Neural Processing of Gravito-Inertial Cues in Humans. I. Influence of the Semicircular Canals Following Post-Rotatory Tilt

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Zupan, L. H., R. J. Peterka, and D. M. Merfeld. Neural processing of gravito-inertial cues in humans. I. Influence of the semicircular canals following post-rotatory tilt. J Neurophysiol 84: 2001–2015, 2000. Sensory systems often provide ambiguous information. Integration of various sensory cues is required for the CNS to resolve sensory ambiguity and elicit appropriate responses. The vestibular system includes two types of sensors: the semicircular canals, which measure head rotation, and the otolith organs, which measure gravito-inertial force (GIF), the sum of gravitational force and inertial force due to linear acceleration. According to Einstein’s equivalence principle, gravitational force is indistinguishable from inertial force due to linear acceleration. As a consequence, otolith measurements must be supplemented with other sensory information for the CNS to distinguish tilt from translation. The GIF resolution hypothesis states that the CNS estimates gravity and linear acceleration, so that the difference between estimates of gravity and linear acceleration matches the measured GIF. Both otolith and semicircular canal cues influence this estimation of gravity and linear acceleration. The GIF resolution hypothesis predicts that inaccurate estimates of both gravity and linear acceleration can occur due to central interactions of sensory cues. The existence of specific patterns of vestibulocoelic reflexes (VOR) related to these inaccurate estimates can be used to test the GIF resolution hypothesis. To investigate this hypothesis, we measured eye movements during two different protocols. In one experiment, eight subjects were rotated at a constant velocity about an earth-vertical axis and then tilted 90° in darkness to one of eight different evenly spaced final orientations, a so-called “dumping” protocol. Three speeds (200, 100, and 50°/s) and two directions, clockwise (CW) and counterclockwise (CCW), of rotation were tested. In another experiment, four subjects were rotated at a constant velocity (200°/s, CW and CCW) about an earth-horizontal axis and stopped in two different final orientations (nose-up and nose-down), a so-called “barbecue” protocol. The GIF resolution hypothesis predicts that post-rotatory horizontal VOR eye movements for both protocols should include an “induced” VOR component, compensatory to an interaural estimate of linear acceleration, even though no true interaural linear acceleration is present. The GIF resolution hypothesis accurately predicted VOR and induced VOR dependence on rotation direction, rotation speed, and head orientation. Alternative hypotheses stating that frequency segregation may discriminate tilt from translation or that the post-rotatory VOR time constant is dependent on head orientation with respect to the GIF direction did not predict the observed VOR for either experimental protocol.

INTRODUCTION

The vestibular system includes two types of sensors: the semicircular canals and the otolith organs. The semicircular canals behave as integrating angular accelerometers measuring head angular velocity (Wilson and Melvill Jones 1979). The otolith organs behave as linear accelerometers measuring the specific gravito-inertial force (GIF), which is the sum of gravitational force and inertial force due to linear acceleration. Using information from these sensors, the human CNS develops perceptions of spatial orientation and generates VORs that help stabilize gaze in response to head rotation and translation. A problem arises when the CNS must distinguish head tilt with respect to gravity from linear translation (acceleration) of the head. For example, a compensatory response for tilting the head toward the left shoulder is a torsional eye movement while acceleration toward the right induces a compensatory horizontal eye movement. In both cases, the interaural shear force measured by the otolith organs might be identical, but the compensatory eye responses are quite different. Ideally, having devices that independently measure gravity and linear acceleration could solve the tilt-translation dilemma. However, Einstein’s equivalence principle states that no physical device can distinguish gravitational force from inertial force due to linear acceleration. This implies that the CNS is unable to solve the tilt-translation problem using only information from the otolith organs or any other combination of linear accelerometers. Indeed, a given GIF (f) measured by the otolith organs can be produced by an infinite number of combinations of gravity (g), and linear acceleration (a). For example, while in a supine orientation, a linear acceleration of the head to the left down a slight slope (Fig. 1A) can lead to the exact same GIF as a slight yaw tilt (φ) to the right (Fig. 1B).

In many situations, the eye movements generated in response to head tilts and translations are appropriately compensatory (Angelaki et al. 1999; Merfeld and Young 1995), implying that the CNS is able to somehow distinguish gravity from linear acceleration. At least three hypotheses have been proposed to explain how the CNS makes use of GIF information from the otolith organs to influence eye movements, peripheral processing, frequency segregation, and GIF resolution.

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Specifically, the CNS systematically separates the otolith GIF (magnitude and direction with respect to the subject) can be obtained by
subtracting the measured acceleration ( \( \hat{a} \)) from the gravitational force ( \( g \)). This hypothesis is in accordance with low-frequency cues elicit translation responses (Mayne 1974; Paige and Tomko 1991). Different combinations of \( g \) and \( a \) can yield exactly the same estimated gravito-inertial force (GIF). \( A \) with a subject in a supine position on a sled, acceleration down the inclined slope produces a GIF with a magnitude of 1 \( g \) toward the back of the head at a slight angle (\( \phi \)) to the subject’s right. \( B \) with no linear acceleration, the exact same GIF (magnitude and direction with respect to the subject) can be obtained by tilting the subject into a position \( \psi \) degrees to the right of a supine orientation. Since the measurement of GIF relative to the head is identical for these 2 situations, additional information is required for the nervous system to distinguish tilt from translation and to determine how much of the measured GIF is due to gravity and how much is due to linear acceleration.

The peripheral processing hypothesis states that some of the separation of the GIF into estimates of gravity and linear acceleration occurs peripherally with the phasic irregular oto-lith affeerent signal interpreted primarily as linear acceleration, while the tonic regular oto-lith affeerent signal might represent gravity (Mayne 1974; Young and Meiry 1967). The frequency segregation hypothesis states that the CNS might resolve the GIF ambiguity using a form of central processing in which low-frequency cues elicit tilt responses and high-frequency cues elicit translation responses (Mayne 1974; Paige and Tomko 1991). This hypothesis is in accordance with low-frequency characteristics of tilt perception during centrifugation (Clark and Graybiel 1951; Glasauer 1992). It also matches VOR data during interaural translation, which has both horizontal translation-related eye movements with high-frequency characteristics and torsional tilt-related eye movements with low-frequency characteristics (Paige and Tomko 1991). However, as observed by Angelaki (1998), frequency segregation during interaural translation is affected by the way translation and tilt sensitivities are expressed (Paige and Tomko 1991).

The GIF resolution hypothesis (Merfeld and Young 1995; Merfeld et al. 1993a), an explicit refinement of the “multisensory integration” hypothesis (Guedry 1974; Mayne 1974; Oman 1982; Young 1984), states that additional sensory information is required for the CNS to resolve the GIF ambiguity. Specifically, the CNS systematically separates the otolith GIF measurement (\( f \)) into estimates of gravity (\( \hat{g} \)) and linear acceleration (\( \hat{a} \)) using multi-sensory convergence, so that the difference between these estimates approximately matches the measured GIF (\( f = g - a \)). The specific gravito-inertial force measured by the otolith organs (\( f \)) is defined as the sum of gravitational force (\( g \)) plus an inertial force per unit mass (\( -a \)) acting on the otolith organs and exactly opposing the direction of linear acceleration (\( a \)). We choose to adopt the notation of Young (1984) for representing the effect that gravity and linear acceleration have on the otolith organs. Physical variables are mathematically represented by three-dimensional vectors, \( f, g, a \).

The GIF resolution hypothesis appears indistinguishable (other than notational differences) from another recently formulated approach used to explain how the CNS uses semicircular canal cues to distinguish sinusoidal tilt from sinusoidal translation (Angelaki et al. 1999).

When visual cues are absent or cannot be used, the semicircular canal and otolith cues may provide the CNS with conflicting sensory information. Consider the sensory situation experienced by a subject statically positioned in a nose-up orientation (Fig. 2A) following a sustained counterclockwise rotation (toward the subject’s left) in darkness about an earth-horizontal axis. First, for this experimental protocol, the otolith organs measure a constant GIF due to gravity alone (\( f = g \)). In the nose-up orientation, this force is aligned with the subject’s naso-occipital axis. At the same time, the semicircular canals, because of their dynamics (Wilson and Melvill Jones 1979), have a post-rotatory response indicating an on-going rotation (\( \hat{\omega} \)) in a clockwise (toward the subject’s right) direction even though the subject is actually at rest. Rotational cues are known to influence the perceived orientation of gravity (Stockwell and Guedry 1970), often leading to illusory tilt (Dichgans et al. 1972; Merfeld et al. 1999; von Holst and Grisebach 1951). This evidence suggests that the yaw rotational cue following post-rotatory tilt (\( \hat{\omega} \)) influences the estimated orientation of gravity (\( \hat{g} \)) such that the estimate of gravity (\( \hat{g} \)) rotates in the same direction as if there was an actual rotation. We hypothesize that the CNS computes estimates of gravity (\( \hat{g} \)) and linear acceleration (\( \hat{a} \)) such that their difference matches the measured GIF, which equals gravity in this example (\( f = g = \hat{g} - \hat{a} \)). Therefore a nonzero estimate of linear acceleration (\( \hat{a} = g - f \)) would be generated whenever the estimate of gravity (\( \hat{g} \)) does not match true gravity (\( g \)), as demonstrated in Fig. 2A.

The estimate of interaural linear acceleration (\( \hat{a}_{i} \)) may induce a horizontal VOR component (Fig. 2B) that should be similar to a horizontal VOR response compensatory to an actual interaural linear acceleration; we refer to this VOR component as an induced VOR. This induced VOR component should combine more or less linearly with the horizontal angular VOR component as previously demonstrated in squirrel monkeys...
(Sargent and Paige 1991). Since the tilt direction of the estimate of gravity (\( \vec{g} \)) depends on rotation direction, the induced VOR component must depend on rotation direction. Similarly, since the estimate of interaural linear acceleration (\( \vec{a}_l \)) depends on subject orientation (\( \theta \), Fig. 2C), the induced VOR component must depend on subject orientation.

To gain insight into how human subjects distinguish tilt from translation, we designed two experiments that created a conflicting sensory situation between semicircular canal and otolith cues, and we measured reflexive slow phase eye movements. In one experiment, subjects were tilted 90° from an upright orientation after they were rotated for 150 s at a constant velocity about an earth-vertical axis ("dumping" protocol). In another experiment, subjects were rotated for 150 s at a constant velocity about an earth-horizontal axis and then decelerated to a stop ("barbecue" protocol). For both protocols, we focused on the reflexive eye movements following deceleration to a stop, referred to as the post-rotatory responses. Both of these protocols are described in detail in the following section.

Horizontal responses alone have been presented in a previous report for 200°/s dumping protocols (Merfeld et al. 1999). The present report extends this previous study by including VOR responses for 50 and 100°/s dumping protocols to investigate the influence of the magnitude of the rotational stimulus on the GIF resolution. In addition, vertical VOR responses are investigated to identify properties of the axis-shift. Moreover, responses following barbecue-spit rotation are presented to evaluate the dynamic influence of post-rotational tilt on the measured responses.

**METHODS**

**Experimental setup and eye movement recording**

Informed consent was obtained in accordance with institutional procedures, and subjects were instructed about potential risks, including motion sickness, prior to each testing session.

All protocols were conducted on a two-axis rotation device. An inner gimbal powered by a 160-N-m DC motor (velocity servo control) provided full-circle rotations about the subject's yaw axis. An outer pitch/roll gimbal powered by a 2,300-N-m hydraulic actuator (position servo control) provided rotations about an earth-horizontal axis. Each subject was seated in a kneeling position on a car-race-type seat mounted in the device's inner yaw gimbal. The subject's body was restrained using a 5-point seat-belt system, lateral shoulder supports, a wide waist belt, and knee restraints. Foam pads were added as needed to ensure maximum stability. During testing the subject gripped a pair of handlebars that provided additional stabilization. The subject’s head was secured in an adjustable foam-lined head restraint. The subject's interaural axis was aligned with the outer gimbal earth-horizontal axis and the interaural axis midpoint was aligned with the inner gimbal yaw axis.

Binocular eye movements were recorded (Panasonic AG-DS850 SVHS VCR) using small video cameras (Machine Vision Hyper CCD Cameras CV-36SH) mounted on a bite-bar assembly. Infrared light-emitting diodes (LEDs) provided lighting for the video cameras. A mold of each subject’s mouth was formed on the bite-bar using dental-impression compound (3 M Express, 3 M Dental Products, St. Paul, MN). The weight of the camera assembly was supported by elastic bands attached to the yaw gimbal.

An off-line application of a custom image-analysis program provided measurements of the horizontal and vertical coordinates of the pupil center for each field of the video image (59.94 video fields/s).

The video system was calibrated by having the subject sequentially direct gaze at 9 horizontal, 9 vertical, and 12 oblique LED target lights. Target viewing evoked horizontal and/or vertical eye movements up to approximately 20°. Measurements of the three-dimensional (3-D) locations in space of both the eyes and target LEDs were used to determine the horizontal and vertical angular orientations (Fick coordinates) of the eyes with respect to the head for each gaze orientation. The calibration procedure used these known gaze orientations to determine polynomial equations that related the horizontal and vertical pupil center coordinates to the horizontal and vertical eye orientation angles. These polynomial equations were applied to video data obtained during subsequent test runs to determine horizontal and vertical eye orientation. The overall accuracy of the video measurements is provided by the root mean square error between the absolute eye position prediction from the polynomial fit and the presumed actual eye position. The rms error was less than 0.5° for both horizontal and vertical eye position measures. All reported eye movement responses are at least one order of magnitude greater than the video-system sensitivity. Horizontal and vertical eye position data were digitally filtered and differentiated to yield horizontal and vertical eye velocity, respectively. Torsional eye position was not calculated. Fast phases were automatically removed using a computer algorithm based on peak acceleration detection, with manual editing by experienced personnel, leaving the slow phase eye velocity (SPV).

**Experimental protocols**

**DUMPING PROTOCOL.** Eight healthy subjects age 26–47 (6 males and 2 females) with no history of peripheral or central vestibular disorders volunteered for this study. Clinical testing (including but not limited to rotating chair test battery, Hallpike maneuvers, computer-ized dynamic posturography, and caloric testing) was performed on seven of the eight subjects and indicated no abnormalities. (The data from the subject not clinically examined were similar to the data from the other subjects.)

The test subjects, with head upright, were accelerated in 2 s to a clockwise (CW) or counter-clockwise (CCW) constant yaw angular velocity about an earth-vertical axis. (A clockwise rotation is defined as a yaw head rotation toward the subject’s right shoulder and a counterclockwise rotation as a yaw head rotation toward the subject’s left shoulder.) As a convention, the post-rotatory period of a trial is designated by the direction of the preceding rotation. Each subject was tested using three different constant velocities: 50, 100, and 200°/s. The constant velocity rotations were maintained for 150 s and were followed by a 2-s angular deceleration to a stop. To control “viewing” distance, a light was turned on, 10 s prior to the stop. During this 5-s “lights-on” period, the subject was instructed to look straight ahead at a poster fixed to the chair 40 cm in front of the subject’s eyes. (Any residual nystagmus was suppressed during this 5-s interval, but a small nystagmus returned by the time the subject was brought to a stop.) Immediately after stopping, the subject was tilted 90° about an earth-horizontal axis through the center of the head (at ear level) in 1.5 s. This passive post-rotatory tilt positioned the subject in one of eight evenly spaced final orientations: nose-up (NU), nose-down (ND), right-down (RD), left-down (LD), and each of the four orientations midway between these principal orientations (NU-RD, NU-LD, ND-RD, ND-LD). The trial order was randomized and secret; the direction of rotation (CW or CCW), and the direction of tilt were counterbalanced across eight subjects for each speed. The same testing order was used for each subject for each speed. The order with which the speeds were presented was counter-balanced across six subjects, and the two remaining subjects were tested using two previously tested speed sequences (200, 100, 50 and 200, 50, 100°/s). The
speed was always the same within a test session, and at least two nights separated test sessions. For each speed, there were three testing sessions: one session with all NU and ND trials, one session with all LD and RD trials, and one session with all in-between orientation trials. As controls, each subject was also tested with no tilt following the upright rotation for each velocity (in the 1st 2 sessions). Each subject was also passively tilted 90° to one of eight orientations (in a separate session).

To minimize order effects, lights were turned on for 2 min between trials while the subjects were upright and stationary. During data collection, subjects were instructed to keep their eyes open and to look straight ahead but not to focus on any point, real or imagined, and were challenged with mental arithmetic to maintain alertness.

BARBECUE SPIT PROTOCOL. Four healthy male subjects, ages 29–49, with no history of peripheral and central vestibular disorders participated in this portion of the study (2 of the 4 also participated in the dumping protocol). The number of subjects performing this protocol was limited because of severe motion sickness that prevented most subjects from completing the test protocols.

Subjects were initially positioned in a supine orientation and were then accelerated in 2 s to a CW or CCW constant yaw angular velocity of 200°/s about an earth-horizontal axis. The constant velocity rotation was maintained for 150 s before decelerating (2 s) to a stop in either the nose-up (NU) or nose-down (ND) orientations. The remainder of the protocol was identical to the dumping protocol. (Ongoing nystagmus was suppressed during the 5-s light interval preceding the deceleration but returned to normal by the time the subject was brought to a stop.)

In addition, two subjects who also participated in the dumping study were tested with the barbecue protocol using all eight stop orientations. The trial order for these two subjects was the same as for their dumping tests.

Data analysis

HEAD-FIXED REFERENCE FRAME. All vector coordinates (physical variables and internal estimates) were expressed in an orthogonal head-fixed frame of reference with x, y, and z axes corresponding to the subject’s nasooccipital, interaural, and rostrocaudal axes respectively. The positive axes were directed nasally (x), toward the left ear (y), and toward the top of the skull (z).

FICK ANGLES. To describe eye position and eye angular velocity, we used Fick angles and angular rates defined by the right-hand rule with positive x, y, and z coordinates corresponding to CW torsional, downward vertical, and leftward horizontal movements, respectively.

SINUSOIDAL FIT. To characterize the variations of the horizontal induced VOR component, horizontal VOR time constant, and vertical VOR as a function of head orientation, we fit spatial sinusoids to these data sets for each direction of rotation. For the horizontal-induced VOR component, a sinusoidal variation with head orientation is expected based on the following considerations. The induced VOR component should be proportional to the interaural projection of the estimate of linear acceleration (\( \hat{a}_x \), Fig. 2B). If the estimate of linear acceleration is constant in a space-fixed frame of reference, its interaural projection and the associated compensatory induced VOR component should vary sinusoidally with head orientation in a head-fixed frame of reference (Fig. 6). This sinusoidal variation was quantified by measuring the mean horizontal induced VOR component between 3 and 4 s after the tilt and fitting a sine function to these data (Figs. 6 and 8).

Similarly for the vertical VOR, if the VOR axis-shift component stays constant in a space-fixed frame of reference, its projection on the vertical axis should vary sinusoidally with head orientation in a head-fixed frame of reference. The sinusoidal variation in the vertical VOR with head orientation was quantified by measuring the mean vertical VOR between 10 and 11 s after the tilt (Fig. 10) and fitting a

\[ C(\theta) = B + M \cos(\theta - \phi) \]  

where \( \theta \) is the orientation angle of the subject in the post-rotatory period (see Fig. 2C), \( B \) is the bias, \( M \) the amplitude, and \( \phi \) the phase of the fit. Phase values in the remainder of this paper always refer to the phase \( \phi \) computed according to Eq. 1.

TIME CONSTANTS. To determine time constants, a constrained nonlinear optimization algorithm was used (function const in Matlab 5.2 for Macintosh, The Mathworks). The slow phase velocity was fit with three different analytical functions \( D(t) \):

\[ D(t) = A \exp(-t/T) \]  

\[ D(t) = A_s + A_e \exp(-t/T_e) \]  

\[ D(t) = A_s \exp(-t/T_s) + A_e \exp(-t/T_e) \]

where \( A \) is the amplitude and \( T \) the time constant of the exponential fit. The decay time constant was also determined by measuring the time interval in which the post-rotatory SVP amplitude reached 37% of its peak amplitude (1/e \( \approx 0.37 \)). For data presented in this paper, we used the parameters obtained from Eq. 2 since they showed the lowest variability. (Except for higher variability, the parameters obtained using the other methods were similar to those from Eq. 2.)

STATISTICAL ANALYSIS. Analysis of variance (ANOVA) was used to determine the statistical significance of velocities and time constants of VOR, angular VOR, and induced VOR components as a function of speed of rotation, direction of rotation, and head final orientation. All statistical analyses were performed with Systat 7.0 (SPSS).

Multivariate ANOVA (MANOVA) methods were applied to the statistical analysis of sinusoidal fit results. Each sinusoidal curve, defined by an amplitude \( M \) and a phase \( \phi \) (Eq. 1), was represented by the complex variable \( Z = M[\cos(\phi + i \sin(\phi)] = X + iY \) where \( i^2 = -1 \). To compare mean phase shifts between two groups (\( \phi_1 \) and \( \phi_2 \)), MANOVA was conducted on the two groups of real pairs \([X_1, Y_1]\) and \([X_2, Y_2]\), where \([X, Y]\) is considered as a pair of related dependent variables in the Hotelling’s \( T^2 \) test (Johnson and Wichern 1982). If the two groups of paired variables \([X_1, Y_1]\) and \([X_2, Y_2]\) were significantly different (MANOVA \( T^2 \)-test) and if the two associated groups of amplitude \((M_1, M_2)\) were not significantly different (ANOVA \( t \)-test), we concluded that the statistically significant difference came from the variations in phase shifts (\( \phi_1 \) and \( \phi_2 \)). This approach is preferred to ANOVA on the independent parameters \( M \) and \( \phi \), since separate statistics on \( M \) and \( \phi \) may lead to erroneous results (Calkins 1998).

RESULTS

This report focuses primarily on the responses following deceleration, i.e., slow phase velocity of the post-rotatory nystagmus. However, the per-rotatory responses to yaw rotations about an earth-vertical axis during dumping protocols had average amplitudes and average decay time constants within the normal range (Table 1) for all speeds (Hess et al. 1985; Honrubia et al. 1984). The per-rotatory horizontal VOR time constants decreased with increasing velocity as previously reported (Balog et al. 1979; Paige 1989). For barbecue spit
TABLE 1. Average decay time constant and peak amplitudes

<table>
<thead>
<tr>
<th>Speed</th>
<th>Time Constant, s</th>
<th>Amplitude, °/s</th>
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<tbody>
<tr>
<td>50°/s</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CW</td>
<td>11.5 ± 0.7</td>
<td>35 ± 4</td>
</tr>
<tr>
<td>CCW</td>
<td>12.2 ± 1.4</td>
<td>-38 ± 3</td>
</tr>
<tr>
<td>100°/s</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CW</td>
<td>11.0 ± 1.1</td>
<td>76 ± 4</td>
</tr>
<tr>
<td>CCW</td>
<td>11.4 ± 1.2</td>
<td>-82 ± 5</td>
</tr>
<tr>
<td>200°/s</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CW</td>
<td>8.5 ± 0.8</td>
<td>150 ± 6</td>
</tr>
<tr>
<td>CCW</td>
<td>9.5 ± 1.0</td>
<td>-156 ± 14</td>
</tr>
</tbody>
</table>

Values are time constants and amplitudes (means ± SE) for per-rotatory responses during post-rotatory tilt protocols (8 subjects, 3 speeds, and 2 directions). Positive (negative) amplitude values indicate horizontal slow phase velocity to the left (right).

trials (Table 2), the per-rotatory responses showed the usual peak amplitudes and sinusoidal modulations (Wall and Furman 1989).

Post-rotatory horizontal eye movements following earth-vertical axis rotations ("dumping")

HORIZONTAL VOR. The horizontal post-rotatory VOR slow-phase velocity was determined in eight subjects for three speeds (200, 100, 50°/s), two directions (CW and CCW) of rotation, and eight final tilt orientations. During the first 20 s following the post-rotatory tilt, the post-rotatory VOR exhibited four very different patterns dependent on rotation direction and head orientations. First, for each of the three speeds tested, the VOR magnitude following a tilt in the NU orientation was greater than the VOR magnitude following a tilt in the ND orientation after identical CCW and CW rotations (Fig. 3, left). We are focusing here on the 20 s following the post-rotatory tilt period that begins 3.5 s after the VOR peaked (see graphs to the right of the vertical dash-dotted line on each plot in Fig. 3). Second, the VOR magnitude was greater for LD trials than for RD trials following identical CCW rotations, but the VOR magnitude was smaller for LD trials than for RD trials following identical CW rotations for each of the three speeds tested (Fig. 3, 2nd column). Third, for NU-RD and ND-LD orientations, little difference was observed following CCW rotation, but the VOR magnitude was greater for NU-RD trials than for ND-LD trials following CW rotation (Fig. 3, 3rd column). Fourth, for NU-LD and ND-RD trials, little difference was observed following CW rotation, but the VOR magnitude was greater for NU-LD trials than for ND-RD trials following CCW rotation (Fig. 3, 4th column). These response patterns were one of our principal findings and were predicted by the GIF resolution hypothesis as discussed later.

Table 2. Average peak amplitudes and sine modulation amplitude

<table>
<thead>
<tr>
<th></th>
<th>Subject 1</th>
<th>Subject 2</th>
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<tbody>
<tr>
<td>Peak amplitude, °/s</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CW</td>
<td>156 ± 2</td>
<td>149 ± 7</td>
</tr>
<tr>
<td>CCW</td>
<td>-164 ± 5</td>
<td>-159 ± 2</td>
</tr>
<tr>
<td></td>
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<td></td>
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<tr>
<td>Sine modulation amplitude, °/s</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CW</td>
<td>21 ± 1</td>
<td>21 ± 1</td>
</tr>
<tr>
<td>CCW</td>
<td>19 ± 1</td>
<td>24 ± 1</td>
</tr>
</tbody>
</table>

Values are amplitudes (means ± SE) for per-rotatory responses during earth-vertical axis rotations ("dumping") at 200°/s for two subjects (2 directions). Positive (negative) peak amplitude values indicate horizontal SPV to the left (right).
orientation pairs separated by 180°. For all four orientation pairs, the peak amplitude of the induced VOR component decreased with decreasing angular velocity (Fig. 5, the mean across 8 subjects is shown). For each speed and orientation pair, the induced VOR component peaked between 3 and 4 s following the post-rotatory tilt. This observation was consistent across all subjects. To rule out the possibility that the induced VOR component was contaminated by the post-rotatory tilt, control experiments were performed where the subjects were tilted 90° to the eight different orientations without being previously rotated. For all subjects, there was no apparent nystagmus 3 s after completion of the tilt (not shown). Therefore, we concluded that the peak amplitude of the induced VOR component between 3 and 4 s after completion of the tilt varied as a function of head orientation for each individual subject (individual data not shown). Individual induced VOR data following CW and CCW rotations varied sinusoidally with head orientation (individual data not shown). For each individual sinusoidal fit, an amplitude $M$ and a phase shift $\phi$ were determined. As described in METHODS, each sinusoidal fit can be represented by a pair of real numbers $(X, Y)$. For all three speeds (50, 100, and 200°/s), the group of real pairs $(X_1, Y_1)$ for CW rotations were significantly different ($P < 0.0004$, $P = 0.0006$, $P = 0.0003$, respectively, using MANOVA Hotelling–$T^2$) from the group of real pairs $(X_2, Y_2)$ for the CCW rotations. Since response amplitudes were not significantly different, we concluded that there was a significant phase difference between the results from CW and CCW rotations. The mean phase shift, for the horizontal induced VOR component following CW rotations (157, 153,
and 137°, respectively) was significantly different from following CCW rotations (22, 37, and 47°, respectively).

The mean peak amplitude across subjects of the induced VOR component calculated between 3 and 4 s after completion of the tilt also varied as a function of head orientation (Fig. 6, left). The CW and CCW mean induced VOR data were well fit by sinusoids shifted with respect to one another. For each stimulus velocity, the induced VOR data supported the GIF resolution hypothesis. Specifically, the sinusoidal fits closely matched the predicted negative of the estimate of interaural linear acceleration ($\hat{a}_i$) plotted as a function of head orientation (Fig. 6, right) for different leftward and rightward tilts of the estimate of linear acceleration, $\hat{a}$, with earth-horizontal (tilt of $\hat{a}$ is specified by $\hat{\alpha}$, see Fig. 2B). The sensitivity between the negative of the estimate of interaural linear acceleration ($-\hat{a}_i$) and the sinusoidal fit to the induced VOR data varied between 8.3 and 11° $\cdot$ s$^{-1}$ $\cdot$ g$^{-1}$. For all three speeds (50, 100, and 200°/s), very good fits were obtained by increasing the tilt of the estimate of linear acceleration with increasing speed ($\hat{a} = 22.5°$, $\hat{\alpha} = 30°$, and $\hat{\alpha} = 45°$, respectively). For each speed, the theoretical angle $\hat{\alpha}$ (Fig. 2B) has been chosen as the mean between $\hat{\alpha}_1 = \phi_1$ and $\hat{\alpha}_2 = 180° - \phi_2$ (for further explanation, see GIF resolution hypothesis in DISCUSSION), where $\phi_1$ and $\phi_2$ are the phases of the sinusoidal fits to the CCW and CW rotation data respectively: for example, $\hat{\alpha} = (22 + 180 - 157)/2 = 22.5°$ following 50°/s rotations.

Figure 6, left, presents sinusoidal fits to the data following CW and CCW rotations between 3 and 4 s after the tilt following 50, 100, and 200°/s yaw rotations. Similar plots were made at 1-s sequential time intervals between 3 and 50 s after completion of the post-rotatory tilt. At each 1-s increment, a sine fit was made to the CW and CCW mean induced VOR amplitude versus head orientation data to estimate the values of $M$ and $\phi$ (Eq. 1) at these points in time. These results were combined to form a parametric estimate of the variation of $M$ and $\phi$ over time [$M(t)$ and $\phi(t)$, respectively]. The induced VOR “experimental trajectories” (Fig. 7, left) are defined as a parametric plot $X(t) = M(t) \cos \phi(t)$ and $Y(t) = M(t) \sin \phi(t)$.

The induced VOR experimental trajectories closely matched the estimated linear acceleration ($\hat{a}$) theoretical trajectories following CW and CCW rotations (Fig. 7, right). Following 50, 100, and 200°/s yaw rotations, very good matches occurred for maximum tilts of the estimate of linear acceleration with earth-horizontal of $|\hat{a}|_{\text{max}} = 22.5°$, $|\hat{a}|_{\text{max}} = 30°$, and $|\hat{a}|_{\text{max}} = 45°$, respectively. The theoretical trajectories of the estimated linear acceleration $\hat{a}$ are portions of a circle, the diameter of which is the constant norm of the estimate of gravity $|\hat{g}|$. The time courses of the tilt of the estimate of linear acceleration with earth-horizontal ($\hat{\alpha}$) are not shown explicitly. But these time courses are very similar to time courses of the induced VOR component (Fig. 5).

**Post-rotatory horizontal eye movements following an earth-horizontal axis rotation (“barbecue”)**

HORIZONTAL EYE MOVEMENTS. Four subjects completed barbecue rotations with constant yaw angular velocity of 200°/s about an earth-horizontal axis followed by a stop in either the NU or ND orientations. The barbecue post-rotatory VOR (Fig. 8A) and induced VOR (Fig. 8B) were very similar to the results

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### TABLE 3. Mean horizontal VOR time constants

<table>
<thead>
<tr>
<th></th>
<th>50°/s</th>
<th></th>
<th>100°/s</th>
<th></th>
<th>200°/s</th>
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<tbody>
<tr>
<td></td>
<td>CW</td>
<td>CCW</td>
<td>CW</td>
<td>CCW</td>
<td>CW</td>
</tr>
<tr>
<td>UP</td>
<td>11.5 ± 1.5</td>
<td>11.0 ± 1.7</td>
<td>12.1 ± 1.5</td>
<td>10.7 ± 1.0</td>
<td>9.4 ± 1.2</td>
</tr>
<tr>
<td>NU</td>
<td>6.3 ± 0.6</td>
<td>5.8 ± 0.7</td>
<td>7.7 ± 0.8</td>
<td>6.9 ± 0.7</td>
<td>7.8 ± 0.9</td>
</tr>
<tr>
<td>ND</td>
<td>4.1 ± 0.5*</td>
<td>5.2 ± 0.7</td>
<td>5.3 ± 0.5*</td>
<td>5.6 ± 0.6*</td>
<td>5.4 ± 0.6*</td>
</tr>
<tr>
<td>LD</td>
<td>6.4 ± 1.0</td>
<td>5.3 ± 0.4</td>
<td>6.2 ± 1.1</td>
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<td>6.6 ± 1.0</td>
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<tr>
<td>RD</td>
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<td>6.4 ± 0.7</td>
<td>7.0 ± 0.6</td>
</tr>
<tr>
<td>NU-RD</td>
<td>6.4 ± 0.8</td>
<td>5.7 ± 0.5</td>
<td>7.2 ± 0.7</td>
<td>7.0 ± 0.8</td>
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<tr>
<td>ND-LD</td>
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<td>4.7 ± 0.5</td>
<td>5.7 ± 1*</td>
<td>6.3 ± 0.6</td>
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<td>NU-LD</td>
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<tr>
<td>ND-RD</td>
<td>5.0 ± 0.9</td>
<td>5.4 ± 0.6</td>
<td>5.9 ± 0.6*</td>
<td>6.5 ± 0.8</td>
<td>6.3 ± 0.6</td>
</tr>
</tbody>
</table>

Mean horizontal vestibuloocular reflex (VOR) time constants (means ± SE in seconds) for eight subjects, three velocities (200, 100, 50°/s), two directions [clockwise (CW) and counterclockwise (CCW)] and 8 orientations [nose up (NU), nose down (ND), left down (LD), right down (RD), NU-RD, ND-LD, NU-LD, ND-RD]. Orientations separated by 180° are grouped together. * Significant difference between two orientations separated by 180°.

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1. Indeed, the tilt angle ($\hat{\alpha}$) of the estimate of linear acceleration with respect to earth-horizontal can be approximated as $\hat{\alpha} = \arctan (\text{VOR}_{\text{LD-RD}}/\text{VOR}_{\text{NU-ND}})$, where $\text{VOR}_{\text{LD-RD}}$ is the induced VOR component for the orientation pair LD-RD and $\text{VOR}_{\text{NU-ND}}$ is the induced VOR component for the orientation pair NU-ND for a given rotation direction.
for 200°/s dumping trials (Figs. 3 and 5). During the 35 s following the tilt, for both CW and CCW rotations, the VOR magnitude following a stop in the NU orientation was greater than following a stop in the ND orientation. For both CW and CCW rotations, the VOR time constant was greater for the NU orientation (12.2 and 12.3 s, respectively) than for the ND orientation (8.7 and 8.9 s, respectively), but due to the small number (n = 4) of subjects tested, the difference was not significant (P = 0.07). These results confirm that the dynamic tilt rotation measured by the semicircular canals in the dumping protocol did not substantially affect or contaminate the horizontal VOR eye movements recorded in the post-rotatory period.

To allow a more complete comparison of the dumping and barbecue rotation protocols, two subjects were tested for two directions of rotation and eight orientations at 200°/s for both barbecue and dumping protocols with the same trial order for each protocol. The mean induced VOR amplitudes between 3 and 4 s after the tilt for dumping protocols and after the stop for barbecue protocols are plotted as a function of head orientation (Fig. 8, C and D). The results were very similar for both protocols, again confirming that the dynamic aspect of post-rotatory tilt did not substantially contaminate the post-rotatory horizontal VOR three or more seconds after the tilt was completed. Therefore head orientation with respect to gravity was the predominant factor influencing post-rotatory eye movement responses and not dynamic head tilt per se.

Post-rotatory vertical eye movements following earth-vertical axis rotations (dumping)

In addition to the postulated induced VOR component discussed previously, previous results in humans (Fetter et al. 1996; Harris and Barnes 1987), rhesus monkeys (Angelaki and Hess 1994), and squirrel monkeys (Merfeld et al. 1993b) demonstrate that a shift in the axis of eye rotation is also observed following post-rotatory tilt. This axis-shift, which is not specifically predicted (nor precluded) by the GIF resolution hypothesis, indicates the tendency of the VOR rotation axis to align with gravity, as described by any one of several spatial orientation hypotheses (Angelaki and Hess 1994; Cohen et al. 1999; Merfeld et al. 1993b). While both AVOR and induced VOR components should be horizontal eye movements, any axis-shift of the VOR rotation axis toward alignment with...
Gravity should induce either vertical or torsional eye movements, depending on the subject’s orientation. The axis-shift of the VOR rotation axis is not directly related to the induced VOR component, although the induced VOR component would influence the magnitude of the axis-shift, since the induced VOR component modifies the horizontal VOR.

We evaluated the spatial reorientation of the post-rotatory VOR induced by head movements in the roll plane by plotting post-rotatory vertical VOR versus horizontal VOR (Fig. 9) for both LD or RD orientations, for all speeds, and for both directions of rotation. The upward vertical components were on average larger than the downward vertical components.

**FIG. 7.** Parametric comparison between experimental trajectories of the induced VOR and theoretical trajectories of the estimate of linear acceleration for 50, 100, and 200°/s yaw rotations. Left: experimental trajectories of the induced VOR following CW and CCW rotations in a space-fixed reference frame. The experimental trajectory of the induced VOR is defined as the parametric plot $X(t) = M(t) \cos \phi(t)$ and $Y(t) = M(t) \sin \phi(t)$, where $M(t)$ and $\phi(t)$ are the amplitude and phase of sinusoidal fits to the induced VOR data at times between 3 and 50 s after completion of the tilt. Right: in a space-fixed frame of reference where gravity $g$ is vertical and oriented downward, the theoretical trajectory of the estimate of linear acceleration $\hat{a}$ is defined by the parametric equations $\hat{X}(t) = |\hat{a}(t)| \cos \hat{\alpha}(t)$ and $\hat{Y}(t) = |\hat{a}(t)| \sin \hat{\alpha}(t)$. The theoretical trajectories of the estimate of linear acceleration are plotted for an estimate of linear acceleration $\hat{a}$ maximally tilted $\hat{\alpha} = 22.5°$ (1st row), $\hat{\alpha} = 30°$ (2nd row), and $\hat{\alpha} = 45°$ (3rd row) from an earth-horizontal axis to the left and to the right (see Fig. 2B for details).

**FIG. 8.** Barbecue protocol experimental data. A: post-rotational horizontal VOR following 200°/s yaw rotations about an earth-horizontal axis for 4 subjects. As before, post-rotational responses are labeled using the actual direction of rotation preceding the tilt (CW or CCW). Time 0 indicates the end of the horizontal rotation plus a 2-s delay corresponding to the tilt duration used on dumping protocols. The mean post-rotatory responses for 4 subjects are shown for NU and ND orientations. B: the induced VOR component is calculated as the NU response minus the ND response (divided by 2). C: peak induced VOR following 200°/s yaw rotations about an earth-horizontal axis (barbecue protocol) for 2 subjects. The peak amplitude of the induced VOR component for each subject and each test condition was defined as the mean of the induced VOR component during a 1-s interval that corresponded to the same interval used for the dumping protocol. The mean peak amplitudes (+1 SE) for 2 subjects are plotted vs. subject orientation following both CW (○) and CCW (●) rotations. Responses are modulated sinusoidally; least-square-error sinusoidal fits to the data are shown. D: for comparison, peak induced VOR following 200°/s yaw rotations about an earth-vertical axis followed by a 90° tilt (dumping protocol) for the same 2 subjects.

**FIG. 9.** Spatial reorientation of the average post-rotatory VOR (8 subjects) in the roll plane. The average post-rotatory vertical VOR for 8 subjects is plotted vs. the average post-rotatory horizontal VOR following both CW and CCW 50, 100, and 200°/s yaw rotations for left-down and right-down orientations. Dashed lines indicate reference axis-shift angles (0, ±15, ±30°) of the slow phase velocity axis of rotation toward gravity following the post-rotatory tilt. Data where the horizontal VOR was less than 5°/s are not plotted to avoid inaccurate computations due to experimental noise.

VOR induced by head movements in the roll plane by plotting post-rotatory vertical VOR versus horizontal VOR (Fig. 9) for both LD or RD orientations, for all speeds, and for both directions of rotation. The upward vertical components were on average larger than the downward vertical components. The
axis-shift was initially small (<10° for all speeds) at the time when the induced VOR component peaked (about 3 s after the post-rotatory tilt, Fig. 5), and then increased and peaked at an amplitude of roughly 15–30° between 10 and 20 s after the tilt, depending on the rotation angular velocity. A slow buildup in the axis-shift has been previously observed following post-rotatory tilt (Fetter et al. 1996) and following off-vertical axis rotation in humans (Furman and Koizuka 1994; Harris and Barnes 1987). Figure 10 shows plots of the mean vertical VOR between 10 and 11 s after completion of the tilt as a function of head orientation.

For each rotation direction and speed, the peak amplitude of the vertical VOR calculated between 10 and 11 s after completion of the tilt varied sinusoidally as a function of head orientation for each individual subject (not shown). As described in METHODS, each individual sinusoidal fit can be represented by a pair of real number \( [X = M \cos \phi, Y = M \sin \phi] \) where \( M \) is the amplitude and \( \phi \) the phase of the sinusoidal fit. For two speeds (100 and 200°/s), the group of real pairs \( [X_1, Y_1] \) for CW rotations were significantly different \( (P = 0.02) \) and \( P = 0.03, \) respectively, for Hotelling \( T^2 \)-test) from the group of real pairs \( [X_2, Y_2] \) for the CCW rotations. Since response amplitudes were not significantly different, we concluded that there was a significant phase difference between the results from CW and CCW rotations. The mean phase shift for vertical VOR following CW rotations (63 and 66°, respectively) was significantly different from following CCW rotations (−58 and −64°, respectively).

The mean peak amplitude across subjects of the vertical VOR calculated between 10 and 11 s after completion of the tilt also varied as a function of head orientation (Fig. 10). The CW and CCW responses were well fit by sinusoids shifted with respect to one another. The amplitude, the bias, and the phase shift absolute value of the sinusoidal fits to the mean vertical VOR data decreased with decreasing speed for both CW and CCW rotations.

**Vertical VOR data decreased with decreasing speed for both CW and CCW rotations.**

**Horizontal VOR decay following post-rotatory tilts**

Previous human studies reported that an eye movement response attenuation (dumping) occurs when graviceptor cues are inconsistent with rotation cues, e.g., after yaw (Benson and Bodin 1966) and roll (Udo de Haes and Schöne 1970) rotation about an earth-horizontal axis and after active (Schradar et al. 1985) and passive (Benson and Bodin 1966) post-rotational tilts following yaw rotation about an earth-vertical axis. Our data confirm these findings, with the decay time constant of post-rotatory VOR significantly smaller for trials with post-rotatory tilt than for trials without post-rotatory tilt. Previous studies also demonstrated asymmetries in VOR responses for orientations separated by 180° after both passive (Benson and Bodin 1966) and active (Schradar et al. 1985) post-rotatory tilts. Other paradigms also appear to induce related orientation-dependent asymmetries. For example, human horizontal optokinetic nystagmus and afternystagmus induced by yaw rotation of an optokinetic surround, with subjects and optokinetic surround aligned with earth-horizontal, have been shown to be greater for NU than for ND orientations (Wall et al. 1999). A similar asymmetry has been observed during caloric stimulation of canal plugged squirrel monkeys (Minor and Goldberg 1990; Paige 1985). These extensive sets of data allow for detailed comparisons of predictions of different hypotheses regarding the interactions of otolith and semicircular canal cues on the generation of VOR eye movements.

**VOR spatial orientation hypothesis**

The VOR spatial orientation hypothesis has been proposed to explain orientation dependent asymmetries in the VOR (Cohen et al. 1999). First, this hypothesis states that the angular VOR time constant (10–20 s) is prolonged when compared with primary semicircular canal afferent (5–6 s) by a velocity-storage mechanism (Raphan et al. 1979). Second, the velocity storage mechanism is dependent on head orientation with respect to the direction of the GIF as demonstrated in rhesus and cynomolgus monkeys (Dai et al. 1991) and humans (Gizzi et al. 1994). Third, a “cross-coupling” in the velocity-storage mechanism occurs from the primary horizontal nystagmus to a secondary vertical nystagmus after a roll tilt or to a secondary torsional component after a pitch tilt (Raphan and Cohen 1990; Paige 1985). These extensive sets of data allow for detailed comparisons of predictions of different hypotheses regarding the interactions of otolith and semicircular canal cues on the generation of VOR eye movements.
Because of this cross-coupling, the rotation axis of reflexive eye movements demonstrates a tendency to shift toward alignment with the GIF direction. In several species of monkeys (rhinocyon, cynomolgus, and squirrel monkeys), this so-called axis-shift has been observed for optokinetic nystagmus (OKN) and afternystagmus (OKAN) (Dai et al. 1991), for VOR during centrifugation (Merfeld and Young 1995; Wearne et al. 1999), for VOR following off-vertical axis rotation (Raphan et al. 1992), and for VOR following a post-rotatory tilt (Angalaki and Hess 1994; Merfeld et al. 1993b). For similar protocols in humans (Fetter et al. 1996; Gizzii et al. 1994; Harris and Barnes 1987; Merfeld et al. 1998), the rotation axis of reflexive eye responses also tends to align with the GIF direction but to a much smaller extent.

According to the VOR spatial orientation hypothesis, a directional gain asymmetry in the secondary nystagmus induced by “cross-coupling” might lead to a time constant asymmetry in the horizontal primary nystagmus (Raphan and Sturm 1991). For example, upward OKN and OKAN are larger than downward OKN and OKAN in rhesus and cynomolgus monkeys (Matsuo et al. 1979). Therefore horizontal OKN and OKAN responses following a roll tilt in either LD or RD orientations demonstrate asymmetries that reverse with the direction of the rotational cues in rhesus and cynomolgus monkeys (Raphan and Cohen 1988). Assuming that a similar upward/downward response symmetry exists for human VOR responses, the VOR spatial orientation hypothesis might be consistent with our observed LD/RD asymmetries in the horizontal VOR and their dependence on rotation direction.

While upward/downward response asymmetries are consistently observed in rhesus and cynomolgus monkeys, the presence of an upward/downward response asymmetry in humans is rather controversial and is certainly not consistent across subjects. An OKN/OKAN upward/downward asymmetry was reported in humans in some studies (Murasugi and Howard 1989; Wei et al. 1994) but not in other studies where asymmetries were reported for only a minority of human subjects (Baloh et al. 1986; Stiefel 1962). No consistent vertical VOR asymmetry has been reported in humans during pitch rotation about an earth-vertical axis (Allum et al. 1988; Baloh et al. 1983) or about an earth-horizontal axis (Baloh and Demer 1991).

It is certainly safe to conclude upward/downward response asymmetries are inconsistent and at best very weak in humans. Furthermore no asymmetries in torsional responses have ever been reported in humans for either optokinetic or vestibular stimulation (Morrow and Sharpe 1993; Peterka 1992; Seidman and Leigh 1989). Therefore the VOR spatial orientation hypothesis cannot explain the observed NU/ND asymmetries in the horizontal VOR. Even if an asymmetry in torsional responses existed, the VOR spatial orientation hypothesis would predict that the NU/ND asymmetry in the post-rotatory horizontal VOR should reverse with opposite rotation direction for both dumping and barbecue protocols. This prediction is refuted by our dumping and barbecue protocol data that demonstrate a similar NU/ND asymmetry following both CW and CCW yaw rotations.

Therefore the VOR spatial orientation hypothesis is unable to predict many characteristics found in the measured human responses. This may be because this hypothesis has primarily been developed to explain monkey but not human responses. Furthermore the fact that models of reflexive eye response spatial orientation (Raphan and Sturm 1991; Wearne et al. 1999) do not implement the influence of rotational cues on the estimation of gravity and linear acceleration may explain some of these shortcomings.

Frequency segregation hypothesis

The frequency segregation hypothesis states that the frequency content of the GIF measured by the otolith organs can be used to separate gravity from linear acceleration (Paige and Tomko 1991; Seidman et al. 1998). Specifically, low-frequency content might contribute to an estimate of gravity while high-frequency content might contribute to an estimate of linear acceleration. Our experimental results are not consistent with this hypothesis.

Rapid tilts yield high-frequency forces measured by the otolith organs. According to the frequency segregation hypothesis, these high-frequency cues should lead to an estimate of linear acceleration in the plane of the post-rotatory tilt and therefore should generate a horizontal linear VOR component when the interaural projection of this estimate of linear acceleration is nonzero. First, there should be a horizontal linear VOR component following a dynamic 90° tilt in either LD or RD orientation with no rotation preceding the tilt. These predictions are inconsistent with the absence of horizontal eye movements for both of these passive tilts. Second, there should be no horizontal linear VOR component when the subject is pitched into either a NU or ND orientation. These predictions are inconsistent with the large asymmetry observed between the NU and ND orientations (Fig. 3). In addition, we have shown that the post-rotatory tilt alone cannot explain the various asymmetries observed in horizontal VOR eye movements since eye responses following yaw rotation about an earth-horizontal axis demonstrated the same asymmetries (Fig. 8). Some additional central processing, probably involving sensory interactions, must be assumed to explain our data.

GIF resolution hypothesis

The GIF resolution hypothesis predicts that the difference between the estimate of gravity (\( \mathbf{g} \)) and the estimate of linear acceleration (\( \mathbf{a} \)) matches the measured GIF (\( \mathbf{f} = \mathbf{g} - \mathbf{a} \)). Therefore the GIF resolution hypothesis predicts a nonzero estimate of linear acceleration (\( \mathbf{a} \)), whenever the measured GIF, in this case gravity (\( \mathbf{g} \)), and the estimate of gravity (\( \mathbf{g} \)) do not match. After a post-rotatory tilt following a yaw rotation about an earth-horizontal axis, the post-rotatory semicircular canal cue induces an illusory tilt (von Holst and Grisbach 1951). Therefore the estimate of gravity (\( \mathbf{g} \)) does not match gravity (\( \mathbf{g} \)) and the GIF resolution hypothesis predicts a nonzero estimate of linear acceleration (\( \mathbf{a} \), Fig. 2A). If present, the interaural estimate of linear acceleration should induce a horizontal VOR. This induced VOR component is similar to the VOR evoked by actual linear acceleration (Paige and Tomko 1991; Schwarz and Miles 1991; Schwarz et al. 1989) but is evoked by an estimate of linear acceleration even in the absence of true linear acceleration. The induced VOR component should depend on both rotation direction and head orientation because the rotation direction influences the direction of illusory tilt and therefore the direction of the interaural estimate.
of linear acceleration and head orientation alters the projection of the estimated linear acceleration on the interaural axis ($\hat{a}_y$, Fig. 2, B and C). For example, the post-rotational response ($\hat{\omega}$) for a CCW rotation is CW. For the NU head orientation, the estimate of gravity ($\hat{g}$) tilts toward the subject’s right (Fig. 3, 1st column, top). Since the estimate of gravity does not match gravity, a nonzero interaural estimate of linear acceleration ($\hat{a}_y$) is therefore induced toward the subject’s right. This compensatory eye response to this interaural estimate of linear acceleration is a horizontal leftward induced VOR component, which adds to the AVOR component. In contrast, for the ND orientation following a CCW rotation, both the predicted tilt and interaural estimate of linear acceleration are toward the subject’s left. This leftward interaural estimate of linear acceleration induces a rightward horizontal induced VOR component, which now deducts from the AVOR component. Consistent with these predictions, in the 20 s following the post-rotatory tilt, the magnitude of the VOR following a tilt in the NU orientation was greater than the VOR following a tilt in the ND orientation after identical CCW rotations for each of the three speeds tested (Fig. 3). When the direction of the rotation preceding the post-rotatory tilt is CW, the predicted AVOR and induced VOR components both reversed. Again the induced VOR component adds to the AVOR component for the NU orientation but deducts for the ND orientation. Therefore the VOR asymmetry is similar for both rotation directions (Fig. 3).

For the LD orientation, the interaural estimate of linear acceleration ($\hat{a}_y$) is toward the subject’s right for both directions of rotation (Fig. 3, 2nd column), inducing a leftward horizontal induced VOR component. This induced VOR component should add to the AVOR component following CCW rotation and deduct from the angular VOR component following CW rotation. For the RD orientation, both the interaural estimate of linear acceleration and the induced VOR component are inverted. Therefore the induced VOR component should deduct from the AVOR component following CCW rotation and add following CW rotation. Consistent with previous data (Schrader et al. 1985), the LD response magnitude was greater than the RD response magnitude following identical CCW rotations and less than the RD response magnitude following identical CW rotations for each of the three speeds tested (Fig. 3).

For orientations midway between the primary tilt orientations, the observed patterns are also consistent with predictions of the GIF resolution hypothesis. If we assume that the estimate of linear acceleration is tilted approximately 45° to the right of vertical following CCW rotations, the interaural estimate of linear acceleration is near-zero for NU-RD and ND-LD orientations and maximal for NU-LD and ND-RD orientations following CCW rotations (Fig. 3). When the rotation direction is opposite (CW), the estimate of linear acceleration tilts 45° to the left of vertical. Therefore the asymmetry patterns are inverted. Indeed the maximal interaural estimates of acceleration for CW trials occur now for NU-RD and ND-LD orientations (Fig. 3), while near-zero estimates of linear acceleration for CW trials occur for NU-LD and ND-RD orientations (Fig. 3).

The dependence of the horizontal VOR time courses on head orientation after a post-rotatory tilt (Fig. 3) are predicted by previous VOR models that implement the GIF resolution hypothesis (Merfeld et al. 1993a; Zupan 1995). These models include mechanisms that allow the combination of otolith and canal information to contribute to the estimates of both gravity and head angular velocity.

The GIF resolution hypothesis is further supported by sudden increases observed in the horizontal VOR immediately following the post-rotatory tilt and by the induced VOR component reversal pattern. First, the VOR actually increases immediately after the post-rotatory tilt in some orientations (Fig. 3): this increase is easily noticeable for CW RD, CW NU-RD, and CCW NU-LD trials at all speeds. This increase is inconsistent with any type of response attenuation but is consistent with additive influence of an induced VOR component. Second, for 200°/s rotations, the induced VOR component reverses after about 30 s for all orientations except for LD and RD orientations (Fig. 5, 3rd row). It is well known that semicircular canal afferents typically show a secondary phase reversal approximately 30 s after deceleration following constant velocity rotation (Goldberg and Fernandez 1971) and a reversal of VOR eye movements consistent with this pattern of afferent discharge is commonly recorded (Correia and Guedry 1966). As the semicircular canal cue diminishes and reverses (Fig. 11), the angle between the estimates of gravity ($\hat{g}$) and gravity ($\hat{g}$) should diminish ($\phi$) and then reverse ($\phi$). Therefore the GIF resolution hypothesis predicts a reversal of the estimate of linear acceleration as well as a reversal of the induced VOR component for most orientations (as illustrated for the NU orientation in Fig. 11B). Such reversals are evident in the horizontal induced VOR component (Fig. 5) following 200°/s yaw rotations. These reversals are also present following 50° and 100°/s yaw rotations but are harder to observe.

However, in the RD and LD positions, the projection of the estimated linear acceleration on the interaural axis is always in a single direction. For example, in the RD orientation (Fig. 11C), this projection is always toward the subject’s left fol-

FIG. 11. A: after a post-rotatory tilt following a CCW rotation, the estimate of head angular velocity ($\hat{\omega}$) decreases in absolute value (from $t_1$ to $t_2$) and even reverses ($t_3$). B: the estimates of gravity and linear acceleration are time varying. As the estimated tilt, driven by the estimate of head angular velocity, decreases ($t_2$) and even reverses ($t_3$), the projection of the estimated linear acceleration on the interaural axis for a subject oriented NU also decreases ($t_2$) and reverses ($t_3$). C: for a subject oriented RD, the projection of the estimated linear acceleration on the interaural axis decreases ($t_2$ and $t_3$) without reversing.
following both CW and CCW rotations. Therefore for the RD and LD orientations, reversal in the estimated tilt does not reverse the interaural estimate of linear acceleration nor does it reverse the induced VOR component even though the VOR for these conditions reverse. Consistent with this prediction, the horizontal induced VOR component does not show a reversal for RD and LD orientations for any of three speeds tested.

According to the GIF resolution hypothesis (Fig. 2), the induced VOR component is proportional to the interaural estimate of linear acceleration ($\dot{a}$) and therefore should vary sinusoidally as a function of head orientation. The induced VOR component should be maximum and positive when the subject’s interaural axis is aligned with the estimate of linear acceleration and when this estimate of linear acceleration is toward the right ear. Therefore the amplitude ($M$) of the sinusoidal fit to induced VOR data (Fig. 6, left) should be proportional to the norm of the estimate of linear acceleration ($\dot{a}$). In addition, the phase shift ($\phi$) of the sinusoidal fits should be related to the tilt angle that the estimate of linear acceleration makes with the earth horizontal ($\dot{a}$, Fig. 2B). Specifically, the phase shift ($\phi$) should be equal to $\dot{a}$ for CCW rotations and equal to $180^\circ - \dot{a}$ for CW rotations. In agreement with this prediction, the induced VOR component varied sinusoidally with subject orientation at each of the three velocities tested (Fig. 6, left). Moreover, these sinusoidal fits to the 50, 100, and 200°/s data closely matched the variations of the projection of the estimate of linear acceleration (Fig. 6, right) onto the subject’s interaural axis ($\hat{a}$) for angles of the estimate of linear acceleration with respect to earth-horizontal ($\hat{a}$, Fig. 2B) of 22.5, 32, and 45°, respectively.

In the simple formulation of the GIF resolution hypothesis discussed in this paper, the estimate of gravity ($\hat{g}$) has a constant norm [i.e., central processing of canal and graviceptor information leads to an estimate of gravity ($\hat{g}$) such that the magnitude of $\hat{g}$ is always a fixed value, presumably 1 g]. Therefore the trajectory of the estimate of linear acceleration ($\hat{a}$) is theoretically an arc of a circle with a radius equal to the magnitude of $\hat{g}$ (Figs. 7, right, and 11). Using simple trigonometry and planar geometry (Fig. 2B), the theoretical trajectory of the estimate of linear acceleration (Fig. 7, right) is defined by the parametric equations $\hat{X}(t) = ||\hat{a}|| \cos \hat{a}(t)$ and $\hat{Y}(t) = ||\hat{a}|| \sin \hat{a}(t)$. In these equations, $t$ is the time after the post-rotatory tilt and $\hat{a}$ is the tilt of the estimate of linear acceleration with earth-horizontal (Fig. 2B). The amplitude of the estimate of linear acceleration ($||\hat{a}||$) is theoretically proportional to the amplitude ($M$) of the induced VOR sinusoidal fit. In addition, the tilt of the estimate of linear acceleration with earth-horizontal for CCW rotations ($\hat{a}$, Fig. 2B) and for CW rotations ($180^\circ - \hat{a}$) is theoretically equal to the phase shift ($\phi$) of the sinusoidal fits to the induced VOR component. Therefore if the GIF resolution hypothesis is valid, the induced VOR experimental trajectories (Fig. 7, left) defined by the parametric equations $\hat{X}(t) = M(t) \cos \phi(t)$ and $\hat{Y}(t) = M(t) \sin \phi(t)$ should closely match the theoretical trajectories of the estimate of linear acceleration (Fig. 7, right). Indeed, the experimental trajectories appear consistent with these predictions.

Influence of speed on the GIF resolution hypothesis

Due to semicircular canal dynamics (Wilson and Melvill Jones 1979), the semicircular canal post-rotatory cue decreases with decreasing angular velocity. Since the tilt of the estimate of gravity ($\hat{g}$) relative to the earth-vertical axis is driven by the post-rotatory semicircular canal cue, this illusory tilt should decrease with decreasing speed. Therefore both the amplitude of the estimate of linear acceleration ($\dot{a}$) and the angle ($\hat{a}$) of the estimate of linear acceleration with earth-horizontal (i.e., the phase shift) should decrease with decreasing speed (Fig. 6, right).

Using trigonometry and planar geometry (Fig. 2B), we can calculate that the magnitude of the estimate of linear acceleration ($||\hat{a}||$) when tilted with respect to earth-horizontal is $||\hat{a}|| = \frac{2||g||}{\sin \hat{a}}$. This magnitude decreases with decreasing velocity since the tilt angle ($\hat{a}$) of the estimate of acceleration decreases with decreasing velocity. Since the amplitude ($M$) of the sinusoidal fits to the induced VOR data are hypothesized to be proportional to the magnitude of the estimate of linear acceleration ($\hat{a}$), this amplitude ($M$) should decrease with decreasing velocity. This expectation is consistent with experimental results showing a decrease in $M$ with decreasing velocity (Fig. 6).

The decrease in the magnitude of the induced VOR component could simply be due to the scaling factor of the rotation angular velocity. However, a simple scaling factor explanation cannot explain the phase shift variation between sinusoidal fits to CW and CCW data with speed (Fig. 6). In fact, according to the GIF resolution hypothesis, the phase shift ($\phi$) of the sinusoidal fit to the induced VOR data are related to the angle ($\hat{a}$) of the estimate of linear acceleration ($\hat{a}$) with earth-horizontal.
Specifically, the orientation angle (θ, see Fig. 2C) where the induced VOR component is at its positive maximum is equal, by definition, to the phase shift (ϕ). This angle also corresponds to the orientation where the subject’s interaural axis is aligned with the estimate of linear acceleration (â), and this estimate of linear acceleration is directed toward the right ear. As a result, θ = ā = ϕ for CCW rotations and θ = 180° − ā = ϕ for CW rotations. Therefore with decreasing speed, the peak of the sinusoidal fits to the induced VOR data should shift toward 0° for CCW rotations and toward 180° for CW rotations. The experimental results confirm this theoretical prediction (Fig. 6).

**Vertical responses**

In addition to horizontal responses, vertical eye movements were also evoked following post-rotatory tilts (Figs. 9 and 10). These vertical VOR eye movements were not compensatory to either the horizontal post-rotatory semicircular canal cues or the post-rotatory tilt itself. Therefore these vertical responses must be due to the interaction of these sensory cues. As previously reported after post-rotatory tilts following yaw rotations in rhesus monkeys (Angelaki and Hess 1994) and squirrel monkeys (Merfeld and Young 1992; Merfeld et al. 1993b), the vertical eye movements observed in the dumping protocol illustrate the tendency of the VOR axis of rotation to align with either gravity (ĝ) or an estimate of gravity (â). Consider a subject tilted to the NU orientation following CW or CCW yaw rotations. If the VOR displays a tendency to align its rotation axis with the direction of gravity (ĝ), the axis-shift component should be exclusively torsional (Fig. 12A, A-shift₁). Alternatively, if the VOR exhibits a tendency to align its rotation axis with the direction of the estimate of gravity (â), the corresponding axis-shift component (Fig. 12A, A-shift₂) should include a secondary vertical-axis-shift component in addition to the torsional component. For both CW and CCW directions of rotation, the post-rotatory secondary vertical VOR component should be positive (downward) for the NU orientation (Fig. 12A) and negative (upward) for the ND orientation (Fig. 12B).

As shown (Fig. 10), the sinusoidal fits to the vertical VOR data for CW and CCW rotations are phase shifted with respect to one another, with a phase shift smaller than 180°. This experimental phase shift is better matched by the predicted phase shift when the VOR rotation axis aligns with the estimate of gravity (ĝ, Fig. 12D) rather than gravity (ĝ, Fig. 12C). In particular, if the VOR rotation axis aligns with gravity (ĝ), no vertical eye movement should be present for NU and ND orientations (Fig. 12C, orientation angle 0 and 180°, respectively). However, experimental results show that a small vertical VOR is present for both NU and ND orientations, consistent with an axis-shift toward alignment with the estimate of gravity (ĝ), as opposed to alignment with gravity.

**Conclusion**

The GIF resolution hypothesis accurately predicts that post-rotatory VOR eye movements recorded during dumping and barbecue protocols include an “induced” VOR component. The induced VOR component is consistent with the idea of a response compensatory to an internally generated neural estimate of linear acceleration even though no physical linear acceleration is present. The GIF resolution hypothesis accurately predicts the VOR and induced-VOR dependency with head orientation, direction, and speed of rotation. Alternative hypotheses, stating that the post-rotatory VOR time constant depends on head orientation relative to the GIF or that gravity can be separated from linear acceleration by frequency segregation are not consistent with the various characteristics of the measured post-rotatory VOR during dumping and barbecue protocols.

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