Behavior of the Position Vestibular Pause (PVP) Interneurons of the Vestibuloocular Reflex During Head-Free Gaze Shifts in the Monkey

Albert F. Fuchs,1,3 Leo Ling,1,3 and James O. Phillips2,3
1Departments of Physiology and Biophysics and 2Otolaryngology, Head, and Neck Surgery and 3Washington Regional Primate Research Center, University of Washington, Seattle, Washington

Submitted 28 January 2005; accepted in final form 18 August 2005

Fuchs, Albert F., Leo Ling, and James O. Phillips. Behavior of the position vestibular pause (PVP) interneurons of the vestibuloocular reflex during head-free gaze shifts in the monkey. J Neurophysiol 94: 4481–4490, 2005. First published August 24, 2005; doi:10.1152/jn.00101.2005. Most behavioral studies indicate that the efficacy (gain) of the vestibuloocular reflex (VOR) in primates is modulated during the voluntary head movements that accompany large shifts in the direction of gaze. However, the timing and degree of this modulation is the subject of some debate. The neurophysiological substrate for this apparent gain reduction has been sought in the behavior of the type I position vestibular pause (PVP) neuron, a well-known type of interneuron in the direct VOR pathway. With the head fixed, PVPs increase their firing rates with contraversive eye position and with ipsiversive passive head rotation and also cease firing (pause) for the duration of ipsiversive saccades. During head-free ipsiversive gaze shifts, the eyes and head move in the same direction. If the vestibular signal carried by PVPs provides the primary drive for the VOR, the vestibular signal should be present during ipsiversive gaze shifts to the degree that the VOR is present. Of 25 type I PVPs recorded, 21 ceased their discharge for the entire duration of the rapid, eye-saccade component of an ipsiversive gaze shift. The resumption of activity occurred, on average, 13 ms after the end of the saccade. These results suggest that the activity of the vast majority of PVP neurons do not reflect the state of the VOR, but rather PVPs are completely eliminated from participation in the reflex during head-free gaze movements. We conclude that if any modulation of the VOR does exist, it must occur through other, probably longer-latency, pathways.

INTRODUCTION

Large changes in the direction of the line of sight (i.e., gaze shifts) toward interesting objects in our peripheral visual world can be accomplished only if the head is free to move and aid the eye movement. However, when the head is rotated passively, it normally produces compensatory eye movements in the opposite direction, i.e., the vestibuloocular reflex (VOR). Therefore during active gaze shifts when the eyes and head must turn in the same direction, the VOR clearly would thwart the head’s attempt to help direct gaze to eccentric locations. Initially, it was suggested that the VOR of monkeys continues to function during an active gaze shift and that the saccadic eye component simply takes its contribution into account to bring gaze accurately onto the target (Bizzzi et al. 1971; Dighgans et al. 1973; Morasso et al. 1973).

Since those early studies, almost all of the data on humans and monkeys suggest that the VOR in fact is reduced or turned off completely during head-free gaze shifts (Cullen et al. 2004; Guitton and Volle 1987; Laurutis and Robinson 1986; Pelisson et al. 1988; Tabak et al. 1996; Tomlinson 1990; Tomlinson and Bahra 1986). In these experiments, the state of the VOR during a head-unrestrained gaze shift was assessed behaviorally by perturbing the head before, during, and after a gaze shift. In both humans and non-human primates, the state of the VOR appears to depend on the amplitude of the gaze shift. The largest reductions in VOR gain occur for the largest gaze shifts (human: Laurutis and Robinson 1986; Tabak et al. 1996; monkey: Cullen et al. 2004; Tomlinson and Bahra 1986). For these large gaze shifts, the depth and time course of VOR suppression varies widely from subject to subject (Cullen et al. 2004; Guitton and Volle 1987; Tabak et al. 1996). In general, however, the VOR operates at its normal gain prior to a gaze shift, drops to a minimum gain (sometimes zero) at gaze onset, and then gradually recovers to reach its normal gain as the eye movement ends (Cullen et al. 2004; Tabak et al. 1996). Because the head is still rotating toward the target when the saccade ends, the now fully functional VOR produces compensatory eye counter-rotations so that gaze remains stable in space and the eyes remain on target. For small gaze shifts (<20°), the operation of the VOR has been proven only in the monkey, in which it has been suggested that the VOR is operating at full capacity (Cullen et al. 2004; Tomlinson and Bahra 1986). However, Tomlinson and Bahra (1986) acknowledged that inserting a perturbation to test the VOR gain of small gaze shifts is technically difficult because of their small durations, so they resorted to producing smaller saccades of longer duration by intravenous injection of diazepam. On balance, the existing data suggest that the VOR is at least partially suppressed during large gaze shifts with a substantial head component, although that opinion is not held universally (Freedman et al. 1998).

The neuronal substrate responsible for the reduction of VOR gain during active gaze shifts is currently in dispute. Vestibular information from the eighth nerve travels through disynaptic and polysynaptic pathways to abducens motoneurons, which produce horizontal gaze saccades (Lorente de Nó 1933; Szentagothai 1950). With the head fixed, the best-established interneuron of the direct three-neuron horizontal VOR increases its rate with contraversive eye position and ipsiversive passive head rotations and exhibits a cessation of firing (a pause) for the duration of ipsiversive saccades. These so-called type I position vestibular pause (PVP) neurons are concentrated in the
ventrolateral vestibular nucleus, just caudal and lateral to the abducens nucleus (Langer et al. 1986; Scudder and Fuchs 1992). For gaze shifts with the head free to turn, our preliminary data (Phillips et al. 1996) indicated that PVP neurons still exhibit a reliable pause that continues for the entire duration of the saccadic eye component of the gaze shift. McCrea and Gdowski (2003) have shown similar full pauses for the PVPs in the squirrel monkey. Therefore vestibular signals that mediate the VOR during a gaze shift must gain access to the motoneurons innervating the horizontal extraocular muscles through some other route, i.e., via another interneuron or polysynaptic circuit. In contrast, Roy and Cullen (1998, 2002) have shown that the pause of their putative PVP neurons does not last for the duration of the eye saccade. Instead, the reactivation of their PVPs begins during the gaze shift, and firing increases gradually as gaze approaches the target in an apparent reflection of the reinstatement of the VOR by gaze end.

Clearly, the question of whether the PVPs are silent during a gaze shift is currently unresolved. It is possible, as argued by Roy and Cullen (1998, 2002), that the VOR interneurons of the most direct vestibuloculomotor pathway relay eye- and head- velocity and eye-position signals throughout the gaze shift. In this scenario, the shortest reflex circuit participates in the control of large active gaze movements. It is also possible, however, that the three-neuron arc is gated off during all gaze shifts, large or small, and that the vestibular contribution to the gaze movement is communicated through other vestibuloculomotor pathways.

To resolve the issue of PVP participation in gaze control, we recorded from a larger number of PVPs during head-free gaze shifts. Because the vestibular nuclei contain many neurons with discharge characteristics somewhat similar to those of PVP neurons, but for which the connectivity is unknown, we were very careful here to consider only those that met the stringent identification criteria for type I PVP interneurons in the three-neuron arc established by Scudder and Fuchs (1992). The overwhelming majority (84%) of our identified PVP neurons paused for the entire gaze shift as described by Phillips et al. (1996) and McCrea and Gdowski (2003). Only a small number resumed firing before gaze end as described by Roy and Cullen (1998, 2002). We discuss possible reasons to reconcile the findings from our lab and theirs.

METHODS

General procedures

Four macaques (Macaca mulatta; O, R, T, and W) participated in these experiments. In completely aseptic surgeries, each received an eye coil for the electromagnetic measurement of eye position, a head post, which, when engaged in a low-friction bearing, constrained head movements to the yaw plane, and a recording cylinder. The cylinder was tilted by 20° from the sagittal plane and aimed 2 mm posterior of ear-bar zero.

With the monkey’s head fixed while we searched for neurons (see Experimental strategy), we measured eye position in the head with an electromagnetic technique that was linear to ±40° with a sensitivity of ~0.25°/s (Fuchs and Robinson 1966; Robinson 1963). When the head was free to rotate about a vertical axis to participate in horizontal gaze shifts, the same eye coil measured eye position in space, i.e., gaze position (\(G\)). Head position (\(H\)) was measured via either a search coil affixed to the head or a single-turn precision potentiometer (linearity: 0.25%) attached to the low-inertia (\(J = 120 \text{~g} \cdot \text{cm}^2\)) head-restraint post. The post was coaxial with the spinal column when the animal was seated comfortably in a primate chair. With the monkey in this position, which corresponds roughly to the stereotaxic orientation, the horizontal canals were tipped slightly upward. Eye position in the head was calculated on-line as \(G-H\).

Monkeys were rewarded for aiming their gaze within ±2° of the illuminated distant light-emitting diode (LED) in an array of LEDs that were positioned every 5° along the horizontal axis. We generated step changes in target position by illuminating a LED while simultaneously extinguishing the fixed LED (for details, see Phillips et al. 1999). With the head fixed, the target stepped within ±20° of straight ahead, and when the head was free, it stepped within ±40°.

With the head either fixed or free, we recorded extracellular unit activity with tungsten microelectrodes that were advanced hydraulically to the brain stem. Neuronal activity was amplified and filtered (band-pass: 300 Hz to 10 kHz), played over an audio monitor and displayed on an oscilloscope.

Both head-fixed and head-free data were saved to a VCR (Vetter 4000A) for off-line analysis. Eye and target position signals were digitized at 1 kHz and spikes were specified within 10 μs using a 16-bit analog/digital board (NB-MIO-16XH50; National Instruments) and stored on a computer (Power Macintosh 7500/120, Apple). Behavioral and unit data associated with head-free gaze shifts were analyzed on a Macintosh G4 computer with an interactive program that detected and displayed each gaze shift on a monitor, calculated and displayed the instantaneous velocities of the gaze, eye, and head movements, and marked their salient features, e.g., movement start and end times and times to peak velocity and the beginning and end of the pause. Movement onset and end were marked as those times when movement velocity first exceeded and then fell below, respectively, 10°/s. The pause was identified as the interspike interval that straddled the time of peak saccadic velocity. The user could correct the occasional erroneous markings, but this seldom was necessary. The program used these markings to determine the metrics of the movements and the duration of the pause. The resultant data file was exported to commercial programs for the plotting of histograms and for statistical analyses. To determine a unit’s vestibular sensitivity, a second program parsed the data obtained during head-fixed, en bloc, periodic oscillations into separate cycles of chair rotation for analysis of the gain and phase of the VOR and the associated unit modulation (Scudder and Fuchs 1992; see Phillips et al. 1999 for details about General procedures).

Experimental strategy

Many PVPs that project to the contralateral abducens nucleus are located in the ventrolateral vestibular nucleus (VLVN), which is just caudal and slightly lateral to the VIth nucleus (Langer et al. 1986; Scudder and Fuchs 1992). Accordingly, we first located the abducens nuclei by their characteristic burst-tonic discharge patterns in association with head-fixed horizontal saccades (Fuchs et al. 1988). Once we had located the abducens nuclei, we searched for vestibular and eye-movement-related activity in the vicinity of the VLVN by requiring the head-fixed monkey to fixate a visual target stationary in space while it was rotated about the vertical axis. We used sinusoidal oscillations between 0.4 and 0.5 Hz and peak velocities between 25.1 and 32.1°/s. When we encountered a responsive unit, we rotated the target with the monkey (VOR suppression) to evaluate possible vestibular sensitivities without compensatory eye movement. All of the PVPs in this study showed a modulation of firing rate with ipsiversive head velocity, i.e., type I activity. Once type I activity had been identified, we stopped the chair and required the monkey to make gaze shifts between illuminated LEDs located along the horizontal meridian. All of the PVPs we describe here showed an increase of steady discharge with contraversive eye position and a cessation of activity, or pause, for ipsiversive saccades. All three of these discharge characteristics had to be present for a neuron to be classified as a type
I PVP neuron (McCrea and Gdowski 2003; Scudder and Fuchs 1992) because other neurons in the vicinity have just ipsiversive head-velocity sensitivity and pause for ipsiversive saccades or have other combinations of the three discharge characteristics. After a type I PVP had been identified qualitatively, we collected ~20 cycles of activity during VOR suppression and an assortment of head-fixed horizontal saccades.

We then allowed the animal to rotate its head about the vertical axis to acquire targets that appeared peripheral to its current direction of gaze. Initially, we concentrated on collecting large gaze shifts to target steps between 40 and 80°, but when a unit remained isolated we collected an assortment of amplitudes at 10° increments from 10 to 80°.

Quantitative description of PVP activity

We fit our data following the procedure of Roy and Cullen (1998, 2002). Each action potential was convolved with a Gaussian (5-ms SD during the saccade; 10-ms SD before and after the saccade) and the smoothed firing rate (FR) was described by the following equation

\[ FR = k_1 + k_2 E + k_3 dE/dt + k_4 dH/dt + e \]

where \( E \), \( dE/dt \), and \( dH/dt \) are eye position, eye velocity, and head velocity, respectively, \( k_1 \) represents a DC term, and \( e \) denotes the residual error of the fit. The coefficients are chosen to minimize the residual variance, the variance of the fit errors. Separate fits were performed for blocks of several gaze shifts with similar amplitudes. A fit was based on all of the gaze shifts within a block. The number of blocks (i.e., different amplitudes) varied from three to five (most were 4). For all blocks, \( k_2 \) was fixed to the slope of the relation between firing rate and steady eye position with the head fixed. The remaining coefficients were determined for a series of time delays, and those coefficients and time delay for which the Variance Accounted For, \( VAF = [1 - \text{(variance of fitted total variance of spike density function)}] \), was maximal were taken as descriptions of the best fit. For each block of data, we fit the intra- and peri-saccadic segments of the trial separately. Pre-peri-saccadic periods ended 25 ms before saccade onset and post-periods began 25 ms after saccade end; for peri-saccadic periods, \( k_3 = 0 \). The model fits were plotted separately for the two segments (Fig. 9).

The Animal Care and Use Committee at the University of Washington approved all the surgical and training procedures. The veterinary staff of the Regional Primate Research Center cared for the animals. The animals were housed under conditions that comply with National Institutes of Health standards as stated in the Guidelines for the Care and Use of Mammals in Neuroscience and Behavioral Research (compiled by the National Research Council. Washington, DC, Natl. Acad. Press in 2003).

RESULTS

We examined the discharge patterns of 25 neurons (10, 3, 9 and 3 in monkeys \( O, R, T, \) and \( W \), respectively) that were located caudolateral to the abducens nucleus. All lay in an area where our previous anatomical study had labeled a high percentage of somata after HRP injections into the contralateral abducens nucleus (Langer et al. 1986). We also had demonstrated previously that many neurons in this same area had PVP discharge characteristics, produced monosynaptic spike-triggered averages in the contralateral lateral rectus muscle, and were activated monosynaptically from the eighth nerve (Scudder and Fuchs 1992). Therefore we conclude that the majority of the PVP neurons reported in this study lay in the ventrolateral vestibular nucleus and that most probably participated as interneurons of a three-neuron vestibulocochlear pathway.

First we will describe the behavior of these neurons with the head restrained from moving (head-fixed) to establish that all behaved like the traditional PVP neurons that have been described in the literature (McCrea and Gdowski 2003; Scudder and Fuchs 1992). Then we will describe their behavior when the head was free to turn (head-free) and to participate in large shifts in the direction of gaze.

Head-fixed discharge characteristics

All 25 of our neurons responded during en bloc rotation of the monkey toward the recording site, showed a steady firing rate that increased in frequency with increasing contraversive eye position, and ceased firing or paused for ipsiversive saccades. The head-velocity sensitivity, taken as the modulation that occurred during suppression of the VOR at frequencies between 0.4 and 0.5 Hz (peak head velocities of 25.1–31.4°/s), averaged 0.80 ± 0.39 (SD) spikes/s per °/s for 19/25 neurons that provided adequate suppression data; the average phase lead was 10.55 ± 7.90° SD. The passive head-velocity sensitivity of these neurons, therefore is similar to that which we reported earlier (1.04 ± 0.85 spikes/s°/s with an average phase lead of 10.7 ± 10.4°; Scudder and Fuchs 1992). The steady firing rate increased linearly with contraversive eye position with an average slope of 1.52 ± 0.69 spikes/s° (r = 0.86 ± 0.07). Again, this slope is similar to that which we reported previously (1.73 ± 0.93 spikes/s°) (Scudder and Fuchs 1992). With the eyes straight ahead, the average firing rate for our PVP neurons was 88.33 ± 35.50 spikes/s.

With the head fixed, all of our 25 neurons showed a complete pause throughout the duration of ipsiversive head-fixed saccades with amplitudes >5°, the smallest size tested for all neurons. Behavior during contraversive saccades varied from unit to unit. Twelve units showed no pause for contraversive saccades, 10 neurons showed a partial pause, usually only for large saccades, and 3 paused completely for contraversive saccades of all sizes.

Head-free discharge characteristics

FULL-PAUSE PVPS. With the head free to rotate, the majority of PVP units in our current sample (21/25) exhibited a pause that usually lasted throughout the duration of the eye-movement component of an ipsiversive gaze shift. Figure 1 illustrates this behavior for an assortment of gaze shifts of different sizes with the associated rasters sorted from top to bottom according to increasing eye-movement duration. The top rasters are associated with gaze shifts that had little or no head-movement component, whereas the rasters toward the bottom are associated with gaze shifts that all required a head component. There was no qualitative difference in the pause behavior for small and large gaze shifts. Furthermore, the sorting with eye-movement duration indicates that the duration of the pause exhibited a qualitative increase with the duration of the eye component.

Similar data obtained in another monkey show that although this animal’s gaze shifts generally were slower, pause behavior clearly was similar for all gaze shifts whether or not head movements were employed (Fig. 2). Again, pause duration appeared to increase with the duration of the eye saccade.
The relation between the duration of the pause and the duration of the eye component is shown directly in Fig. 3. For the units illustrated in Figs. 1 (Fig. 3A) and 2 (Fig. 3B), pause duration was linearly correlated with saccade duration (□) with slopes of 0.93 and 1.16, respectively, and these relations describe the data extremely well ($r^2 = 0.99$ and 0.97, respectively). These high correlations are the result of a combination of the timing of the beginning and end of the pause relative to saccade onset. As anticipated from the data in Figs. 1 and 2, the lead time of the pause was relatively constant as the duration of the eye saccade increased. For all our neurons, pause onset relative to saccade onset ranged from little variation with saccade duration (Fig. 3B, ○) to a slight decrease (Fig. 3A). On average, the slope of the relation for such PVP neurons was $-0.03 \pm 0.03$ ($n = 21$). Thus for a 10-fold increase in eye duration from 30 to 300 ms, this relation would produce an average decrease in the lead time of the pause, and hence pause duration, of 7.29 ms. In contrast, the timing of the end of the pause relative to saccade onset increased with eye duration at essentially the same rate as did pause duration (Fig. 3, □). When the timing of pause onset did not vary with eye duration, as for the unit in Fig. 3A, the pause end time relation increased faster than the pause duration relation to compensate.

The tight relation between the end of the eye saccade and the end of the pause also can be demonstrated by aligning the histograms of Fig. 1 and 2 on the end of the eye movement. As shown in Fig. 4, the pause for our two exemplar neurons was complete throughout the eye saccade of a gaze shift, and firing resumed slightly before or after the end of the eye movement. For the unit in Fig. 4A, the pause ended, on average, 7.85 ± 5.70 ms before the end of the eye saccade, whereas for the unit in Fig. 4B, it ended 5.11 ± 22.74 ms after the eye saccade.

We have summarized the timing data for all of our 25 neurons by plotting the timing of pause end relative to eye end (eye end latency) as a function of the slope of the pause duration versus eye duration relation (Fig. 5). The data separate reasonably well into two groups. For 21 neurons, the average eye end latency exceeded −20.6 ms, and the slope of the pause duration versus eye duration relation exceeded 0.73. For 15 of the 21, the pause lasted, on average, at least until the saccade ended (mean eye end latencies ≥0). For the entire population of 21 neurons, these PVPs resumed firing an average of 13.11 ± 19.87 ms after the saccade landed. We therefore call these 21 neurons full-pause PVPs.

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When the pause lead decreased with eye duration, as for the unit in Fig. 3A, the pause end time relation increased faster than the pause duration relation to compensate.

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Many gaze shifts end with the end of the eye saccade. When they do not, it is because the eye movement does not move beyond a certain position in the orbit (i.e., it “plateaus,” but gaze continues toward the target on the back of the head movement or because gaze continues toward the target as a glissade (Freedman and Sparks 1997; Phillips et al. 1995). In either case, the gaze movement ends after the eye saccade. In the current study, the pause of 21 of 25 neurons ended, on average, after the saccade but before the end of the gaze shift by 8.16 ± 10.8 ms, on average.

PARTIAL-PAUSE PVPs. For 4 of the 25 PVP neurons recorded in this study, the average eye end latency was −45 ms, and the slope of the linear regression of pause duration with eye movement duration was <−0.55 (Fig. 5). Because the pause ended well before the end of both the eye and gaze movements, we describe their pause as partial. These four partial-pause PVPs resumed firing an average of 61.1 ± 15.18 ms before the saccade ended and 75.82 ± 12.57 ms before the end of the gaze shift.

The behavior of these partial-pause PVPs differed qualitatively from that of the full-pause neurons illustrated in Figs. 1–4. Figure 6 shows data for a typical partial-pause PVP in the monkey that made the smallest head movements. In this recording, most gaze shifts were either small (<12°) or large −50°. Although the monkey’s 50° gaze shifts varied substantially in duration by almost 100 ms (Fig. 6A, from \( \langle \rangle \) to \( \langle \rangle \)), there was no commensurate change in pause duration for the associated rasters, which again are ordered from top to bottom according to increasing eye movement duration. That the pause did not continue through the entire eye saccade becomes quite obvious when the rasters are aligned on saccade end (Fig. 6B). As eye duration increases from top to bottom, the pause of this PVP ends ever earlier. Whereas there was only occasional encroachment of spikes into the eye component of a full-pause neuron, cf., Fig. 4B, this partial-pause neuron exhibited a pause that was substantially shorter than eye-movement duration for all longer-duration eye saccades. Note that the presence of spikes during the eye saccade also occurred for smaller gaze shifts. These firing patterns are similar to those associated with the majority of PVPs recorded by Roy and Cullen (1998; their Fig. 3).

As might be expected from the rasters in Fig. 6, the pause of a partial-pause neuron is poorly related to eye-movement duration. Figure 7 shows plots of pause duration as a function of horizontal saccade duration (HED). All 6 data sets are fit with linear regressions: ---, pause duration and pause start time plots; - - - , pause end time plots. In A, the equations are: 0.99 HED + 4.38 (\( r^2 = 0.99 \)), −0.03 HED + 11.39 (\( r^2 = 0.25 \)), and 1.02 HED − 7.83 (\( r^2 = 0.99 \)) respectively. In B, the equations are: 1.16 HED − 7.72 (\( r^2 = 0.97 \)), −0.01 HED + 8.57 (\( r^2 = 0.02 \)), and 1.16 HED − 16.08 (\( r^2 = 0.97 \)), respectively.

Many gaze shifts end with the end of the eye saccade. When they do not, it is because the eye movement does not move beyond a certain position in the orbit (i.e., it “plateaus,” but gaze continues toward the target on the back of the head movement or because gaze continues toward the target as a glissade (Freedman and Sparks 1997; Phillips et al. 1995). In either case, the gaze movement ends after the eye saccade. In the current study, the pause of 21 of 25 neurons ended, on average, after the saccade but before the end of the gaze shift by 8.16 ± 18.87 ms, on average.
of eye-movement duration for the unit in Fig. 6 (○), one of three units with similar behaviors recorded in monkey T and the single unit with a partial pause recorded in monkey O. For partial-pause neurons, pause duration increased with shorter eye-movement durations after which it either reached a maximum and then declined (Fig. 7, □; 3 neurons) or appeared to saturate (Fig. 7, ●; 1 neuron) for longer durations. Also, for a
particular eye-movement duration, the associated pause durations were more variable than for typical full-pause neurons (compare Fig. 7 with Fig. 3). As might be expected from the data in Fig. 7, the average slope of a linear fit of the pause duration versus eye-movement duration relation was less for the four partial-pause neurons (0.35 ± 0.18) than for the full-pause neurons (1.04 ± 0.22) with $r^2$ values of 0.54 ± 0.51 and 0.91 ± 0.06, respectively. The pause-duration versus eye duration plots for the two partial-pause neurons illustrated in Fig. 7 are better fit with quadratic functions ($r^2$ values of 0.73 and 0.88 for the units recorded from monkeys T and O, respectively).

The partial-pause neurons also differed with regard to their sensitivity to eye position with the head fixed. The average slope of their rate-position relations (0.73 ± 0.23 spikes/s/°) was less than half that of full-pause neurons (1.67 ± 0.64 spikes/s/°). On the other hand, there was no difference in the vestibular sensitivity or pause lead times between the two types of PVPs.

Partial-pause neurons do not seem to be segregated anatomically from full-pause neurons. In one monkey (T), we recorded three partial-pause neurons and six full-pause neurons. Within the limits of our placement accuracy, we estimate that we recorded all nine PVPs on tracks that lay within 250 μm of each other in the anterior-posterior and medial-lateral dimensions. Furthermore, on one track, we recorded a full-pause neuron just 600 μm deeper than a partial-pause neuron.

OBSERVATIONS CONCERNING THE OCCURRENCE OF A PARTIAL PAUSE. Some insight regarding the source of signals that cause a pause to end early in a gaze shift can be obtained by considering the idiosyncratic gaze-shifting behavior of our individual monkeys. The gaze shifts of two monkeys occasionally exhibited an eye-movement plateau where the eye stayed at a fixed eccentricity in the head while the gaze movement continued to the target on the back of the head movement. As the gaze shift ended, the eye began to counter-rotate. For the nine neurons recorded during some eye-movement plateaus, we determined the SDs of the time that the pause ended relative to the end of the eye movement and relative to the start of eye counter-rotation. For seven of the nine, the end of the pause showed the lowest variability with the beginning of eye counter-rotation ($F$ test for difference in variances; $P < 0.05$). We argue in the DISCUSSION that this more consistent timing of the end of the pause with the onset of eye counter-rotation implicates the brain-stem saccade generator and therefore signals associated with eye rather than head velocity.

As mentioned in the preceding text, monkey T accomplished its gaze shifts with very small head movements, relying mostly on saccadic eye movements. Furthermore, its saccadic gaze shifts occasionally were rather slow. In five of six full-pause neurons in monkey T, even slow saccades were accompanied by complete pauses. However, in the remaining full-pause neuron, the pause associated with some gaze shifts ended well before the eye movement ended. On those trials, the eye velocities were rather slow with lengthy deceleration phases. In Fig. 8, we show seven such low-velocity saccades in comparison with two brisk saccades with symmetrical acceleration and deceleration phases; all are aligned on the end of the saccade and are presented in order (top to bottom) of increasing eye-movement duration. For the two brisk gaze shifts, the pause ended just before the end of the saccade. For the seven slow gaze shifts, the end of the pause appears to reflect the rate of eye deceleration. For example, the saccades identified as 1 through 3 show increasingly slower decelerations that reached comparable low velocities earlier and earlier in the gaze shift and their associated pauses also ended earlier and earlier. Head movements in these trials had total amplitudes of $<5°$.

At the insistence of the reviewers and section editor, we used the procedure of Roy and Cullen (1998, 2002) to fit the discharge of our neurons during a gaze shift even though, as we have emphasized repeatedly, 84% of our PVPs cease firing completely during the movement so there is little, if any, data to fit in the intra-saccadic interval. Figure 9A illustrates the success of Eq. 1 (METHODS) in fitting the instantaneous firing rates of gaze shifts from a representative full-pause PVP (O 37:3). For the $\sim22°$ gaze shift in A1, the fitted firing rate (red curve), an average from 19 similar trials in this block, is a poor match (VAF = 30.6%) to the spike density function, which, in this trial, is the result of only three spikes (thick green vertical lines) at the end of the intra-saccadic interval. In the intra-saccadic intervals of all of the 19 trials in this block, a total of only 19 spikes contributed to the average fit. The fit is even more problematic for; large gaze shifts ($\sim65°$) with a substantial head movement (A3). Here, the fitted firing rate, an average from 19 similar trials in this block, again is a poor match...
the number of spikes per trial occurring during saccades >20° ranges from 0.0 to 3.3 with a median of 0.33 spikes/trial. Moreover, a fit based on the intra-saccadic behavior (thin red line) consistently falls way short of describing the peri-saccadic behavior (gray lines).

Figure 9B shows an application of the fitting procedure in Eq. 1 to a partial-pause neuron (T 162/1). For the approximately 55° gaze shift in B, the fitted firing rate (red curve), based on 11 similar trials in this block, follows the main outline of the spike density function even though the fit still is a relatively poor match (VAF = 51.4%); the analysis here is based on 233 spikes in the intra-saccadic intervals of 11 trials (23 in the trial shown). By comparison, similar analyses applied during VOR suppression in the post-saccadic period yielded a VAF between 35 and 50%. Again, the fit based on the intra-saccadic data (thin red line) does not capture the peri-saccadic behavior (gray lines). Moreover, unlike the PVPs described by Roy and Cullen (1998, 2002), the contribution of the head-velocity term, i.e., \( k_4 \), did not change with the size of the gaze shift for our partial-pause neurons. For example, for the unit in Fig. 9B, \( k_4 \) for gaze shifts with means of 10, 45, and 54° was 0.94, 0.83, and 1.07 spikes/°, respectively; the relation between the head-velocity coefficient and gaze-shift amplitude was not significant. The relations for the remaining three partial-pause neurons also were not significant. Moreover, the fitted discharge profiles over the duration of the saccade resembled eye rather than head velocity.

**DISCUSSION**

We have shown that the vast majority (84%) of type I PVPs in the vestibular nuclei of the rhesus macaque exhibit a complete cessation of activity throughout the entire eye-movement component of an ipsiversive gaze shift. Our data indicate that the same tight relation between the end of the pause and the end of the eye movement is maintained whether or not the gaze shift is accomplished with the participation of a head movement. Others have presented similar results for the squirrel monkey (McCrea and Gdowski 2003). Type I PVPs receive monosynaptic excitation from the ipsilateral vestibular nerve and project monosynaptically to the contralateral abducens nucleus (Scudder and Fuchs 1992). Therefore they constitute one of the interneurons in the excitatory three-neuron VOR pathway. The complete pause in our PVPs occurs for large gaze shifts that only can be accomplished with a head movement. In contrast, when similar head rotation is produced passively by whole-body rotation, type I PVP neurons show a substantial vestibular modulation that increases with ipsiversive head velocity. The complete absence of unit modulation during a rapid gaze shift accomplished with the participation of an ipsiversive head movement indicates that the vestibular component of PVP discharge is completely turned off for the duration of the saccade component of the gaze shift.

On the basis of the data presented here, we conclude that if the VOR is modulated during head-free gaze shifts, that modulation is not the result of a head-velocity signal that leaks through the pause of the full-pause neurons, which constitute the majority of type I PVPs. Furthermore, it seems highly unlikely that the putative VOR modulation is controlled by the much smaller percentage of partial-pause PVPs. Instead, if modulation of the VOR does indeed occur, we suggest that it...
would have to result from modulation of the activity of other VOR interneurons in the vestibular nuclei. One possibility would be neurons that discharge for both eye and head velocity, some of which also are interneurons in the ipsilateral three-neuron VOR pathway (McCrea and Gdowski 2003; Scudder and Fuchs 1992). Of course, vestibular signals also might be delivered to the abducens nucleus over polysynaptic pathways with more than three neurons. Finally, it should be cautioned that the conclusion that the VOR is modulated at all during the monkey VOR is not secure. In the three studies that have applied small head perturbations to test VOR efficacy during a gaze shift, one mentions the difficulties of producing head perturbations during small gaze shifts (Tomlinson and Bahra 1986), a second finds that the effects of perturbations vary from little to modest from subject to subject (Cullen et al. 2004), and a third reports no VOR modulation at all (Freedman et al. 1998).

As we mentioned earlier, Roy and Cullen (1998, 2002) posit that the firing rate modulation of PVPs during ipsiversive gaze shifts is the result of a head-velocity signal. In contrast, we suggest that the pause in all of our PVP neurons, partial and full pause alike, reflects an eye- and not a head-velocity signal. First, in the monkey that made little head movement during large gaze shifts, we still found partial-pause PVPs—indeed three of the four we recorded. Second, in that same animal, on the infrequent trials where a truncated pause occurred for one full-pause PVP, the end of the pause occurred earlier on those trials where eye deceleration, the rate of change of eye velocity, was slower (Fig. 8); note that in the examples of Fig. 8, the total head movements were <5° in amplitude and therefore the head contribution during the gaze shift itself was even less. Finally, it is clear from a comparison of the data in Figs. 4 and 6 that the partial-pause PVPs resumed firing during the saccade when eye velocity was high, and full-pause PVPs resumed their discharge toward the end of the saccade, when eye velocity was much lower. This observation could be explained if there were a common source of eye-velocity-related inhibition to both the full- and partial-pause PVPs, and the efficacy (gain) of the inhibition to the full-pause neurons was very high and that to the partial-pause neurons was low. In this scenario, even when the eye velocity was quite low at saccade end, the low-eye-velocity signal would be multiplied by a high gain and the pause of the full-pause neurons would be maintained. In contrast, to produce a sufficient inhibitory signal to maintain the pause of a partial-pause neuron, the eye velocity would have to be much higher, causing the pause to end during the saccade.

What could be the source of an eye-velocity input to PVPs during gaze shifts? In the animals that exhibited delayed counter-rotation of the eye because of eye-movement plateaus, the end of the pause was delayed to occur near the onset of eye counter-rotation. The end of the pause of omnidirectional pause neurons (OPNs), which, because they cease firing for the duration of saccades in all directions, are thought to control the firing of saccadic burst neurons (Scudder et al. 2002), also is best tied to the onset of eye counter-rotation during gaze shifts (Phillips et al. 1999). Therefore it seems reasonable to suggest that the pause of type I PVPs is primarily the result of an inhibitory signal from the saccadic burst generator (Scudder et al. 2002) and that the time course of inhibition reflects eye velocity. Indeed, when the pause of PVPs is modeled, it is the eye-velocity term in the equation that accounts for the cessation of firing during ipsiversive gaze shifts (Roy and Cullen 2002; their Fig. 2).

The most likely candidate in the burst generator to provide such a signal during a gaze shift would be an inhibitory burst neuron (IBN), the firing rate of which closely resembles instantaneous eye velocity, e.g., Cullen and Guitton (1997). Although the known IBNs, which are located caudal to the abducens nucleus, project strongly to the ventrolateral vestibular nucleus (Strassman et al. 1986), the projection is crossed and thus would be expected to provide inhibition for contra- versus not ipsiversive saccades. Therefore at present, we cannot identify the putative burst neurons that, we suggest, provide the firing rate modulation of PVPs during ipsiversive gaze shifts.

Our data and conclusions differ from those of Roy and Cullen, who wrote “none of the PVP neurons in our sample paused for the entire duration of ipsilaterally directed gaze shifts. In fact, for many neurons, activity resumed before the completion of the ocular saccade component of a gaze shift” (Roy and Cullen 1998). In contrast, 15 of 21 of our frequently encountered full-pause neurons ended their pauses, on average, at or after the end of the eye saccade. It was only the occasionally encountered partial-pause neurons that had a pause that ended well before the saccade did. Roy and Cullen (1998) also concluded “the head-velocity signal carried by VOR pathways is reduced during gaze shifts in an amplitude-dependent manner.” Their PVPs showed little pause for small gaze shifts of ~25°, which had durations between 60 and 70 ms (their Fig. 3). In contrast, our neurons typically showed frank pauses for eye saccades of this duration, indicating that neither a vestibular signal nor any other signal was being supplied over our PVPs during these gaze shifts.

We are at a loss to explain the difference in the data from our study and theirs. All of the neurons considered here were definitely type I PVPs because we subjected them to the strict criteria that define their behavior in the literature (McCrea and Gdowski 2003; Scudder and Fuchs 1992). Furthermore, although we did not confirm their connections electrophysiologically, we believe that many of our PVPs were interneurons of the direct VOR because their reconstructed anatomical locations placed them in or near the VLVN, the vestibular nucleus that houses the highest density of PVPs projecting to abducens motoneurons (Scudder and Fuchs 1992). It may be that there are at least two populations of PVP neurons with different discharge patterns, and possibly different functions, during a gaze shift. However, it seems unlikely that the minority partial-pause neurons alone constitute the substrate for the control of the VOR when the head is free. Moreover, even if the pause in a small number of PVPs is partial, it is unlikely that the encroaching spikes during a gaze shift are the result of a head movement because most of our partial-pause neurons were recorded in the animal that made the smallest head movements.

Modeling our data with the equation used by Roy and Cullen (1998, 2002) did not resolve the discrepancy. First, for the majority (84%) of our PVP neurons, the fits were based on very few spikes in the intra-saccadic interval so any conclusions based on such modeling results are suspect. Of course, the partial-pause neurons did at least provide some data in the intra-saccadic interval to fit. Although the fits of the four partial-pause neurons have VAFs comparable to those of Roy...
and Cullen (1998, 2002), our calculated head-velocity sensitivities do not exhibit the decreases with gaze amplitude that they report. Indeed, our data show no significant change in head-velocity sensitivity with gaze amplitude. Therefore even our partial-pause neurons do not behave like their PVPs. Finally, for the partial-pause neurons, our fits strongly resemble the time course of eye velocity, e.g., Fig. 9B, suggesting, as we do, that the intra-saccadic firing rate may indeed be the consequence of an inhibitory eye-velocity signal.

Finally, it is possible that the disparate results of the two studies may be due to differences in methodology. Whereas the data of Roy and Cullen (1998, 2002) were recorded with the head completely unrestrained, ours were obtained during head movements constrained to rotate about a vertical axis. However, there is no difference in the characteristics of the overall gaze shift or the relative contributions of the eye and head components to a gaze shift whether the head is completely free or constrained to rotate about a vertical axis (Freedman and Sparks 2000). Furthermore, the discharge characteristics of other brain stem neurons, such as abducens motoneurons, are similar under both conditions (Cullen et al. 2000; Ling et al. 1999). Therefore we consider that differences in methodology provide an unlikely explanation for the discrepant results.

We conclude that those type I PVPs that are one of the interneurons of the VOR pause throughout the eye saccade of ipsiversive gaze shifts whether the head is fixed or free. The exact characteristics of the pause are probably controlled by an inhibitory input from burst neurons that discharge with eye velocity and do not reflect the PVP’s excitatory input related to head velocity.

Acknowledgments

We are grateful for the incisive comments of C. Kaneko, F. Robinson R. Soetjedo, and A. Weiss on an early version of this manuscript and for the deft editorial manipulations of K. Elias.

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