Horizontal Vestibuloocular Reflex Evoked by High-Acceleration Rotations in the Squirrel Monkey. I. Normal Responses

LLOYD B. MINOR, DAVID M. LASKER, DOUGLAS D. BACKOUS, AND TIMOTHY E. HULLAR

Departments of Otolaryngology—Head and Neck Surgery, Biomedical Engineering, and Neuroscience, The Johns Hopkins University, Baltimore, Maryland 21287-0910

Minor, Lloyd B., David M. Lasker, Douglas D. Backous, and Timothy E. Hullar. Horizontal vestibuloocular reflex evoked by high-acceleration rotations in the squirrel monkey. I. Normal responses. J. Neurophysiol. 82: 1254–1270, 1999. The horizontal angular vestibuloocular reflex (VOR) evoked by high-frequency, high-acceleration rotations was studied in five squirrel monkeys with intact vestibular function. The VOR evoked by steps of acceleration in darkness (3,000°/s² reaching a velocity of 150°/s) began after a latency of 7.3 ± 1.5 ms (mean ± SD). Gain of the reflex during the acceleration was 14.2 ± 5.2% greater than that measured once the plateau head velocity had been reached. A polynomial regression was used to analyze the latency of the responses to steps of acceleration. A better representation of the data was obtained from a polynomial that included a cubic term in contrast to an exclusively linear fit. For sinusoidal rotations of 0.5–15 Hz with a peak velocity of 20°/s, the VOR gain measured 0.83 ± 0.06 and did not vary across frequencies or animals. The phase of these responses was close to compensatory except at 15 Hz where a lag of 5.0 ± 0.9° was noted. The VOR gain did not vary with head velocity at 0.5 Hz but increased with velocity for rotations at frequencies of ≥4 Hz (0.85 ± 0.04 at 4 Hz, 20°/s; 1.01 ± 0.05 at 100°/s, P < 0.0001). No responses to these rotations were noted in two animals that had undergone bilateral labyrinthectomy indicating that inertia of the eye had a negligible effect for these stimuli. We developed a mathematical model of VOR dynamics to account for these findings. The inputs to the reflex come from linear and nonlinear pathways. The linear pathway is responsible for the constant gain across frequencies at peak head velocity of 20°/s and also for the phase lag at higher frequencies being less than that expected based on the reflex delay. The frequency- and velocity-dependent nonlinearity in VOR gain is accounted for by the dynamics of the nonlinear pathway. A transfer function that increases the gain of this pathway with frequency and a term related to the third power of the nonlinear pathway. A transfer function that increases the gain of the system with frequency and a term related to the third power of the nonlinear pathway. A transfer function that increases the gain of the system with frequency and a term related to the third power of the nonlinear pathway. A transfer function that increases the gain of the system with frequency and a term related to the third power of the nonlinear pathway.

INTRODUCTION

The response dynamics of the angular vestibuloocular reflex (VOR) have been most extensively studied for a relatively limited range of lower frequencies and accelerations of head movement. The eye movements in monkeys produced in response to such rotations have a phase and gain (when accounting for the effects of vergence) that are approximately compensatory for head movements over the range of 0.2–4.0 Hz (Böhmer and Henn 1983; Paige 1983; Telford et al. 1996). The frequencies and accelerations of angular head movements over which the VOR is needed to produce gaze-stabilizing eye movements extend to considerably more dynamic stimuli. For example, running produces head movements with substantial energy in the power spectrum over the range of 8–20 Hz (Grossman et al. 1988). Because motion of images on the retina at velocities as low as 3–5°/s can produce oscillopsia (Demer et al. 1994), it would be useful for the VOR to produce compensatory eye movements for this higher range of stimuli. This need is reinforced by the observation that visual following mechanisms operate at significantly longer latencies than the VOR, thereby precluding their utility in stabilizing gaze during such rapid movements (Martins et al. 1985).

The VOR appears to function well for these more dynamic stimuli. The gain of the reflex in humans for responses to brief, unpredictable, steps of acceleration is close to or slightly >1.0 (Aw et al. 1996; Collewijn 1998)—a marked contrast to the VOR elicited by less dynamic stimuli where the gain has been reported to vary from 0.6 to 0.8 (Wall et al. 1984). Because these more dynamic stimuli include accelerations between 2,000 and 4,000°/s² and frequency components ≤15 Hz, investigations and models of vestibuloocular processes need to extend to this range of stimuli.

The dynamics of the VOR over the lower and middle range of frequencies and velocities of sinusoidal head movement have been modeled with linear transfer functions (Paige 1983; Robinson 1981). The comparatively few studies exploring responses to rotations of higher frequency, acceleration, and velocity in monkeys (Böhmer and Henn 1983; Keller 1978) and in humans (Das et al. 1995; Tabak and Collewijn 1994; Tabak et al. 1997) have led to findings that are sometimes conflicting and that cannot always be explained based on traditional linear models.

A complete description of the response dynamics of the VOR over the frequency range of naturally occurring head movements will require a comparison of responses to steps of acceleration with those to sinusoidal rotations. Such data have been related for a lower range of frequencies and/or accelerations (Minor and Goldberg 1991; Raymond and Lisberger 1996) with the findings for both types of stimuli being predicted based on linear transfer functions. Responses to steps of acceleration have been compared with those to sinusoidal rotations delivered with a reactive torque helmet in humans (Tabak and Collewijn 1994; Tabak et al. 1997). The gain of the VOR rose with frequency up to a maximum of 1.2 at 20 Hz, and phase lag (thought to be related to the latency of the reflex) increased with frequency up to a 45° lag at 20 Hz. Such
findings would not be predicted based on the linear transfer functions that traditionally have been used in models of the VOR: either the gain would be predicted to rise with frequency while phase lag remained low or gain would be predicted to remain constant while phase lag increased with frequency (Minor and Goldberg 1991). These issues are made more complicated by findings from other studies suggesting that inertia of the eye, independent of neural mechanisms, may be responsible for eye movements that are compensatory for head movements at higher rotational frequencies and accelerations (Khater et al. 1993; Vercher et al. 1984).

The goal of this study was to define the dynamics of the horizontal VOR evoked by yaw rotations for a higher range of frequencies and accelerations. Responses to steps of angular acceleration at 3,000°/s² and to sinusoidal rotations ±15 Hz were studied. Visual following mechanisms were investigated in animals with and without vestibular function to define the contribution of these responses to vestibuloocular function for more dynamic stimuli. We show that ocular inertia has a negligible effect on responses to these stimuli. The VOR evoked by steps of acceleration and sinusoidal rotations displayed a frequency- and velocity-dependent gain increase that could not be predicted based on linear transfer functions. A model for the horizontal VOR evoked by rotations in the yaw plane with linear and nonlinear components is presented. The dynamic elements of each of these pathways were derived from the experimental data. As shown in the companion study (Lasker et al. 1999), the findings and model provide a basis for understanding changes in the reflex following unilateral vestibular lesions.

METHODS

Surgical preparation

Surgery was done under sterile conditions in seven adult squirrel monkeys anesthetized with inhalation of Halothane/nitrous oxide/oxygen. A head bolt was cemented to the occiput at a position such that the animal was pitched 15° nose-down relative to the horizontal stereotaxic plane when in the upright position. The horizontal semicircular canals are in the earth-horizontal plane when the head is in this position (Blanks et al. 1985; Minor and Goldberg 1990). A prefabricated search coil was implanted in the frontal plane about the limbus of each eye (Minor and Goldberg 1991; Paige and Tomko 1991), and the leads were soldered to plugs cemented to the skull.

Labyrinthectomy procedures were performed in separate surgical sessions after implantation of the head bolt and eye coils in two animals (G52 and R10). These procedures began on each side with a cortical mastoidectomy followed by successive obliteration of the horizontal, posterior, and superior semicircular canals. The sensory epithelium of each of these canals was removed. The vestibule was opened and the utriculus and sacculus were removed. Temporalis muscle and fascia were used to obliterate the mastoidectomy and labyrinthectomy cavities.

All surgical and other animal care procedures used in this study were done in accordance with a protocol approved by the Animal Care and Use Committee of the Johns Hopkins University School of Medicine.

Eye-movement recording

Experiments took place in an enclosed, light-isolated room. The animal was seated in a plastic chair, and the head was restrained by securing the implanted bolt to a chair-mounted clamp. The chair was placed in a superstructure mounted to the top surface of a rotation table capable of generating a peak torque of 100 ft-lb (125 N-m). The motion of this rotation system was controlled by a digital servomechanism with position feedback (Acutronic, Pittsburgh, PA). The horizontal VOR was tested with the animal seated in the upright position in the superstructure and aligned such that the horizontal canals were in the earth-horizontal plane of rotation. In some experimental sessions, D-amphetamine (0.2–0.3 mg/kg, im) was injected 15 min before recording eye movements.

Two pairs of field coils, 45 cm side length, were rigidly attached to the superstructure and moved with the animal. The horizontal field oscillated at 50,000 Hz and the vertical field at 75,000 Hz. Voltages induced in the scleral search coils were monitored by a detection circuit (Remmel Labs) that extracted signals proportional to horizontal and vertical eye position. The peak-to-peak noise at the output of the circuit was equivalent to an eye movement of 0.02°. All signals transducing motion of the head or the eye were passed through eight-pole Butterworth anti-aliasing filters with a corner frequency of 100 Hz. These signals then were digitized by 16-bit A/D converters interfaced to a PC-486 microcomputer. A sampling rate of 1,000 Hz was used for acceleration steps and sinusoidal rotations at frequencies ≥2 Hz. A sampling rate of 200 Hz was used for sinusoidal rotations <2 Hz.

The eye-coil system was calibrated in two ways. A search coil identical to the one implanted about each eye was placed in a gimbal located where the animal’s head is positioned in the field coil. This search coil then was moved to angles of 5, 10, and 15° right-left and up-down with respect to center and calibration factors relating volts to degrees were determined. The second method involved sinusoidal rotation of the animal in light at 0.5 Hz, ±60°/s, a stimulus in which the gain of the visual-vestibuloocular reflex has been shown to be 1.0 (Minor and Goldberg 1990; Paige 1983). Calibration factors obtained from these methods typically agreed to within 5%.

The onset of the head movement was further confirmed in two ways. A linear accelerometer was mounted on the superstructure eccentric to the animal’s head. A search coil identical to the one implanted on the animal’s eye was attached to a rod made of phenolic that extended from the ceiling through the middle of the field. This earth-fixed search coil was located in the center of the field. The onset points measured from the accelerometer trace, the earth-fixed coil, and the servomechanism on the rotator agreed to within 1 ms.

It was particularly important to measure any motion of the head relative to the field coils in analysis of responses to steps of acceleration. For this purpose, an identical search coil was implanted on the acrylic securing the animal’s head bolt directly superior to the right eye. For determination of latency in animals with intact vestibular function and for evaluation of responses to steps of acceleration after bilateral labyrinthectomy (both of which involve analyses of small eye movements), the head-fixed coil signal was subtracted from the eye movement signal to obtain a corrected representation of the eye movement.

Rotational testing

Responses to steps of acceleration (3,000°/s²) acceleration to a peak velocity of 60 or 150°/s followed by a plateau of head velocity lasting 0.9–1.1 s and then deceleration at 3,000°/s² to rest) were recorded with animals in darkness. The acceleration magnitude, direction, duration, and interstimulus interval were varied randomly from one trial to the next.

Sinusoidal head rotations (0.5–15 Hz, peak velocity 20–150°/s) were given with animals in darkness and in light with a patterned visual surround located 1 m in front of the animal. Each stimulus frequency was given for 60 s. The order in which different frequencies and velocities were tested as well as the trials performed in darkness and in light were varied.

The possible role of predictive mechanisms in responses of the
VOR in darkness was investigated with a sum-of-sines stimulus. The component frequencies in this stimulus were 1, 3, 7, and 15 Hz with each having a peak velocity of 17°/s.

Relating steps of acceleration to sinusoidal rotations

We needed to determine the relative frequency components of the steps of acceleration to relate these stimuli to the sinusoidal rotations. Our goal was to define the sinusoidal frequencies that directly related to the steps of acceleration.

Figure 1A displays the head velocity signal for the 3,000°/s² rotations that reached a peak velocity of 150°/s. We used a Hamming-windowed, linear-phase filter with an order of 1,000 (finite-impulse-response filter) and varied the corner frequency between 4 and 40 Hz. This filter was designed from the fir1 function in Matlab (The Math Works, Natick, MA). The frequency-response characteristics for the various corner frequencies are shown in Fig. 1B. The goal of this analysis was to identify the change in the signal as the corner frequency was changed. Lines were fit to the head velocity signal during the period of 20–40 ms into the response (indicated by the line on the abscissa in Fig. 1A) and to the eye velocity signal during this same interval. An acceleration gain was calculated for each corner frequency from the ratio of the slopes of the lines fit to the eye and head velocity signals. These values for acceleration gain were calculated from each of the following corner frequencies: 4 Hz, 0.39; 8 Hz, 0.77; 15 Hz, 1.12; 20 Hz, 1.07; and 40 Hz, 1.00.

These findings indicate that frequencies up to 15 Hz are important for forming the trajectory of the head velocity stimulus.

Data analysis

The data were analyzed off-line using software that we wrote in the Matlab (The Math Works) programming environment.

ACCELERATION STEPS. The analyses reported here were obtained mainly from the responses to 3,000°/s² steps of acceleration that reached a peak velocity of 60 or 150°/s. The eye-position data were first passed through a 50-point, finite-impulse-response filter with a corner frequency of 100 Hz (to calculate latency) or 40 Hz (to assess dynamics of the response). Eye velocity was obtained from a seven-point central difference algorithm. The data from 10 to 30 trials in each direction were averaged to obtain a characterization of the response. All data were taken before the first fast phase.

Response latency was measured by two techniques. First, in the linear fit method, head and eye velocity signals from each trial in each direction for an individual animal were fit with lines. Points over the interval of 20–40 ms after the onset of the command signal were used to determine each line. The difference in intercept on the head velocity axis of each line was defined as latency. Second, in the 3-SD method, the mean and standard deviation of eye and head velocity signals were measured during the 20-ms interval before the onset of the command signal to the rotation table. The onset of the head and eye movements were determined to be the points at which the velocity signals deviated from the mean value measured before onset of the stimulus for head and eye velocity, respectively, by >3 SD. The difference in these two onset points measured for each trial was defined as response latency.

The initial VOR during the step of acceleration was evaluated with linear and polynomial fits relating eye to head velocity. An average response from the steps of acceleration was obtained from 10 to 30 trials in each direction. The averaged eye and head velocity data beginning at 10 ms into the response were aligned at the origin to compensate for the effects of the latency of the reflex. The traces for the rightward rotations were then concatenated with those for the leftward rotations. First- through fifth-order polynomial fits were then made to head and eye velocity data extending from 10 to 40 ms after the onset of the stimulus. The order of the polynomial necessary and sufficient to account for the trajectory of the response was specified by the Bayesian information criterion (BIC) (Cullen et al. 1996; Galiana et al. 1995). This analytic method takes into account the decrease in the difference between the fit and the data that will occur simply from the addition of high-order parameters to the model and weighs this decrease against the order of the model (Schwarz 1978). A reduction in BIC value justifies the use of a more complex (higher order) model, whereas an unchanged or increased value of BIC indicates that no additional information is obtained from an increase in the complexity of the model.

The relationship between the stimuli for these steps of acceleration and the responses that were recorded is inherently better represented by an odd-order polynomial. On the basis of the direction conventions that we have used, a positive head velocity will give rise to a positive eye velocity and vice versa. Therefore the data always will be located in the first and third quadrants and will be better fit by odd-rather than even-order polynomials. Asymmetries in responses to rotations in one direction in comparison with the other would lead to larger values for coefficients of the even-order terms in the polynomial fit to the data.

Measurements of the gain of the VOR also were made during the step of acceleration and after the plateau of head velocity had been reached. The acceleration gain of the VOR, $G_A$, was measured for each trial as the ratio of the slope of a line through the eye velocity points to the slope of a line through the head velocity points during the latter portion of the step of acceleration. For the steps of acceleration that reached a maximum velocity of 150°/s, this period was 20–40 ms.

**FIG. 1.** A: head velocity signal ($H_v$) from acceleration steps of 3,000°/s² that reach a maximum velocity of 150°/s and the signals resulting from passing $H_v$ through finite-impulse-response filters with corner frequencies of 4, 8, and 15 Hz. Time period during which the stimulus and response were analyzed is indicated by the line projecting above the abscissa. B: frequency-response characteristics of these filters (same symbols as A).
after the onset of the stimulus when head velocity was increasing from 60 to 120°/s. For those that reached a maximum velocity of 60°/s, $G_A$ was measured during the period of 10–20 ms after stimulus onset when head velocity was increasing from 30 to 60°/s. The velocity gain of the VOR, $G_V$, was measured from the ratio of the mean eye and head velocity evaluated at 100–300 ms after the plateau head velocity had been reached for each trial. Both $G_A$ and $G_V$ were determined for the same trials used in the averages from which the linear and polynomial fits for the initial responses were made. For display of the data, fast phases were removed from each trace and an average response was calculated at each point based on the traces without fast phases at that point. This method avoided any distortion of the data due to interpolation or smoothing at the time of saccades.

SINUSOIDAL ROTATIONS. For responses to single-frequency stimuli, individual cycles of the data were defined by zero-crossings of the stimulus. Eye-position data were differentiated with a four-point central difference algorithm to obtain eye velocity. Saccades were removed from responses at frequencies <4 Hz and replaced with interpolated values obtained from a least-squares sinusoidal fit of the velocity record (Ichingolo and Spanio 1985). Responses at frequencies <4 Hz were not desaccaded, and only cycles without saccades were included in the analysis. Successful cycles (5–10 at 0.5 Hz, 10–35 at 2–6 Hz, and 25–75 at 8–20 Hz) were averaged. The amplitude and phase of the response fundamental were obtained from a Fourier analysis as were the corresponding values for the head-velocity signal. Gains and phases for eye re head velocity were expressed with the convention that a unity gain and zero phase imply a perfectly compensatory VOR. A negative phase indicates that eye movements lag head movements. A harmonic analysis was performed on the average cycle at each rotational frequency to determine any distortion in the stimulus or the response. Harmonic distortion of the stimulus was 9% at 15 Hz and was <5% at all other frequencies and velocities. This harmonic distortion at 15 Hz was principally due to an asymmetry in the velocities generated by the rotation motor (peak velocities were 6% greater for the rightward half-cycles in comparison with the leftward half-cycles). This difference in peak head velocity was taken into account in the determinations of gain and of response asymmetry.

We looked for a velocity dependence in these sinusoidal responses in a manner analogous to that used for the responses to steps of acceleration. The data were displayed as plots of eye versus head velocity. First- through fifth-order polynomials were fit to the data, and the order of the polynomial that was necessary and sufficient to account for the relationship between eye and head velocity was calculated with the BIC.

Responses to the sum-of-sines stimulus were analyzed by dividing the record into increments of 1 s and performing a Fourier analysis to measure gain and phase for each component frequency.

**Modeling of the VOR**

Mathematical models of the VOR were formulated in Simulink (The Math Works). The Dormand-Prince method with a fixed step size of 0.001 s was used for simulation of the ordinary differential equations. Fourier analysis was used to calculate gain and phase of the simulated responses to sinusoidal inputs.

**Statistical analysis**

Results were described as means ± SD. Data from two groups were compared with an unpaired $t$-test. ANOVA was used to compare data from more than two groups.

**RESULTS**

The horizontal VOR evoked by steps of head acceleration and by sinusoidal rotations was examined in five squirrel monkeys with intact vestibular function and in two squirrel monkeys after bilateral labyrinthectomy.

**Responses to steps of acceleration**

Steps of angular acceleration delivered with the animal in darkness evoked a robust VOR. Responses to 3,000°/s² acceleration steps were shown as eye position and velocity for leftward (Fig. 2, A and C) and rightward (Fig. 2, B and D) rotations. In this and all other figures depicting eye responses evoked by head rotations, the head movement signal was inverted in direction to facilitate direct comparison of traces representing motion of the head and the eye. The initial response consisted of a slow phase that was compensatory for head velocity followed by a fast phase that reset the eye toward the center of the oculomotor range. Successive slow and fast phases of nystagmus then followed.

Eye-velocity responses from seven stimulus repetitions are displayed as superimposed traces for rotations to the left (Fig. 3A) and right (Fig. 3B). The average of these responses to 30 stimulus repetitions in each direction are shown after the fast phases were removed in Fig. 3, C and D. There was little variability in the velocities or trajectories of the initial slow phase of the VOR during the period of the acceleration. The time of onset of the first fast phase did, however, differ between trials, and there was more variance in the gain of the VOR after the first fast phase.

The differences in the onset of the first fast phases could be predicted based on horizontal eye position immediately before onset of the rotation. The slow-phase components were longer in duration and in position amplitude when eye position at the start of the acceleration step was in the direction opposite to the slow phase evoked by the rotation. The relationship between initial eye position and amplitude of the first slow phase is shown in Fig. 4. The initial slow phase of the VOR evoked by the rotation was longer in duration when, immediately before the rotation, the eye was deviated in the direction opposite to that of the slow phase. As a consequence, the slow phase had

![Graphs](http://example.com/graphs.png)
a position amplitude, in terms of change in eye position before the first fast phase, that was dependent on eye position at the start of the rotation (Fig. 4A). Responses showed the same dependence on eye position for leftward and rightward rotations, therefore data for each direction were pooled. Eye position was plotted as deviation toward (positive values) or away from (negative values) the direction of the subsequent slow phase. The relationship between the amplitude of the initial slow phase ($L$) and starting eye position ($E_p$) was expressed in the following regression equation where the units of each parameter are degrees: $L = -0.56E_p + 8.0$, ($r = 0.8$).

### Latency

The initial responses in one animal used for calculating latency by the linear fit and 3-SD methods are shown in Fig. 5. For the five animals in the study, the latency measured with the 3-SD method was 7.4 ± 1.5 ms (rightward rotations) and 7.1 ± 1.5 ms (leftward rotations), whereas that measured from the linear fit method was 7.2 ± 1.8 ms (rightward) and 7.1 ± 1.8 ms (leftward). These differences between values with respect to the method of measurement and direction were not significant ($P > 0.6$). There was also no change in the measured value of latency when a method based on the intercept on the time axis for higher-order polynomial fits was used. Pooling the latency data in the five animals calculated by the 3-SD method gave a latency of 7.3 ± 1.5 ms.

To determine if the eye-movement responses we observed with the acceleration step stimuli were due to mechanisms other than a neurally mediated VOR (such as ocular inertia), we studied responses to steps of acceleration in two animals after bilateral labyrinthectomy. There were no discernible eye movements evoked by the steps of acceleration (3,000°/s²; duration of acceleration = 250 ms, peak head velocity = 750°/s) or by the sinusoidal rotations (0.5–15 Hz; peak velocity of 20–100°/s for rotations at 0.5–4 Hz and 20°/s for 6–15 Hz). Figure 6 displays averaged position records from the frontal search coil and from an identical coil mounted above the animal’s eye. These two signals were the same during the period of acceleration, indicating that the small (<0.15°) position deflection seen at the onset of the acceleration was due to mechanical factors such as vibration of the superstructure at the onset of the rotation and not to inertia of the eye.

### Dynamics

The initial VOR during the step of acceleration was evaluated with linear and polynomial fits relating eye to head velocity (Fig. 7). The coefficients for the first- through third-order fits as well as the fifth-order fit to the data records that were formed from concatenating responses to rightward and leftward rotations in each animal along with the mean squared error of each fit are presented in Table 1. The fit to the data differed little for a second-order (squared) in comparison with a first-order (linear) fit. This finding indicates that the responses are symmetric with regard to the eye velocity evoked by rotations in each direction. A greater response for rotations in one direction in comparison with the other would have resulted in larger coefficients for the second-order term. If this had been the case, the fit to the data would have been improved.

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**Figure 3**. Superposition of responses to leftward (A) and rightward (B) accelerations at 3,000°/s² reaching a peak velocity of 150°/s in M798. Head velocity is indicated by the dashed line and eye velocity by the solid line. Averages of these responses are represented by the open line with 1 SD indicated by shading around this line in C and D.

**Figure 4**. A: responses to leftward rotations at an acceleration of 3,000°/s² for different eye positions at the onset of rotation in M34. In each case, the rotation begins at 0.2 s. B: amplitude of the initial slow phase component of the eye movement responses to 3,000°/s² rotations at different starting eye positions for the 5 animals in the study.
substantially with second-order polynomial in comparison with a linear fit. A considerably better fit was obtained with a polynomial that included a third-order (cubic) term. The value of the BIC was substantially lower for a third-order in comparison with a linear fit but was either unchanged or increased for a fifth-order fit. This finding indicated that a third-order fit provided the best representation of the data.

The coefficients from the third-order polynomial fits in each of the five animals given in Table 1 were pooled to calculate the mean coefficients as shown in the following equation.

$$E_V = -1.37 + (0.97)H_V + (-3.8 \times 10^{-3})H_V^2 + (1.0 \times 10^{-3})H_V^3$$

$E_V$ and $H_V$ are relative eye and head velocity, respectively. When $E_V$ is evaluated from Eq. 1 at an $H_V$ of 100°/s, the squared term is noted to make a contribution of <0.5% to the response, whereas the cubic term accentuates the response by ~10%.

The trajectory of the initial slow phase eye movements evoked by the rotations differed somewhat between the individual animals in the study. As we will show, these differences also were reflected in the polynomial fits of responses to sinusoidal rotations at higher frequencies and velocities. The values of the coefficients for the polynomial fits to the steps of acceleration are presented in Table 1. For M51, M34, and M314, mean squared error between the fit for the response and the data was reduced by ~4.0 deg²/s² for the cubic in comparison with the linear fit. In contrast, the reduction in mean squared error for the cubic in comparison with the linear fit was ~2.5 deg²/s² for both M798 and M330. The value of the linear...
term for the first- and third-order fits also showed variation in accord with the differences between these fits. The coefficient of the linear term for the first-order fit in M51, M34, and M314 was 1.01 ± 0.05 and was 1.04 ± 0.05 in M798 and M330. This coefficient decreased by 0.09 ± 0.01 for M51, M34, and M314 when a cubic fit was used (P < 0.01) but was unchanged (0.00 ± 0.03) for a cubic in comparison with a linear fit in M798 and M330. The findings indicate that the nonlinear increase in the eye velocity at higher head velocities during the step of acceleration, manifested as a better representation of the increase in the eye velocity at higher head velocities during the acceleration was negligible effect on the gain of the VOR (Telford et al. 1996, 1997).

\( G_A \) and \( G_V \) also were evaluated for the 3,000°/s\(^2\) rotations that reached a maximum velocity of 60°/s in three animals to determine the effects of velocity on these responses. \( G_A \) for the rotations at 150°/s (\( G_{A150} \)) was greater than \( G_A \) at 60°/s (\( G_{A60} \)) in two of the three animals (M51 and M34).

The following values of \( G_{A150} \) and \( G_{A60} \) were calculated when data from these two animals were pooled: \( G_{A150} = 1.08 \pm 0.10 \) and \( G_{A60} = 0.99 \pm 0.10 \) (P < 0.01). In a third animal (M798), \( G_{A150} \) did not differ from \( G_{A60} \): \( G_{A150} = 0.95 \pm 0.07 \) and \( G_{A60} = 0.92 \pm 0.07 \) (P > 0.15). The velocity gain measured from the 60°/s rotations (\( G_{V60} \)) did not differ from that measured from the 150°/s rotations in any of the animals (P > 0.2). The following values were obtained from pooling the data in these three animals: \( G_{V60} = 0.93 \pm 0.07, G_{V150} = 0.92 \pm 0.07 \) (P > 0.5).

### Table 1. Polynomial fits to steps of acceleration for each of the 5 animals

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<th>M798</th>
<th>M330</th>
<th>M314</th>
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</tr>
<tr>
<td>BIC</td>
<td>1.74</td>
<td>1.48</td>
<td>-0.89</td>
<td>0.26</td>
<td>2.00</td>
<td></td>
</tr>
<tr>
<td>Third order</td>
<td>( A_1 H_V )</td>
<td>1.83</td>
<td>1.59</td>
<td>0.300</td>
<td>-0.502</td>
<td>1.90</td>
</tr>
<tr>
<td></td>
<td>( B_1 H_V )</td>
<td>44.20</td>
<td>7.20</td>
<td>-43.9</td>
<td>-44.4</td>
<td>17.8</td>
</tr>
<tr>
<td></td>
<td>( C_2 H_V )</td>
<td>0.957</td>
<td>0.867</td>
<td>0.981</td>
<td>1.09</td>
<td>0.931</td>
</tr>
<tr>
<td></td>
<td>( D_3 )</td>
<td>-0.985</td>
<td>-1.85</td>
<td>-0.730</td>
<td>-1.71</td>
<td>-1.59</td>
</tr>
<tr>
<td>MSE</td>
<td>0.39</td>
<td>0.37</td>
<td>0.21</td>
<td>0.79</td>
<td>1.33</td>
<td></td>
</tr>
<tr>
<td>BIC</td>
<td>-1.21</td>
<td>-0.94</td>
<td>-2.17</td>
<td>-0.58</td>
<td>0.29</td>
<td></td>
</tr>
<tr>
<td>Fifth order</td>
<td>MSE</td>
<td>0.26</td>
<td>0.34</td>
<td>0.10</td>
<td>0.49</td>
<td>0.65</td>
</tr>
<tr>
<td></td>
<td>BIC</td>
<td>-1.14</td>
<td>-0.87</td>
<td>-2.10</td>
<td>-0.51</td>
<td>-0.23</td>
</tr>
</tbody>
</table>

A1, B1, C2, coefficients of the first-order term for the linear, second-order, and third-order fits, respectively; \( A_1 \), \( B_1 \), \( C_1 \), \( D_3 \), intercept on the head-velocity axis for the linear, second-order, and third-order fits, respectively; \( H_V \), head velocity; MSE, mean squared error of the difference between the fit and the data; BIC, Bayesian Information Criterion calculated from the MSE and the order of the polynomial fit.

### Table 2. Gains of the VOR measured during the step of acceleration and at the velocity plateau

<table>
<thead>
<tr>
<th>Animal</th>
<th>( G_A^* )</th>
<th>( G_V^* )</th>
<th>0.5 Hz, 60°/s</th>
</tr>
</thead>
<tbody>
<tr>
<td>M51</td>
<td>1.12 ± 0.10</td>
<td>0.96 ± 0.06</td>
<td>0.97 ± 0.03</td>
</tr>
<tr>
<td>M34</td>
<td>1.03 ± 0.08</td>
<td>0.92 ± 0.04</td>
<td>0.87 ± 0.02</td>
</tr>
<tr>
<td>M798</td>
<td>0.97 ± 0.06</td>
<td>0.85 ± 0.03</td>
<td>0.81 ± 0.03</td>
</tr>
<tr>
<td>M330</td>
<td>0.98 ± 0.06</td>
<td>0.90 ± 0.03</td>
<td>0.91 ± 0.01</td>
</tr>
<tr>
<td>M314</td>
<td>1.11 ± 0.09</td>
<td>0.91 ± 0.03</td>
<td>0.96 ± 0.03</td>
</tr>
</tbody>
</table>

Values are given for each animal as means ± SD. *P < 0.001.

Acceleration and velocity gains were measured from 3,000°/s\(^2\) rotations that reached a peak velocity of 150°/s. Velocity gain was also measured from responses to 0.5 Hz, ±60°/s rotations. \( G_A \), acceleration gain of the vestibulo-ocular reflex (VOR); \( G_V \), velocity gain of the VOR.
Sinusoidal responses

Figure 8 displays data from the sinusoidal rotations with peak head velocity of 20°/s at the frequencies tested between 2 and 15 Hz. An eye-velocity response that was compensatory for the head-velocity stimulus was present at all of the frequencies that were tested. Figure 9 gives the plots for gain and phase averaged across the five animals. Gain measured 0.83 ± 0.06 and did not differ across frequencies or animals (P > 0.2). Phase measured −1.4 ± 0.8° for frequencies up to and including 12 Hz. Phase at 15 Hz measured −5.0 ± 0.9°. Gains measured in light were greater than those measured in darkness at 0.5, 2, and 4 Hz (P < 0.05 at each frequency) but did not differ from those measured in darkness frequencies >4 Hz (P > 0.8 at each frequency).

Ocular tracking responses in light in an animal (R10) after bilateral labyrinthectomy had a gain identical to that in animals with intact vestibular function for rotations at 0.2 Hz, ±20°/s. These responses declined in gain at higher rotational frequencies and had an increasing phase lag. When calculated from the phase measurements for rotations at 0.5–6 Hz, the delay in these tracking responses was 86 ± 30 ms.

Similar gain and phase values were calculated from the responses to sum-of-sines rotations evaluated in two animals. Figure 10 shows a 1-s interval for head and eye velocity from a sum-of-sines rotation. Gains and phases re head velocity at 1, 3, 7, and 15 Hz measured: 0.87 ± 0.06, 0.3 ± 2.1°; 0.88 ± 0.02, 0.2 ± 3.6°; 0.88 ± 0.02°, −1.8 ± 0.2°; and 0.92 ± 0.03, −3.8 ± 1.4°; respectively. Neither the gain nor the phase measured at each frequency for the sum-of-sines or single frequency sinusoidal rotations differed from one another (P > 0.9).

Figure 11 gives the plots for gain and phase of responses at 0.5–15 Hz for different velocities in the lower and middle range of these frequencies measured in three animals (M51, M798, and M34). Gain did not vary with velocity at 0.5 Hz: gain at 20°/s = 0.91 ± 0.01 and at 100°/s = 0.86 ± 0.04, (P > 0.08). Gain increased with velocity at frequencies of ≥2 Hz.
Gain at 4 Hz measured 0.85 ± 0.04 at 20°/s and 1.01 ± 0.05 at 100°/s (P < 0.0001). Phase lag decreased slightly as velocity increased at 4 Hz: phase = −1.9 ± 0.9° at 20°/s and −0.2 ± 0.6° at 100°/s (P < 0.025).

Harmonic distortion and asymmetries in the eye movement response were calculated after having taken into account the values of these parameters measured in the stimulus. The additional distortion present in the eye movement response was <2% at all frequencies for rotations with a peak velocity of 20°/s. Harmonic distortion increased at higher velocities for the frequencies tested to reach a maximum of 4.3 ± 0.8% at 4 Hz, ± 100°/s. This increase in harmonic distortion at the highest velocity tested at 4 Hz is expected based on the nonlinearity in response dynamics that is both frequency and velocity dependent.

Polynomial fits also were made to data from the 4-Hz rotations at 100°/s in the three animals that were tested with this stimulus (Table 3). As was the case for the fits to the data from responses to steps of acceleration, little difference was noted between the second-order in comparison to the first-order fits. The largest reduction in the value for BIC came with the third-order fit, and BIC was either unchanged or increased for higher-order fits.

**DISCUSSION**

**Latency of the VOR**

Our findings indicate that the horizontal VOR evoked by a step of acceleration at 3,000°/s² begins after a latency of 7 ms. This value is consistent with the latency measured in humans in response to passive head-on-body rotations (Maas et al. 1989; Tabak and Collewijn 1994) and whole-body rotations (Crane and Demer 1998) of similar acceleration. It is substantially shorter than the 14-ms latency reported in previous studies of the VOR of monkeys (Lisberger and Pavelko 1986; Minor and Goldberg 1991). The reason for this apparent discrepancy between the earlier monkey studies and the findings in humans as well as those in this study may be related to differences in stimuli and the time required to elicit a measurable eye movement. Lisberger and Pavelko (1986) and Minor and Goldberg (1991) used acceleration steps of 600°/s². The minimum eye movement that could be resolved in these studies was likely to be between 0.05 and 0.1°, so a rotation at this acceleration would require 13–19 ms to produce a discernible eye movement.

The latency of 7 ms from onset of head to eye movement is in accord with the delays measured for the neural components of the reflex. The delay from deflection of stereocilia on a hair cell to a change in firing rate in an afferent receiving activation from the hair cell has been estimated to be 0.7 ms (Rabbit et al. 1996). The delay from activation of vestibular-nerve afferents to change in discharge of secondary vestibular neurons has been measured as between 0.8 and 1.0 ms (Goldberg et al. 1987). A similar latency can be estimated for transmission from secondary neurons to abducens motor neurons. The latency from shock stimulation of the abducens nerve to the onset of contraction in the lateral rectus is 2.8 ms with peak tension developing an additional 2.5 ms later (Fuchs and Luschei 1971).

We did not observe any difference in the value of latency according to the measurement method that was used (linear fit, 3-SD, or fit of higher-order polynomials). Because of the nonlinearity that we measured, the agreement between values calculated with these different methods at first might appear unexpected. We showed that the responses to these steps of acceleration have a nonlinear increase in gain at higher velocities. This nonlinearity did not have a significant effect on the measurement of the intercept on the time axis of fits to the trajectory of the eye velocity. As will be seen in the companion study (Lasker et al. 1999), these nonlinearities are accentuated after canal plugging and result in substantially different estimates of latency.

**TABLE 3. Polynomial fit to sinusoidal rotations at 4 Hz, ±100°/s**

<table>
<thead>
<tr>
<th>Fit Term</th>
<th>Animal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Linear</td>
<td></td>
</tr>
<tr>
<td>A₁Hᵥ</td>
<td></td>
</tr>
<tr>
<td>Bᵥ</td>
<td></td>
</tr>
<tr>
<td>MSE</td>
<td></td>
</tr>
<tr>
<td>BIC</td>
<td></td>
</tr>
<tr>
<td>A₂Hᵥ(×10⁻⁴)</td>
<td></td>
</tr>
<tr>
<td>BᵥX</td>
<td></td>
</tr>
<tr>
<td>Cᵥ</td>
<td></td>
</tr>
<tr>
<td>Dᵥ</td>
<td></td>
</tr>
<tr>
<td>MSE</td>
<td></td>
</tr>
<tr>
<td>BIC</td>
<td></td>
</tr>
<tr>
<td>MSE</td>
<td></td>
</tr>
<tr>
<td>BIC</td>
<td></td>
</tr>
</tbody>
</table>

Coefficients and abbreviations are the same as those described in Table 1.
Effects of ocular inertia on vestibuloocular responses

Previous studies have concluded that the inertia of the eye, independent of neurally mediated eye movements, results in an eye movement in the direction opposite to head movement for rotations that are of higher frequency and acceleration. Vercher et al. (1984) injected lidocaine into the extraocular muscles of one eye of a baboon and found that vestibuloocular responses from this eye were abolished at rotational frequencies < 8 Hz during the period the lidocaine was active. Gain of responses to rotations > 8 Hz increased with frequency to the point that at 12 Hz the eye with muscles putatively paralyzed by lidocaine moved conjugately with the nonparalyzed eye. They concluded that “mechanical resonance oscillation,” and not a neurally mediated VOR, accounted for these high-frequency responses. Khater et al. (1993) identified an eye movement with an amplitude of 0.2° occurring at the initiation (no delay) of 4,000°/s² rotations in the cat. This initial response was also present after bilateral labyrinthectomy. Inertia of eye was proposed to be responsible for this motion that began without latency relative to movement of the head. Gilchrist et al. (1998) concluded that the mass of the coil on the eye led to an increase in the moment of inertia of the eye that resulted in an eye movement that was compensatory to head movement at the onset of steps of acceleration in the guinea pig.

Although the reason for the differences in these findings from those in our study cannot be determined with absolute certainty, the motion transduced from the head-fixed coil in our experiments indicated the importance of measuring any relative movement of the head in comparison with the field coils during these high-acceleration stimuli. Even a small uncoupling of the motion of the head and field coils can, if not measured, appear to be an eye movement in the direction opposite to the head movement.

The origin of initial eye movements in response to acceleration steps is critical to analyses of the dynamics of the VOR. We did not observe an eye movement occurring simultaneously with the onset of head acceleration in any of the monkeys in this study. In the two monkeys after bilateral labyrinthectomy, there was no discernible eye movement evoked by 3,000°/s² accelerations given in darkness. The findings indicated that the eye movements we measured in response to the rotational stimuli in this study were due to the neurally mediated VOR and not to mechanical properties of the eye or the structures with which it is associated. This issue is considered quantitatively in terms of a model of the oculomotor plant in the Appendices.

Responses to steps of acceleration

The gain of the VOR during the period of acceleration for the 3,000°/s² rotations that reached a maximum velocity of 150°/s ($G_{A_{150}}$) was greater than the gain at the plateau of head velocity ($G_{V_{150}}$). This increase in gain that occurred during the acceleration was related to the trajectory of the response; this was better represented by a third- in contrast to a first-order polynomial. The cubic relationship between head and eye velocity resulted in a VOR gain that was greater than unity during the higher velocity portions of the step of acceleration.

A comparison of the responses to 3,000°/s² rotations that reached a maximum velocity of 60 or 150°/s provided confirmation of these observations. $G_{A_{150}}$ was greater than $G_{A_{60}}$ in two of the animals but did not differ in a third animal. The animal for which no difference in these parameters was observed ($M798$) showed only a small difference in third-order in comparison to first-order fits to the 3,000°/s² steps that had a duration of 50 ms (Table 1). Values of the velocity gain calculated from eye and head velocity at the plateau of the stimuli that reached 60°/s did not differ from those that reached 150°/s. This finding indicated that the greater values for $G_{A_{150}}$ than $G_{V_{150}}$ were not attributable to a saturation in gain due to head velocity.

Such a nonlinear dependence of gain based on head velocity during the higher velocity components of steps of acceleration is evident in the figures relating eye to head velocity for rotations in the yaw plane in the study of subjects with normal vestibular function by Aw et al. (1996). In the present study, the gain of the VOR during the latter portion of the step of acceleration stimulus, as evaluated by the values of $G_{A}$ averaged across animals, was 1.04 ± 0.02. Collewijn (1998) recently has reported similar findings for the human VOR where initial responses to 1,000°/s² rotations evaluated over an analogous time period were reported to have a gain of 1.1 ± 0.1. These gains of greater than unity for dynamic stimuli may reflect a precalibration of the VOR for a specific target eccentricity and axis of rotation. Such a preset calibration would be beneficial for rapid responses because changes in gain of the angular VOR due to target eccentricity have been reported to lag the onset of VOR by ~20 ms and changes in gain due to shifts of the axis of rotation relative to the otoliths follow an additional 10 ms (Snyder and King 1992).

Responses to sinusoidal rotations

Gain did not vary with frequency over the range of 0.5–15 Hz for stimuli with a peak velocity of 20°/s. Phase also remained relatively constant over the frequencies tested with only a 5° lag at 15 Hz. The delay of 7 ms in the reflex pathway would give rise to a predicted phase lag in the reflex of 38° at 15 Hz. The relatively small phase lag that was observed at these higher frequencies indicates that a phase lead arising from dynamic elements of the reflex pathway are compensating for the phase lag due to the delay. The resulting VOR has a phase that is close to compensatory for higher frequencies. Similar values for phase with respect to velocity were noted in responses to sum-of-sine rotations. Because such stimuli are more “random” than single-frequency rotations, it is unlikely that predictive components along VOR pathways are responsible for the phase lag being less than expected based on the delay of the reflex. What is the source of this phase lag that increases with frequency in the dynamics of the VOR pathways? One possibility, considered in further detail in the following text, is that the inherent response dynamics of the irregularly discharging vestibular-nerve afferents provide the linear inputs to the VOR (Hullar and Minor 1999; Minor and Goldberg 1991).

Fits to the sinusoidal responses were made from the data displayed as eye versus head velocity. As was the case for the responses to steps of acceleration, the trajectories of the eye velocity responses for rotations at 4 Hz, ±100°/s were better fit with a third-order in contrast to a first-order polynomial (Table 3). Differences between animals also were noted in the coef-
considerable variation in phase was noted with a lag of 5°; but rose conti-
nuously from 0.6 at 8 Hz to 30 Hz. VOR gain decreased for rotations be-
tween 2 and 8 Hz, a rise in peak stimulus velocity from 13°/s at 2 Hz to 188°/s at 

The studies of Keller and of Böhmer and Henn as well as our data indicate that the monkey VOR has a substantially lower phase lag at higher rotational frequencies than would be predicted based on the delay in the reflex pathways. This is in contrast to the findings from rotations at higher frequencies in humans that, while techniques of data acquisition and analysis vary considerably between studies, seem to generally indicate that phase lag increases with frequency in a manner that would be predicted based on a fixed delay transmitted through the reflex pathways. One obvious difference between the human and monkey studies is that the VOR was elicited by head-on-body rotations in humans but by whole-body rotations in monkeys. Activation of the cervicoocular reflex could have had an effect on the response dynamics recorded in humans.

The nonlinearity in VOR dynamics that we have observed in our data from sinusoidal rotations at higher frequencies and
Model of the dynamics of the horizontal VOR

The most appropriate discussion of the findings in this study is in the form of a mathematical model that accounts for the responses to various stimuli. The model that we have developed uses transfer functions to represent the known elements in vestibuloocular signal processing, the frequency- and velocity-dependent nonlinearities that we have identified, and the signal transformations required to obtain the appropriate gain and phase at the output. Figure 12 shows a schematic diagram with the elements of the model.

The inputs to the reflex come from linear and nonlinear pathways. The linear pathway confers the dynamics of the reflex responses to sinusoidal rotations over the frequency range of 0.5–15 Hz at 20°/s peak stimulus velocity. This pathway is also responsible for the linear component of the polynomial fit to the responses for steps of acceleration. The nonlinear pathway is responsible for the frequency- and velocity-dependent increase in gain noted in the sinusoidal responses and manifested in the coefficients for the higher-order polynomial fits.

The output of the linear and nonlinear pathways from each side are summed and passed through the neural integrator. Gains of the pulse, slide, and step components of the neural integrator are set to cancel the poles of the fourth-order model of the oculomotor plant (Minor and Goldberg 1991). The model predicts that the signal processing important for the dynamics after lens-induced modification on the adapting and the horizontal VOR at 2.8 Hz. Keller's data over the frequency range of 0.5–15 Hz, ±20°/s.

In model 1, the initial transfer function is that derived for regularly discharging vestibular-nerve afferents recorded in the squirrel monkey by Goldberg and Fernández (1971). This transfer function has a zero at the origin and a second zero that has a value of 0.015 s. The parameters of this transfer function were calculated from data collected mainly at rotations of ±2-Hz frequencies. This afferent transfer function predicts a phase lead and gain enhancement at higher rotational frequencies (Fig. 13). Such a phase lead is beneficial in compensating for the phase lag that would be predicted in the frequency responses based on the 7-ms delay in the reflex. The phase lag predicted based on the delay would be 38° at 15 Hz, whereas the observed response has only a 5° lag at that frequency. Although the phase of the VOR is accurately accounted for by summation of the predicted lead of the regular afferents and the lag due to the reflex delay, the gain of the reflex does not follow that expected from the afferent. Rather, this afferent transfer function leads to the prediction that the VOR gain at 15 Hz should be 60% greater than that at 0.5 Hz. The VOR data in this study indicate that the gain remains constant across all frequencies studied for stimulus velocities of 20°/s.

To compensate for the predicted increase in gain of the afferent with frequency and to match the observed dynamics of the reflex at higher frequencies and lower velocities, we proposed a first-order transfer function with a pole and a zero determined from a least-squares optimization method. This technique for independently adjusting gain and phase in a frequency-specific way is reminiscent of the models used by Lisberger et al. (1983) to account for the dependence of VOR dynamics after lens-induced modification on the adapting and testing frequencies. With this central gain-phase compensator, we were able to more closely predict the gain and phase of the VOR across all of the frequencies tested at a peak velocity of 20°/s (see Fig. 13).

In model 2 of the linear pathway (Fig. 14), we propose that the dynamics of regularly discharging vestibular-nerve afferents at higher rotational frequencies differ from those predicted by the Goldberg-Fernández transfer function. We

FIG. 12. Schematic diagram of a model to account for the dynamics of the horizontal VOR in response to higher-frequency rotations. Inputs to the reflex come from linear and nonlinear pathways. These signals from each pathway are summed on each side and then the outputs from the 2 sides are summed. Overall signal is then passed through a neural integrator (NI) with terms representing pulse, slide, and step dynamics set to compensate for the dynamics of a 4th-order model of the oculomotor plant. Time delay in the reflex pathways (Td) is also included in the model.
derived a transfer function with a single pole (the long-time constant of the torsion pendulum model of the semicircular canals) and two zeroes. We did not include the second pole with a shorter (0.003 s) time constant of the torsion pendulum model because we saw no evidence of this pole in the data at 15 Hz. The second pole would result in a gain decrease and phase lag as frequency increased. Neither of these effects was observed.

One zero in the second model of the linear pathway was at the origin, and the second zero (0.00625 s) was calculated from a least-squares fit to the VOR data across frequencies at a peak velocity of 20°/s and the known time delay of 7 ms in the reflex pathway.

**FIG. 13.** Model of the linear pathway arising from one labyrinth with inputs coming from regularly discharging afferents having the response dynamics predicted by the Goldberg-Fernández transfer function. Resting rate of the afferents is set to 90 spikes/s. Saturation element is set to a maximum firing rate of 500 spikes/s and inhibitory cutoff of 0 spikes/s. Proposed central transfer function then lowers the increase in gain arising from the afferent transfer function at higher frequencies to maintain a relatively constant gain from the pathway as frequency is increased to 15 Hz. Linear pathway continues to have an increasing phase lead with frequency. Coefficients in the model are $T_c = 5.7 \text{ s}$, $T_v = 0.015 \text{ s}$, $T_p = 0.043 \text{ s}$, $p_l = 0.43 \text{ spikes} \cdot \text{s}^{-1}$, $k_l = 1.0$. Delay element ($e^{-e^t}$) is included with the measured delay of 7 ms. Gain plot shows simulations for the afferent, the central transfer function that is responsible for the gain and phase adjustment, and the product of these two which is the predicted gain of the VOR. Phase plot shows simulations for the lead resulting from the transfer function for the afferent, the lag resulting from the time delay, the response from the central gain and phase adjustment, and the sum of these 3 phases which represents the phase predicted for the VOR.

**FIG. 14.** Model of the linear pathway arising from one labyrinth with inputs coming from a modified transfer function for regularly discharging afferents. This afferent transfer function incorporates a single pole representing the long time constant of the cupula ($T_c = 5.7 \text{ s}$) and a zero ($T_g = 0.00625 \text{ s}$) that was optimized to maintain a rotational sensitivity that remained relatively constant as frequency was increased to 15 Hz and a phase lead that increased with frequency. Resting rate of the afferents was set to 90 spikes/s. Saturation element was set to a maximum discharge rate of 500 spikes/s and inhibitory cutoff of 0 spikes/s. Other coefficients in the model: $p_l = 0.43 \text{ spikes} \cdot \text{s}^{-1}$, $k_l = 1.0$. Simulations for gain are shown for the afferent (normalized to 0.4 spikes $\cdot \text{s}^{-1}$) and the VOR. Note that the predicted gain of the VOR remains relatively constant across frequencies with a small gain enhancement at the higher frequencies. Data for the VOR at peak stimulus velocities of 20°/s and the known time delay of 7 ms in the reflex pathway. Difference between the afferent phase lead and lag due to the delay is a predicted VOR phase that closely matches the data.
pathways. Data obtained from single-unit recordings of regularly discharging afferents in chinchillas at rotational frequencies $\approx 15$ Hz indicate that this modified transfer function is representative of afferent response dynamics (Hullar and Minor 1999).

The gain increase in the VOR at higher frequencies as velocity is increased cannot be described by a linear transfer function. This nonlinear component of the VOR is only observed at frequencies $>0.5$ Hz. The model for the nonlinear pathway begins with a transfer function that has two first-order high-pass filters. One of these is specified by the dominant transfer function of the semicircular canals ($T_c = 5.7$ s) and the second has a shorter time constant ($T_h = 0.11$ s; Fig. 15). The time constant of this second high-pass filter was calculated by first subtracting the contribution of the linear pathway determined from the gains at rotations at 0.5–10 Hz with a peak velocity of 20°/s from the gains at 50 and 100°/s for the specific frequencies tested. This difference then was used in a least-squares fit analysis to determine the time constant. The effect of this second high-pass filter is to increase the gain of the transfer function as frequency rises. The frequency dependence of the nonlinear pathway was, therefore, conferred by this transfer function. The output was next passed through a saturation element with peak discharge rate of 500 spikes/s and inhibitory cutoff at 0 spikes/s.

The data for responses to the more dynamic stimuli indicated that the nonlinear increase in gain of the VOR with rising head velocity at higher rotational frequencies was best modeled by a third-order polynomial fit. The average coefficient of the third-order term in the fits to the steps of acceleration were used to specify the gain of the element in the model. The model for the nonlinear pathway was based only on a third-order term because the values calculated for the second-order term were small and did not improve the fits for the stimuli used in this study. Because we proposed that this higher-order relationship applied to head velocity independent of resting rate, we subtracted the assumed spontaneous firing rate of 90 spikes/s before the cubic term.

Figure 15 shows the excitatory contribution of the nonlinear pathway to the response gain and phase at higher frequencies and velocities (inset on the gain and phase plots). The frequency- and velocity-dependent increases in gain resulted in this pathway being driven into inhibitory cutoff for more dynamic stimuli. The nonlinear pathway provides, in effect, a rectified signal that accentuates responses for excitatory stimuli but is driven into cutoff for inhibitory ones. Also shown on Fig. 15 are the gain and phase plots for the sum of the linear and nonlinear pathways. The phase of the output from the nonlinear pathway was independent of velocity. Because the gain of the nonlinear pathway rose with frequency and velocity, the contribution of its phase to the overall response phase was larger at higher frequencies and velocities. The increases in gain with velocity at frequencies of $\approx 4$ Hz, but not at 0.5 Hz, match the VOR data for this range of stimuli.

This model with linear and nonlinear pathways also predicts a greater value for $G_A$ in comparison with $G_V$ for responses to the 3,000°/s$^2$ steps of acceleration that reach a maximum velocity of 150°/s. The value of $G_A$ and $G_V$ from simulations in response to this stimulus were 0.97 and 0.80, respectively. $G_A$ measured from the five animals in the study was 1.04 ± 0.07 and $G_V$ was 0.91 ± 0.04. The higher values of $G_V$ observed than predicted may be due to fast phases resetting the spontaneous activity or sensitivity of central vestibular neurons (Galiana 1991).

The model presented above provides a quantitative description of transfer functions that will account for the behavioral data. We can hypothesize as to the neuronal elements underlying these signal transformations, but a definitive understanding of these pathways will require data from single-unit recordings of peripheral and central neurons involved in control of the VOR at the frequencies, accelerations, and velocities used in this study. As a first estimation, it can be suggested that the linear and nonlinear pathways might arise from separate groups of vestibular-nerve afferents. The response dynamics of the linear pathway resemble those of regularly discharging afferents. Irregularly discharging afferents have a gain enhancement that grows with the frequency of rotational stimulation making them candidates for mediating the nonlinear pathway. Also, these afferents would be expected to be in inhibitory cutoff during significant portions of the sinusoidal rotational stimuli used in this study. Their excitatory responses in such situations need to be defined with respect to frequency and velocity.

The dynamics of the nonlinear pathway need not necessarily be encoded in the response properties of vestibular-

![Model of the nonlinear pathway from 1 side. Dynamics of this pathway are represented by 2 signal processing blocks: a transfer function that has the long time constant of the torsion pendulum model followed by a high pass filter that gives the pathway frequency selectivity and a function that establishes a cubic dependence of gain on velocity. Resting rate of the afferent is set to 90 spikes/s. Saturation element has a maximum discharge rate of 500 spikes/s and inhibitory cutoff of 0 spikes/s. Gain and phase plots for the sum of the linear and nonlinear pathways are shown. Insets: excitatory contribution of the nonlinear pathway. Coefficients in the model are $T_c = 5.7$ s, $p_{a1} = 3.0$ spikes $\cdot s^{-1/2} \cdot s^{-1}$, $T_h = 0.11$ s, $p_{a2} = 0.333, k_1 = 1 \times 10^{-3}$.](http://jn.physiology.org/content/1267/4/1220/F15)
nerve afferents. The increase in gain with velocity for high-frequency rotations could arise from the intrinsic dynamics of secondary vestibular neurons involved in control of the VOR. Recent studies of N-methyl-D-aspartate-receptor-mediated synaptic currents in secondary vestibular neurons have indicated that these receptors produce larger depolarizations for higher frequency stimuli (Kinney et al. 1994; Peterson et al. 1996).

**APPENDIX**

The potential role of ocular inertia in inducing an eye movement in response to these dynamic rotational stimuli merits quantitative consideration. We simulated the Robinson fourth-order linear model of the oculomotor plant (from Robinson 1964). In this model, the active portion of the muscle is divided into a contractile component ($R_\text{ac}$) and a series elastic component ($K_\text{s}$). All passive elements of the orbit and muscles are grouped into slow ($K_2, R_2$) and fast ($K_1, R_1$) viscoelastic (Voigt) elements. The eye has a moment of inertia ($m_o$) onto which three forces may act in the case of eye movements evoked in response to head movements. $F_h$ is the force exerted by the added tension of the horizontal recti and results from the neural command to the muscles ($F_m$). $F_m$ is the net restraining force of all passive tissues in the orbit, and $F_p$ is the force acting on the eye due to rotation of the head. The direction of the forces is such that $F_p$ and $F_o$ are directed opposite to $F_m$. A representation of the model in transfer function notation is shown in Fig. A1B.

The moment of inertia, $m$, of the human eye as a rigid, spherical body is determined to be $6.0 \times 10^{-3} \text{ g} \cdot \text{s}^2$. Because the vitreous body is largely left behind during rapid eye movement (Hilding 1954), the functional moment of inertia is estimated to be about half of this value (Robinson 1964). An estimate of the moment of inertia for the squirrel monkey eye is derived from the ratio of the radii of the radian ($r_h = 24 \text{ mm}$) and squirrel monkey ($r_s = 15 \text{ mm}$) eyes as follows:

$$3.0 \times 10^{-3} \left( \frac{r_h}{r_s} \right)^3 = 7.3 \times 10^{-4} \text{ g} \cdot \text{s}^2.$$  

The anticipated eye movement due to inertia, calculated from the plant model and coefficients shown in Fig. A1B, during the first 10 ms of the $3,000/\text{s}^2$ stimulus used in this study is $0.002^\circ$—an order of magnitude smaller than the position resolution of our eye movement recording system. A 100-fold increase in inertia is required for the model to produce a $0.2^\circ$ eye movement during the initial 10 ms of the rotation. Such a large moment of inertia would, if present, have consequences on the stability of saccades as shown in Fig. A2. In such high-inertia conditions, saccades would be expected to overshoot and ring due to the increased gain in the feedback pathway. We have never observed this type of saccade trajectory nor has it been described in the studies that attribute initial vestibuloocular responses to inertia. The data and the results of the model are therefore consistent with the conclusion that even for the higher range of frequencies and accelerations used in this study, ocular inertia has a negligible effect on mechanics of the eye.

A conclusion of this quantitative analysis is that the dynamics of saccades should be studied in any experimental situation where the inertia of the eye or the coil used to transduce its motion is thought to

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**FIG. A1.** A: mechanical model of the oculomotor plant (from Robinson 1964). Active portion of the muscle is divided into a contractile component ($R_\text{ac}$) and a series elastic component ($K_\text{s}$). All passive elements of the orbit and muscles are grouped into slow ($K_2, R_2$) and fast ($K_1, R_1$) viscoelastic (Voigt) elements. Globe has a moment of inertia ($m$). Coefficients in the model were determined from data gathered in monkeys. Net muscle force-velocity slope ($R_\text{ac}$) for the lateral rectus was $0.04 \text{ g} \cdot \text{s}^2$. Stretch of the series-elastic element, $K_\text{s}$, was $3.6 \text{ g} \cdot \text{s}^2$. Robinson (1964). $F_m$ is the neural signal arriving from extracranial motoneurons. $F_p$ is the external force imposed on the eye which is the force due to movement of the head in the case of the VOR and is 0 in the case of saccades. $F_m$ and $F_p$ are the resultant forces from the active and passive components of the orbit, respectively. B: transfer function in block diagram form of the oculomotor plant derived from the mechanical model in A. Time constant of the muscle, $T_{\text{ac}}$, was estimated to be $0.01 \text{ s}$ (Fuchs et al. 1988). Time constants for the Voigt elements were as follows: $T_1 = R_1/K_1 = 0.012 \text{ s}$, $T_2 = R_2/K_2 = 0.260 \text{ s}$, $T_3 = 1/(K_3 + 1/K_1) = 1.0 \text{ g} \cdot \text{s}^2$. Fuchs et al. (1988) determined a value for $T_h = (R_1 + R_2)/(K_1 + K_3) = 0.140 \text{ s}$ from a fit to smooth pursuit data in the rhesus monkey at 0.5 Hz. Moment of inertia for the squirrel monkey’s eye was estimated from the following relationship: $3.0 \times 10^{-3} \left( \frac{r_h}{r_s} \right)^3 = 7.3 \times 10^{-4} \text{ g} \cdot \text{s}^2$ where $3.0 \times 10^{-3} \text{ g} \cdot \text{s}^2$ is the estimated moment of inertia of the human eye (Robinson 1964), $r_h$ is radius of the squirrel monkey eye = 15 mm, and $r_s$ is radius of the human globe = 24 mm.

**FIG. A2.** Simulations for the eye movement resulting from a pulse stimulus passed through the neural integrator and to the 4th-order model of the oculomotor plant described in Fig. A1. Moment of inertia of the eye was multiplied by the values corresponding to each simulation shown in the figure. Note that as the estimated moment of inertia of the eye is increased, the resulting saccadic eye movement overshoots its intended amplitude and then oscillates prior to reaching the final position.
have an effect on the initial ocular response to a head movement. As predicted by the model of the oculomotor plant and as observed experimentally when ocular inertia was increased mechanically to the levels required to elicit a discernible eye movement from rotational stimuli within the physiological range (Robinson 1964), saccades should have underdamped dynamics with an overshoot and ringing.

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Address for reprint requests: L. B. Minor, Dept. of Otolaryngology—Head and Neck Surgery, Johns Hopkins University School of Medicine, 601 N. Caroline St., Rm. 6253, Baltimore, MD 21287-0910.

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