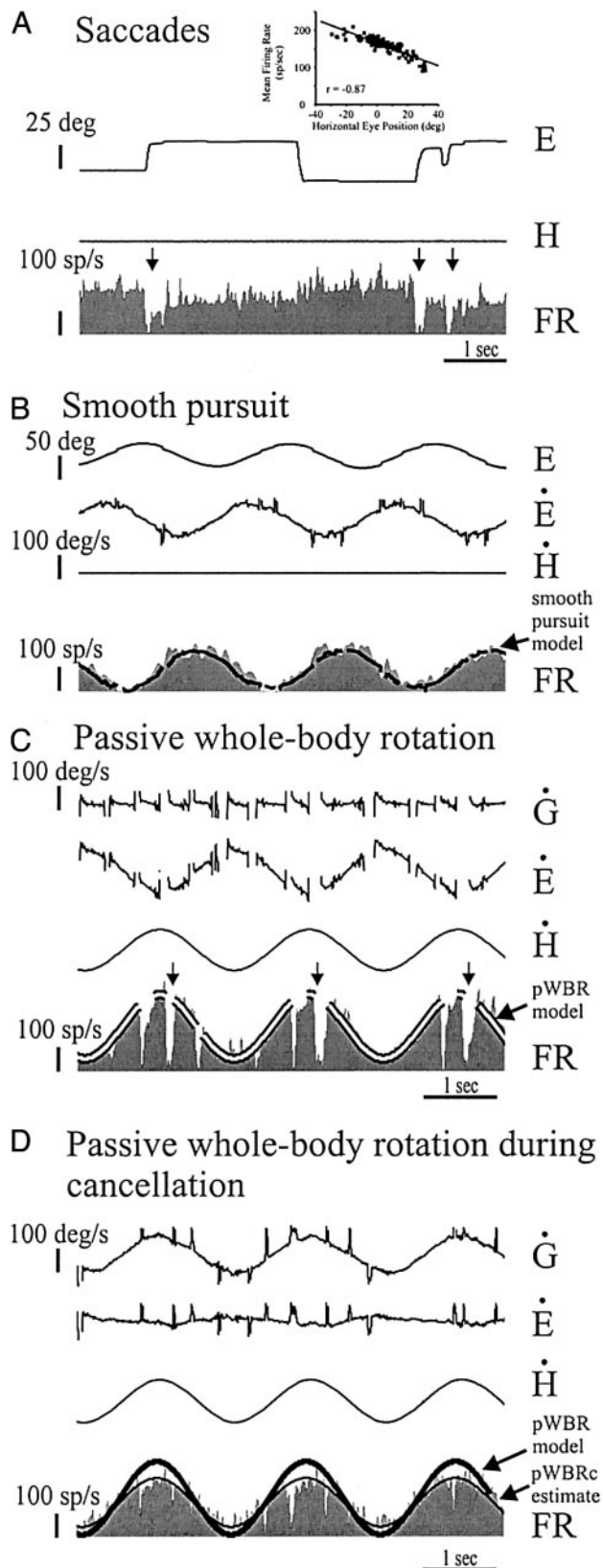


FIG. 1. Activity of an example type I position-vestibular-pause (PVP) neuron (unit *b39_1*) during the head-restrained condition. **A:** the neuron increased its discharge for contralaterally directed eye movements and paused for ipsilaterally directed saccades (vertical arrows). *Inset:* mean neuronal firing rate was well correlated with horizontal eye position during periods of steady fixation. **B:** the neuron also increased its discharge during contralaterally directed smooth pursuit. A model based on the bias discharge, the eye-position sensitivity, and the eye-velocity sensitivity of the neuron provided a good fit to the neural activity (smooth pursuit model, thick trace). **C:** passive whole-body rotation (pWBR) was used to characterize the neuron's response to head movements during VOR in the dark. A model based on the bias discharge, the eye-position sensitivity, and the head-velocity sensitivity during the compensatory eye movements made during pWBR (solid trace) is superimposed on a model fit that also included a head-acceleration term (gray shaded trace). The vertical arrows indicate pauses in activity for ipsilaterally directed vestibular quick phases. **D:** unit *b39_1* was typical in that its modulation was less during pWBR while the monkey cancelled its VOR (pWBRc) by fixating a target that moved with the table (pWBRc estimate, thin trace) than during pWBR (pWBR model, thick trace). Traces directed upward are in the ipsilateral direction. E, eye position; H, head position; $\dot{E}$, eye-in-head velocity; $\dot{H}$, head-in-space velocity; $\dot{G}$, gaze velocity ($= \dot{E} + \dot{H}$); FR, firing rate.

sensitivity from its eye-movement related modulation. As can be seen in Fig. 1D, type I PVP neurons remained well modulated in response to ipsilateral head velocity during this paradigm.

The eye- and head-movement sensitivities of type I PVP neurons were quantified during fixation, smooth pursuit, and pWBR (see METHODS for details) using an analysis approach similar to that employed in previous studies (e.g., Cullen and McCrea 1993; Scudder and Fuchs 1992; Tomlinson and Robinson 1984). First, mean eye positions and firing rates were calculated during periods of steady fixation. A regression analysis (Fig. 1A, *inset*) was done to determine each neuron's eye-position sensitivity (slope = k_x) and resting discharge rate (y intercept = bias_x). The firing rate of type I PVP neurons was generally well correlated with eye position during ocular fixation (sample mean $R^2 = 0.63 \pm 0.04$). The neuron illustrated in Fig. 1 had a k_x of 1.9 (sp/s)/° [sample mean = 1.38 ± 0.14 (sp/s)/°] and a bias_x of 116 sp/s (sample mean = 93 ± 11 sp/s). Second, we determined each neuron's eye-position sensitivity (k_{sp}), eye-velocity sensitivity (r_{sp}), and bias discharge (bias_{sp}) during 0.5-Hz smooth pursuit using the following model

$$\text{fr} = \text{bias}_{sp} + (k_{sp} * \text{eye position}) + (r_{sp} * \text{eye velocity}) \quad (\text{smooth pursuit model})$$

where fr is the firing rate. In general, type I PVP neuron discharges during smooth pursuit were well described by the linear combination of eye velocity, eye position, and bias terms in this model (sample mean VAF = 0.68 ± 0.05 ; Fig. 1B, smooth pursuit model, thick trace). During this paradigm, the example neuron had a k_{sp} of 1.6 (sp/s)/° [sample mean = 1.21 ± 0.14 (sp/s)/°], a r_{sp} of 0.7 (sp/s)/(°/s) [sample mean = 0.39 ± 0.08 (sp/s)/(°/s)], and a bias_{sp} of 121 sp/s (sample mean = 89 ± 12 sp/s). The mean phase lag with respect to eye velocity for the sample of neurons was $73 \pm 2.1^\circ$. Third, we determined each neuron's bias discharge (bias_{pWBR}), sensitivity to eye position (k_{pWBR}), sensitivity to head velocity (g_{pWBR}), and sensitivity to head acceleration (a_{pWBR}) during the compensatory eye movements made during pWBR using the following model

$$\text{fr} = \text{bias}_{pWBR} + (k_{pWBR} * \text{eye position}) + (g_{pWBR} * \text{head velocity}) + (a_{pWBR} * \text{head acceleration})$$

The model fit to the example neuron is illustrated in Fig. 1C (gray shaded trace). The estimated head acceleration term was relatively small [0.07 ± 0.02 (sp/s)/(°/s²)], indicating that neuronal modulation only slightly led head velocity (mean: $10 \pm 0.75^\circ$ at 0.5 Hz). As a result, removing this term from the model had little effect on our ability to fit neuronal activity. For example, during pWBR, model formulations with and without a head-acceleration term provided similar fits of neuronal modulation (mean VAF for our sample of neurons = 0.75 ± 0.04 vs. 0.71 ± 0.04 , respectively). Furthermore, removing head acceleration from the model formulation had no significant effect on our estimates of bias, eye position, and head-velocity coefficient estimates (paired t -test: $P > 0.1$). Because similar results were found in our preliminary analysis of neuronal discharges during the other behavioral tasks used in this study (e.g., pWBRC, passive head-on-body rotation, and gaze shifts; see METHODS), we simplified our model to the following form

$$\text{fr} = \text{bias}_{pWBR} + (k_{pWBR} * \text{eye position}) + (g_{pWBR} * \text{head velocity}) \quad (\text{pWBR model})$$

The pWBR model fit to the example neuron is illustrated in Fig. 1C (solid trace) and superimposed on the model fit that included the head-acceleration term. This neuron had a bias_{pWBR} of 116 sp/s (sample mean = 98 ± 13), a k_{pWBR} of 1.23 (sp/s)/° [sample mean = 1.32 ± 0.14 (sp/s)/°], and a g_{pWBR} of 1.45 (sp/s)/(°/s) [sample mean = 1.25 ± 0.15 (sp/s)/(°/s)]. The eye-position sensitivities and bias values estimated by this model were comparable to those obtained during fixation, smooth pursuit, and pWBR (for both parameters paired t -tests were computed across all combinations of paradigms and none indicated a significant difference; $P > 0.5$).

Note that because gaze is stable during pWBR, eye- and head-motion trajectories are equal and opposite. Thus it is not possible to use a regression model that includes both eye- and head-velocity terms. Furthermore, it is largely a matter of semantics whether PVP neurons encode "head" or "eye" velocity during gaze stabilization. Because PVP neurons are the primary interneurons of the VOR, they function to produce a compensatory eye movement in response to head motion. It then follows that during gaze stabilization, PVP neuron modulation is at the same time both a response to the vestibular stimuli and a motor command signal to drive the VOR. Because in the present study we asked what head-velocity signals are carried by PVP neurons to the extraocular motoneurons, a model formulation containing a head-velocity term, rather than eye-velocity term was used.

To characterize the head-velocity-related modulation of type I PVP neurons when the animals cancelled their VOR (pWBRC paradigm), we first determined whether each neuron's activity could be predicted by its behavior during pWBR. We found that the "pWBR model" consistently over-predicted the firing rate (Fig. 1D; pWBR model, thick trace). We next estimated the head-velocity sensitivity (g_{est}) during this paradigm by using the model

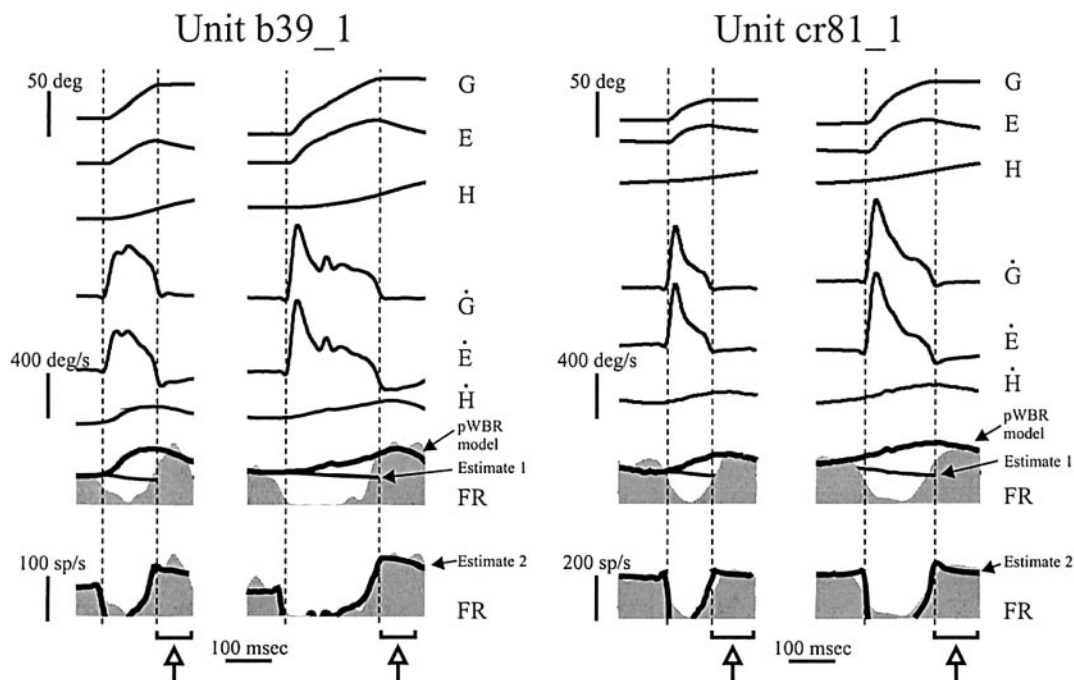
$$\text{fr} = \text{bias}_{pWBR} + (k_{pWBR} * \text{eye position}) + (g_{est} * \text{head velocity}) \quad (\text{Estimate 1})$$

where bias_{pWBR} and k_{pWBR} values were taken from the pWBR model, and the value of g_{est} was optimized. The activity of each neuron was well described by this model (mean sample VAF = 0.69 ± 0.03). The example neuron was representative in that its estimated head-velocity sensitivity during pWBRC was reduced by ~25% as compared with pWBR [$g_{est} = 0.94$ (sp/s)/(°/s); sample mean $g_{est} = 0.94 \pm 0.07$ (sp/s)/(°/s); pWBRC estimate, thin trace]. This finding is consistent with prior studies (Cullen and McCrea 1993; McCrea et al. 1987; Roy and Cullen 1998). To facilitate comparison across experimental paradigms, a given neuron's head-velocity sensitivity during each task was normalized relative to its sensitivity during pWBR (normalized sensitivity = $[g_{est} \text{ for a given task} / g_{pWBR}]$). Thus during pWBRC the normalized head-velocity sensitivity of type I PVP neurons was $[0.94/1.25] = 0.75$ (sp/s)/(°/s), corresponding to an attenuation of ~25% ($P < 0.02$).

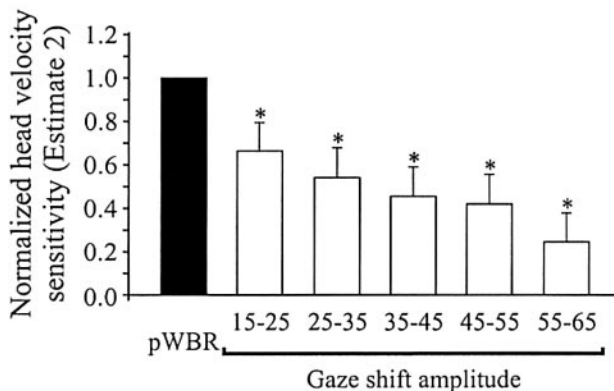
VOLUNTARY HEAD-ON-BODY MOTION. Rapid gaze redirection. After the head-restrained characterization had been completed, the monkey's head was slowly released to allow a wide range of motion in all three axes (yaw, pitch, and roll). Unit activity was carefully monitored during the transition from the head-restrained to head-unrestrained condition to ensure that neurons remained isolated and undamaged.

The firing rate of each type I PVP neuron was then recorded

A Ipsilateral Gaze Shifts



B Gaze Shift Interval



C Post Gaze Shift Interval

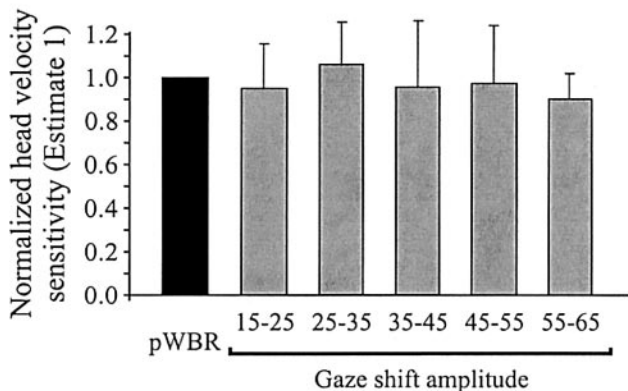


FIG. 2. Activity of example type I PVP neurons (units *b39_1* and *cr81_1*) during and after voluntary ipsilaterally directed combined eye-head gaze shifts. **A:** the pWBR model overpredicted the discharge of this neuron during small- and large-amplitude gaze shifts (pWBR model, thick trace, 2nd row from bottom). *Estimate 1* provided a poor fit to the firing rate during gaze shifts (*Estimate 1*, thin trace, 2nd row from bottom). *Estimate 2*, with its additional eye-velocity term, provided a much improved fit to the neural activity (*Estimate 2*, thick trace, bottom row). Dotted vertical lines indicate the onset and offset of gaze shifts using a $\pm 20^\circ/\text{s}$ criterion. Open arrows indicate the post-gaze-shift intervals. **B:** during gaze shifts, the head-velocity sensitivity of our sample of type I PVP neurons, obtained using *Estimate 2*, decreased significantly as gaze shift amplitude increased from 15 to 65° (open columns), and for all gaze shift amplitudes, responses were significantly smaller than those resulting from pWBR (solid column). **C:** in contrast, head-velocity sensitivities in the post-gaze-shift interval (denoted by open arrows in **A**; gray shaded columns) were comparable to those measured during pWBR (solid column). Error bars show SE. Asterisks, $P < 0.05$. G, gaze position.

during voluntary combined eye-head gaze shifts. For analysis, ipsilaterally directed gaze shifts (i.e., gaze shifts for which the head motion was in the neuron's "on direction") were sorted by amplitude into five separate data sets, each spanning 10° and ranging from 15 to 65° . In agreement with what we have previously shown (Roy and Cullen 1998), the pWBR model consistently over-predicted the discharge of type I PVP neurons during small as well as large gaze shifts (Fig. 2A, pWBR model, 2nd row from bottom, thick trace). To estimate the

head-velocity signal carried by type I PVP neurons during gaze shifts we first used *Estimate 1*. Consistent with the findings of our previous report (Roy and Cullen 1998), the head-velocity sensitivity estimated was significantly reduced relative to that observed during pWBR. However, *Estimate 1* provided an extremely poor fit of neuronal firing rates (Fig. 2A, *Estimate 1*, 2nd row from bottom, thin trace; mean VAF = -0.97 ± 0.47). We have previously argued that the addition of an eye-velocity term to the model would dramatically improve our ability to

describe type I PVP neuron activity during gaze shifts (Roy and Cullen 1998). To specifically test this proposal, neuronal discharges were fit using the following model

$$fr = \text{bias}_{\text{pWBR}} + (k_{\text{pWBR}} * \text{eye position}) + (r_{\text{est}} * \text{eye velocity}) + (g_{\text{est}} * \text{head velocity}) \quad (\text{Estimate } 2)$$

in which eye- and head-velocity sensitivities (r_{est} and g_{est} , respectively) were estimated (Fig. 2A, *Estimate 2*, bottom row, thick trace). Recall that only data for which the firing rate was greater than zero were included in the model optimization (see METHODS). Furthermore because negative firing rates are physiologically meaningless, the model was plotted only when firing rate values were greater than zero.

As predicted, *Estimate 2* provided a better fit of neuronal firing rates (mean VAF = 0.54 ± 0.06) than did *Estimate 1* during gaze shifts. On a neuron-by-neuron basis, the head-velocity sensitivities obtained using *Estimate 2* were well correlated with those that had been obtained using *Estimate 1* for each gaze shift amplitude range (e.g., for gaze shifts of $55\text{--}65^\circ$; slope = 0.81; $R^2 = 0.66$). The relationship between a neuron's head-velocity sensitivity during gaze shifts (using *Estimate 2*) and gaze-shift amplitude is shown in the histogram of Fig. 2B. As gaze-shift amplitude increased, type I PVP neuron responses to head velocity diminished significantly [e.g., mean normalized $g_{\text{est}} = 0.67 \pm 0.13$ (sp/s)/($^\circ$ /s) for $15\text{--}25^\circ$ vs. 0.25 ± 0.12 (sp/s)/($^\circ$ /s) for $55\text{--}65^\circ$; $P < 0.05$] and the attenuation was always significant relative to pWBR ($P < 0.05$).

We carried out a comparable analysis to estimate the head-velocity signal carried by type I PVP neurons during the interval 10–80 ms immediately following gaze shifts (Fig. 2A, denoted by open arrows) where gaze was stable but the head was still moving. The pWBR model provided a good fit to the firing rate of type I PVP neurons (Fig. 2A, pWBR model, thick trace, top firing rate). Accordingly during the post-gaze shift interval, the head-velocity sensitivities obtained using *Estimate 1* were not significantly different from those estimated during pWBR for all gaze shift amplitudes (Fig. 2C; $P > 0.4$). Therefore the model fits of the pWBR and *Estimate 1* overlap

during this interval (Fig. 2A, thick trace, top firing rate). Note that during this interval, eye- and head-motion trajectories are equal (and opposite), and as a result (as during pWBR, see above) *Estimates 2* and *1* are virtually equivalent. Thus here and for each of the behavioral paradigms described in the following text, *Estimate 1* was used whenever gaze was stable in space (i.e., when eye velocity = $-\text{head velocity}$) and *Estimate 2* was used whenever gaze velocity $\neq 0$.

Type I PVP neuron activity was also characterized during contralaterally directed gaze shifts (i.e., off direction of the neuron's head-velocity sensitivity). The majority of neurons (96%) did not pause during contralaterally directed head-restrained saccades of all amplitudes (Fig. 3A). The same neurons also did not pause or burst for small contralaterally directed gaze shifts $<35^\circ$ (Fig. 3B, left). As shown in Fig. 3B (left), the pWBR model superimposed well on the neuronal discharges for small gaze shifts. However, for larger-amplitude gaze shifts, the pWBR model described the activity only until the neuronal discharges were driven to inhibition as a result of the head velocity becoming sufficiently large (Fig. 3B, right). Accordingly, we found that whether a neuron's firing rate was driven to zero during a gaze shift depended on the balance between the bias and the head-velocity sensitivity of the individual neuron. In general, head velocities were large enough to drive the firing rate to zero for gaze shifts $>35^\circ$ in amplitude.

Gaze pursuit. The behavioral goal during both pWBRc (Fig. 1D) and gaze shifts (Fig. 2A) was different from that during the pWBR (Fig. 1C); during pWBRc and gaze shifts, the animal's goal was to redirect rather than stabilize its gaze-in-space. We found that during pWBRc and gaze shifts the head-velocity signals carried by the direct VOR pathways (i.e., type I PVP neurons) were reduced. This reduction in the head-velocity sensitivity of the direct VOR pathways is consistent with the behavioral goal of the animal because the VOR functions to generate an eye movement in the opposite direction to that of the intended change in gaze. We next tested whether the discharge activity of type I PVP neurons was significantly attenuated in a third gaze-redirection task in which the monkey

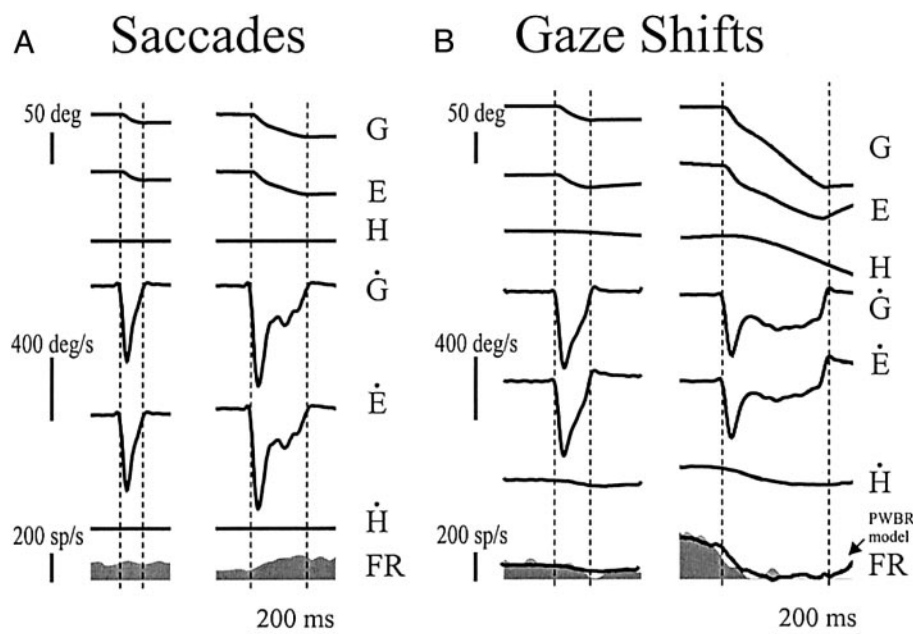


FIG. 3. Activity of an example type I PVP neuron (unit b39_1) during voluntary contralaterally directed head-restrained saccades and combined eye-head gaze shifts. A: during small (left) and large (right) saccades, the majority of type I PVP neurons did not pause or burst in activity. B: during small-amplitude gaze shifts ($<35^\circ$, left), the pWBR model (thick trace) provided a good prediction of neural discharge. Similarly, during large-amplitude gaze shifts (right), the model provided a good fit until the discharge was driven to 0 by the faster head velocities.

made voluntary combined eye-head movements to pursue a moving target (i.e., gaze pursuit). The example neuron shown in Fig. 4A was representative of our sample of type I PVP neurons in that the pWBR model provided a poor prediction of the discharge activity (pWBR model, thin trace; VAF = 0.21 ± 0.21). *Estimate 2* provided a good fit of each neuron's modulation (Fig. 4A, *Estimate 2*, bottom row, thick trace; sample VAF = 0.64 ± 0.03). For the neurons tested ($n = 19$), the head-velocity sensitivity was significantly less than that measured during pWBR [mean normalized $g_{\text{est}} = 0.54 \pm 0.08$ (sp/s)/(°/s); $P < 0.05$]. Interestingly, on a neuron-by-neuron basis, the eye-velocity sensitivity obtained with *Estimate 2* during gaze pursuit was comparable to that obtained during smooth pursuit (Fig. 4B; $R^2 = 0.67$).

In summary, the head-velocity related modulation of type I PVP neurons was significantly reduced when the monkey redirected its gaze. This was true for the head rotations that were *passively* applied to the monkey during pWBRc as well as for the *actively* generated head-on-body rotations that were

made by the monkey during ipsilaterally directed gaze shifts and gaze pursuit.

Do type I PVP neurons differentially encode head velocity during self-generated vs. passively applied rotations of the head-in-space?

Both gaze shifts and gaze pursuit involve the voluntary movement of the head on the body. To determine whether type I PVP neurons might differentially encode head-velocity during self-generated versus passively applied rotations of the head-in-space, we used a paradigm in which head-restrained monkeys voluntarily drove or controlled the direction and rotation velocity of the turntable, thus moving both their heads and bodies together in space. The monkeys were trained to align a turntable mounted laser target (T_{table}) with a computer controlled target (T_{goal} ; Fig. 5A, see schema), which either stepped from one location to another or moved sinusoidally. The data traces shown in Fig. 5A illustrate the discharge activity of an example type I PVP neuron during the two behavioral tasks. When the monkey redirected its gaze ipsilaterally to align the turntable with a target that stepped (Fig. 5A; middle, ↓), the pWBR model over-predicted the discharge of the neuron (pWBR model, thick trace). Indeed, for the neurons tested ($n = 8$), the estimated head-velocity sensitivity was significantly attenuated relative to pWBR to a level comparable to that observed during gaze shifts [*Estimate 2* mean normalized $g_{\text{est}} = 0.18 \pm 0.21$ (sp/s)/(°/s); Fig. 5B, □]. Similarly, when the monkey pursued the target (Fig. 5A; right), the pWBR model overpredicted the discharge of the neuron (pWBR model, thick trace), and the estimated head-velocity sensitivity was significantly reduced relative to pWBR [*Estimate 2* mean normalized $g_{\text{est}} = 0.64 \pm 0.04$ (sp/s)/(°/s); Fig. 5B, ■]. This attenuation was comparable to that described for gaze pursuit and pWBRc above ($P > 0.7$ and > 0.27 , respectively).

In contrast, in the intervals where the monkey had acquired the new target, but the turntable was still moving (i.e., gaze was stable) the pWBR model provided a good fit to the firing rate (Fig. 5A, middle, pWBR model, thick trace; mean VAF = 0.64 ± 0.07) and accordingly the estimated head-velocity sensitivity was not significantly different from that during pWBR [mean normalized $g_{\text{est}} = 0.92 \pm 0.05$ (sp/s)/(°/s); Fig. 5B, compare □ and ■]. This result is analogous to that described in the preceding text for the *active* head-on-body motion made when gaze is immobile immediately following gaze shifts. Thus the head-velocity information carried by type I PVP neurons was the same regardless of whether the head was voluntarily moved on the body or whether the head and body were voluntarily moved together; head-velocity sensitivities were similarly reduced when the monkey redirected its gaze and were unaltered when the monkey stabilized its gaze. Taken together, these findings support the hypothesis that type I PVP neuron responses to head motion vary in a manner that depends exclusively on the monkey's current gaze goal.

Type I PVP neurons

SIMULTANEOUS VOLUNTARY AND PASSIVE MOTION. In the behavioral tasks presented until this point, the head motion has been either passively imposed or self-generated, yet, under natural circumstances, passive perturbations of the head and/or

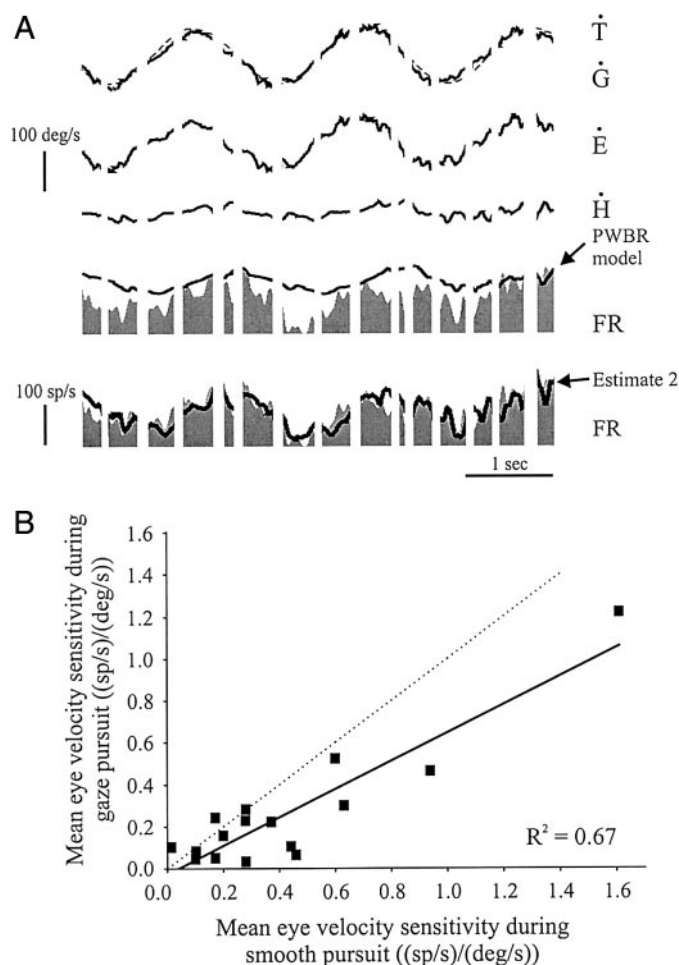


FIG. 4. Responses of a typical type I PVP neuron (unit b39_1) to voluntary head-on-body motion during combined eye-head gaze pursuit. A: the neuron's response to self-generated head motion was overpredicted by the neuron's sensitivity during pWBR (pWBR model, thick trace, 2nd row from bottom). *Estimate 2* provided a good of the firing rate (*Estimate 2*, thick trace, bottom row) and the estimated head-velocity sensitivity was significantly reduced as compared with pWBR. B: on a neuron-by-neuron basis, the eye-velocity sensitivities estimated during gaze pursuit were similar to those estimated during smooth pursuit. Dotted line represents unity (slope = 1). $\dot{T}$: target velocity.

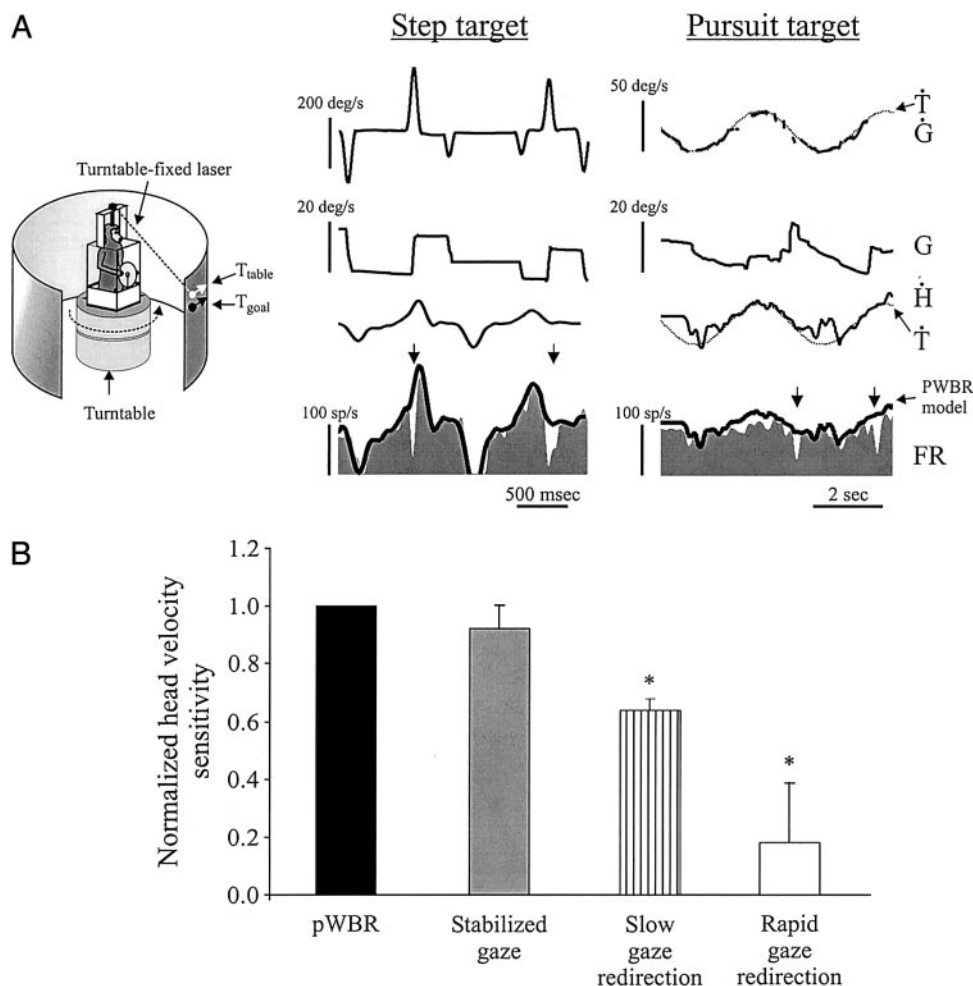


FIG. 5. Type I PVP neuron responses to voluntary combined head-body motion. **A:** head-restrained monkeys manually controlled a steering wheel to rotate the vestibular turntable relative to space (schema). Their goal was to align a turntable-fixed laser target (T_{table} ; schema) with a computer-controlled target (T_{goal} ; schema) that either stepped in location (middle) or moved sinusoidally (right panel). This example neuron (unit *br23_1*) was typical in that its response was well predicted by its sensitivity to head velocity during pWBR whenever the monkey stabilized gaze (pWBR model, thick trace). The neuron paused in activity for rapid ipsilaterally directed eye-head/body gaze redirections ($\uparrow$) and was less responsive to head motion when the target was pursued with both its eyes and head/body as compared with pWBR (right). **B:** type I PVP neurons had a greater attenuation during rapid gaze redirection ($\square$) than during slow gaze redirection ($\square$) and were not attenuated when gaze was stabilized ($\square$) as compared with pWBR ($\blacksquare$).

body can occur at the same time as voluntary head motion. To further test the proposal that the head-velocity information carried by type I PVP neuron modulation depends only on current gaze goal, we characterized neuronal discharges during simultaneous passive and self-generated head motion. Head-unrestrained monkeys were encouraged to generate voluntary head-on-body movements (Fig. 6A, dashed line arrow in schema) while being passively whole-body rotated (Fig. 6A, solid arrow in schema). During this paradigm, the head-in-space motion is the sum of the passive turntable rotation and the active head-on-body motion.

We characterized type I PVP neuron discharge activity with respect to both the passively applied and actively generated components of the head-in-space motion during gaze redirection using the following model

$$fr = \text{bias}_{pWBR} + (k_{pWBR} * \text{eye position}) + (r_{est} * \text{eye velocity}) + (\text{pass}_{est} * \text{passive component}) + (\text{act}_{est} * \text{active component}) \quad (\text{Estimate 3})$$

in which the eye-velocity sensitivity (r_{est}) and the sensitivities to the passive and active components of the head-in-space velocity (pass_{est} and act_{est} respectively) were estimated. Note that during gaze stabilization, the eye-velocity sensitivity (r_{est}) was not estimated (as during pWBR, see preceding text) because eye- and head-motion trajectories were equal (and opposite). For all neurons tested ($n = 12$), responses differed significantly during gaze redirection versus gaze stabilization

($P < 0.02$). During rapid gaze redirection (gaze shifts; Fig. 6A, denoted by vertical arrows), the responses of type I PVP neurons to both the passive and the active components of head-in-space motion were significantly attenuated as compared with pWBR (Fig. 6B; compare open columns to the solid column). During slow gaze redirection (Fig. 6A, region labeled slow gaze redirection), type I PVP neuron responses to the passive and active components of head-in-space motion were also significantly attenuated (Fig. 6B, compare vertically striped columns to the solid column) though this attenuation was less than that seen during rapid gaze redirection. Finally, when the monkey stabilized its gaze relative to space (Fig. 6A, regions labeled gaze stabilization), neuronal discharges were underpredicted by a model based on the passive component of head motion and the neuron's sensitivities during pWBR (Fig. 6A, pWBR model, thin trace; mean VAF = 0.44 ± 0.13) but were well predicted by a model based on the head-in-space motion and the same pWBR parameters (Fig. 6A, $\dot{H}$ -in-space model, thick trace; mean VAF = 0.73 ± 0.06). Consistent with the latter model prediction, the head-velocity sensitivities to both passive and active components of head-in-space motion obtained using *Estimate 3* were comparable to the head-velocity sensitivity during pWBR (Fig. 6B, compare gray shaded columns to solid column). In summary, neuronal sensitivities to the passive and active components of head motion were comparable during rapid gaze redirection ($P > 0.2$), during

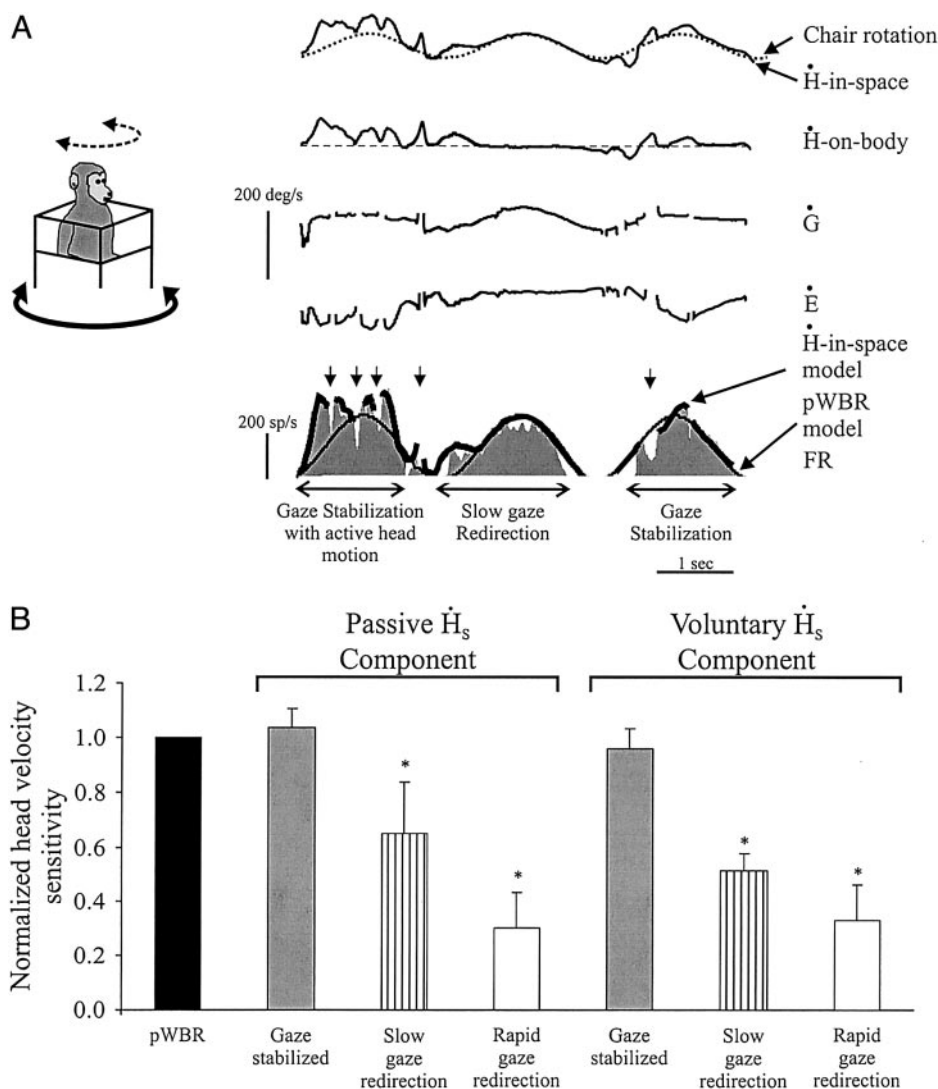


FIG. 6. Type I PVP neuron responses to combined voluntary and passive head-in-space motion. **A**: head-unrestrained monkeys generated voluntary head-on-body movements (dashed arrow in schema) while being passively rotated by the vestibular turntable (thick arrow in schema). Head-in-space velocity ($\dot{H}$ -in-space) is the sum of the passive rotation velocity (chair rotation) and voluntary head-on-body velocity ($\dot{H}$ -on-body). The modulation of the example neuron (unit *c131_1*) was well correlated with the head-in-space motion ($\dot{H}$ -in-space model, thick trace) whenever the monkey stabilized its gaze but was poorly related whenever the monkey rapidly redirected (vertical arrows) or slowly redirected its gaze (middle). **B**: the responses to both the passive and the voluntary components of head-in-space motion were significantly attenuated when the monkey either rapidly redirected (open columns) or slowly redirected (vertically striped columns) its gaze as compared with pWBR (solid column). In contrast, the neurons showed no attenuation during gaze stabilization (gray shaded columns).

slow gaze redirection ($P > 0.2$), and during gaze stabilization ($P > 0.3$). These results further support the hypothesis that type I PVP neuron head-velocity responses do not depend on whether head motion was actively or passively generated but rather depend on the current behavioral goal of the monkey.

INFLUENCE OF PASSIVE NECK PROPRIOCEPTOR ACTIVATION. To determine whether afferent inputs from neck muscle proprioceptors influence the activity of type I PVP neurons, we used two different paradigms. First we passively rotated the monkey's body while its head was held earth-stationary (Fig. 7A, see schema). The torque produced by the monkey against the head restraint was concurrently measured and found to be small (less than ± 0.5 Nm) compared with that produced when orienting to food target (more than ± 3.5 Nm). Thus during these passive rotations, the neck motor efference signals generated by the monkeys were minimal, yet the musculature was stretched such that neck proprioceptors were activated. The neuron shown in Fig. 7A was typical in that its activity was not significantly affected by the passive rotation of the neck. Its firing rate was well predicted by the pWBR model (note, in this case: head velocity = 0; pWBR model, thick trace). This finding is best appreciated when the firing rate is corrected for the neuron's eye-position sensitivity (Fig. 7A; FR_{corr}). For all

neurons tested ($n = 12$), the neck-related signals were negligible [mean neck-velocity sensitivity = 0.07 ± 0.05 (sp/s)/($^{\circ}$ /s)].

Because eye movements were simultaneously recorded during this task, we also were able to assess the status of the cervicoocular reflex (COR). The gain of the COR (gain = eye velocity/neck velocity) was not significantly different from zero over the range of frequencies and velocities tested (Fig. 7, B and C for 20 and 40°/s, respectively). The mean VOR gain (gain = eye velocity/−head velocity) of the monkeys is shown in the same figure for comparison (0.9 ± 0.06 ; Fig. 7, B and C). VOR gain was measured at 0.5 Hz and assumed to be constant over the range of frequencies used in this study (see for example: Bohmer and Henn 1983; Keller 1978; Paige 1983; Telford et al. 1996). Prior studies have reported comparable COR gains in humans and rhesus monkeys. We consider the implication of this result in the DISCUSSION.

To further investigate whether afferent inputs from neck muscle proprioceptors affect type I PVP neuron discharge activity, the monkey's head was passively rotated on its stationary body to elicit comparable head velocities and trajectories to those observed during natural head motion (Fig. 8A, see schema). The example neuron illustrated in Fig. 8A was typical in that when gaze was stable, the pWBR model provided a

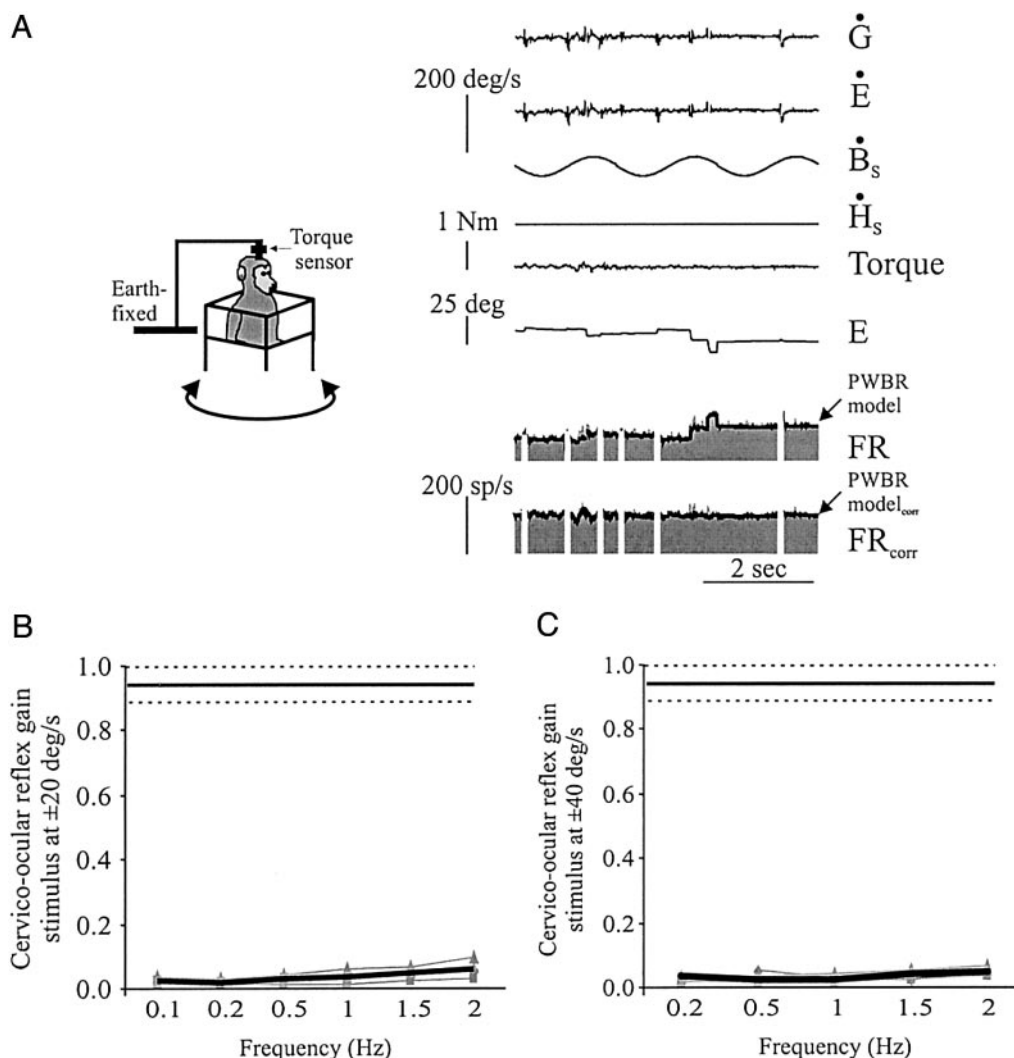


FIG. 7. Response of type I PVP neurons to passive neck rotation. *A*: the response of example neuron (*unit gr11_2*) was typical in that it was not modulated by neck-related signals when the monkey's body was passively rotated beneath its stationary head. The neural discharge was well described by the pWBR model (thick trace, 2nd row from bottom). This is emphasized when the firing rate and pWBR model are corrected for the neuron's eye-position sensitivity: $FR_{corr} = FR - (k_{pWBR} * E)$ and $pWBR_{corr} = pWBR \text{ model} - (k_{pWBR} * E)$. *B* and *C*: during this task, the status of the cervicoocular reflex was simultaneously assessed by calculating the resulting gain (eye velocity/neck velocity). The gains of the monkeys tested are shown by the gray traces (triangle, monkey *C*; square, monkey *G*; diamond, monkey *J*) and were not significantly different from 0 over the range of frequencies and velocities (20°/s, *B*; 40°/s, *C*) tested. The average gain of the 3 monkeys is indicated by the solid black trace. The mean $\pm$ SE VOR gain (eye velocity/head velocity) is plotted for comparison (0.94 ± 0.06 ; see text). $\dot{H}_s$, head-in-space velocity; $\dot{B}_s$, body-in-space velocity; Torque: reaction torque produced by the monkey against the head-restraint.

good prediction of its activity during the head trajectories generated during this paradigm (pWBR model, thin trace; mean VAF = 0.56 ± 0.04). The head-velocity sensitivities of the neurons tested ($n = 12$) were found to be comparable to pWBR values during gaze stabilization [mean normalized $g_{est} = 0.99 \pm 0.04$ (sp/s)/(°/s); Fig. 8*B*, $\square$]. However, neuron responses to head velocity were significantly attenuated when the monkey rapidly redirected its gaze during the passive head rotations [see $\uparrow$ in Fig. 8*A*; mean normalized $g_{est} = 0.21 \pm 0.18$ (sp/s)/(°/s); Fig. 8*B*, $\triangle$].

The results illustrated in Figs. 7 and 8 demonstrate that the dynamic activation of the neck proprioceptors had no influence on the activity of type I PVP neurons. To test whether type I PVP neurons might carry static neck position signals, we again passively rotated the monkey's body under its earth-fixed head

(as in Fig. 7), but this time held the body of the monkey immobile at different positions. The pWBR model (where head velocity = 0) provided an accurate fit to the discharge activity (Fig. 9, pWBR model, thick trace) during this paradigm. The mean static neck-position sensitivity of the neuron illustrated in Fig. 9 was not significantly different from zero ($P > 0.4$), which was representative of all neurons tested ($n = 11$). This result can be clearly observed once the firing rate has been corrected for the neuron's eye-position sensitivity (Fig. 9; FR_{corr} and inset). Thus we conclude that type I PVP neurons in the alert rhesus monkey are not influenced by either the dynamic or static activation of neck proprioceptors.

SUMMARY OF NEURAL DISCHARGE DURING PASSIVE AND VOLUNTARY HEAD MOTION. Type I PVP neurons responses to both passive and self-generated head motion were influenced by the

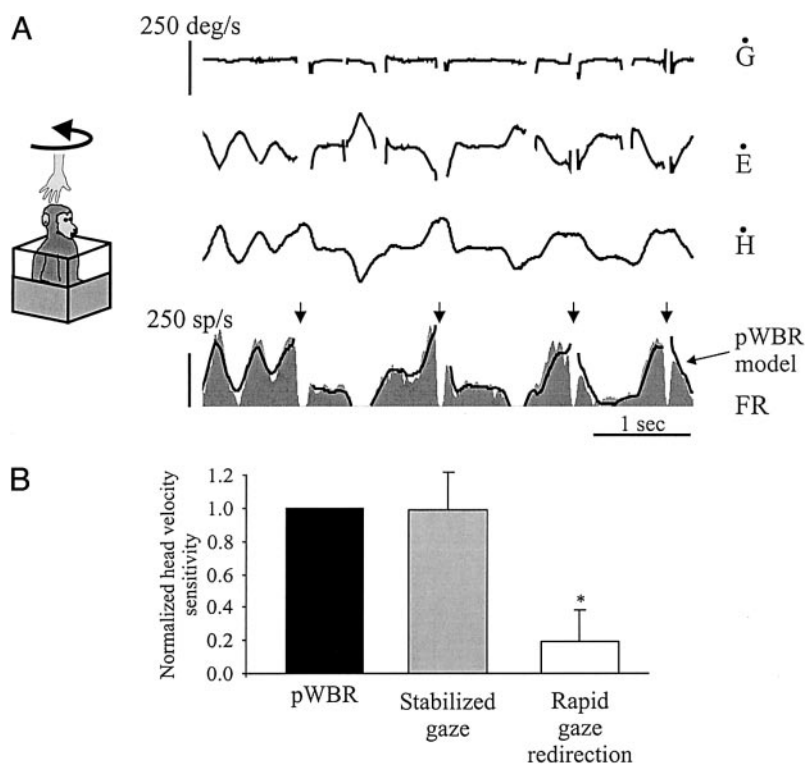


FIG. 8. Response of type I PVP neurons to passive rotation of the head-on-body. **A**: the experimenter (hand in schema) passively rotated the monkey's head relative to its earth stationary body. The discharge of example neuron (*unit gr11_2*) was reliably predicted by the pWBR model whenever the monkey stabilized its gaze (thin trace). In contrast, the neuron paused in activity whenever the monkey rapidly redirected its gaze ($\uparrow$). **B**: neuron responses during passive head-on-body rotation were comparable to those during pWBR when gaze was stable ($\square$) and significantly attenuated when gaze was rapidly redirected ($\square$) as compared with pWBR ($\blacksquare$).

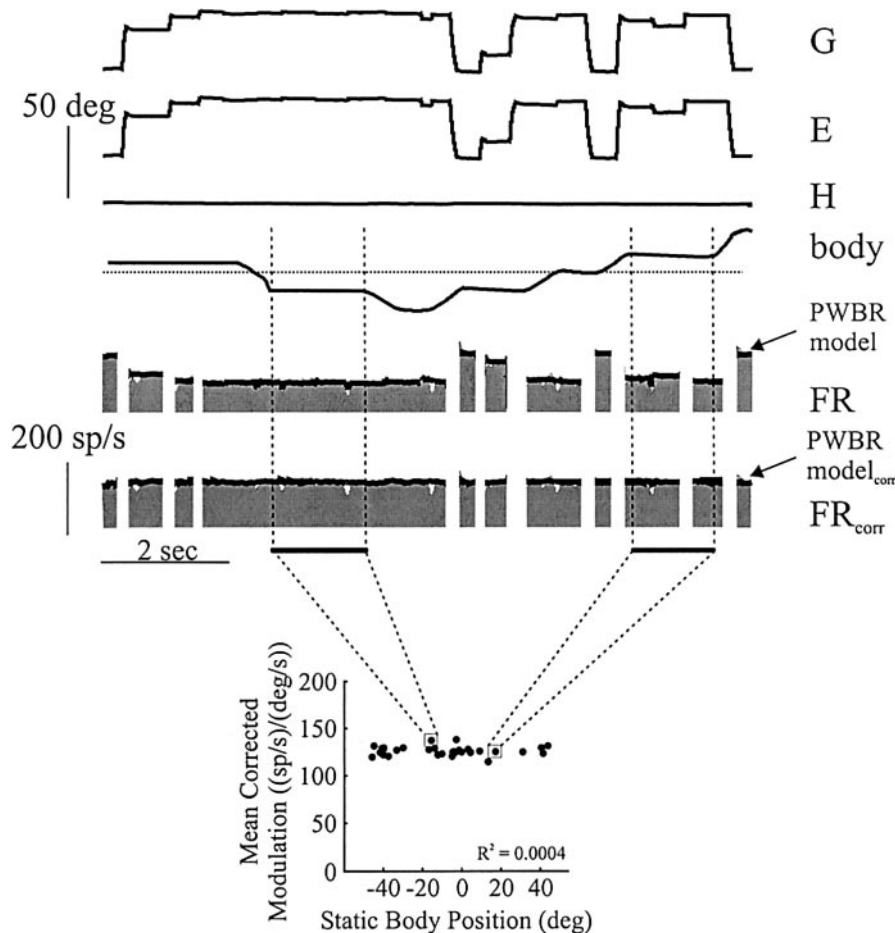


FIG. 9. Response of type I PVP neurons to static body positions. The pWBR model accurately predicted the discharge activity of the example neuron (*unit gr11_2*) during stable gaze and body positions (thick trace, 2nd row from bottom). This is emphasized when the firing rate and pWBR model (bottom) are corrected for the eye-position sensitivity of the neuron (see Fig. 7 legend). *Inset*: the mean corrected firing rate was not correlated to static body position. Body: body position in space.

gaze goal of the monkey. When the monkey stabilized its gaze, the head-velocity sensitivity of the neurons was comparable to that obtained during pWBR (Fig. 10; ■). In contrast, when the monkey redirected its axis of gaze either slowly (Fig. 10; ▨) or rapidly (Fig. 10; □), the head-velocity sensitivity of the neurons was significantly attenuated as compared with pWBR. The neuronal responses were more attenuated during rapid gaze redirection than during slow gaze redirection (Fig. 10; compare □ and ▨). Whether the head was passively or actively moved or whether the head moved relative to the body or not did not affect the neural discharges once the gaze goal was taken into account.

Type II PVP neurons

In the present study, we also characterized type II PVP neurons. These neurons have opposite eye- and head-motion sensitivities to type I PVP neurons during the head-restrained paradigms shown in Fig. 1 and were included in the present report because they behaved very much like type I PVP neurons during each of the paradigms tested in our study. The only significant difference in firing behavior that we observed was that these neurons frequently discharged a burst during ipsilaterally directed saccades, vestibular quick phases, and gaze shifts. This difference is detailed in the following text.

The type II PVP neuron illustrated in Fig. 11 was typical of the neurons tested ($n = 14$) in that its firing rate increased for ipsilateral eye positions during spontaneous eye movements (Fig. 11A, see *inset*). The firing rate of type II PVP neurons was generally well correlated with eye position during ocular fixation (sample mean $R^2 = 0.64 \pm 0.06$). The example neuron

had a k_x of 1.31 (sp/s)/° [sample mean = 1.67 ± 0.37 (sp/s)/°] and a bias of 50 sp/s (sample mean = 55 ± 10 sp/s) during periods of fixation. During smooth pursuit, type II PVP neuron firing rate phase lagged ipsilateral eye velocity and led ipsilateral eye position (Fig. 11B). In general, neuron discharges were well described by the linear combination of eye velocity, eye position, and bias terms (sample mean VAF = 0.56 ± 0.09 ; Fig. 11B, smooth pursuit model, thick trace). The example neuron had a k_{sp} of 0.61 (sp/s)/° [sample mean = 1.52 ± 0.6 (sp/s)/°], a r_{sp} of 0.44 (sp/s)/(°/s) [sample mean = 0.54 ± 0.14 (sp/s)/(°/s)], and a bias_{sp} of 59 sp/s (sample mean = 64 ± 12 sp/s). The mean phase lag with respect to eye velocity for the sample of neurons during smooth pursuit was $64 \pm 4.5^\circ$. During passive whole-body rotation in the dark (pWBR, Fig. 11C), the neuron increased its firing rate in response to contralateral head motion (i.e., a type II response). A model based on a combination of head velocity, eye position, and bias terms (*Estimate 1*) provided a good fit of type II PVP neuron activity during pWBR (sample mean VAF = 0.59 ± 0.06). The example neuron had a bias_{pWBR} of 67 sp/s (sample mean = 80 ± 10), a k_{pWBR} of 0.65 (sp/s)/° [sample mean = 1.25 ± 0.37 (sp/s)/°], and a g_{pWBR} of 1.71 (sp/s)/(°/s) [sample mean = 0.89 ± 0.08 (sp/s)/(°/s); Fig. 11C, pWBR model, thick trace]. In addition, each type II PVP neuron stopped firing or “paused” during contralaterally directed saccades and vestibular nystagmus quick phases (note vertical arrows in Fig. 11, A and C). The head-velocity sensitivity of type II PVP neurons was obtained during pWBRc using *Estimate 1* (mean sample VAF = 0.50 ± 0.1). The example neuron was representative in that its estimated head velocity was reduced by $\sim 21\%$ as

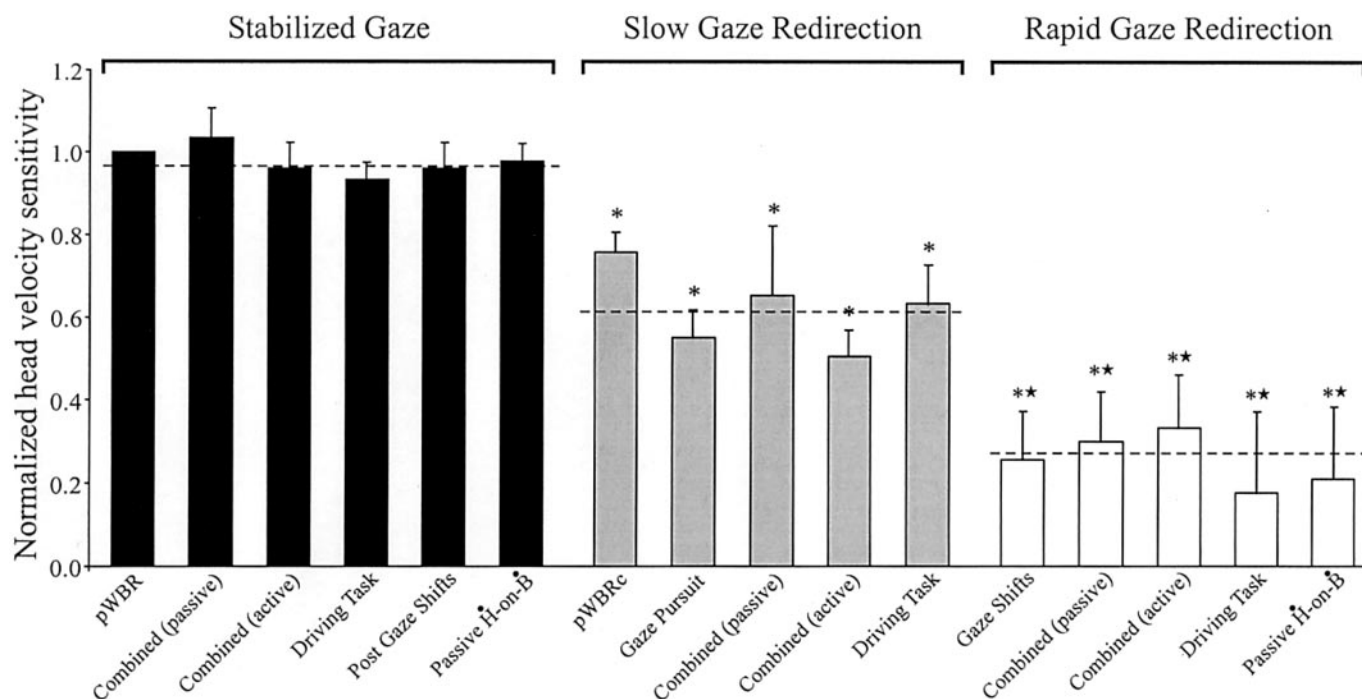


FIG. 10. Summary of type I PVP neuron discharge activity during passive and voluntary head motion. When the monkey redirected its axis of gaze either slowly (▨) or rapidly (□), the head-velocity sensitivity of the neurons was significantly attenuated as compared with pWBR (*, $P < 0.05$ relative to pWBR). The neuronal responses were significantly less during ipsilaterally directed rapid gaze redirection than during slow gaze redirection (*, $P < 0.05$ relative to slow gaze redirection). In contrast, when the monkey stabilized its gaze, the head-velocity sensitivity of the neurons was comparable to that obtained during pWBR (■). ---, the average normalized head-velocity sensitivities across conditions with the same gaze goal.

compared with pWBR [normalized $g_{\text{est}} = 0.79$ (sp/s)/(°/s); mean normalized $g_{\text{est}} = 0.71 \pm 0.06$ (sp/s)/(°/s); Fig. 11D, pWBRc estimate, thin trace]. This reduction was comparable to what we observed for type I PVP neurons. However, while

type II PVP neurons paused during vestibular nystagmus quick phases and saccades in the “off direction” for eye motion (see contralateral saccade in Fig. 12A, left), they most often ($n = 9/14$) burst during saccades in the “on direction” (ipsilateral saccade shown in Fig. 12A, right). This latter behavior differed from that of type I PVP neurons. During ipsilaterally directed saccades, the eye-velocity sensitivity (r_{sac}) of type II PVP neurons was estimated [$\text{fr} = \text{bias}_x + (k_x * \text{eye position}) + (r_{\text{sac}} * \text{eye velocity})$] and found to be 0.27 ± 0.05 (sp/s)/(°/s).

Similar to their responses during head-restrained saccades, most (10/13) type II PVP neurons paused for the duration of eye-head gaze shifts in the contralateral direction (Fig. 12B). In addition, most (8/13) neurons burst for the duration of gaze shifts in the ipsilateral direction (Fig. 12C). Recall that the activity of type I PVP neurons was attenuated, in an amplitude-dependent manner, during ipsilaterally directed gaze shifts. We estimated the eye- and head-velocity sensitivity of each type II PVP neuron during ipsilaterally directed gaze shifts using *Estimate 2*. Even though they burst, the head-velocity sensitivities of type II PVP neurons were significantly reduced for gaze shifts of all amplitudes (Fig. 12D; compare ■ and ■). While the attenuation was not as great as that observed for type I PVP neurons (Fig. 2B), the level of attenuation did significantly increase with the increasing amplitude ($R^2 = 0.83$). In addition, the estimated eye-velocity sensitivities were comparable to those estimated during saccades on a neuron-by-neuron basis [sample mean = 0.27 ± 0.05 (sp/s)/(°/s); slope = 0.90, $R^2 = 0.96$]. Type II PVP neurons showed similar responses when the monkey rapidly redirected its gaze during all of the behavioral tasks employed. Thus in light of the results that we obtained from type I PVP neurons, we elected to limit our analysis of rapid gaze redirections to saccades and gaze shifts (as described in the preceding text).

Type II PVP neurons behaved similarly to type I PVP neurons whenever the monkey slowly redirected its gaze. The head-velocity sensitivity of the type II PVP neurons was reduced as compared with pWBR (Fig. 13; solid column) when the monkeys cancelled their VOR (pWBRc; Fig. 13; diagonally striped column) and during eye-head gaze pursuit (Fig. 13; vertically striped column). The attenuated response to head velocity was not dependent on whether the head motion was passively or actively generated but rather on the gaze goal of the monkey. This is illustrated by the response of the neurons during simultaneous passive whole-body rotation and voluntary head motion. When gaze was stable, the pWBR model

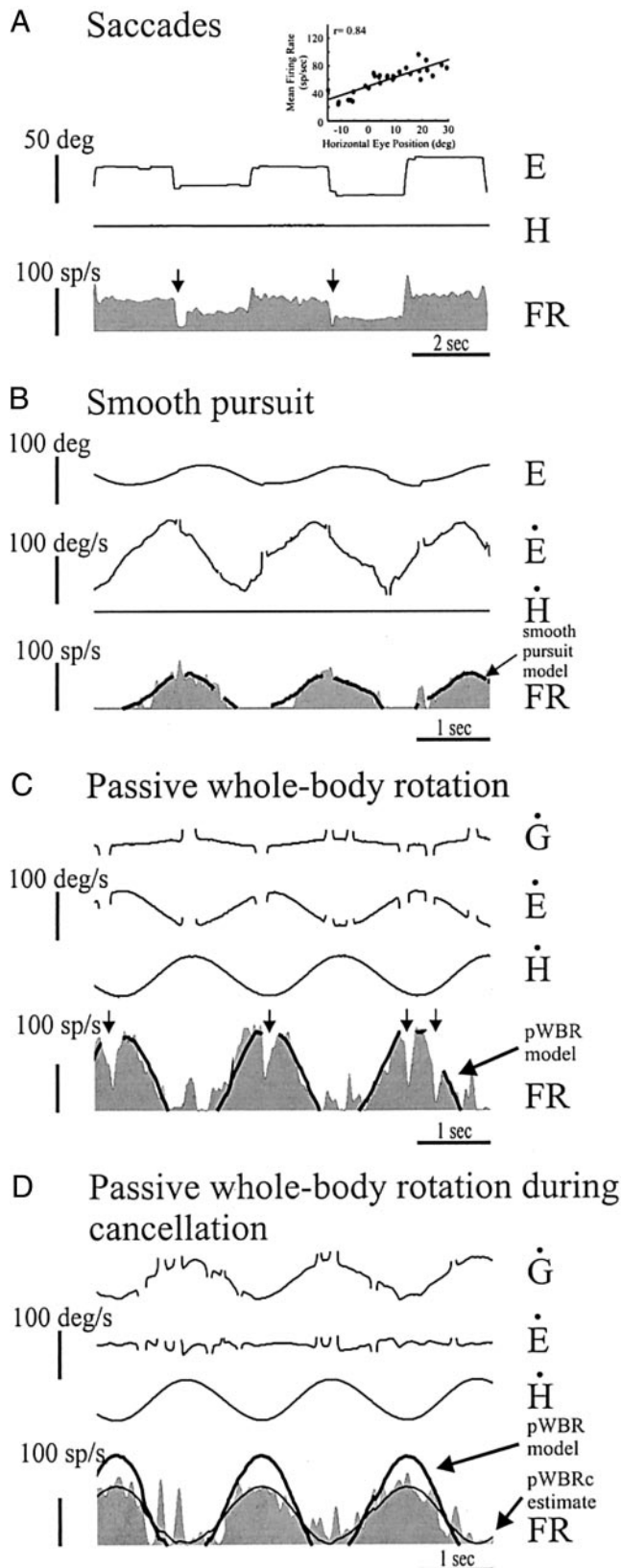
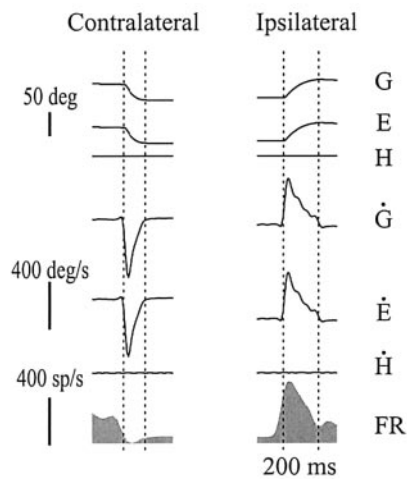
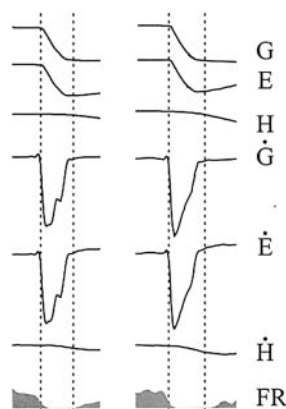


FIG. 11. Activity of an example type II PVP neuron (unit c66_1) during the head-restrained condition. A: the neuron increased its discharge for ipsilaterally directed eye movements and paused for contralaterally directed saccades (vertical arrows). Inset: mean neuronal firing rate was well correlated with horizontal eye position during periods of steady fixation. B: the neuron also increased its discharge during ipsilaterally directed smooth pursuit. A model based on the bias discharge, the eye-position sensitivity, and the eye-velocity sensitivity of the neuron provided a good fit to the neural activity (smooth pursuit model, thick trace). C: passive whole-body rotation was used to characterize the neuron's response to head movements during VOR in the dark (pWBR). A model based on the bias discharge, the eye-position sensitivity, and the head-velocity sensitivity during the compensatory eye movements made during pWBR is superimposed on the firing rate trace. The vertical arrows indicate pauses in activity for contralaterally directed vestibular quick phases. D: unit b39_1 was typical in that its modulation was less during passive whole-body rotation while the monkey cancelled its VOR (pWBRc) by fixating a target that moved with the table (pWBRc estimate, thin trace) than during pWBR (pWBR model, thick trace).

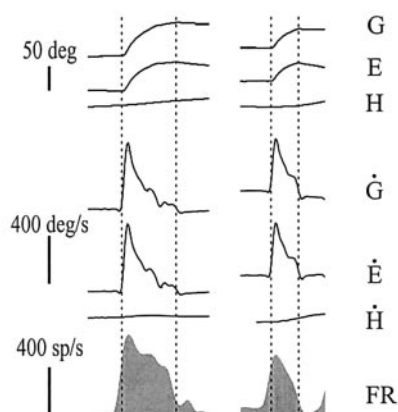
A Saccades



B Contralateral Gaze Shifts



C Ipsilateral Gaze Shifts



D

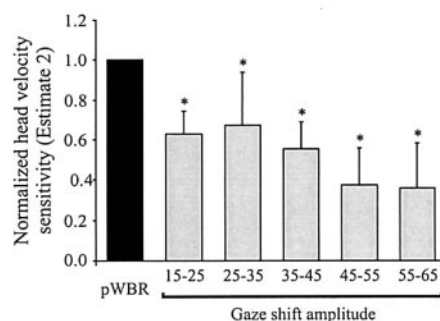


FIG. 12. Activity of an example type II PVP neuron (*unit cr93_1*) during saccades and eye-head gaze shifts. A: this unit was typical in that it paused for contralaterally directed saccades (left) and burst for ipsilaterally directed saccades (right). B: during contralaterally directed gaze shifts of all amplitudes, the neuron paused in activity. C: the neuron burst in activity during both large (left) and small (right) ipsilaterally directed gaze shifts. D: as with type I PVP neurons, the head-velocity sensitivities of type II PVP neurons decreased as a function of amplitude for ipsilaterally directed gaze shifts (compare $\square$) and were always significantly reduced as compared with pWBR ($\blacksquare$).

provided a good prediction of the neural firing rate (sample mean VAF = 0.52 ± 0.07) and the head-velocity sensitivity was not attenuated as compared with pWBR (Fig. 13; gray shaded columns). When gaze was redirected the head-velocity sensitivity of the neurons was significantly attenuated (Fig. 13; horizontally striped columns). In addition, during the driving paradigm, where the monkey moved its head and body together in space, the neurons were less responsive when gaze was redirected (Fig. 13; open column) than when gaze was stabilized (Fig. 13; gray shaded column with horizontal stripes). The pWBR model provided a good prediction of the neural activity when gaze was stable during the driving paradigm (sample mean VAF = 0.64 ± 0.14). During ipsilaterally directed rapid gaze redirections (Fig. 13; gray shaded column with diagonal stripes), type II PVP neurons responses were more attenuated than during slow gaze redirection, similar to what was observed for type I PVP neurons (Fig. 10). The influence of afferent inputs from neck muscle proprioceptors on the activity of type II PVP neurons was tested using the same paradigms as described for type I PVP neurons [i.e., passive rotation of the head on the body (Fig. 13; gray shaded column with vertical stripes) and passive rotation of the body under an earth stationary head (data not shown)]. As with type I PVP neurons, the type II PVP neurons tested were not

influenced by passive activation (dynamic or static) of the neck proprioceptors.

DISCUSSION

Gaze stabilization vs. gaze redirection

The main finding of the present study is that the head-velocity-related response of the direct VOR pathways is modulated in a manner that is consistent with the behavioral goal of the animal. Neuronal activity of VOR interneurons (type I PVP neurons) was recorded during a diverse range of vestibular stimuli protocols including: passive whole-body rotation, passive head-on-body rotation, active eye-head gaze shifts, active eye-head gaze pursuit, self-generated whole-body motion (i.e., driving), and active head-on-body movements made while the monkey was passively rotated. Regardless of the stimulation condition, head-velocity-related modulation of type I PVP neurons was comparable whenever monkeys stabilized their gaze relative to space. In contrast, whenever the monkeys' behavioral goal was to redirect their gaze relative to space, type I PVP neuron responses to head motion were significantly reduced. We also found that type II PVP neurons, which are likely to contribute indirectly to the VOR, generally behaved in

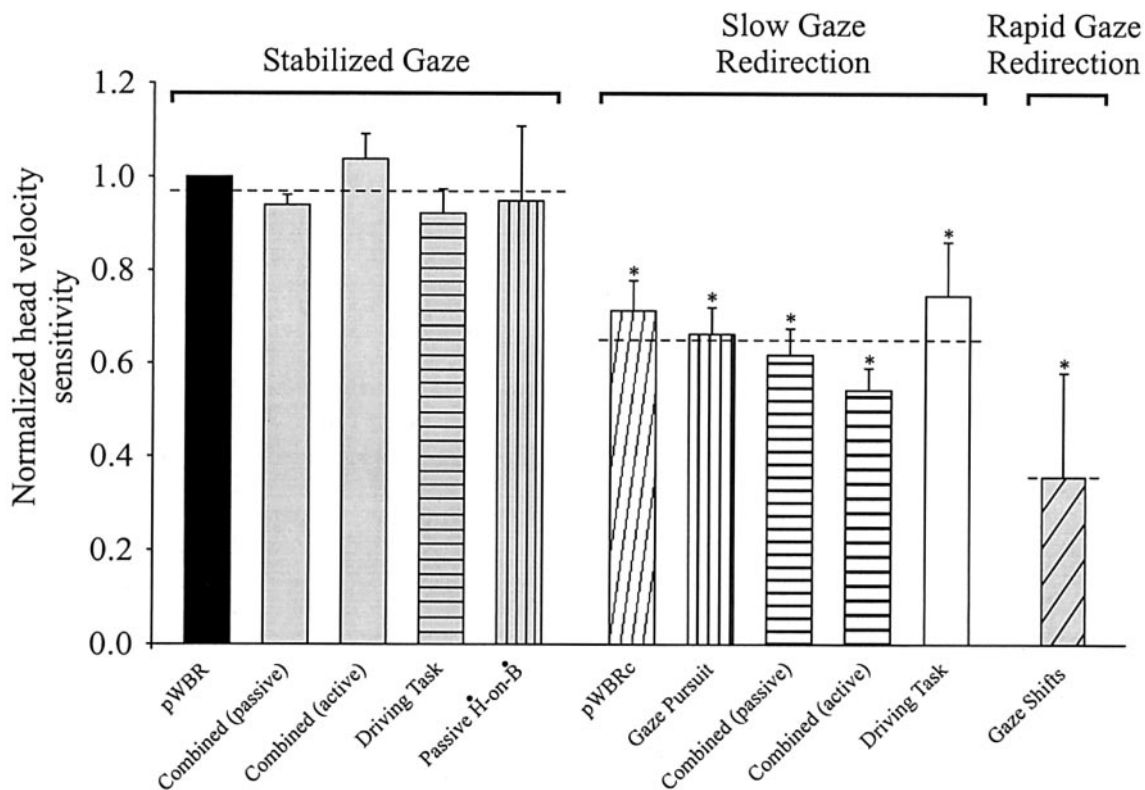


FIG. 13. Summary of type II PVP neuron discharge activity during passive and voluntary head motion. Neuronal responses to head velocity were significantly attenuated when gaze was redirected during both passive and voluntary head motion as compared with pWBR (solid column). Such attenuation occurred during pWBRC (diagonally striped column), eye-head gaze pursuit (vertically striped column; $n = 12$), and the driving task (open column; $n = 4$). Similarly, when monkeys made voluntary head-on-body movements during simultaneous passive whole-body rotation, neuronal responses to both the voluntary and passive components of head-in-space motion (compare horizontally striped columns; $n = 5$) were attenuated. Neurons were attenuated to a greater extent during ipsilaterally directed gaze shifts than during slow gaze redirection (gray shaded column with diagonal stripes). Neurons were not attenuated when the monkey stabilized its gaze during simultaneous passive and voluntary head motion (gray shaded columns), the driving task (gray shaded column with horizontal stripes), and passive head-on-body rotations (gray shaded column with vertical stripes; $n = 10$). The horizontal dashed lines represent the average normalized head-velocity sensitivities across each condition with the same gaze goal.

a similar manner. However, there were some important differences which we consider later in this discussion.

Absence of influence from neck proprioceptive inputs

In the present study, we found that neither static nor dynamic activation of neck proprioceptors alone influenced the activity of PVP neurons (Fig. 14). This result is very different from that of a recent study (Gdowski and McCrea 2000) in which it was reported that the majority of type I PVP neurons are sensitive to static head position relative to the trunk (61%) and dynamic neck motion (76%). These investigators noted that their findings might have important implications regarding the COR, which functions to generate compensatory eye movements in response to neck motion. They proposed that because PVP neurons carry neck-related information, these same premotor VOR interneurons might also mediate the COR. On the one hand, the difference between our results and those of McCrea and colleagues is surprising given that neurons were recorded during the same paradigms: passive rotation of the monkey's body under its earth-fixed head and/or passive rotation of its head on its body. On the other hand, an important difference between these two studies is that neurons were characterized in old world (rhesus) monkeys in the present

study and in new world (squirrel) monkeys in that of Gdowski and McCrea (2000).

Prior studies have determined that COR gains are small to nonexistent in most species including: rhesus monkeys (Bohmer and Henn 1983; Dichgans et al. 1973), humans (Barlow and Freedman 1980; Bronstein 1992; Bronstein and Hood 1986; Huygen et al. 1991; Jürgens and Mergner 1989), rabbits (Barmack et al. 1981, 1989, 1992; Fuller 1980; Gresty 1976), and cats (Fuller 1980). The results of the present study are consistent with these prior reports; none of our rhesus monkeys had COR gains that differed significantly from zero (Fig. 7, B and C). However, it is interesting to note that squirrel monkeys may be an exception to this general rule. In this species, COR gains in the range of 0.4 have been recently reported (Godowski and McCrea 2000). This marked difference between the COR gain of rhesus and squirrel monkeys is consistent with the apparent difference that neck proprioceptive inputs have on premotor vestibular nuclei neurons for these two species. In addition, prior reports by our laboratory and McCrea and colleagues have revealed an analogous difference regarding the influence of neck proprioceptors on another class of vestibular nuclei neurons, vestibular-only neurons. These neurons, which are thought to contribute to the VCR, appear to carry neck

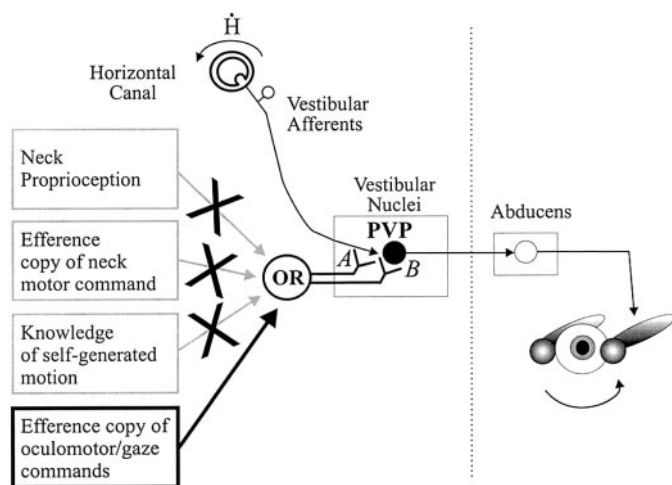


FIG. 14. Proposed mechanism mediating the gaze goal dependence of type I PVP neurons. Our findings suggest that neither neck proprioceptive information nor an efference copy of neck motor commands influenced neuron activity. In addition, the monkey's knowledge of self-generated head-in-space motion did not contribute to the attenuation. (Note: $\times$, hypothetical pathways that have been eliminated.) We propose that an inhibitory signal representing an efference copy of the oculomotor/gaze command mediates the attenuation either at the level of the PVP neurons (A) and/or presynaptically to the PVP neurons (B).

afferent signals in the squirrel monkey (McCrea et al. 1999) but not in the rhesus monkey (Roy and Cullen 2001). In summary, the results of this and previous studies suggest that use of neck proprioceptive inputs by vestibular reflex pathways in rhesus and squirrel monkeys differs greatly.

Absence of influence from neck efference copy

An unresolved question in the vestibular literature is whether or not the gain of the VOR differs for active versus passive head motion. Two previous studies have reported higher VOR gains during active head-on-body motion as compared with pWBR when subjects fixated an earth-fixed target (Jell et al. 1988) and in the dark (Demer et al. 1993). The gain enhancement observed by Demer and colleagues (1993) was attributed to an efference copy of the motor command to the neck. However, there is much accumulated evidence that suggests the VOR gains are comparable during active and passive head motion. First, the gains of the VOR during sinusoidal (0.25–1.0 Hz) passive whole-body rotation and active head-on-body motion were similar (Hanson and Goebel 1998). Second, numerous studies have reported that the gain of the VOR was comparable during passive and active head-on-body motion (Foster et al. 1997; Hanson and Goebel 1998; Pulaski et al. 1981; Santina et al. 1999, 2000; Thurtell et al. 1999). Third, in the present report, we have recorded from the VOR interneurons and show that the head-velocity-related modulation of type I PVP neurons was comparable during pWBR and active head movements made when gaze was stable (Figs. 2C, 5B, and 6B). Finally, our neurophysiological results agree with our observation in the present study that there was no significant difference in the gain of the behavioral VOR during pWBR (Fig. 1C; VOR gain $\approx$ 0.94) and immediately following gaze shifts during the active head motion that occurred once gaze was stable (Fig. 2C; VOR gain $\approx$ 0.98). Thus taken together, the results of behavioral and single-unit recording experiments strongly suggest that an efference copy of the neck motor

command does not influence to status of the VOR during active head-on-body motion (Fig. 14).

Our findings appear to be consistent with those of a recent report by Gdowski and McCrea (1999). These investigators recorded the responses of PVP neurons in squirrel monkeys when slow head-on-body movements were made during passive whole-body rotation. They attributed these head-on-body movements to the vestibulocollic reflex and found that neuronal modulation was better related to head-in-space motion than to passive turntable motion. It is probable (although it is not explicitly stated) that the analysis was limited to intervals in which the axis of gaze was stable. Accordingly, these results could be interpreted as further evidence that PVP neurons similarly encode active and passive head motion when gaze is stable.

Influence of knowledge of self-generated motion

Traditionally the vestibular system is associated with generating the reflexes that are crucial for our daily activities, such as stabilizing gaze (Grossman et al. 1988, 1989) and posture (for review, see Peterson and Richmond 1988). However, the role of the vestibular system is not limited to these functions. The development of an accurate spatial representation, proper implementation of navigation, and gaze control involves the interaction between many brain structures that receive vestibular information and in turn project back to the vestibular nuclei. It is possible that these cortical (reviewed in Fukushima 1997) and cerebellar (Voogd et al. 1996) projections could impinge on type I PVP neurons and result in the differential encoding of head velocity. Here, we have examined whether a monkey's knowledge of its self-generated motion modified the head-velocity signals carried by type I PVP neurons. We found that for active head movements made while gaze was stable, the discharge of type I PVP neurons could be accurately predicted by their head-velocity-related response during passive whole-body rotation. This finding was consistent for active head-on-body movements, active movements of the head and body together in space (i.e., the driving paradigm), and combined active and passive head rotations. In all cases, the attenuation of vestibular responses was limited to the specific intervals in which monkeys actively redirected their gaze. We therefore conclude that knowledge of self-motion, per se, does not directly influence the vestibular sensitivity of type I PVP neurons (Fig. 14). Note, we have previously shown that another class of neurons in the vestibular nuclei—vestibular-only neurons, which are thought to mediate the vestibulocollic reflex—are also not directly influenced by the monkey's knowledge of self-generated motion (Roy and Cullen 2001). Thus our results support the hypothesis that a monkey's knowledge of its self-generated head motion relative to space does not alter the processing of vestibular information at the level of the vestibular nuclei.

Convergence of signals on type I PVP neurons

Although the head-velocity-related modulation of type I PVP neurons was significantly attenuated whenever the monkey wanted to redirect its gaze in space, the amount of suppression differed depending on the type of gaze movement. Type I PVP neurons were more attenuated during rapid gaze

redirections (Fig. 10, □), which included vestibular quick phases, saccades, eye-head gaze shifts, and head/body-eye gaze shifts (i.e., driving paradigm step target), than during slow gaze redirection (Fig. 10, ▨), which included VOR cancellation, gaze pursuit, and head/body-eye pursuit (i.e., driving paradigm pursuit target). We propose efference copies of oculomotor/gaze motor commands are responsible for the behaviorally dependent modulation of type I PVP neurons—and as a result, for the status of the VOR—during gaze redirection (Fig. 14). Accordingly, the differing levels of suppression result

from the different gaze premotor circuitries that generate rapid versus slow gaze redirection.

MECHANISMS FOR VOR SUPPRESSION DURING RAPID GAZE REDIRECTION. During the rapid redirection of gaze (i.e., saccades, vestibular quick phases, and gaze shifts), the brain stem burst generator is active. We have previously proposed that this premotor brain stem circuitry mediates the attenuation of type I PVP neuron responses, which can be observed during each of these behaviors (Fig. 15A) (Roy and Cullen 1998). Burst neurons in the paramedian pontine reticular formation (PPRF)

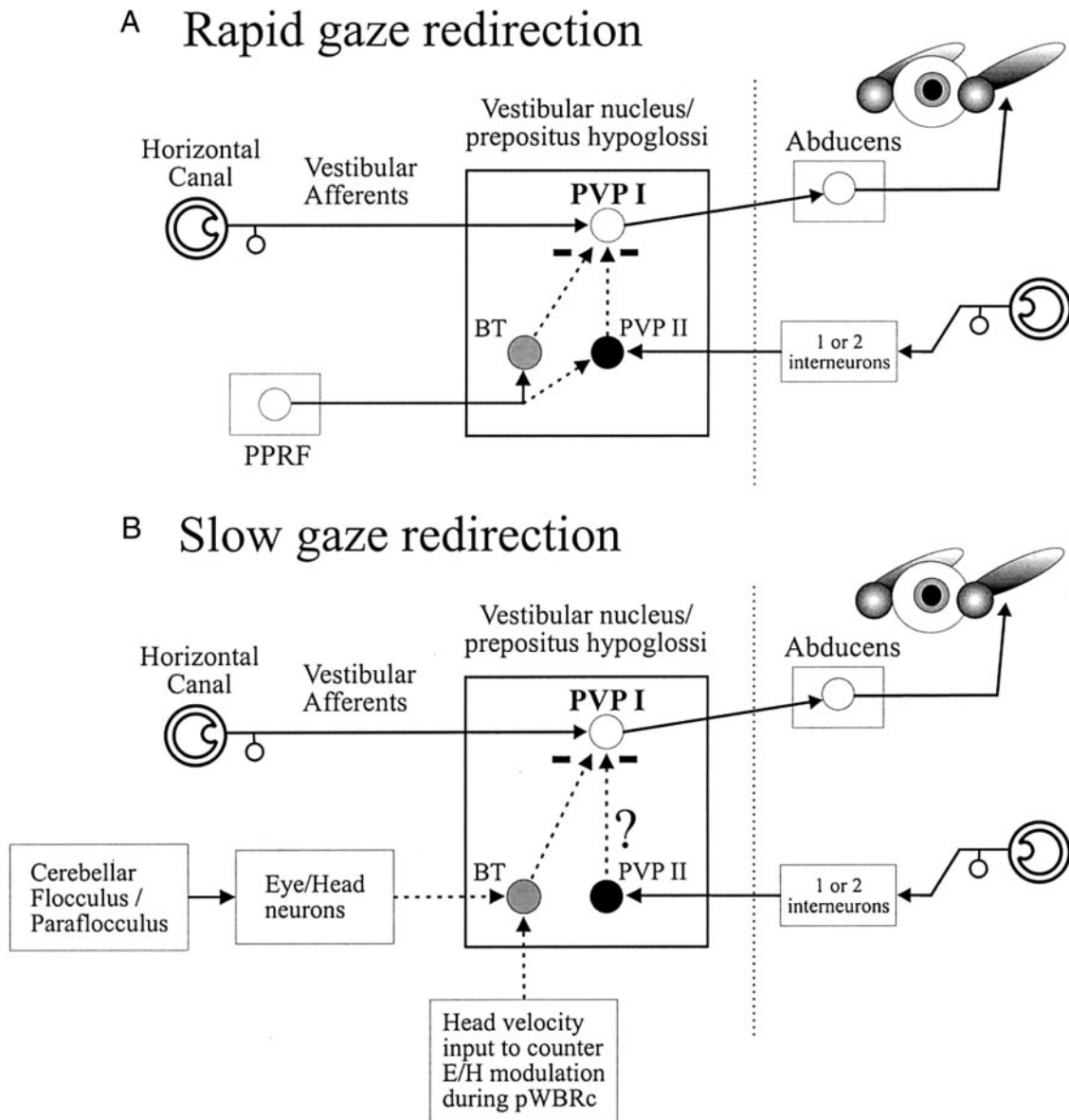


FIG. 15. Possible brain stem premotor circuitries involved in the attenuation of type I PVP neurons during gaze redirection. **A:** mechanisms for VOR suppression during rapid gaze redirection. Type I PVP neurons receive a strong monosynaptic connection from the ipsilateral vestibular afferents and in turn project directly to extraocular motoneurons. During saccades, vestibular quick phases, and gaze shifts, brain stem burst neurons in the PPRF are active. These neurons are known to project to neurons with type II vestibular responses, which in turn would inhibit the type I PVP neurons. Type II PVP neurons and burst-tonic (BT) neurons are possible candidates for this interneuron. **B:** mechanisms for VOR suppression during slow gaze redirection. Eye/head (E/H) neurons receive information from the cerebellum during slow gaze redirection and are likely to project to BT neurons. An inhibitory projection from BT neurons could attenuate vestibular responses of type I PVP neurons during gaze pursuit and pWBRC. E/H neurons are modulated during pWBRC, such that an additional head-velocity-related input is required to offset this input on BT neurons, which are not modulated. The role of type II PVP neurons is not clear (?) because their activity during slow gaze redirection is not appropriate to suppress type I PVP neurons.

generate a burst in activity to drive the eye during saccades and gaze shifts (Cullen and Guitton 1997). Burst neurons project to type II neurons in the vestibular nucleus (Sasaki and Shimazu 1981), and in turn, type II neurons send an inhibitory projection to type I PVP neurons (Nakao et al. 1982). Because the type II-type I vestibular projection is inhibitory, this pathway would effectively invert the "burst" behavior of burst neurons to create the "pause" in the type I PVP response observed during rapid redirection of gaze.

It was not possible to determine whether the type II response of the neurons in the Nakao et al. (1982) study was vestibular in origin or eye movement related because decerebrate cats were studied. Accordingly, within the vestibular nuclei and nearby nucleus prepositus hypoglossi, there are at least two classes of neurons that match the description of the type II neurons. The first class of neurons are the type II PVP neurons described in the present study, which increase their modulation in response to contralateral passive whole-body rotation and burst in activity during ipsilaterally directed saccades, vestibular quick phases, and gaze shifts. While the projection pattern of type II PVP neurons is not known, it is likely that they are involved in the inhibitory commissural pathways between vestibular nuclei (Goldberg et al. 1987; Highstein et al. 1987; Shimazu 1972; Shimazu and Precht 1966). The second class of neurons are the burst-tonic (BT) neurons in the medial vestibular nucleus/nucleus prepositus hypoglossi. In addition to a type II response during passive whole-body rotation, these neurons burst for ipsilaterally directed saccades and vestibular quick phases (Cullen et al. 1993; McConville et al. 1996; McFarland and Fuchs 1992). Using intracellular staining, the strongest projections of BT neurons have been traced to the contralateral abducens nucleus and PPRF, the vestibular nuclei, and the prepositus hypoglossi (reviewed in McCrea 1988). The projections to the abducens nucleus have been shown to be inhibitory (Spencer et al. 1989), and thus it is likely that the projection to the vestibular nuclei would be as well. The discharges of type II PVP neurons and/or BT neurons could mediate the pause in activity of type I PVP neurons during ipsilaterally directed saccades, vestibular quick phases, and gaze shifts (Fig. 15A). While the behavior of type II PVP neurons is consistent with their proposed role in the attenuation of type I PVP neuron activity during gaze shifts, further experiments are required to confirm whether the behavior of BT neurons during combined eye-head gaze shifts is equally appropriate.

MECHANISMS FOR VOR SUPPRESSION DURING CANCELLATION AND SLOW GAZE REDIRECTION. Because less is known about the connectivity of the brain stem premotor circuits that mediate smooth pursuit and VOR cancellation than those that mediate saccades, elucidating the mechanism responsible for the attenuation in type I PVP neuron responses during slow gaze redirection is less straightforward. During smooth pursuit eye movements in head-restrained animals, the cerebellar flocculus and paraflocculus send pursuit command signals to neurons in the vestibular nuclei (Lisberger et al. 1994a). Based on their responses during eye movements and head-rotation paradigms, it is generally agreed that these neurons are part of the same population of neurons that have been termed smooth-pursuit and eye-head neurons (Cullen et al. 1993 and Scudder and Fuchs 1992, respectively). Thus for the sake of simplicity,

we will refer to them as eye-head (E/H) neurons here. There is no evidence that E/H neurons project to PVP neurons. It is possible that pursuit information reaches the vestibular nuclei indirectly via the BT neurons, which show robust modulation during smooth pursuit (Cullen et al. 1993; McConville et al. 1996; McFarland and Fuchs 1992). A schema in which E/H neurons project to BT neurons and BT neurons, in turn, send inhibitory pursuit signals to type I PVP neurons is shown in Fig. 15B.

This projection offers an explanation for the attenuated responses of type I PVP neurons during pWBRC and slow gaze redirection. BT neurons are not modulated during pWBRC but are well modulated during pWBR (Cullen et al. 1993; McConville et al. 1996; McFarland and Fuchs 1992). An ipsilateral inhibitory projection from the BT neurons would result in a decrease in the modulation of type I PVP neurons during pWBRC as compared with pWBR. If this attenuation is a result of the reduced eye-motion-related input from BT neurons, then it follows that the modulation of type I PVP neurons during pWBR should be equal to the sum of their modulation during pWBRC and smooth pursuit. Overall, for our sample of neurons, this was the case: the sum of the head-velocity sensitivity during pWBRC [1.03 ± 0.13 (sp/s)/(°/s)] and eye-velocity sensitivity during smooth pursuit [0.39 ± 0.08 (sp/s)/(°/s)] approximated the mean head-velocity sensitivity during pWBR [1.4 vs. 1.3 ± 0.12 (sp/s)/(°/s), respectively]. However, on a neuron-by-neuron basis, the slope of the relationship between pWBR and pWBRC + smooth pursuit was significantly less than unity (slope = 0.72, $R^2 = 0.70$, $P < 0.02$), suggesting that this explanation cannot fully account for differences in type I PVP neuron activity observed across these paradigms. Our findings are consistent with those of Cullen and McCrea (1993) and Scudder and Fuchs (1992). In addition, the projections shown in Fig. 15B could also explain the attenuation of type I PVP neurons during other slow gaze-redirection tasks. For example, if during gaze pursuit BT neuron modulation remains related to eye motion, then type I PVP neurons would be suppressed by the resulting inhibitory drive.

One limitation of the preceding mechanism is that E/H neurons are strongly modulated during pWBRC (Cullen and McCrea 1993; Scudder and Fuchs 1992), whereas BT neurons are not. Thus if E/H neurons project to BT neurons, as proposed, an additional head-velocity signal would be required to offset the modulation of E/H neurons at the level of the BT neurons. Such a signal could originate from neurons within the ipsilateral or contralateral vestibular nucleus or from the ipsilateral vestibular afferents (Goldberg et al. 1987; Straka and Dieringer 2000). Nevertheless, the lack of BT neuron modulation during pWBRC could mediate, at least in part, the nonvisual suppression of the VOR that has been described in previous studies (Cullen and McCrea 1993; Cullen et al. 1991; Lisberger 1990). Finally, another possible explanation for the reduced response of type I PVP neurons to head velocity during pWBRC and gaze pursuit is that a yet-to-be determined inhibitory pursuit-related signal exists. Candidates for this signal could be the ipsilateral E/H neurons and/or neurons in the contralateral vestibular/prepositus nuclei complex.

Type II PVP neurons

The responses of type II PVP neurons during slow gaze-redirection tasks were not consistent with their playing a primary role in mediating the attenuation of type I PVP neurons if one assumes an inhibitory ipsilateral projection from type II PVP neurons to the type I PVP neurons (as we did in Fig. 15A). For instance during pWBRC, type II PVP neuron responses are attenuated as compared with during pWBR, which means that their modulation is opposite to what would be required to mediate the suppression of type I PVP neurons. This is not only a problem for pWBRC but also for all of the other slow gaze-redirection tasks because type II PVP neuron responses were attenuated (see Fig. 13). Thus while it is conceivable that type II PVP neurons project to type I PVP neurons, their activity does not appear to be integral for the short-term modulation of type I PVP neuron responses across different behavioral conditions. Given the complex interconnections between the vestibular nuclei, the prepositus hypoglossi, and the cerebellum, it is more likely that over the long term they play a role in balancing vestibular function across these structures.

Conclusion

In conclusion, we have shown that the activity of type I and II PVP neurons is modulated in a manner that depends strictly on the current gaze strategy of the monkey. Neuronal discharges were comparable during active and passive head motion whenever the monkey's gaze was stable. Similarly, discharges were attenuated during active and passive head motion when a monkey redirected its gaze. Thus the neuronal responses to head motion are altered in a manner that is consistent with maximizing the VOR gain when the goal is to stabilize gaze and reducing the VOR gain when the behavioral goal is to redirect gaze. We propose that the attenuation of the direct VOR pathways is mediated via inputs from the premotor circuitries that are known to generate saccades and smooth pursuit eye movements in head-restrained animals.

We thank P. A. Sylvestre, J.T.L. Choi, J. Mok, and M. C. Taylor for critically reading the manuscript and E. Moreau, W. Kucharski, J. Knowles, and A. Smith for excellent technical assistance.

This study was supported by the Canadian Institutes of Health Research.

REFERENCES

- ANASTASOPOULOS D AND MERGNER T. Canal-neck interaction in vestibular nuclear neurons of the cats. *Exp Brain Res* 46: 269–280, 1982.
- BARLOW D AND FREEDMAN W. Cervicocolic reflex in the normal adult. *Acta Otolaryngol* 89: 487–496, 1980.
- BARMACK NH, ERRICO P, FERRARESI A, AND PETTOROSSO VE. Interactions of cervicocolic and vestibuloocular fast-phase signals in the control of eye position in rabbits. *J Physiol (Lond)* 410: 213–225, 1989.
- BARMACK NH, NASTOS MA, AND PETTOROSSO VE. The horizontal and vertical cervicocolic reflexes of the rabbit. *Brain Res* 224: 261–278, 1981.
- BARMACK NH, PIERANGELO E, FERRARESI A, AND PETTOROSSO VE. Cervicocolic reflexes with and without simultaneous vestibular stimulation in rabbits. In: *The Head-Neck Sensory Motor System*. Oxford, UK: Oxford Univ. Press, 1992, p. 201–207.
- BOHMER A AND HENN V. Horizontal and vertical vestibuloocular and cervicocolic reflexes in the monkey during high frequency rotation. *Brain Res* 277: 241–248, 1983.
- BOYLE R AND POMPEIANO O. Responses of vestibulospinal neurons to sinusoidal rotation of the neck. *J Neurophysiol* 44: 633–649, 1981.
- BRONSTEIN AM. Plastic changes in the human cervicocolic reflex. *Ann NY Acad Sci* 656: 708–715, 1992.
- BRONSTEIN AM AND HOOD JD. The cervicocolic reflex in normal subjects and patients with absent vestibular function. *Brain Res* 373: 399–408, 1986.
- CULLEN KE, BELTON T, AND MCCREA RA. A non-visual mechanism for voluntary cancellation of the vestibulo-ocular reflex. *Exp Brain Res* 83: 237–252, 1991.
- CULLEN KE, CHEN-HUANG C, AND MCCREA RA. Firing behavior of brain stem neurons during voluntary cancellation of the horizontal vestibuloocular reflex. II. Eye-movement-related neurons. *J Neurophysiol* 70: 844–856, 1993.
- CULLEN KE AND GUITTON D. Analysis of primate IBN spike trains using system identification techniques. II. Relationship to gaze, eye, and head movement dynamics during head-free gaze shifts. *J Neurophysiol* 78: 3283–3306, 1997.
- CULLEN KE AND MCCREA RA. Firing behavior of brain stem neurons during voluntary cancellation of the horizontal vestibuloocular reflex. I. Secondary vestibular neurons. *J Neurophysiol* 70: 828–843, 1993.
- CULLEN KE, REY CG, GUITTON D, AND GALIANA HL. The use of system identification techniques in the analysis of oculomotor burst neuron spike train dynamics. *J Comp Neurosci* 3: 347–368, 1996.
- DEMER JL, OAS JG, AND BALOH RW. Visual-vestibular interaction in humans during active and passive, vertical head motion. *J Vestibul Res* 3: 101–114, 1993.
- DICHGANS J, BIZZI E, MORASSO P, AND TAGLIASCO V. Mechanisms underlying recovery of eye-head coordination following bilateral labyrinthectomy in monkeys. *Exp Brain Res* 18: 548–562, 1973.
- FOSTER CA, DEMER JL, MORROW MJ, AND BALOH RW. Deficits of gaze stability in multiple axes following unilateral vestibular lesions. *Exp Brain Res* 116: 501–509, 1997.
- FUCHS AF AND KIMM J. Unit activity in vestibular nucleus of the alert monkey during horizontal angular acceleration and eye movement. *J Neurophysiol* 38: 1140–1161, 1975.
- FUCHS AF AND ROBINSON DA. A method for measuring horizontal and vertical eye movements in the monkey. *J Physiol (Lond)* 191: 609–631, 1966.
- FUKUSHIMA K. Corticovestibular interactions: anatomy, electrophysiology, and functional considerations. *Exp Brain Res* 117: 1–16, 1997.
- FULLER JH. The dynamic neck-eye reflex in mammals. *Exp Brain Res* 41: 29–35, 1980.
- FULLER JH. Chronic recording of neck sensory input to vestibular neurons. In: *Control of Head Movement*. Oxford, UK: Oxford Univ. Press, 1988, p. 120–128.
- GDOWSKI GT AND MCCREA RA. Integration of vestibular and head movement signals in the vestibular nuclei during whole-body rotation. *J Neurophysiol* 81: 436–449, 1999.
- GDOWSKI GT AND MCCREA RA. Neck proprioceptive inputs to primate vestibular nucleus neurons. *Exp Brain Res* 135: 511–526, 2000.
- GOLDBERG JM AND FERNANDEZ C. Physiology of peripheral neurons innervating semicircular canals of the squirrel monkey. I. Resting discharge and response to constant angular accelerations. *J Neurophysiol* 34: 635–660, 1971.
- GOLDBERG JM, HIGHSTEIN SM, MOSCHOVAKIS AK, AND FERNANDEZ C. Inputs from regularly and irregularly discharging vestibular nerve afferents to secondary neurons in the vestibular nuclei of the squirrel monkey. I. An electrophysiological analysis. *J Neurophysiol* 58: 700–718, 1987.
- GRESTY MA. A reexamination of “neck reflex” eye movements in the rabbit. *Acta Otolaryngol* 81: 3886–3394, 1976.
- GROSSMAN GE, LEIGH RJ, ABEL LA, LANSKA DJ, AND THURSTON SE. Frequency and velocity of rotational head perturbations during locomotion. *Exp Brain Res* 70: 470–476, 1988.
- GROSSMAN GE, LEIGH RJ, BRUCE EN, HUEBNER WP, AND LANSKA DJ. Performance of human vestibuloocular reflex during locomotion. *J Neurophysiol* 62: 264–271, 1989.
- HANSON JM AND GOEBEL JA. Comparison of manual whole-body and passive and active head-on-body rotational testing with conventional rotary chair testing. *J Vestibul Res* 8: 273–282, 1998.
- HAYES AV, RICHMOND BJ, AND OPTICAN LM. A UNIX-based multiple process system for real-time data acquisition and control. *WESCOM Conf Proc* 2: 1–10, 1982.
- HIGHSTEIN SM, GOLDBERG JM, MOSCHOVAKIS AK, AND FERNANDEZ C. Inputs from regularly and irregularly discharging vestibular nerve afferents to secondary neurons in the vestibular nuclei of the squirrel monkey. I. Correlation with output pathways of secondary neurons. *J Neurophysiol* 58: 719–738, 1987.

- HUYGEN PLM, VERHAGEN WIM, AND NICOLASEN MGM. Cervicoocular reflex enhancement in labyrinthine-defective and normal subjects. *Exp Brain Res* 87: 457–464, 1991.
- JELL RM, STOCKWELL CW, TURNIPSEED GT, AND GEUDRY FE. The influence of active versus passive head oscillation, and mental set on the human vestibuloocular reflex. *Aviat Space Environ Med* 59: 1061–1065, 1988.
- JÜRGENS R AND MERGNER T. Interaction between cervicoocular and vestibuloocular reflexes in normal adults. *Exp Brain Res* 77: 381–390, 1989.
- KELLER EL. Gain of the vestibuloocular reflex in monkey at high rotational frequencies. *Vision Res* 18: 311–315, 1978.
- KELLER EL AND DANIELS PD. Oculomotor related interaction of vestibular and visual stimulation in vestibular nucleus cells in alert monkey. *Exp Neurol* 46: 187–198, 1975.
- KELLER EL AND KAMATH BY. Characteristics of head rotation and eye-movement-related neurons in alert monkey vestibular nucleus. *Brain Res* 100: 182–187, 1975.
- LISBERGER SG. Visual tracking in monkeys: evidence for short-latency suppression of the vestibuloocular reflex. *J Neurophysiol* 63: 676–688, 1990.
- LISBERGER SG. Neural basis for motor learning in the vestibuloocular reflex of primates. III. Computational and behavioral analysis of the sites of learning. *J Neurophysiol* 72: 974–998, 1994.
- LISBERGER SG, PAVELKO TA, AND BROUSSARD DM. Responses during eye movements of brain stem neurons that receive monosynaptic inhibition from the flocculus and ventral paraflocculus in monkeys. *J Neurophysiol* 72: 909–927, 1994a.
- LISBERGER SG, PAVELKO TA, AND BROUSSARD DM. Neural basis of motor learning in the vestibuloocular reflex of primates. I. Changes in the responses of brain stem neurons. *J Neurophysiol* 72: 928–953, 1994b.
- MC CONVILLE K MV, TOMLINSON RD, AND NA EQ. Behavior of eye-movement-related cells in the vestibular nuclei during combined rotational and translational stimuli. *J Neurophysiol* 76: 3136–3148, 1996.
- MC CREA RA. Neuroanatomy of the oculomotor system. The nucleus prepositus. *Rev Oculomot Res* 2: 203–223, 1988.
- MC CREA RA, CHEN-HUANG C, BELTON T, AND GDOWSKI GT. Behavior contingent processing of vestibular sensory signals in the vestibular nuclei. *Ann NY Acad Sci* 781: 292–303, 1996.
- MC CREA RA, GDOWSKI GT, BOYLE R, AND BELTON T. Firing behavior of vestibular neurons during active and passive head movements: vestibulospinal and other non-eye-movement-related neurons. *J Neurophysiol* 82: 416–428, 1999.
- MC CREA RA, STRASSMAN EM, AND HIGHSTEIN SM. Anatomical and physiological characteristics of vestibular neurons mediating the horizontal vestibuloocular reflex of the squirrel monkey. *J Comp Neurol* 264: 547–570, 1987.
- McFARLAND JL AND FUCHS AF. Discharge patterns of nucleus prepositus hypoglossi and adjacent vestibular nucleus during horizontal eye movement in behaving macaques. *J Neurophysiol* 41: 319–332, 1992.
- MILES FA. 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, 1975.
- NAKAO S, SASAKI S, SCHOR RH, AND SHIMAZU H. Functional organization of premotor neurons in the cat medial vestibular nucleus related to slow and fast phases of nystagmus. *Exp Brain Res* 45: 371–385, 1982.
- PAIGE GD. Vestibuloocular reflex and its interactions with visual following mechanisms in the squirrel monkey. I. Response characteristics in normal animals. *J Neurophysiol* 49: 134–151, 1983.
- PETERSON B AND RICHMOND FJ. *Control of Head Movement*. Oxford, UK: Oxford Univ. Press, 1988.
- PULASKI PD, ZEE DS, AND ROBINSON DA. The behavior of the vestibuloocular reflex at high velocities of head rotation. *Brain Res* 222: 159–165, 1981.
- ROY JE AND CULLEN KE. A neural correlate for vestibuloocular reflex suppression during voluntary eye-head gaze shifts. *Nat Neurosci* 1: 404–410, 1998.
- ROY JE AND CULLEN KE. Selective processing of vestibular reafference during self-generated head motion. *J Neurosci* 21: 2131–2142, 2001.
- SANTINA CC, CAREY JP, CREMER PD, AND MINOR LB. Comparison of passive head impulses and sinusoidal vestibular autorotation as measures of human vestibuloocular reflex function. *Soc Neurosci Abstr* 25: 264, 1999.
- SANTINA CC, CREMER PD, CAREY JP, AND MINOR LB. Shortened latency and improved alignment imply preprogrammed mechanisms contribute to VOR during active head rotation after unilateral labyrinthectomy. *ARO Conf Abstr* 5233, 2000.
- SASAKI S AND SHIMAZU H. Reticulovestibular organization participating in generation of horizontal fast eye movement. *Ann NY Acad Sci* 374: 130–145, 1981.
- SATO H, OHKAWA T, UCHINO Y, AND WILSON VJ. Excitatory connections between neurons of the central cervical nucleus and vestibular neurons in the cat. *Exp Brain Res* 115: 381–386, 1997.
- SCUDDER CA AND FUCHS AF. Physiological and behavioural identification of vestibular nucleus neurons mediating the horizontal vestibuloocular reflex in trained rhesus monkeys. *J Neurophysiol* 68: 244–264, 1992.
- SHIMAZU H. Organization of the commissural connections: physiology. *Prog Brain Res* 37: 177–190, 1972.
- SHIMAZU H AND PRECHT W. Inhibition of central vestibular neurons from the contralateral labyrinth and its mediating pathway. *J Neurophysiol* 29: 467–492, 1966.
- SPENCER RF, WENTHOLD RJ, AND BAKER R. Evidence for glycine as an inhibitory neurotransmitter of vestibular, reticular, and prepositus hypoglossi neurons that project to the cat abducens nucleus. *J Neurosci* 9: 2718–2736, 1989.
- STRAKA H AND DIERINGER N. Convergence pattern of uncrossed excitatory and inhibitory semicircular canal-specific inputs onto second-order vestibular neurons of frogs. *Exp Brain Res* 135: 462–473, 2000.
- SYLVESTRE PA AND CULLEN KE. Quantitative analysis of abducens neuron discharge dynamics during saccadic and slow eye movements. *J Neurophysiol* 82: 2616–2632, 1999.
- TELFORD L, SEIDMAN SH, AND PAIGE GD. Canal-otolith interactions driving vertical and horizontal eye movements in the squirrel monkey. *Exp Brain Res* 109: 407–418, 1996.
- THURTELL MJ, BLACK RA, HLMAGYI GM, CURTHOYS IS, AND AW ST. Vertical eye position dependence of the human vestibuloocular reflex during passive and active yaw head rotations. *J Neurophysiol* 81: 2415–2428, 1999.
- TOMLINSON RD AND ROBINSON DA. Signals in vestibular nucleus mediating vertical eye movements in the monkey. *J Neurophysiol* 51: 1121–1136, 1984.
- VOOGD J, GERRITS M, AND RUIGROK JH. Organization of the vestibulocerebellum. *Ann NY Acad Sci* 781: 553–579, 1996.
- WILSON VJ, YAMAGATA Y, YATES BJ, SCHOR RH, AND NONAKA S. 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, 1990.