Horizontal Vestibuloocular Reflex Evoked by High-Acceleration Rotations in the Squirrel Monkey. II. Responses After Canal Plugging

DAVID M. LASKER,1 DOUGLAS D. BACKOUS,1 ANNA LYSAKOWSKI,4 GRIFFIN L. DAVIS,1 AND LLOYD B. MINOR1-3
Departments of 1Otolaryngology—Head and Neck Surgery, 2Biomedical Engineering, and 3Neuroscience, The Johns Hopkins University, Baltimore, Maryland 21287-0910; and 4Department of Anatomy, University of Illinois College of Medicine, Chicago, Illinois 60612-7500

Lasker, David M., Douglas D. Backous, Anna Lysakowski, Griffin L. Davis, and Lloyd B. Minor. Horizontal vestibuloocular reflex evoked by high-acceleration rotations in the squirrel monkey. II. Responses after canal plugging. J. Neurophysiol. 82: 1271–1285, 1999. The horizontal angular vestibuloocular reflex (VOR) evoked by high-frequency, high-acceleration rotations was studied in four squirrel monkeys after unilateral plugging of the three semicircular canals. During the period (1–4 days) that animals were kept in darkness after plugging, the gain during steps of acceleration (3,000°/s², peak velocity = 150°/s) was 0.61 ± 0.14 (mean ± SD) for contralesional rotations and 0.33 ± 0.03 for ipsilesional rotations. Within 18–24 h after animals were returned to light, the VOR gain for contralesional rotations increased to 0.88 ± 0.05, whereas there was only a slight increase in the gain for ipsilesional rotations to 0.37 ± 0.07. A symmetrical increase in the gain measured at the plateau of head velocity was noted after animals were returned to light. The latency of the VOR was 8.2 ± 0.4 ms for ipsilesional and 7.1 ± 0.3 ms for contralesional rotations. The VOR evoked by sinusoidal rotations of 0.5–15 Hz, ±20°/s had no significant half-cycle asymmetries. The recovery of gain for these responses after plugging was greater at lower than at higher frequencies. Responses to rotations at higher velocities for frequencies ≥4 Hz showed an increase in contralesional half-cycle gain, whereas ipsilesional half-cycle gain was unchanged. A residual response that appeared to be canal and not otolith mediated was noted after plugging of all six semicircular canals. This response increased with frequency to reach a gain of 0.23 ± 0.03 at 15 Hz, resembling that predicted based on a reduction of the dominant time constant of the canal to 32 ms after plugging. A model incorporating linear and nonlinear pathways was used to simulate the data. The coefficients of this model were determined from data in animals with intact vestibular function. Selective increases in the gain for the linear and nonlinear pathways predicted the changes in recovery observed after canal plugging. An increase in gain of the linear pathway accounted for the recovery in VOR gain for both responses at the velocity plateau of the steps of acceleration and for the sinusoidal rotations at lower peak velocities. The increase in gain for contralesional responses to steps of acceleration and sinusoidal rotations at higher frequencies and velocities was due to an increase in the gain of the nonlinear pathway. This pathway was driven into inhibitory cutoff at low velocities and therefore made no contribution for rotations toward the ipsilesional side.

INTRODUCTION

Disruption of vestibular signals from one labyrinth results in asymmetries in angular vestibuloocular reflexes (see Curthoys and Halmagyi 1995 for review). These asymmetries are subtle for less dynamic rotations (lower frequency, velocity, and acceleration) and may resolve as the gain of the VOR recovers through processes of vestibular compensation (Fetter and Zee 1988; Paige 1983). Entirely different findings are noted for responses to more dynamic stimuli.

Halmagyi et al. (1990) observed a marked asymmetry in vestibuloocular responses to manually delivered, high-frequency, high-acceleration head movements in humans after unilateral ablative vestibular lesions. For the horizontal angular VOR, rotations toward the intact labyrinth resulted in a VOR with a gain that was slightly reduced in comparison with prelesion values (0.85–0.95). In contrast, rotations toward the lesioned side elicited a VOR with a gain that was markedly lower (0.25–0.45). This asymmetry changed little during the course of time that the responses were studied after the lesion. Similar findings were noted when these high-acceleration, rotatory stimuli were given in guinea pigs after unilateral labyrinthectomy or vestibular neurectomy (Gilchrist et al. 1998). These effects have been studied most extensively for the horizontal VOR evoked by rotations in the yaw plane, but analogous asymmetries in the magnitude and alignment of the VOR have been noted when responses from humans were analyzed in three dimensions (Aw et al. 1996). Rotations produced with a reactive torque helmet revealed similar asymmetries after unilateral ablative vestibular lesions and also indicated a longer delay in the initiation of the reflex (Tabak et al. 1997).

Asymmetries in the gain of the VOR, lower for ipsilesional in comparison with contralesional rotations, also have been noted for lower acceleration and frequency rotations that reach a higher peak velocity in studies performed in monkeys. For sinusoidal rotations, these asymmetries are manifested as a diminished gain for half-cycles of the rotation toward the lesioned side and a bias velocity (slow phase components directed toward the lesioned ear) during the rotation (Paige 1989). For velocity-step rotations, the asymmetry is observed as a diminished gain for rotations toward the lesioned ear noted immediately after reaching the peak head velocity (Fetter and Zee 1988; Fetter et al. 1988).

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We sought to determine the interaction of frequency, velocity, and acceleration in producing asymmetries of the horizontal VOR after disruption of vestibular function from one labyrinth. The lesion used for this study was unilateral plugging of the three semicircular canals. Evidence is presented indicating that canal plugging in squirrel monkeys results in a reduction in the dominant time constant of the canal and attenuation in the response gain while preserving both the spontaneous activity of the afferents and otolith function. The findings indicate that there is a frequency- and velocity-dependent asymmetry in the horizontal VOR evoked by rotations in the yaw plane after plugging. For more dynamic stimuli, rotations toward the lesioned labyrinth resulted in a VOR with a lower gain. The findings were interpreted in terms of a mathematical model of the VOR with inputs from linear and nonlinear pathways the parameters of which were derived from data in squirrel monkeys with normal vestibular function. The responses from steps of acceleration and sinusoidal rotations after plugging were accounted for by a selective increase in gain of the nonlinear pathway which, because of its dynamics at higher rotational frequencies and velocities, was prone to inhibitory cutoff.

**METHODS**

**Surgical procedures**

The methods for implantation of the head restraining bolt and eye coils were described in the companion paper (Minor et al. 1999).

The postauricular mastoid bone was removed with an otologic drill and curettes to expose the horizontal and posterior semicircular canals. The petrous bone was further removed anteriorly and superiorly to visualize the superior canal near its union with the common crus. This surgical exposure required gentle retraction of the petrosal lobe to visualize the superior canal near its union with the common crus. The dura overlying the petrosal lobe remained intact and there was no evidence of hemorrhage or injury to this structure after the retraction had been released.

A fenestra was made in the osseous portion of each canal at a point that was approximately the maximal distance from its ampulla. The membranous canal remained intact and was compressed against the walls of the osseous canal by packing the osseous canal with bone dust and fascia.

Animals showed a slight (5–10°) head tilt and minimal gait ataxia during the initial 2 days after the plugging procedure. Their head orientation and gait were relatively normal thereafter. Two animals underwent plugging of the three canals on the opposite side 3–4 mo later. These animals had a head tilt toward the side on which the plugging procedure had been performed most recently that was of similar magnitude and resolved over a similar time course to that noted after the initial plugging procedure. Their gait returned close to normal within 1 wk after the remaining three canals had been plugged although their heads would occasionally oscillate for 2–3 s after rapid movements.

When testing was completed, animals were anesthetized deeply with sodium pentobarbital and perfused transcardially with 10% formalin. For three of the four animals in the study (M20, M31, and M330), the right and left temporal bones were removed, decalcified, embedded in celloidin, and cut in horizontal sections (80 μm). The sections were stained with cresyl violet.

Examination of the histological sections indicated that the lumen of each plugged canal was occluded. The sensory epithelia of the cristae and the otoliths as well as the afferent nerve fibers and cells in Scarpa’s ganglion were intact and normal in histological appearance. Figure 1 shows a representative temporal bone specimen demonstrating intact sensory epithelia and plugged canals.

**Eye-movement responses**

The experimental procedures used for recording eye movements were identical to those described for the animals before plugging. Animals typically were tested 8 h after the plugging procedure, 18–24 h after return to light, and on days 10 and 30 after plugging.

**Rotational testing and data analysis**

The testing paradigms and analysis procedures used for calculating gain and phase parameters were identical to those described in the companion paper. For steps of acceleration, responses to 10–15 stimulus repetitions in the ipsilesional and contralesional directions were studied. 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 after the onset of the stimulus when head velocity was increasing from 60 to 120°/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. Responses to steps of acceleration that reached a lower peak velocity (3,000°/s², 60°/s) were studied to define the transition between acceleration and velocity gains independent of fast phases. For these briefer rotational steps, the gain during the period of acceleration was measured as the ratio of the peaks of eye and head velocity, whereas the gain during the velocity plateau was defined as the ratio of eye and head velocity from 200 ms after the onset of the stimulus to the occurrence of the first fast phase.

Distinctly different responses, requiring different analytic fits, were noted for contra- and ipsilesional steps of acceleration after the plugging procedure. We analyzed the ipsilesional and contralesional responses separately. To compare the contralesional and ipsilesional responses with the data obtained from animals with normal vestibular function, we inverted the eye- and head-velocity signals for the averaged response to rotations in each direction and concatenated this signal with the corresponding noninverted trace. Polynomial fits were made for the contralesional responses, and the ipsilesional responses were fit with a hyperbolic tangent function. For example, in Fig. 6 the responses to rightward (contralesional) rotations are shown as positive values for eye and head velocity. These signals were inverted to form the head velocity responses that would have been expected if the lesion had been on the right instead of the left side. These two responses then were concatenated at the origin. The best fit to the contralesional data will be with an odd-order polynomial, without contribution from even-order terms, because the method for forming the signal insured that the responses were symmetric about the origin. All full description of these techniques for polynomial fits is given in Minor et al. (1999).

**Correction for response arising from plugged canals**

As shown in Fig. 13, a response rising in amplitude and declining in phase lead re velocity with increased rotational frequency was noted in animals after plugging of the six semicircular canals. We wished to correct for the contribution that this response was making to the gains and phases measured with sinusoidal rotations. We assumed that the responses measured in animals after all canals had been plugged were due to equal contributions from excitation and inhibition of the respective canals. The gain at each frequency was measured from linear and nonlinear pathways the parameters of which were derived from data in squirrel monkeys with normal vestibular function. We sought to determine the interaction of frequency, velocity, and acceleration in producing asymmetries of the horizontal VOR after disruption of vestibular function from one labyrinth.
The responses attributable to the intact canals were fit with a transfer function with a single pole and zero, the values of which were determined from a least squares regression that minimized error between the fit and the observed values of gain and phase.

Eccentric rotations

The two animals that had undergone plugging of all six semicircular canals were tested with eccentric rotations to verify that their linear VOR (LVOR) was intact. The superstructure to which the animal was secured was placed 58 cm eccentric to the rotational axis. Rotations at 4 Hz, $\pm 20^\circ/s$ were given with animals facing toward and away from the axis of rotation. The peak tangential force for this stimulus was 5.0 m/s$^2$ which is equivalent to 0.51g. Animals were tested in darkness and cycles with a vergence of $<1$ meter angle (MA) were used in the averages.

RESULTS

The horizontal VOR evoked by steps of head acceleration and by sinusoidal rotations was examined in four squirrel monkeys after unilateral plugging of the three semicircular canals. Semicircular canals were plugged on the right in three animals and on the left in one. Unless otherwise noted, all responses were measured in darkness.

Spontaneous nystagmus

These four animals were kept in darkness after the plugging procedure. There were no restrictions on movement within their cages at any time after the procedure. When evaluated 8 h after plugging while animals were still in darkness, there was a spontaneous nystagmus with slow phase components directed toward the plugged side in three of these animals (M314, M20, and M51). The horizontal slow-phase eye velocity of this nystagmus was $9.0 \pm 6.4^\circ/s$. On the first day after plugging (while the animal was still being kept in darkness) the slow-phase eye velocity had fallen to $5.4 \pm 3.4^\circ/s$. This nystagmus increased in amplitude to $15.3 \pm 3.2^\circ/s (P < 0.02$ with respect to slow phase velocities before animals were brought into light) when tested in darkness 8 h after they had been returned to light. The slow-phase velocity of the spontaneous nystagmus decreased to $3.8 \pm 2.8^\circ/s$ after the animals had been in light for 18–24 h. At 10 and 30 days after plugging, the spontaneous nystagmus measured $2.9 \pm 3.0$ and $3.1 \pm 2.0^\circ/s$, respectively.

One animal (M330) had a spontaneous nystagmus with slow-phase components toward the intact labyrinth when measured while the animal was being kept in darkness 8 h after the plugging procedure. The slow-phase velocity was $6.9 \pm 3.2^\circ/s$. The spontaneous nystagmus in this animal reversed in direction on the first day after surgery when the animal was still in darkness and had a slow phase velocity of $6.4 \pm 1.8^\circ/s$. The nystagmus continued to beat toward the intact ear and had a slow-phase velocity of $5.2 \pm 1.7^\circ/s$ after the animal had been in light for 18–24 h. It measured $3.5 \pm 1.6$ and $4.1 \pm 1.6^\circ/s$ at 10 and 30 days, respectively, after the plugging procedure.

Steps of acceleration

The VOR evoked by steps of acceleration showed a reduction in gain after plugging with responses to ipsilesional rotations having a lower gain than those for contralesional rota-
When tested 18–24 h after return to light, the asymmetry in $G_A$ had increased: $G_{A,\text{ipsi}}$ for ipsilesional rotations ($G_{A,\text{ipsi}} = 0.37 \pm 0.07$ and $G_{A,\text{contra}} = 0.88 \pm 0.05$ ($P < 0.001$). This increased asymmetry was due to a large rise in $G_{A,\text{contra}}$ after animals were returned to light ($P < 0.02$), whereas $G_{A,\text{ipsi}}$ was unchanged ($P > 0.11$). The rise in $G_{A,\text{contra}}$ after animals were returned to light brought this parameter close to its value before the plugging procedure. $G_V$ remained asymmetric when initially evaluated after return to light: $G_V$ for ipsilesional rotations ($G_{V,\text{ipsi}} = 0.49 \pm 0.07$ and $G_{V,\text{contra}} = 0.62 \pm 0.04$ ($P < 0.03$). In contrast to $G_A$, return to light resulted in increases in $G_{V,\text{ipsi}}$ and $G_{V,\text{contra}}$ that were significant for each direction ($P < 0.04$ for $G_{V,\text{ipsi}}$, $P < 0.01$ for $G_{V,\text{contra}}$).

One animal, M51, was kept in darkness for 4 days after the plugging procedure. The findings in this animal provided further support for the notion that return of the animal to light, and not simply the elapse of time after the procedure, provided the stimulus required for an increase in $G_{A,\text{contra}}$. There was a small increase in $G_{A,\text{contra}}$ from 0.60 ± 0.04 measured 8 h after the plugging procedure to 0.68 ± 0.09 measured on day 4 after plugging but before return of the animal to light ($P < 0.05$). A large increase in $G_{A,\text{contra}}$ to 0.86 ± 0.04 occurred within the first 8 h after the animal was returned to light on day 4 ($P < 0.01$). When tested 18–24 h after return to light, the asymmetry in $G_A$ had increased: $G_{A,\text{contra}}$ from 0.60 ± 0.04 measured 8 h after the plugging procedure to 0.68 ± 0.09 measured on day 4 after plugging but before return of the animal to light ($P < 0.05$). A large increase in $G_{A,\text{contra}}$ to 0.86 ± 0.04 occurred within the first 8 h after the animal was returned to light on day 4 ($P < 0.01$).

To account for the possible effects of small differences in the values of $G_A$ and $G_V$ between animals before the plugging procedure, these gains measured after plugging were normalized in each animal to that of the comparable parameter before the procedure. $G_A$ for ipsilesional rotations when measured 8 h after plugging (while animals were still in darkness) was $0.33 \pm 0.03$ and $0.61 \pm 0.14$ for contralateral rotations ($P < 0.05$). $G_V$ for ipsilesional rotations was also reduced in comparison with that for contralateral rotations at the time of this initial evaluation after plugging: $0.40 \pm 0.05$ and $0.52 \pm 0.05$, respectively ($P < 0.01$).

The findings in this animal provided further support for the notion that return of the animal to light, and not simply the elapse of time after the procedure, provided the stimulus required for an increase in $G_{A,\text{contra}}$. One animal, M51, was kept in darkness for 4 days after the plugging procedure. The findings in this animal provided further support for the notion that return of the animal to light, and not simply the elapse of time after the procedure, provided the stimulus required for an increase in $G_{A,\text{contra}}$.
on day 4 at 8 h after return to light (P reached a lower peak velocity (3,000°/s², 60°/s). The contrale-

rotations (gain is appreciably greater than that measured for ipsilesional

in Fig. 3. These findings indicate that the decrease in gain that occurs at

0.73

6

0.71

0.09 for acceleration and 0.70

6

0.09. At day 30, Gv,ipsi was unchanged when its value on
day 30 (0.98 ± 0.15) was compared with that after initially returning to light (P > 0.20). The data for GA and GV at intervals of ≤30 days after unilateral canal plugging are shown in Fig. 3.

Gv for rotations in each direction increased during the 30 days after the plugging procedure. When data from the four animals were pooled, the difference between values for Gv,ipsi in comparison with Gv,contra rotations ceased to be significant. At day 10 after the plugging procedure, Gv,ipsi = 0.65 ± 0.07 and Gv,contra = 0.71 ± 0.09 (P > 0.09). At day 30, Gv,ipsi = 0.67 ± 0.09 and Gv,contra = 0.79 ± 0.10 (P > 0.08). When data from each animal were considered separately, the difference between ipsilesional and contralesional values of GV was not significant at day 30 in three of the animals (P > 0.15). One animal, M51, had asymmetries in GV that persisted throughout the initial 30-day period of evaluation and even at day 63 after the plugging procedure: Gv,ipsi = 0.73 ± 0.03 and Gv,contra = 0.87 ± 0.03 (P < 0.0001).

Figure 4 shows the responses to steps of acceleration that reached a lower peak velocity (3,000°/s², 60°/s). The contralesional gain values were 0.88 ± 0.10 for acceleration and 0.73 ± 0.06 for velocity (P < 0.002), whereas the ipsilesional gains were 0.52 ± 0.05 for acceleration and 0.70 ± 0.03 for velocity (P < 0.0001). Note that the contralesional acceleration gain is appreciably greater than that measured for ipsilesional rotations (P < 0.0001), whereas the velocity gains for ipsi- and contralesional rotations were indistinguishable (P > 0.43). These findings indicate that the decrease in gain that occurs at

the end of the acceleration for contralesional rotations and the increase in gain that occurs at that point for ipsilesional rotations are both independent of fast phases.

**Latency**

Whereas the latency calculated by the linear fit and 3-SD methods (see Minor et al. 1999 for a description of these methods) were identical before plugging, the diminished gain of the ipsilesional responses after plugging resulted in a shorter latency (4.0 ± 3.5 ms) with the linear fit method than that measured prior to the lesion (Fig. 5A). In contrast, the increasing gain with velocity noted for the contralesional responses gave a longer estimate of latency (11.4 ± 1.0 ms) in comparison with prelesion values when the linear fit method was used. The 3-SD method was less sensitive to such differences in gain (Fig. 5B). The latency for ipsilesional responses on day 10 after
plugging for the four animals measured 8.4 ± 0.4 ms and that for contralesional responses was 7.2 ± 0.1 (P < 0.01).

Latency values calculated by the 3-SD method in the four monkeys are listed at various times after the plugging procedure in Table 1. There were no differences between the measures at specific times after plugging for contralesional (P > 0.5) or for ipsilesional (P > 0.9) rotations. The data for all of the measurement times in the animals were pooled to compare the responses in each direction. The contralesional latency measured 7.1 ± 0.3 ms and the ipsilesional latency measured 8.2 ± 0.4 ms (P < 0.0001).

Fits to steps of acceleration

**CONTRALESIONAL.** The gain of the VOR was noted to increase with head velocity after plugging. Responses to contralesional rotations were analyzed with linear and polynomial fits to the data. Figure 6 shows a plot of these responses and the fits at day 10 after plugging in MS1. Table 2 gives the values for the coefficients of the terms for each of these fits. As described in METHODS, the responses were symmetric about the head- and eye-velocity axes and the coefficient of the second-order term was zero in each case.

When animals were evaluated 8 h after plugging (while still in darkness), there was little difference in the gain values calculated by the linear and cubic fit methods. The coefficient of the first-order term calculated by the linear fit method was 0.53 ± 0.18. This first-order term calculated by the cubic fit method measured 0.50 ± 0.18 (P > 0.8).

There was a substantial increase in the contribution of the third-order term to the response dynamics after the animals were brought into the light. The value of the third-order term calculated from the cubic fit increased from (0.38 ± 0.27) x 10^{-5} when evaluated 8 h after plugging (while still in darkness) to (2.21 ± 0.39) x 10^{-5} when evaluated 18–24 h after return to light (P < 0.001). The third-order term did not change at later times after the animal had been evaluated 8–24 h after return to light (P > 0.65). Pooling the values of the third-order terms after animals were returned to light gave a mean value of (2.17 ± 0.52) x 10^{-5} in comparison with the value of (1.02 ± 1.07) x 10^{-5} obtained before plugging (P < 0.01). The increased contribution of the third-order term to the response when the animal was brought into light was also apparent in the increase in mean-squared error for the linear in comparison with the cubic fit. The improved fit with the third-order polynomial was reflected in the decrease in the value of the Bayesian information criterion (BIC) with this higher-order fit after the animal was brought into light. As explained in the companion study (Minor et al. 1999), a reduction in the value of the BIC justified the use of a more complex (higher-order) model (Cullen et al. 1996; Galiana et al. 1995).

**IPSILESIONAL.** The responses to ipsilesional rotations, in contrast to those for contralesional rotations, showed no increase in gain with velocity. In fact, for the initial two testing sessions (day 1 in the dark and day 1 in the light) there was a decrease in gain with increasing stimulus velocity. Therefore we fit the ipsilesional data obtained early after plugging with a hyperbolic tangent optimized to match the trajectory of the relationship between eye and head velocity (Fig. 7). The coefficients of this equation varied in accord with the
Traces of sinusoidal rotations (0.5–15 Hz, Responses to sinusoidal rotations with time after plugging. indicate that the ipsilesional response becomes more linear velocity. This was also the case for day 21. These findings because their gains did not decrease with increasing head data from day 10 could not be made in the other three animals day on which the data were obtained. On the day of surgery, \( \alpha = 0.01 \pm 0.0016 \) and \( k = 35.1 \pm 8.9 \). On day 1 in the light, \( \alpha = 0.0076 \pm 0.0018 \) and \( k = 63.6 \pm 13.8 \). The data from M51 on day 10 were fit with \( \alpha = 0.005 \) and \( k = 105.2 \). This fit for data from day 10 could not be made in the other three animals because their gains did not decrease with increasing head velocity. This was also the case for day 21. These findings indicate that the ipsilesional response becomes more linear with time after plugging.

**Responses to sinusoidal rotations**

Figure 8 displays the gain and phase plots of responses to sinusoidal rotations (0.5–15 Hz, ± 20°/s) measured while animals were in darkness 8–12 h after plugging. 18–24 h after return to light, and days 10 and 30 after plugging. The gain recovered across all frequencies over time after plugging. The gain measured in darkness after plugging was 0.49 ± 0.06 and did not change with respect to frequency (\( P > 0.9 \)). The reduction in gain compared with prelesion values was 42 ± 4%. Gain increases were noted for each successive testing session after animals were returned to light. The recovery of gain evaluated at day 30 after plugging was largest over the frequency range of 0.5–6 Hz. The gain at these frequencies measured 0.70 ± 0.04 and did not differ between individual frequencies (\( P > 0.7 \)). Less recovery of gain was noted for 8- to 15-Hz rotations. The gain at these frequencies was 0.61 ± 0.02 and did not differ for individual frequencies (\( P > 0.8 \)). The difference in the mean gain values for these two frequency groups was significant (\( P < 0.01 \)).

The phase of the VOR evaluated on day 30 after plugging showed a slight lead at 0.5 and 2 Hz (4.5 ± 4.7°) and did not differ between these frequency values (\( P > 0.4 \)). The phase declined with frequency to have a lag that measured −11.7 ± 1.3° at 12 and 15 Hz and did not differ between these frequency values (\( P > 0.4 \); Fig. 9). This difference in mean phase

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Ev = k \cdot \tanh(\alpha \cdot Hv)
\]

FIG. 7. Fit to data from ipsilesional rotations in the 4 monkeys expressed as eye vs. head velocity at 8–12 h after plugging while animals were still in the dark and day 1 after return to light. This fit was also made from day 10 after plugging in M51. The other 3 monkeys had linear responses for ipsilesional rotations at day 10.

As described in the following text, data from two animals that underwent subsequent plugging of the three remaining semicircular canals indicate that, at higher frequencies, responses do arise from the plugged canals. These residual responses after bilateral plugging of the six semicircular canals were subtracted at each frequency from that measured after unilateral canal plugging (see METHODS). This computation gave a representation of responses arising from the intact labyrinth.

Figure 9 displays gain and phase after correction for the response from the plugged canals for the following parameters: responses at day 30 after canal plugging, residual responses attributable to the plugged canals, the resultant responses arising from signals mediated by the intact canals, and the fit of a transfer function to these responses from the intact canals. Recovery of gain was greater at 0.5–4 Hz than it was at the higher frequencies. The gain at 0.5–4 Hz measured 0.70 ± 0.11 and did not differ between frequencies within this interval (\( P > 0.5 \)). The gain at 6–15 Hz measured 0.54 ± 0.07 and did not differ with frequency (\( P > 0.5 \)). The difference in mean gain values for these two frequency groups was significant (\( P < 0.01 \)).

The phase of the VOR evaluated on day 30 after plugging showed a slight lead at 0.5 and 2 Hz (4.5 ± 4.7°) and did not differ between these frequency values (\( P > 0.4 \)). The phase declined with frequency to have a lag that measured −11.7 ± 1.3° at 12 and 15 Hz and did not differ between these frequency values (\( P > 0.4 \); Fig. 9). This difference in mean phase

FIG. 8. Gain and phase of responses to sinusoidal rotations at 0.5–15 Hz, ± 20°/s measured 8–12 h after plugging while animals were still in the dark (dark 1), 18–24 h after return to light (light 1), day 10 and day 30 after plugging.
values for these two groups was significant ($P < 0.02$). The phase lag at these highest frequencies was greater than that observed at these frequencies before plugging ($P < 0.0001$).

Responses to sinusoidal rotations of 0.5–15 Hz, ±20°/s also were analyzed in terms of half-cycle gains (Fig. 10). Although mean values of half-cycle gain for contralesional motion were typically higher than those for the corresponding ipsilesional half-cycle, these differences were not significant at any single frequency on each day tested ($P > 0.05$). There was also no difference in contra- or ipsilesional half-cycle gain across frequencies on any day tested ($P > 0.10$).

MS1 was tested at 4 Hz, ±100°/s after plugging, and considerably larger half-cycle gain asymmetries were noted (Fig. 11). At 0.5 Hz, there was no half-cycle asymmetry at any of the velocities that were tested ($P > 0.6$). At 4 Hz, the contralesional and ipsilesional half-cycle gains for 100°/s rotations measured 0.81 ± 0.05 and 0.53 ± 0.03 ($P < 0.0001$). An increased contralesional in comparison with ipsilesional half-cycle gain also was noted at 10 Hz, ±50°/s. This difference in half-cycle gain was due to an increase in the gain of the contralesional response at higher velocities. The ipsilesional half-cycle gain, in contrast, did not change as velocity was increased. Phase did not change as velocity was varied across these frequencies ($P > 0.05$). This asymmetry in half-cycle gains resulted in a harmonic distortion in the response that measured 8.8% at 4 Hz, ±100°/s.

A bias velocity, defined as a DC shift in the response, was measured from the Fourier analysis of the data. The bias velocity was directed toward the plugged side and measured 2.8 ± 3.1°/s in responses to sinusoidal rotations of 2–15 Hz, ±20°/s on day 1 in the dark, 10, and day 21. The bias velocity was 9.5 ± 2.0°/s when measured 18–24 h after animals were brought into light. Responses to rotations at a peak velocity of 20°/s had a bias velocity that did not change with respect to frequency ($P > 0.6$) and that was indistinguishable from the spontaneous nystagmus measured for each testing session ($P > 0.5$). The bias velocity measured from data pooled at 2 and 4 Hz increased with head velocity, measuring 0.02 ± 4.5°/s and 10.9 ± 3.2°/s at peak velocities of 20 and 100°/s, respectively ($P < 0.002$).

The coefficients of polynomial fits to the contralesional half-cycles for 4 Hz, ±100°/s in MS1 were similar to those calculated from the contralesional steps of acceleration. At day 21 after plugging, the coefficient of the cubic term calculated

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**FIG. 9.** Gain and phase of the horizontal VOR for rotations at 20°/s before and after correction for the response from the plugged canals. Traces shown depict the measured gains and phases before correction (uncorrected), the responses measured at these frequencies in the animals that had undergone bilateral canal plugging (bilateral plug), the gain and phase after correction for responses arising from the plugged canals (corrected), and the fit of a low-pass filter model to the data (- - -).

**FIG. 10.** Half-cycle gains for responses to sinusoidal rotations at 0.5–15 Hz, ±20°/s measured 8–12 h after plugging while animals were still in the dark (A), day 1 (18–24 h) after return to light (B), day 10 (C), and day 30 (D) after plugging.

**FIG. 11.** Gain and phase of responses to sinusoidal rotations at 0.5–15 Hz, ±20, 50, and 100°/s in MS1 at day 10 after unilateral canal plugging. Gain is shown for half-cycles with solid symbols for contralesional and open symbols for ipsilesional rotations.
from the fit to the contralesional steps of acceleration was $1.74 \times 10^{-5}$, whereas that calculated from the sinusoidal data was $1.77 \times 10^{-5}$. As also noted for the steps of acceleration, the responses to ipsilesional half-cycles of rotations had a constant gain over the velocities tested.

Responses after bilateral plugging of the semicircular canals

Two monkeys underwent plugging of the three semicircular canals of the left labyrinth at 137 days (M20) and 70 days (M314) after the canals had been plugged on the right. Responses to steps of acceleration (3,000°/s² to 150°/s) recorded 2 wk after the left semicircular canals were plugged in M314 and M20 are shown in Fig. 12. The responses were symmetric for rightward and leftward rotations. The following first-order transfer function was derived from a least-squares fit to the data

\[ E_v = \frac{0.25(0.032s)}{0.032s + 1} 

\]

where \( H_v \) and \( E_v \) are head and eye velocity, respectively. Figure 12, A and B, shows the responses and fits to steps of acceleration in the leftward and rightward steps of acceleration, respectively. Similar responses were observed at 4 and 6 wk after the remaining canals were plugged.

Responses to sinusoidal rotations at 0.5–15 Hz at 2 wk after the left semicircular canals had been plugged in M314 and M20 are shown in Fig. 13. The gain of the response grew with frequency to reach 0.23 ± 0.03 at 15 Hz. The response had a phase lead re head velocity of 52.4 ± 7.9° at 4 Hz and 16.0 ± 13.0° at 15 Hz. We also fit a first-order transfer function similar to Eq. 1 to the sinusoidal data. The best fit had a gain and time constant of 0.21 and 0.023 s, respectively. These values are quite similar to those noted in the fits to steps of acceleration. Figure 13 also shows the response that is predicted based on the coefficients of the first-order transfer functions derived from the responses to steps of acceleration and from the sinusoidal rotations.

FIG. 12. Responses to leftward (top) and rightward (bottom) rotations in M314 and M20 recorded after all 6 semicircular canals had been plugged. Responses were averaged from 15 rotations in each direction for each animal. Mean (center curve in white) and ±1 SD interval (shaded area) are shown for responses in each direction. Head velocity and the fit of the model to the plugged data discussed in the text also are shown.

FIG. 13. Gain and phase plots for sinusoidal rotations at 0.5–15 Hz, ±20°/s for M314 and M20 recorded after all 6 semicircular canals had been plugged. Also shown are the fits of a first-order model with coefficients derived from the responses to steps of acceleration with an amplitude of 3,000°/s² and reaching a peak velocity of 150°/s (transient fit) and the fit to the data from sinusoidal rotations (sinusoidal fit).

Responses to eccentric rotations after plugging of the six semicircular canals

The sensitivity of the linear vestibuloocular reflex, LVOR, at 4 Hz in M314 after all semicircular canals had been plugged measured 18.4 ± 4.7° · s⁻¹ · g⁻¹ with a phase re head velocity of 168.5 ± 0.3° for rotations with the animal facing the axis of rotation and 20.0 ± 5.1° · s⁻¹ · g⁻¹ with a phase re head velocity of 14.3 ± 1.1° for rotations with the animal facing away from the axis of rotation. For M20, the LVOR sensitivity with the animal facing the axis of rotation was 19.6 ± 5.5° · s⁻¹ · g⁻¹ and a phase re head velocity of 160.5 ± 0.6°. The LVOR sensitivity in M20 was 18.8 ± 5.5° · s⁻¹ · g⁻¹ with a phase of −6.2 ± 0.2° for rotations with the animal facing away from the axis of rotation. Although we did not measure the sensitivity of the LVOR in these animals before plugging, these gain and phase values are comparable with those measured with similar stimuli in animals with normal vestibular function (Sargent and Paige 1991).

Discussion

Asymmetries after unilateral plugging of the three semicircular canals

The asymmetry that we observed after unilateral canal plugging in responses to ipsilesional in comparison with contralesional steps of acceleration was comparable with that reported for similar stimuli after ablative lesions of the vestibular pe-
hippory in humans (Aw et al. 1996; Crane and Demer 1998; Halmagyi et al. 1990). Because we have presented evidence that spontaneous activity in the labyrinth is preserved after canal plugging, this finding indicates that the asymmetry arises from the dynamics of these responses and is not dependent on a static imbalance in activity between the two vestibular nerves or nuclei.

This asymmetry was most prominent during the step of acceleration in comparison with the velocity plateau of the stimulus. The difference in $G_A$ between contralesional and ipesional responses was greater for steps of acceleration that had a longer duration and, as a consequence, reached a higher velocity. This observation indicates that acceleration is not the sole determinant of the asymmetry. There was only a small asymmetry in $G_V$ between contralesional and ipsilesional responses in contrast to the much larger asymmetry in the corresponding values for $G_A$. The stimulus velocity was greater for the portion of the response during which $G_V$ was measured in contrast to the lower stimulus velocities over the interval used to measure $G_A$. If stimulus velocity were the only parameter involved in the asymmetry, then a greater difference between ipsilesional and contralesional responses would have been expected for $G_V$ in comparison with $G_A$. The findings indicate that the asymmetry increases with the velocity of the stimulus but only during the dynamic portion of the stimulus not at the plateau of head velocity. Thus a parameter other than acceleration and velocity also must be involved in the etiology of the asymmetry. The frequency content of the stimulus, in association with velocity, is an obvious suggestion for such a parameter.

The data from sinusoidal rotations at increasing stimulus velocities support an interactive role of both frequency and velocity in the origin of the asymmetry. Sinusoidal rotations at frequencies of $\leq 15$ Hz at a peak velocity of $20^\circ/s$ showed only a slight, and often insignificant, asymmetry between ipsilesional and contralesional responses. A prominent asymmetry was present at frequencies of $\geq 4$ Hz as the stimulus velocity was increased. The gain of responses to the contralesional half-cycles of the rotation increased at higher stimulus velocities, but the gain of ipsilesional responses stayed the same or decreased slightly as peak stimulus velocity was raised. No change in gain was seen as stimulus velocity was increased to $\leq 100^\circ/s$ at 0.5 Hz.

$G_A$ measured from contralesional steps of acceleration showed a marked increase in gain within the initial day after animals were returned to light. The error signal driving this gain increase was most likely retinal slip resulting from a low-gain VOR. In contrast, there was only a slight increase in $G_A$ for ipsilesional responses. These findings support the existence of a highly modifiable, but rectified, signal that is more prominent for stimuli with a combination of both higher frequency and velocity components.

As will be shown later in this DISCUSSION, the model that we developed for responses to steps of acceleration and sinusoidal rotations in monkeys with intact vestibular function (Minor et al. 1999) can be used to explain the findings after unilateral canal plugging. The asymmetries arise because of a greater increase in the gain of the nonlinear, in comparison with the linear, pathway. A more gradual rise with time after the lesion in the gain of the linear pathway accounts for the relatively symmetric increase in gain of responses to stimuli with lower frequency and velocity components.

**Effects of plugging on transduction in the semicircular canals**

Our findings indicate that plugging attenuates the responses of the affected canal to rotations while having little effect on the spontaneous activity of afferents innervating that labyrinth. The temporal bone histology showed that the plugging procedure obliterated the lumen of the canal while preserving the sensory epithelia of the semicircular canals and otoliths.

Four lines of evidence indicate that the plugs do not result in an ablation of spontaneous activity of afferents innervating the affected canals.

First, the spontaneous nystagmus recorded after plugging was considerably lower than the horizontal slow-phase velocity of $43^\circ/s$ noted when monkeys were tested in darkness acutely after labyrinthectomy (Fetter and Zee 1988). This spontaneous nystagmus after plugging was indicative of a decrease in activity from the labyrinth on which plugging had been performed in three animals and was excitatory with respect to the side of surgery in a fourth. An alteration of endolymphatic pressures within the labyrinth or to a transient inflammatory response resulting from the surgical procedure are two potential explanations for the nystagmus.

Second, the postural signs after canal plugging were more subtle and transient than the head tilt and ataxia noted in animals after labyrinthectomy (Fetter and Zee 1988; Precht 1986). In particular, the two animals in our companion study that had undergone bilateral labyrinthectomy (Minor et al. 1999) had significantly impaired movement and ataxia in contrast to the relatively subtle behavioral changes noted in the animals in which all six canals had been plugged.

Third, a small response to higher-frequency rotations was noted after all six canals were plugged in contrast to animals after bilateral labyrinthectomy in which responses to these same stimuli were completely absent.

Fourth, the linear VOR as evaluated by eccentric rotations was intact after all six canals had been plugged. The LVOR sensitivity for these 4-Hz rotations measured $19^\circ \cdot s^{-1} \cdot g^{-1}$ comparable with that reported in animals with no prior surgical manipulation of the labyrinth (Paige and Tomko 1991; Sargent and Paige 1991). As expected, the phase of the LVOR response shifted by $\sim 180^\circ$ when the animal was moved from a position facing toward a position facing away from the axis of rotation indicating that the response was of otolith and not canal origin.

Our data on the residual responses after plugging of all canals are similar to those recently reported in cynomolgus monkeys by Yakushin et al. (1998). They showed a persistent response in the plane of the plugged canal that increased with rotational frequency. The monkeys in our study that had undergone plugging of the six semicircular canals also showed small VOR gains that increased in magnitude as rotational frequency was increased. The phase of this residual VOR led head velocity by $60-80^\circ$ at 2 Hz and returned to being more in phase with velocity as the rotational frequency was increased to 15 Hz.

Yakushin et al. (1998) suggested that the effect of canal plugging was to alter the low-frequency 3-dB roll-off and...
Changes in the VOR after unilateral canal plugging

LATENCY. The latency calculated from the linear fit and 3-SD methods in animals with intact vestibular function was identical. These methods did not produce equivalent findings when used on the data after canal plugging. The linear fit method led to an erroneously short estimate of VOR latency for ipsilesional responses because the gain decreased with increasing head velocity. This method also led to a longer estimate of latency for contralesional responses due to the nonlinear rise in eye velocity with head velocity over the interval of 20–40 ms after the onset of the stimulus.

The 3-SD method was less susceptible to these differences in VOR gain between contra- and ipsilesional responses. The latency measured by this method was identical for contralesional rotations in comparison with prelesion values. In contrast, the latency was 1 ms longer for ipsi- than for contralesional rotations after plugging. The reason for this slight asymmetry between latencies for ipsi- and contralesional responses after plugging is not clear. Ipsilesional responses do have a lower gain that could have affected the time at which an eye movement response could be discerned.

The latency measured by the 3-SD method did not change with time after plugging. This finding indicates that the mechanisms responsible for changes in acceleration and velocity gain after plugging occurred independent of signals conveying the onset of the head rotations.

RESPONSES TO STEPS OF ACCELERATION. $G_A$ and $G_v$ for ipsi- and contralesional rotations were reduced by ~43% when measured during the first testing session after plugging in comparison with prelesion values. The attenuation in responses to head velocity arising from the labyrinth with plugged canals provides the most obvious explanation for the initial reduction in VOR gain. We observed three effects that appeared to result from an inhibitory process during the period animals were kept in darkness after plugging.

First, the spontaneous nystagmus present after plugging was noted to transiently increase when animals were returned to light and then rapidly declined during the course of 1 day to an amplitude of ~3°/s. Paige (1983) observed a similar change in spontaneous nystagmus after plugging when his animals were returned to active head movements in light after plugging. Retinal slip may cause the removal of an inhibitory process that arose immediately after the lesion.

Second, the ipsilesional responses showed a saturation in the VOR at head velocities as low as 25°/s during the initial period after plugging (see Figs. 1 and 7). Inhibitory cutoff in pathways with low resting discharge rates could account for this observation.

Third, the polynomial fits to the contralesional responses from this initial testing session showed that the trajectory of the eye velocity was linear. The cubic term of the VOR noted in the prelesion responses was absent during the period animals were kept in darkness after plugging. Such an inhibitory effect could be explained based on a threshold discharge rate required to produce this nonlinear increase in gain at higher frequencies and velocities.

The recovery of contralesional acceleration gain occurred rapidly (within 18–24 h) after animals were returned to light. This recovery resulted in a larger asymmetry between values of $G_A$ for contra- and ipsilesional rotations. The increase in $G_A$ was manifested as a rise in the coefficient of the cubic term relating eye to head velocity. This term reached a value that was two-fold larger than noted before the lesion. $G_A$ did not change with time after its initial rise on return to light.

The recovery of $G_A$ occurred more slowly than that for $G_A$. Responses initially showed a saturation in the VOR at higher head velocities but linearity returned over the course...
of 10 days after plugging. There was no evidence of a nonlinear increase in gain with velocity (i.e., cubic term) for ipsilesional rotations during the recovery period. The absence of a nonlinear increase in gain with velocity for $G_{A-ipsi}$ may be due to inhibitory cutoff that is inherent in the nonlinear pathway arising from the intact labyrinth.

Asymmetries in $G_V$ were smaller and more variable than those noted for $G_A$. After animals had been returned to light, $G_{V-ipsi}$ values were greater than those measured for $G_{A-ipsi}$. Conversely, $G_{V-contral}$ values were less than $G_{A-contral}$ for each of the days tested. $G_V$ increased for rotations in each direction after plugging with the largest increase occurring when animals were returned to light and a smaller increase occurring over the next week. When evaluated at 30 days after plugging, there was no asymmetry between $G_V$ for ipsi- and contralesional rotations, whereas the corresponding values of $G_A$ remained asymmetric.

We also used steps of acceleration ($3,000°/s^2$) that reached a lower peak velocity of 60°/s because fast phases are typically not seen until later times in the responses to these stimuli in contrast to those that reach a peak velocity of 150°/s. As in the responses to steps of acceleration that reached a peak velocity of 150°/s, an asymmetry during the period of acceleration was noted between ipsi- and contralesional rotations, whereas the velocity gains were symmetric. The transition from gains during the acceleration to those at the velocity plateau was characterized by a decrease in the gain for contralesional rotations and an increase in the gain for ipsilesional rotations. Both of these transitions were noted before the occurrence of a fast phase. This observation is important because fast phases have been proposed to restore linearity to the VOR (Galiana 1991). Such effects of fast phases may be responsible for increases in the VOR gain at later times in the stimulus, but the initial return to symmetry after reaching the velocity plateau is due to response dynamics and not to resetting by fast phases.

The higher gain noted during the period of acceleration in contrast to the velocity plateau for contralesional rotations is due to the frequency and velocity dependence of the nonlinear pathway involved in VOR dynamics (see Fig. 11). This pathway accentuates the gain during the acceleration but does not make a contribution to the response after the velocity plateau has been reached. The increase in gain at the velocity plateau in comparison with the period of acceleration for ipsilesional rotations is most likely related to the frequency-dependent recovery of gain in the linear pathway (see Fig. 7). Gain recovery is greater at lower frequencies than at higher ones. The velocity plateau of the acceleration step stimulus is analogous to a low-frequency stimulus.

The asymmetry between gains measured during the period of acceleration for ipsi- and contralesional rotations is similar to that observed in humans (Aw et al. 1996) and in guinea pigs (Gilchrist et al. 1998) after ablative vestibular lesions and in cats after unilateral plugging of the horizontal canal (Broussard and Bhatia 1996). This finding and the evidence showing that our canal plugging procedures are not resulting in an ablation of spontaneous activity indicate that these asymmetries are linked to the dynamics of the reflex pathways. Similar asymmetries in the VOR that results from inhibition in comparison with excitation of signals related to a canal that is coplanar to a plugged canal is provided by responses to high acceleration rotations in humans after posterior canal occlusion (Aw et al. 1996; Cremer et al. 1998).

**Responses to sinusoidal rotations.** The data from rotations at 0.5–15 Hz, ±20°/s before animals were brought into light at higher frequencies showed a phase lead at higher frequencies that was not present prior to the lesion. This small phase lead may be due to greater inhibition for lower-frequency responses and/or to the residual response arising from the plugged canals. There was a return of the phase lag at higher frequencies and an increase in gain at the lower frequencies noted after the animals were returned to light. We derived the transfer function in Eq. 2 with a single pole and zero to fit the gain and phase data (see Fig. 9) at day 30 after plugging

$$E_V = \frac{(0.019s + 1)}{(0.029s + 1)} \cdot H_V$$

where $H_V$ and $E_V$ are head and eye velocity, respectively. As noted for lens-induced adaptation of the VOR (Lisberger et al. 1983), compensation shows frequency specificity with greater recovery of gain at lower frequencies.

The half-cycle gains for these sinusoidal rotations at lower peak velocity indicate that asymmetries in the VOR after canal plugging are not simply determined by frequency. If frequency alone was responsible, then a larger asymmetry might be expected at 15 Hz than at 0.5 or 2 Hz. Instead, the asymmetry did not reach significance for any frequency tested at peak velocities of ±20°/s (Fig. 10). The findings at higher frequencies and velocities establish the etiology of the asymmetry (Fig. 11). At 4 Hz, ±100°/s, the half-cycle gains are larger for contralesional than for ipsilesional rotations. The asymmetry was due to an increase in the gain of the contralesional in comparison with ipsilesional half-cycle. An increase in the gain of the nonlinear pathway is the most likely cause of the asymmetry. There is no change in the ipsilesional gain because the nonlinear pathway is rapidly driven into inhibitory cutoff for rotations toward the lesioned side after plugging. As noted for the responses to steps of acceleration, the ipsilesional responses are due exclusively to the linear pathway.

Previous studies have defined asymmetries in the VOR with lower-frequency sinusoidal rotations after unilateral canal plugging or ablative vestibular lesions (Fetter and Zee 1988; Paige 1989). These asymmetries typically are observed at peak head velocities of >150°/s and are characterized by a cutoff in responses at higher velocities for rotations toward the lesioned side. A bias velocity defined as a DC shift in the response that is greater than the underlying spontaneous nystagmus typically was observed in association with the asymmetries.

The asymmetries that we have identified in this study appear to arise from a fundamentally different mechanism than that discussed for lower-frequency responses. Rather than cutoff in ipsilesional responses (as reported in the studies at lower frequencies), the asymmetries we observe are due to an increase in the gain of the contralesional response resulting from the excitatory contribution of the nonlinear pathway.

**Modeling of asymmetries in the VOR after unilateral canal plugging.**

Figure 14 shows a bilateral model of the VOR that we have used to simulate the asymmetries in ipsi- and contralesional
responses identified in our study. The inputs, arising from linear and nonlinear pathways, and coefficients used in the model are described in the companion paper (Minor et al. 1999). Because we were concerned mainly with modeling the asymmetries that persist after a unilateral vestibular lesion, we used data from 10 days after the plugging procedure (i.e., after the inhibitory effects had resolved). To simulate the effect of the lesion, we removed the inputs from the plugged side while maintaining the spontaneous rate. We could account for the changes observed in responses to the stimuli used in this study after canal plugging by adjusting the central gain elements of the linear and nonlinear pathways ($k_l$ and $k_n$). The other coefficients in this model were calculated from data in the animals before plugging and were not changed in the simulations of the findings after canal plugging.

Because there was no manifestation of the nonlinear pathway for ipsilesional rotations after plugging, we propose that this pathway is driven into inhibitory cutoff for velocities of $>30°/s$. This cutoff point is predicted based on the sensitivity of neurons in the nonlinear pathway ($p_{n1} = 3.0$ spikes $· s^{-1}° · s^{-1}$). On the basis of this premise, the gains for the ipsilesional responses could be used to specify $k_l$, the central gain element for the linear pathway. The data support the conclusion that the gain of the linear pathway is symmetric for rotations in each direction. We therefore calculated this gain of the linear pathway ($k_l$) from the ipsilesional responses. The gain of the nonlinear pathway ($k_n$) then was calculated from the contralesional responses by subtracting the component of these responses that arose from the linear pathway.

Figure 15 shows the gain and phase plot of the simulated responses at day 10 after canal plugging. The increase in gain for contralesional responses was accounted for by an increase in $k_n$ from $1.0 \times 10^{-5}$ before to $1.5 \times 10^{-5}$ after plugging. The

![Figure 14. Schematic diagram of the bilateral model used in the simulations. Model has linear and nonlinear pathways each of which receive an angular head velocity signal. Linear pathway has a sensitivity to head velocity, $p_l$, that is 0.4 spikes $· s^{-1}° · s^{-1}$. Time constants in the transfer function are $T_c = 5.7 s$, $T_g = 0.00624 s$. There is a central gain element, $k_l$, that has a value of 1.0. Coefficients in the nonlinear pathway are $p_{n1} = 3.0$ spikes $· s^{-1}° · s^{-1}$, $p_{n2} = 0.33$, $k_n = 1.0 \times 10^{-5}$, $T_h = 0.11 s$. The resting rate of units in both the linear and nonlinear pathways is 90 spikes/s and saturation element is set to have cutoff at 0 spikes/s and excitatory saturation at 500 spikes/s. Signals from both sides are passed through the neural integrator and 4th-order model of the oculomotor plant (Minor et al. 1999).](http://jn.physiology.org/)

![Figure 15. Gain and phase plot for simulation of responses to sinusoidal rotations with bilateral model after removal of inputs from 1 side. For the simulation, $k_l$ was increased by a factor of 1.25 and $k_n$ was increased by a factor of 1.5. Inset: comparison of the response to 4 Hz, ±100°/s rotations at day 10 after plugging M51 to the predictions of the model.](http://jn.physiology.org/)
value of \( k_i \) was increased from 1.0 before to 1.25 after plugging. The increase in \( k_i \) occurred more gradually and was responsible for the increase in gain at lower frequencies and lower velocities seen with time after the lesion.

The inset in Fig. 15 shows the agreement between the simulation of the model and the data from 4 Hz, \( \pm 100^\circ/\text{s} \) rotations plotted as eye versus head velocity at day 10 after plugging in M51. The differences between the ipsi- and contralesional responses are apparent on the plot. Note the contralesional response has a trajectory that is similar to that observed in the contralesional responses to steps of acceleration (see Fig. 6). The ipsilesional responses have a linear trajectory also similar to those noted for the steps of acceleration, at day 10 and longer, after plugging.

The coefficients determined for \( k_i \) and \( k_c \) at different days after plugging were used to fit the responses to steps of acceleration. Figure 16 shows the response asymmetries between ipsi- and contralesional rotations observed in the data and predicted by the model. The trajectories of the eye velocity during the period of the acceleration are predicted well by the model. The model predicts a lower gain at the velocity plateau and in restoring linearity during the velocity plateau.

Concluding remarks

The physiological basis of asymmetries between ipsi- and contralesional responses for high-frequency, high-acceleration rotations after unilateral plugging of the three semicircular canals can be summarized as follows.

First, there is inhibitory cutoff at stimulus velocities of \( \sim 30^\circ/\text{s} \) in the nonlinear pathway that is inherent in the dynamics of the normal VOR. The nonlinear pathway therefore makes no contribution to the ipsilesional responses after canal plugging.

Second, the gain of the nonlinear pathway is selectively increased when animals are returned to light, and experience retinal slip, after plugging. As a result, contralesional responses for more dynamic stimuli show a large increase in gain within 18–24 h after return to light.

Third, the gain of the linear pathway is increased more slowly after plugging and contributes to the symmetrical rise in responses to less dynamic stimuli with time after plugging.

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

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REFERENCES


FIG. 16. Comparison of responses in M51 at day 10 after plugging to simulation of responses to steps of acceleration with the bilateral model after removal of inputs from one side. For the simulation, \( k_i \) was increased by a factor of 1.25 and \( k_c \) was increased by a factor of 2.0. Mean (center curve in white) and \( \pm 1 \) SD interval (shaded area) are shown for ipsilateral and contralateral responses.

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