Origin of Orientation-Dependent Asymmetries in Vestibulo-Ocular Reflexes Evoked by Caloric Stimulation

Robert J. Peterka,1 Claire C. Gianna-Poulin,1 Lionel H. Zupan,2 and Daniel M. Merfeld2
1Neurological Sciences Institute, Oregon Health & Science University, Portland, Oregon 97006; and 2Jenks Vestibular Physiology Laboratory, Massachusetts Eye and Ear Infirmary, Department of Otolaryngology, Harvard Medical School, Boston, Massachusetts 02114

Submitted 24 February 2004; accepted in final form 25 May 2004

PETERKA, Robert J., Claire C. GIANNA-POULIN, Lionel H. ZUPAN, and Daniel M. MERFELD. Origin of orientation-dependent asymmetries in vestibulo-ocular reflexes evoked by caloric stimulation. J Neurophysiol 92: 2333–2345, 2004. A caloric stimulus evokes primarily a horizontal vestibulo-ocular reflex (VOR) when subjects are in a supine or prone orientation with the horizontal semicircular canal plane oriented vertically. In both monkeys and humans, the magnitude of VOR eye movements is greater in the supine than in the prone orientation, indicating that some factor or factors, other than the conventionally accepted convective stimulation of the horizontal canals, contributes to the generation of the VOR. We used long-duration caloric irrigations and mathematical models of canal-otolith interactions to investigate factors contributing to the prone/supine asymmetry. Binaural caloric irrigations were applied for 7.5 or 9.5 min with subjects in a null orientation with horizontal canals in the earth-horizontal plane (control trial), or with the subject’s pitch orientation periodically changing between null, supine, and prone positions with each orientation held for 30 s (caloric step trial). The control trial responses identified a small response attributable to a direct thermal effect on vestibular afferent activity that accounted for only 15% of the observed prone/supine asymmetry. We show that the gravito-inertial force resolution hypothesis for sensory integration of canal and otolith information predicts that the central processing of canal and otolith information produces an internal estimate of motion that includes both a rotational motion component and a linear acceleration component. These components evoke a horizontal angular VOR and linear VOR, which combine additively in the supine orientation, but subtract in the prone orientation, thus accounting for the majority of the observed prone/supine asymmetry.

INTRODUCTION

It has long been known that, in humans, horizontal vestibulo-ocular reflex (VOR) responses to caloric irrigations are larger with the subject lying in a supine position than in a prone position (Coats and Smith 1967). A similar supine greater than prone asymmetry has been demonstrated in squirrel monkeys (Minor and Goldberg 1990; Paige 1985). Although an opposite prone greater than supine asymmetry has been reported in rhesus (Böhmer et al. 1992, 1996) and cynomolgus monkeys (Arai et al. 2002), this opposite asymmetry is attributable to very strong cold water caloric irrigations that were sufficient to drive the horizontal canal afferent activity in the irrigated ear to an inhibitory cutoff in the supine orientation. Böhmer et al. (1992) demonstrated a supine greater than prone asymmetry similar to the asymmetry observed in humans and squirrel monkeys when less intense irrigations were used.

The supine greater than prone asymmetry in eye movement responses has often been attributed to a direct thermal effect on afferent nerve activity, which increases neural discharge for warm caloric irrigation and decreases neural discharge for cold caloric irrigation, thus adding to or subtracting from the primary convective effect resulting from changes in endolymph density (Coats and Smith 1967; Hood 1989). However, two studies in squirrel monkeys demonstrated that a direct thermal effect could not account for the entire prone/supine asymmetry (Minor and Goldberg 1990; Paige 1985). Both studies postulated the existence of another factor, dependent on head position and affecting both the convective and thermal components of the afferent neural discharge.

Paige (1985) suggested that this factor may represent a positional (possibly otolith) dependent modification of the horizontal canal VOR, or might reflect a stimulus artifact. Minor and Goldberg (1990) also proposed the existence of a position-dependent factor that they postulated was likely attributable to an otolith-mediated modulation of the horizontal VOR time constant. Specifically, they observed that the monkey horizontal VOR time constant was shorter during yaw rotation about an earth-vertical axis when the whole body was pitched 45° nose down (ND) compared with 45° nose up (NU). Because the VOR acceleration gain is related to the product of VOR velocity gain and the VOR time constant, the short ND VOR time constant should produce a lower ND VOR acceleration gain if the VOR velocity gain remains constant. Therefore because the conventional caloric stimulus is effectively a very low frequency stimulus, where VOR responses are expected to be proportional to rotational acceleration (Wilson and Jones 1979), the NU/ND caloric response asymmetry would be expected to correspond to the predicted VOR time constant asymmetry, and thus to a VOR acceleration gain asymmetry.

However, differences in horizontal VOR time constants, derived from pre- and postrotatory constant velocity rotations, appear small in humans for vertical axis rotations with NU and ND head tilts (Fetter et al. 1986). Therefore as pointed out by Minor and Goldberg (1990), a position-dependent modulation of the horizontal VOR time constant could make only a limited contribution to the prone/supine caloric asymmetry observed in humans. Indeed, Minor and Goldberg (1990) also pointed out that the prone/supine caloric asymmetry reported in humans (Clarke et al. 1988; Coats and Smith 1967) is smaller than that in the squirrel monkey, and suggest that the caloric response in humans may not include a position-dependent component. That is, they suggested that the prone/supine caloric asymmetry.

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

First published June 2, 2004; 10.1152/jn.00174.2004.

Address for reprint requests and other correspondence: R. J. Peterka, Neurological Sciences Institute, OHSU West Campus, Building 1, 505 NW 185th Ave., Beaverton, OR 97006 (E-mail: peterkar@ohsu.edu).
try in humans might be entirely attributable to a direct thermal effect, as originally hypothesized by Coats and Smith (1967). However, more recent results do show a consistent and significant difference between horizontal VOR time constants derived from postrotatory tilts into supine and prone orientations (Zupan et al. 2000), suggesting that it may be premature to dismiss this potential contribution to the prone/supine caloric asymmetry.

Alternatively, recent experimental and modeling results (Merfeld et al. 1999; Zupan and Merfeld 2003; Zupan et al. 2000, 2002) offer a different explanation for the existence of an otolith-mediated prone/supine caloric asymmetry based on the gravito-inertial force (GIF) resolution hypothesis. Specifically, the GIF resolution hypothesis predicts that caloric stimulation of the horizontal canals will evoke both an angular VOR and a linear VOR response. The linear VOR response arises from the central processing of canal and otolith information that attempts to resolve the apparent canal-otolith sensory conflict caused by an angular rotation cue from the horizontal canal that is not accompanied by a corresponding change in otolith afferent activity signaling a head tilt with respect to gravity. (More detailed explanation is provided in the DISCUSSION.) The prone/supine caloric asymmetry is consistent with the GIF resolution hypothesis because this hypothesis predicts that the linear VOR component always adds to the angular VOR magnitude in the supine position, and always subtracts from the angular VOR magnitude in the prone position.

A final possible factor, which has not been previously considered as a possible explanation for the prone/supine asymmetry, is a difference in vertical eye position during prone/supine caloric irrigation. Using passive rotation testing, Fetter et al. (1986) showed that horizontal eye velocity is attenuated by the cosine of the angle made between the optical axis and the plane of head rotation. A prone/supine caloric response asymmetry could occur if there were systematic differences in the vertical orientation of the eyes in their orbits in prone versus supine head orientations.

To identify the origin and the magnitude of the factors contributing to the prone/supine asymmetry in humans, we conducted long-duration caloric irrigation experiments with rapid changes in whole body position into supine and prone orientations. This type of caloric test protocol is referred to as a caloric step stimulus (Bock et al. 1979; Formby and Robinson 2000). A constant thermal gradient is assumed to be established across the vestibular labyrinth after a 2- to 3-min, constant-temperature caloric irrigation (Formby and Robinson 2000). Once a constant gradient is established, a step change of position from a “null” orientation (horizontal canal plane perpendicular to earth-vertical) into a supine or prone orientation induces a step change in convective force acting on the cupula of the horizontal canal. The simple torsion-pendulum model of the canal indicates that this step change in force causes a deflection of the cupula that follows second-order dynamics (Steinhausen 1933; Wilson and Jones 1979), but with the low-frequency dynamics determined by a single dominant time constant. The cupula deflection excites or inhibits canal afferents and generates VOR eye movements with an exponential rise in slow-phase velocity (Formby and Robinson 2000). Additional peripheral [e.g., adaptation (Goldberg and Fernandez 1971)], central [e.g., velocity storage (Merfeld et al. 1993; Raphan et al. 1979; Robinson 1977)], and multisensory interaction (Zupan et al. 2000) factors are expected to contribute to the dynamic VOR response. If head orientation is maintained in the null orientation throughout a long-duration caloric irrigation, then VOR eye movements recorded after 2–3 min should be indicative of the caloric response attributable to the direct thermal effect.

METHODS

Subjects

Twelve healthy subjects with no history of peripheral or central vestibular disorders participated in this study (8 males and 4 females, age 23–49 yr). Subjects gave their informed consent before being tested using a protocol approved by the Institutional Review Board at Oregon Health & Science University and in accordance with the 1964 Helsinki Declaration. Before taking part in the experiments, subjects were informed of the high likelihood that these tests would induce motion sickness. Subjects were asked questions related to their sensitivity to motion sickness during various activities so they could judge their willingness to participate.

Caloric stimulus

Two Brookler-Grams (Grams Medical Products, Costa Mesa, CA) closed-loop caloric irrigators were modified to provide constant-temperature irrigations for ≤10 min. The modifications included the addition of external reservoirs with circulating heaters and cooling fans for the pump and pump motor. Calibration runs with monitoring of irrigator tip temperature showed that the temperature reached a steady state in about 1 min and was maintained ±0.2°C for 10 min.

Irrigations were applied binaurally for the entire duration of each trial with one ear maintained at a temperature 4°C above normal body temperature and the other ear 4°C below body temperature. Left ear warm (41°C) and right ear cool (33°C) irrigations (LW-RC) were used in 11 subjects. Left ear cool and right ear warm irrigations (LC-RW) were also performed in 3 of these 11 subjects and in one additional subject. The 3 subjects tested with both irrigation protocols underwent the second irrigation protocol (LW-RC or LC-RW) 6 to 31 days after the first test session.

Binaural irrigations were chosen for 3 reasons. First, binaural irrigations provided a more natural push-pull activation of afferents from the horizontal semicircular canals. This avoided a potential sensory conflict between rotational information from the 2 horizontal canals that may have interfered with the interactions between canal and otolith inputs. Second, preliminary studies showed that monaural irrigations resulted in asymmetric dynamic responses that were related to excitation versus inhibition of the irrigated ear and not related to prone versus supine orientations. Specifically, the VOR time constant was always shorter when the irrigation evoked inhibitory canal activation (by convective forces) versus excitatory activation. This effect was independent of supine versus prone orientation and of warm versus cold irrigation. Such a time constant asymmetry is consistent with previously observed time constant asymmetry in canal afferent responses in the squirrel monkey (Goldberg and Fernandez 1971). Third, studies of peripheral afferent physiology in the squirrel monkey (Goldberg and Fernandez 1971) also indicate that the sensitivity of canal afferents to inhibitory accelerations is less than that to excitatory accelerations. Use of a binaural caloric stimulus minimized the influence of afferent sensitivity asymmetry as a factor contributing to the observed prone/supine asymmetry in the caloric-evoked VOR.

Pitch-tilt stimulus

The subject was seated and restrained in a kneeling position on a race car-type seat mounted in a hydraulically powered rotation device (2.300 Nm position servo-controlled actuator) with the earth-horizon-
tal pitch-tilt rotation axis aligned with the subject’s interaural axis. The subject’s head was secured using a bite-bar assembly attached to the motion device and an adjustable foam-lined head restraint. A mold of each subject’s teeth was formed on the bite bar using a dental-impression compound (3M Express, 3M Dental Products, St Paul, MN).

With the device’s pitch orientation at 0°, the subject’s head was oriented to place Reid’s plane earth-horizontal [Reid’s plane is defined by the upper margins of the external auditory meati and the infraorbital margin (Haslwanter et al. 1994)]. Standard conventions were followed to define the positive directions of eye and head rotations (Paige and Tomko 1991a).

Two types of trials were used: control trials and step trials. For the control trials, the subject’s whole body was quickly tilted +20° (head oriented 20° ND), thus placing the horizontal semicircular canals in the earth-horizontal plane (Curthoys et al. 1977) and in the null orientation that provides no convective stimulation of the horizontal canals. Caloric irrigations were initiated at the onset of the tilt and maintained for 7.5 min with the subject remaining in a 20° ND orientation.

For the caloric step trials, the subject’s whole body was tilted +20° (ND), as the caloric irrigations were initiated, and remained in this null orientation for 120 s to allow stabilization of the thermal gradient in the ear (Formby and Robinson 2000). The subject was then sequentially pitched and held for 30 s in a series of orientations that were pitched +90° from the original +20° orientation (i.e., +110° for the prone position and −70° for the supine position). The sequence also included 30-s null-orientation intervals between prone and supine orientations. Pitch position changes were accomplished in 1.5 s. Caloric irrigations were started at the onset of the initial 20° ND tilt and maintained for 9.5 min while the subject changed pitch position. Two orientation sequences were used: 1) prone, null, supine, null (repeated 3 times total); and 2) supine, null, prone, null (repeated 3 times total). The final null orientation was maintained for 90 s. (See Fig. 1 for schematic representations of each of the stimuli.) The prone and supine orientations were chosen to provide maximal excitatory or inhibitory convective stimulation to the horizontal semicircular canals. The null orientation was selected to provide zero convective stimulation.

A full test session consisted of a step trial (starting with prone or supine orientation), followed by a control trial, followed by a step trial (starting with opposite orientation as that used for the first step trial). All trials were performed in complete darkness. Subjects were instructed to keep their eyes wide open, and were given a mental-alertness task. A 5-min break was given between each trial during which the room lights were on and the subject was upright (0° tilt).

Eye movement recording and analysis

Binocular eye movements were recorded using infrared illumination for small video cameras (Machine Vision Hyper CCD Cameras, model CV-36SH) mounted on the bite-bar assembly. Reid’s plane was the horizontal reference plane for the eye movement coordinate system. Details of the eye movement recording system, image analysis, and calibration procedures are described in Zupan et al. (2000).

Data analysis was performed for the left eye. Horizontal and vertical eye position data were digitally processed to yield horizontal and vertical eye velocity. Fast phases were automatically removed from the eye velocity data using a computer algorithm based on peak acceleration detection, with manual editing by experienced personnel. Fast phase removal yielded slow-phase eye velocity (SPV). Positive horizontal and vertical SPV indicated eye movements with slow phases directed to the left and downward, respectively.

Examples of control and caloric step responses

Horizontal slow-phase eye velocities recorded in one subject who performed all trials for both LW-RC and LC-RW caloric irrigation protocols are shown in Fig. 1. For both LW-RC and LC-RW irrigations, eye movement responses in the supine orientations (−70°) were consistently stronger than responses in the prone orientations (+110°). Control trials produced small eye movements that were in opposite directions for LW-RC and LC-RW irrigations. These responses are representative of responses obtained from all subjects for both control and step trials.

Control trials

Data for control trials were available in 7 subjects for LW-RC irrigations and in 3 subjects for LC-RW irrigations. Horizontal SPV showed a transient time course in all subjects for the first 150–200 s, followed by a low-amplitude, steady-state SPV throughout the remaining 200–250 s of the trial (Fig.
FIG. 1. Horizontal slow-phase eye velocity (SPV) recorded in one subject who underwent a full test session for 2 irrigation protocols. Positive eye velocities correspond to slow-phase eye movements to the left. This subject first underwent LC-RW irrigations (A–C), and then underwent LW-RC irrigations 6 days later (D–F). Control trials (C and F) were always performed between the 2 step trials. Step trials started either with a pitch into the supine orientation (A and D) or with a pitch into the prone orientation (B and E).
Slow-phase velocities were of similar amplitude but opposite in direction for LW-RC and LC-RW irrigations (Fig. 2B).

The transient component of the responses reached a peak value between 22 and 49 s after initiation of the caloric stimulation. The change in eye velocity from its value at the onset of the caloric stimulation to its peak value ranged from 1.2 to 4.5°/s for LW-RC irrigations (mean of 2.7°/s, n = 7), and from −1.6 to −5.1°/s for LC-RW irrigations (mean of −3.1°/s, n = 3). For all subjects, the direction of the peak transient SPV was opposite to the direction expected for a direct thermal effect.

The steady-state component of the responses measured at the end of the control trials was in the direction expected from a direct thermal effect on all but one trial. The steady-state SPV was to the right for 6 of the 7 subjects tested with LW-RC irrigations. The amplitude of the steady-state component ranged from 2.5 to 0.5°/s (mean of 1.3°/s, 0.9 SD, n = 7), and the mean was significantly different from zero (t-test, P < 0.01). As expected for a direct thermal effect for LC-RW irrigations, steady-state slow-phase velocity was to the left for the 3 subjects tested (range: 1.0 to 1.8°/s, mean of 1.5°/s, n = 3; mean significantly different from zero, P < 0.05). These same 3 subjects had steady-state SPV of comparable magnitude, but opposite direction during LW-RC irrigations (range: −1.4 to −1.8°/s, mean −1.6°/s; mean significantly different from zero, P < 0.05). The overall results from these control trials indicate that the direct thermal effect on afferent nerve activity and subsequent eye movements was small under our caloric irrigation conditions.

**Caloric step trials**

**HORIZONTAL SPV.** Figures 3 and 4 show normalized mean horizontal SPV responses to LW-RC and LC-RW caloric step trials, respectively. SPV data from each subject were normalized by dividing by the peak SPV magnitude before averaging so that the dynamic characteristics of the mean response were not dominated by the subjects with the largest responses. Small transient responses in horizontal SPV were observed during the first 120 s of caloric step trials (Figs. 3 and 4), consistent with those seen in control trials (Fig. 2). The first pitch into the supine or prone orientation produced an exponential rise in SPV in a direction consistent with convective canal stimulation (i.e., SPV to the left for prone head orientation and to the right for supine head orientation with LW-RC irrigation; Fig. 3). After the return to null orientation, the SPV exponentially declined toward a value close to zero. The peak amplitudes of SPV responses for the first and second pitches to prone/supine orientations were smaller than those in the subsequent 4 prone/supine orientations (Figs. 3 and 4). The smaller responses for the first and second pitches may be attributed to the fact that a steady-state temperature gradient was not established until about 200 s, as indicated by the control trial responses (Fig. 2A).
been tilted to a supine or to a prone orientation. Measurements for 3 of these 9 subjects and for one additional subject were also obtained during LC-RW irrigations.

Individual and average responses to step trials showed a large prone/supine asymmetry in SPV (Figs. 3 and 4, Table 1). The magnitude of SPV amplitude (average SPV over the last 15 s of each pitch orientation) was on average about 40% smaller during the prone orientation than during the supine orientation for both LW-RC and LC-RW irrigations (Table 1). For the 9 subjects with data from LW-RC irrigations, the ratio of SPV during prone orientation to SPV during supine orientation varied from 0.4 to 0.78, and there was a significant difference in response magnitude between supine and prone orientations (paired t-test, \( P < 0.001 \)). For the 3 of the 9 subjects who were also tested with LC-RW irrigations, the ratio varied from 0.32 to 0.95.

A systematic deviation of vertical eye position could potentially contribute to the observed prone/supine asymmetry because the horizontal SPV amplitude depends on the alignment between the eye’s rotation axis and the axis of the rotational motion stimulus (Fetter et al. 1986), which in our case was provided by the yaw caloric stimulation that is roughly orthogonal to the horizontal canals. Because the horizontal semicircular canals were in the vertical plane during prone/supine orientation, maximum horizontal SPV would be expected to occur when the subjects looked \(-20^\circ\) from Reid’s plane, thus aligning the orbital axis with the horizontal canal axis. Therefore to account for the difference in vertical eye position as a possible factor for the asymmetry between horizontal SPV in supine and prone orientations, we corrected the measured horizontal eye velocity as: corrected \( \text{SPV} = \text{measured eye velocity} / \cos(20^\circ + \text{measured vertical eye position}) \).

Vertical eye position, measured for each subject over the last 15 s of each tilt, varied from \(-14.9^\circ\) to \(10.6^\circ\) during prone orientation (mean: \(-0.13^\circ\), SD: \(7.0^\circ\) for LW-RC irrigations and mean: \(-0.74^\circ\), SD: \(7.0^\circ\) for LC-RW irrigations) and from \(-18.0^\circ\) to \(16.9^\circ\) during supine orientation (mean: \(-1.6^\circ\), SD: \(9.4^\circ\) for LC-RW irrigations and mean: \(1.18^\circ\), SD: \(8.1^\circ\) for LC-RW irrigations). The corrected horizontal SPVs are shown in Table 1 (numbers in parentheses). Because the corrected horizontal SPVs differ only slightly from the uncorrected horizontal SPVs, we conclude that vertical eye position did not account for the prone/supine asymmetry in horizontal SPV.

**VERTICAL SPV.** Nine of the 10 subjects who underwent caloric step trials showed some vertical nystagmus in the null orientation. The direction of the nystagmus was consistent within subjects across trials (including trials for LW-RC and LC-RW irrigations, which were performed on different days). Seven subjects had upbeat nystagmus (mean SPV: \(1.8^\circ/s\), range: \(0.6^\circ\) to \(3.9^\circ/s\)), and 2 had downbeat nystagmus (\(-0.3^\circ\) and \(-0.74^\circ\)).

![Normalized horizontal SPV](image-url)

**FIG. 4.** Normalized horizontal SPV (mean ± 1SD) evoked during caloric step trials with LC-RW irrigations (\( n = 3 \)). A: data obtained with a step trial starting with a pitch-to-prone orientation. B: data obtained with a step trial starting with a pitch-to-supine orientation.

2). Therefore detailed data analysis was performed only for the last 4 pitch orientations of a step trial.

For the last 4 pitch orientations of each caloric step trial, measurements obtained for the 2 pitch orientations in one direction (prone or supine) were averaged together for the 9 subjects who were able to complete at least one LW-RC caloric step trial. Additional response averaging was performed for responses from the 6 subjects who completed 2 LW-RC caloric step trials. This additional averaging was possible because responses to each supine or prone tilt during the last 4 pitch orientations did not depend on whether the subject had first

TABLE 1. **Amplitude of the horizontal SPV evoked during LW-RC and LC-RW caloric step trials in prone and supine orientations**

<table>
<thead>
<tr>
<th></th>
<th>LW-RC Irrigations (( n = 9 ))</th>
<th>LW-RC Irrigations (( n = 3 ))</th>
<th>LC-RW Irrigations (( n = 3 ))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supine orientation</td>
<td>(-48.9^\circ/s, SD: 22.1 ) ((-52.5^\circ/s, SD: 24.4 ))</td>
<td>(-37.3^\circ/s, SD: 21.5 ) ((-40.0^\circ/s, SD: 24.0 ))</td>
<td>(38.1^\circ/s, SD: 13.3 ) ((41.6^\circ/s, SD: 15.8 ))</td>
</tr>
<tr>
<td>Prone orientation</td>
<td>(29.0^\circ/s, SD: 14.0 ) ((31.0^\circ/s, SD: 14.9 ))</td>
<td>(27.7^\circ/s, SD: 14.8 ) ((30.3^\circ/s, SD: 16.2 ))</td>
<td>(-23.3^\circ/s, SD: 12.5 ) ((-24.7^\circ/s, SD: 12.8 ))</td>
</tr>
<tr>
<td>Prone/supine ratio</td>
<td>0.60, SD: 0.14 (0.60, SD: 0.15)</td>
<td>0.76, SD: 0.03 (0.77, SD: 0.05)</td>
<td>0.61, SD: 0.32 (0.60, SD: 0.33)</td>
</tr>
</tbody>
</table>

Third column shows LW-RC data for the 3 subjects who also underwent LC-RW irrigations. The horizontal SPV data shown are the mean SPV values measured during the last 15 s of a tilt. Results shown in parentheses are horizontal SPV measures corrected for possible attenuation attributed to deviation of vertical eye position.
thermal component was obtained from the control-trial steady-state responses. The second, indirect estimate of the direct thermal effect assumed that 1) only thermal and convective components contribute to the VOR and 2) thermal and convective components combine additively. If these assumptions are true then: \( \text{VOR}_{\text{thermal}} = \text{VOR}_{\text{convective}} + \text{VOR}_{\text{thermal}} \) and \( \text{VOR}_{\text{prone}} = \text{VOR}_{\text{convective}} - \text{VOR}_{\text{thermal}} \). The thermal component of the VOR response can be calculated as: \( \text{VOR}_{\text{thermal}} = (\text{VOR}_{\text{supine}} - \text{VOR}_{\text{prone}})/2 \). This calculation gave a mean eye velocity of \(-9.9°/s\) for LW-RC irrigations (SD: 5.2°/s, \( n = 9 \)), and a mean eye velocity of 7.4°/s for LC-RW irrigations (SD: 5.8°/s, \( n = 3 \)). These values are about 6 times larger than the estimate of the direct thermal contribution obtained from the steady-state component of SPV measured during control trials (about 1.5°/s). Measures of the direct thermal effect from both the control trials and step trials were available from 7 subjects. There was a significant difference between these 2 measures of the direct thermal effect (paired \( t \)-test, \( P < 0.01 \)). The discrepancy between measures of the direct thermal effect from control and caloric step trials indicates that another factor, in addition to a direct thermal effect, must be contributing to the large prone/supine asymmetry observed during caloric step trials.

Horizontal eye movements and motion sickness

Five of the 11 subjects tested with LW-RC irrigation and one of the 4 subjects tested with LC-RW irrigation were not able to complete a full test session because of motion sickness. Although not part of the experimental design, the results from these 6 subjects were compared with the results from the 6 subjects who were able to complete a full test session to determine whether test results revealed systematic differences between responses from more-susceptible and less-susceptible motion-sick subjects.

The mean horizontal SPV measured over the last 15 s of supine and prone tilt were significantly larger in the 6 motion-sick subjects (mean: 71°/s, SD: 11°/s for supine orientation; mean: 43°/s, SD: 10°/s for prone orientation) than in the other 6 subjects (mean: 42°/s, SD: 16°/s for supine orientation: mean 24°/s, SD: 12°/s for prone orientation) (paired \( t \)-test, \( P < 0.01 \) for supine orientation; \( P < 0.02 \) for prone orientation). There were no significant differences between the 2 subject groups for the ratio (prone SPV/supine SPV) or for the difference (supine SPV – prone SPV).

### Estimates of direct thermal contribution

The thermal component to the eye movement response was estimated using 2 techniques. First, a direct measure of the

---

1 The large mean vertical SPV in the supine orientation for LC-RW irrigations probably demonstrates a sampling bias from testing only 3 subjects, given that mean vertical SPVs were small for the LW-RC irrigations where data from 9 subjects were available.

---

![Figure 5](http://jn.physiology.org/)

**FIG. 5.** Vertical SPVs measured in prone, null, and supine orientations for LW-RC irrigations (9 subjects). Vertical SPV was averaged for the whole duration of a tilt (i.e., over a 30-s interval) because some subjects had increasing or decreasing vertical SPV during the whole duration of a tilt, whereas others had mostly constant vertical SPV.

-0.6°/s). The magnitude of this nystagmus is consistent with the magnitude of vertical positional nystagmus previously reported without caloric stimulation (Bisdorff et al. 2000).

In the supine and prone orientations, vertical SPV was considerably smaller than horizontal SPV. For LW-RC irrigations, the mean vertical SPV was 3.0°/s (SD 4.9°/s, \( n = 9 \)) for the prone orientation and 0.6°/s (SD 7.2°/s, \( n = 9 \)) for the supine orientation. For LC-RW irrigations, the mean vertical SPV was 1.1°/s (SD 2.4°/s, \( n = 3 \)) for prone orientation and 11.1°/s (SD 11.2°/s, \( n = 3 \)) for supine orientation. Vertical SPVs were variable in amplitude and direction between subjects (Fig. 5) but were consistent within each trial for each subject. Some subjects had nystagmus beating in the same direction for both supine and prone positions, whereas others had nystagmus beating in the opposite direction for supine and prone positions (Fig. 5).

### TIME CONSTANTS OF CALORIC STEP RESPONSES

The mean time constants measured for different portions of the pitch movements are given in Table 2. The largest mean time constant was obtained for pitch movements from prone-to-null orientations and the smallest mean time constant for movements from null-to-prone. A comparison of all paired combinations of the time constants obtained from LW-RC irrigations showed significant differences between null-to-supine and null-to-prone, null-to-prone and prone-to-null, and supine-to-null and prone-to-null time constants (paired \( t \)-test, \( P < 0.05 \) with Bonferroni correction for 6 paired comparisons, \( n = 9 \)). Similar time constant values were obtained from responses to LC-RW irrigations (Table 2), but statistical comparison of these results was not possible because of the small number of subjects (\( n = 3 \)).

### TABLE 2. Time constants of the SPV responses evoked by the pitch movements during LW-RC and LC-RW irrigations; LW-RC data for the subset of subjects who underwent both irrigations are also shown

<table>
<thead>
<tr>
<th>Pitch Condition</th>
<th>LW-RC Irrigations (( n = 9 ))</th>
<th>LW-RC Irrigations (( n = 3 ))</th>
<th>LC-RW Irrigations (( n = 3 ))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Null to supine</td>
<td>7.33 s</td>
<td>6.32 s</td>
<td>6.20 s</td>
</tr>
<tr>
<td>SD: 2.35 s</td>
<td>SD: 0.60 s</td>
<td>SD: 2.24 s</td>
<td></td>
</tr>
<tr>
<td>Null to prone</td>
<td>5.44 s</td>
<td>5.38 s</td>
<td>4.62 s</td>
</tr>
<tr>
<td>SD: 2.28 s</td>
<td>SD: 1.43 s</td>
<td>SD: 0.37 s</td>
<td></td>
</tr>
<tr>
<td>Supine to null</td>
<td>7.66 s</td>
<td>7.33 s</td>
<td>7.43 s</td>
</tr>
<tr>
<td>SD: 2.81 s</td>
<td>SD: 2.49 s</td>
<td>SD: 2.23 s</td>
<td></td>
</tr>
<tr>
<td>Prone to null</td>
<td>13.0 s</td>
<td>11.5 s</td>
<td>13.1 s</td>
</tr>
<tr>
<td>SD: 4.47 s</td>
<td>SD: 4.94 s</td>
<td>SD: 5.01 s</td>
<td></td>
</tr>
</tbody>
</table>
larger response amplitude would be more likely to become motion sick because one would expect a larger sensory conflict with a larger rotational response.

Time constants for tilts from null-to-prone/supine orientation and from prone/supine-to-null orientation were not significantly different between the motion-sick subjects and the subjects able to complete full testing. However, as an anecdotal observation, one of the motion-sick subjects had a response that differed noticeably from the average results in other subjects. This subject was distinguished from other subjects in having a long VOR time constant, particularly for the prone-to-null tilts (24.9 s) and supine-to-null tilts (18.7 s). However, this subject also had a large response amplitude in addition to a long time constant. Therefore we cannot be certain that the long time constant contributed to the motion-sickness susceptibility of this subject.

**DISCUSSION**

For both LW-RC and LC-RW irrigations, the magnitude of the horizontal SPV demonstrated a clear dependency on head orientation with a larger SPV magnitude for the supine orientation. Horizontal SPV magnitude in the prone orientation was 41% smaller than that in the supine orientation during LW-RC irrigations and 39% smaller during LC-RW irrigations (Table 1). Our results are in agreement with previous human studies on the effect of body position on caloric responses (Clarke et al., 1988; Coats and Smith, 1967). Using a unilateral caloric stimulus (40-s irrigation), Coats and Smith (1967) found that horizontal SPV magnitude was 36% and 48% smaller during prone orientation than during supine orientation for cold and warm irrigations, respectively (Table 1 of Coats and Smith 1967). Using binaural continuous irrigations, Clarke et al. (1988) found SPV in the prone orientation that was about 33% smaller than the responses in the supine orientation (based on peak slow-phase velocity estimated from Fig. 2 in Clarke et al. 1988). These results in humans are similar to those seen in a single rhesus monkey, which showed a 33% smaller response in the prone orientation when mild warm irrigations were performed (Böhmer et al. 1992).

Larger prone/supine asymmetries have been reported in squirrel monkeys (Minor and Goldberg 1990, 1996) and in squirrel monkeys (Minor and Goldberg 1990; Paige and Coats 1985). Using a unilateral ice-water caloric stimulus, Paige et al. (1985) reported responses in the prone orientation 78% (for a 5-s irrigation) and 63% (for a 10-s irrigation) smaller than in the supine orientation. Similarly, Minor and Goldberg (1990) reported monaural caloric responses 71% smaller for prone than for supine orientation during cold irrigations and 73% smaller during warm irrigations.

In the following, we discuss various factors that could have contributed to the observed asymmetry of eye velocity magnitude with head orientation. We will show that the GIF resolution hypothesis that characterizes interactions between otolith and semicircular canal cues is consistent with experimentally determined features of the VOR evoked by caloric step irrigations.

**Possible factors contributing to the prone/supine asymmetry in horizontal SPV**

**DIRECT THERMAL EFFECT.** The prone/supine asymmetry in eye movement responses has often been attributed to a direct thermal effect on afferent nerve responses. In our study, control trials consisting of long-duration caloric stimulation in the null orientation were performed to investigate any contribution of such a thermal effect to the eye movement responses evoked during caloric step trials. Our experimental design assumed that the steady-state SPV evoked by the control-trial irrigations provided a direct measure of the direct thermal effect. If this assumption is correct then the SPV attributed to the direct thermal effect was much smaller than the SPV attributed to convective effects and was too small to account for the prone/supine asymmetry. This small direct thermal effect accounted for only about 15% of the difference between the SPV magnitude in the supine (mean 49°/s with LW-RC irrigations) and prone (mean 29°/s) positions (15% = 2 × (control trial steady-state SPV)/(supine SPV − prone SPV)).

However, there is reason to question whether the steady-state control-trial SPV provided an accurate measure of the direct thermal effect. Specifically, we expected to see an exponential increase in SPV magnitude over time as the continuous irrigations established steady-state thermal gradients across the labyrinths. However, we actually recorded a more complex transient response in the first 100 s where SPV initially developed in a direction opposite to that expected for a direct thermal effect, but then reversed and ultimately reached a steady-state SPV after about 300 s with the expected direction (Fig. 2). The direction of the initial transient we observed is consistent with the results reported by Arai et al. (1998) who showed low-amplitude rightward SPV in the first 60 s after the initiation of warm caloric irrigation of the right ear with the subject positioned in the null orientation.

The origin of this initial transient response is unclear and it is possible that it could influence the estimated SPV attributed to the direct thermal effect. For example, if this initial transient were the result of some unknown process that had a nonzero steady-state response in the null orientation, then our estimate of the direct thermal effect would obviously be in error. However, if this unknown process produced a steady-state SPV that was independent of pitch orientation, then our conclusion remains valid that the steady-state SPV amplitude identified in our control trials is not large enough to account for the prone/supine asymmetry seen on caloric step trials.

Alternatively, if this unknown process contributed a response that changed with pitch orientation, then the above conclusion could be wrong. A worst-case example might be that this unknown process did not contribute to the SPV in the supine or prone orientations, but did contribute in the null orientation in a manner that reduced the steady-state SPV on control trials. In this case, our measure of the direct thermal effect would be too small. Therefore in this worst-case example, the direct thermal effect might truly be responsible for the prone/supine asymmetry observed in caloric step trials, but because this unknown process interfered with our estimate of
the direct thermal effect, our conclusion would be wrong about the limited contribution of the direct thermal effect. Future research, both experimental and theoretical, is required to determine the cause of the initial transient response seen in control trials.

Another consideration in evaluating the accuracy of our estimate of the direct thermal effect is that our estimate depends on accurately positioning the horizontal canals in the null orientation. Anatomic measurements in 10 subjects (20 canals) showed a SD of about 6° in the naso-occipital inclination of the canals (Blanks et al. 1975). Given this variability, the tight distribution of our steady-state responses is surprising. This unexpectedly tight distribution may be because the SD of 6° includes both anatomic variability as well as the influence of measurement “noise”. The tight distribution of our steady-state thermal responses suggests that anatomic variability may be less than the measurement noise.

TABLE 3. Changes in VOR time constant with head orientation. For conventional, transient monaural caloric irrigations, Minor and Goldberg (1990) suggested that the prone/supine asymmetry in peak slow-phase velocity observed in squirrel monkeys results from the large difference in VOR time constants for symmetrical head tilt (i.e., time constant of 28 s for 45° NU rotation vs. 17 s for 45° ND rotation). That is, if the VOR velocity gain remains constant, then the VOR acceleration gain, which is related to the caloric irrigation response amplitude, changes in proportion to the VOR time constant. Previous experimental results suggest that a time constant change could not explain the prone/supine caloric asymmetry in humans because humans, unlike squirrel monkeys, have similar VOR time constants for symmetrical head tilts (Fetter et al. 1986, 1992).

However, more recent experimental results in humans do show a significant difference between the supine and prone VOR time constants (Table 3 in Zupan et al. 2000). Specifically, this study showed a mean ND postrotatory time constant of 5.22 s and a mean NU postrotatory time constant of 7.00 s. These time constants are very similar to the null-to-prone and null-to-supine time constants that we identified using exponential fits to caloric step responses (5.44 and 7.33 s, respectively, Table 2). Following the logic of Minor and Goldberg (1990), the prone/supine ratio of these time constants (5.22/7.00 = 0.75 from postrotatory results or 5.44/7.33 = 0.74 from caloric step results) should predict the ratio of prone/supine SPV from the caloric step responses if this change in time constant is indeed responsible for the observed prone/supine caloric asymmetry. However, the experimental prone/supine SPV ratio of 0.60 (Table 1) is substantially smaller than the time constant ratio. Therefore even if the time constant change does contribute to the observed prone/supine caloric asymmetry, it cannot account for all of the asymmetry and some other orientation-dependent factor must be present. Below we consider such a factor (i.e., the GIF resolution hypothesis) and then go on to show that this hypothesis can explain both the prone/supine SPV asymmetry and the apparent time constant asymmetry.

GIF RESOLUTION HYPOTHESIS. The gravito-inertial force (GIF) resolution hypothesis (Merfeld 1990, 1995; Merfeld and Zupan 2002; Merfeld et al. 1993) was developed to explain how the nervous system uses motion information from multiple sensors to resolve the ambiguity that arises from motion information provided by any single motion sensor (Angelaki et al. 1999, 2001; Green and Angelaki 2003). This hypothesis has been successful in explaining VOR responses from postrotational tilt dumping experiments (Merfeld et al. 1999; Zupan et al. 2000), VOR and perceptions evoked by eccentric tilts (Merfeld et al. 2001; Zupan et al. 2002), VOR during off-vertical axis rotations (Zupan et al. 2002), and modeling experimental results involving combinations of tilt and translations (Merfeld and Zupan 2002). When applied to responses to caloric step irrigations, the GIF resolution hypothesis predicts that horizontal nystagmus evoked by caloric stimulation in the supine or prone positions will contain both an angular VOR component and a linear VOR component.

For example, when the subject is supine (Fig. 6, left panel), LW-RC irrigations produce a clockwise (CW) convective endolymph flow that generates a horizontal canal response signaling a counterclockwise (CCW) head rotation indicated by \( \omega_{\text{caloric}} \). If the subject was truly rotating CCW, the CNS expectation is that the gravity vector \( \mathbf{g} \) should be rotating to the left with respect to the subject. This expectation is represented by the vector \( \mathbf{g}_{\text{CNS}} \), which indicates the internal neural estimate of the orientation of gravity with respect to the head. However the otoliths, which sense the net combination of linear acceleration and gravity (Young 1984), continue to sense the true direction of gravity \( \mathbf{g} \). This apparent “conflict” between the direction of gravity derived from canal and otolith measures can be resolved by the CNS if the nervous system interprets the dispar-

TABLE 3. Model parameters generating the best fits of the average horizontal slow-phase velocities obtained for LW-RC and LC-RW irrigations

<table>
<thead>
<tr>
<th>Test Condition</th>
<th>( \tau_{AV,PN} )</th>
<th>( \tau_{AV,SN} )</th>
<th>( \tau_{AV,NP} )</th>
<th>( \tau_{AV,NS} )</th>
<th>( \tau_s )</th>
<th>( \tau_L )</th>
<th>( K_{AV} )</th>
<th>( K_L )</th>
</tr>
</thead>
<tbody>
<tr>
<td>LW-RC (till ND first)</td>
<td>9.93</td>
<td>9.13</td>
<td>6.70</td>
<td>7.09</td>
<td>128.6</td>
<td>2.51</td>
<td>25.8</td>
<td>0.265</td>
</tr>
<tr>
<td>LW-RC (till NU first)</td>
<td>10.1</td>
<td>9.67</td>
<td>5.77</td>
<td>5.42</td>
<td>110.3</td>
<td>1.82</td>
<td>24.8</td>
<td>0.228</td>
</tr>
<tr>
<td>LC-RW (till ND first)</td>
<td>7.97</td>
<td>9.90</td>
<td>3.68</td>
<td>5.38</td>
<td>96.5</td>
<td>0.860</td>
<td>24.6</td>
<td>0.284</td>
</tr>
<tr>
<td>LC-RW (till NU first)</td>
<td>8.27</td>
<td>10.1</td>
<td>5.30</td>
<td>5.02</td>
<td>127.1</td>
<td>2.91</td>
<td>25.7</td>
<td>0.265</td>
</tr>
</tbody>
</table>

The normalized average data shown in Figs. 3 and 4 was multiplied by 50 before using it to estimate the parameters of the model shown in Fig. 8. Multiplication by 50 gave a SPV signal with a peak amplitude close to that reported in Table 1. \( K_{AV} \) is the only parameter scaled by this multiplication.
ity between $\mathbf{g}$ and $\hat{\mathbf{g}}$ to mean that the subject is concurrently accelerating linearly in the direction $\hat{\mathbf{a}} = \hat{\mathbf{g}} - \mathbf{g}$. The VOR is assumed to include 2 components: a horizontal angular VOR compensatory for $\omega_{\text{caloric}}$ and a horizontal linear VOR compensatory for $\hat{\mathbf{a}}_y$ (the interaural component of $\hat{\mathbf{a}}$). We refer to the linear VOR component as an “induced” linear VOR because it arises as a consequence of canal-otolith interactions rather than in direct response to an actual linear acceleration. For LW-RC irrigations in the supine position, $\hat{\mathbf{a}}_y$ is directed toward the subject’s left and therefore evokes a rightward linear VOR that adds to the rightward angular VOR component. For LW-RC irrigations in the prone position, the induced linear acceleration $\hat{\mathbf{a}}$ is directed toward the subject’s left, and the linear VOR evokes rightward-directed eye movements that decrements from the magnitude of the angular VOR (Fig. 6, right panel). For both supine and prone LC-RW irrigations, the angular VOR and linear VOR components change direction from those shown in Fig. 6. Therefore the magnitudes of the angular and linear VOR components still add in the supine position, and subtract in the prone position.

The above descriptive explanation is embodied in explicit mathematical models that predict the time course of internal estimates of rotation, direction of gravity, and linear acceleration (Merfeld and Zupan 2002; Merfeld et al. 1993; Zupan et al. 2002). An example prediction from the model of Zupan and colleagues (2002) is shown in Fig. 7 for LW-RC irrigations. The input to the model was an angular acceleration applied to the horizontal canals that depended on pitch position. The canal dynamics were represented by a second-order high-pass filter with a dominant time constant of 6 s and an adaptation time constant of 100 s. The angular acceleration input was zero in the null orientation, $+3.5^\circ/s^2$ for the supine orientation, and $-3.5^\circ/s^2$ for the prone orientation. The other input was a change in the orientation of the gravity vector with respect to the head that was dependent on pitch position. The time course of pitch position changes (Fig. 7A) was identical to stimulus profiles used in the experiments. The outputs of the model show changes in the vector components of the internal estimate of the direction of gravity (Fig. 7B), the interaural component of estimated linear acceleration (Fig. 7C), the angular VOR (Fig. 7D), and the horizontal induced linear VOR (Fig. 7E). The horizontal VOR (Fig. 7F) is the sum of the angular and induced linear VOR.

A scaled version of the mean SPV response from Fig. 3A is also shown in Fig. 7F to illustrate that the prone/supine asymmetry and the general response pattern is predicted by the model representing the GIF resolution hypothesis. The parameters of this model were derived from a variety of previous experiments (Cohen et al. 1981; Koenig et al. 1978; Merfeld et al. 2001; Wall and Furman 1990; Zupan et al. 2000), and there were no modifications made to fit the current experimental results. The GIF model could have been modified to provide a better fit to the caloric step data of these particular subjects, but
this would have detracted from the point that the existing GIF model accounts for the main features of the caloric step data.

A simplified GIF resolution model is shown in Fig. 8A. This model captures other features of the caloric step response (response adaptation and possible dynamics of the induced linear VOR mechanism) and permits parameterization of experimental responses. The model input is a normalized angular acceleration that depends on pitch position. The model includes angular VOR dynamics with a dominant response time constant \( (\tau_{AV}) \), gain constant \( (K_{AV}) \), and a VOR adaptation time constant \( (\tau_a) \). The output of the induced linear VOR component is a low-pass filtered version of the angular VOR (time constant \( \tau_{LV} \) and gain constant \( K_{LV} \)). The “tilt switch” controls the pitch position-dependent contribution to the final combined angular and linear VOR.

A least-square-error technique was used to determine the model parameters that generate the best fits of the average data shown in Figs. 3 and 4. Before fitting, the normalized SPV data in Figs. 3 and 4 were multiplied by a factor of 50 to give SPV values that closely matched mean SPV values (Table 1). Only SPV data from the last 2 cycles of pitch position changes were included in the fit procedure. The fit procedure assumed that the values of \( \tau_a, \tau_{LV}, K_{AV}, \) and \( K_{LV} \) were constant over time. However, the angular VOR time constant \( \tau_{AV} \) was permitted to assume a different value for each movement into a different pitch orientation. That is, the curve fit provided estimates of 4 angular VOR time constants for movements from the prone-to-null (\( \tau_{AV,PN} \)), supine-to-null (\( \tau_{AV,SN} \)), null-to-prone (\( \tau_{AV,NP} \)), and null-to-supine (\( \tau_{AV,NS} \)) positions.

In all cases, the curve fit matched the experimental SPV data very closely (e.g., Fig. 8B shows fit to LW-RC data from Fig. 3A results). There was relatively little variation in parameter estimates across conditions (Table 3). The mean VOR adaptation time constant across all conditions was \( \tau_a = 116 \) s and the mean linear VOR time constant was \( \tau_{LV} = 2.0 \) s. The mean value of \( K_{LV} \) was 0.26, indicating that the contribution of the linear VOR component was 26% of the angular VOR in the supine and prone orientations.

The angular VOR time constants were similar for tilts from prone-to-null orientation and for tilts from supine-to-null orientation (\( \tau_{AV,PN} \) and \( \tau_{AV,SN} \) with mean \( \pm SD \) of 9.4 \( \pm 0.8 \) s across all conditions). Angular VOR time constants were also similar for tilts from null-to-prone and null-to-supine orientation (\( \tau_{AV,NP} \) and \( \tau_{AV,NS} \), with mean \( \pm SD \) of 5.6 \( \pm 1.0 \) s across all conditions), but were notably shorter than for tilts into the null orientation. This pattern of angular VOR time constant changes is consistent with velocity storage being increased in the upright position, as indicated by the lengthening of the human VOR time constant, but not increased in the tilted positions (Fetter et al. 1986, 1992; Zupan et al. 2000). Additionally, the observation that \( \tau_{AV,SN} \) and \( \tau_{AV,NS} \) had similar values is consistent with the idea that, in the tilted position, angular VOR dynamics are not dependent on NU versus ND orientation. A similar result was obtained from postrotatory tilt experiments (Fig. 18.8 in Merfeld and Zupan 2003).

Our model-based interpretation of caloric step responses helps explain the VOR time constant asymmetry used by Minor and Goldberg (1990) to explain the observed prone/supine caloric asymmetry. First, the entire prone/supine SPV asymmetry, both amplitude and time constant asymmetries, can be explained by additive or subtractive contributions of the angular and linear VOR components predicted by the GIF...
resolution hypothesis. Second, the GIF resolution hypothesis accounts for the variation in time constants obtained by direct measurements of SPV responses (Table 2) for different portions of the stimulus. Because the model simulations shown in Fig. 8 account for the SPV time course during all segments of the caloric step stimulus, we infer that the differences in time constants for tilts from null-to-supine and from null-to-prone orientations, and the differences in time constants for tilts from supine-to-null and from prone-to-null orientations (Table 2), are caused by an interaction between the dynamic responses of the induced linear VOR and the angular VOR. That is, rather than the VOR time constant variation explaining the prone/supine SPV asymmetry, both the prone/supine time constant asymmetry and the SPV asymmetry are seen as a consequence of the canal-otolith sensory interaction, which elicits an angular VOR and an induced linear VOR.

One might consider testing the GIF prediction that a linear VOR component contributes to the caloric response by evaluating whether the response was correlated with vergence, given that the gain of the linear VOR correlates with vergence (Paige and Tomko 1991b). There are 2 considerations that need to be taken into account before performing such an evaluation. First, the gain of the angular VOR also increases with vergence (Snyder and King 1992; Viirre et al. 1986). Therefore even a positive finding would remain ambiguous. Second, the correlation between vergence and the linear VOR gain, observed at 1 Hz and higher (Telford et al. 1997), was not observed at 0.5 Hz. Therefore because the frequency content of the predicted linear VOR responses induced by our caloric stimulation paradigm and the earlier “dumping” studies (Merfeld et al. 1999; Zupan et al. 2000) falls below 0.5 Hz, we would not expect the linear VOR induced by these paradigms to show a strong correlation with vergence.

In summary, the caloric step stimulus was used to investigate the orientation-dependent dynamic properties of the VOR and factors influencing the prone/supine asymmetry previously observed in caloric responses. Our results suggest that a change in horizontal canal afferent activity caused by a direct thermal effect is insufficient to explain the prone/supine asymmetry. Previous studies in squirrel monkeys concluded that some position-dependent, possibly otolith-mediated effect must contribute to the prone/supine asymmetry (Minor and Goldberg 1990; Zupan et al. 2000). We demonstrate that canal-otolith interactions could also be responsible for the prone/supine asymmetry observed in humans, and suggest a specific mechanism based on the GIF resolution hypothesis. Therefore the response to a caloric test, which has long been considered to provide clinically relevant information about horizontal semicircular canal function only, can now be seen to involve the processing of both canal and otolith information.

Acknowledgments
We thank J. Roth and S. Clark-Donovan for assistance.

Grants
This work was supported by a National Institute of Deafness and Other Communication Disorders Grant R01 DC-04158.

References


