Effects of Tilt of the Gravito-Inertial Acceleration Vector on the Angular Vestibuloocular Reflex During Centrifugation

SUSAN WEARNE, THEODORE RAPHAN, AND BERNARD COHEN
Departments of Neurology, Physiology, and Biophysics, Mount Sinai School of Medicine, New York, 10029; and Department of Computer and Information Sciences, Brooklyn College, City University of New York, Brooklyn, New York 11210

Wearne, Susan, Theodore Raphan, and Bernard Cohen. Effects of tilt of the gravito-inertial acceleration vector on the angular vestibuloocular reflex during centrifugation. J. Neurophysiol. 81: 2175–2190, 1999. Interaction of the horizontal linear and angular vestibuloocular reflexes (IVOR and aVOR) was studied in rhesus and cynomolgus monkeys during centered rotation and off-center rotation at a constant velocity (centrifugation). During centered rotation, the eye velocity vector was aligned with the axis of rotation, which was coincident with the direction of gravity. Facing and back to motion centrifugation tilted the resultant of gravity and linear acceleration, gravito-inertial acceleration (GIA), inducing cross-coupled vertical components of eye velocity. These components were upward when facing motion and downward when back to motion and caused the axis of eye velocity to reorient from alignment with the body yaw axis toward the tilted GIA. A major finding was that horizontal time constants were asymmetric in each monkey, generally being longer when associated with downward than upward cross-coupling. Because of these asymmetries, accurate estimates of the contribution of the horizontal IVOR could not be obtained by simply subtracting horizontal eye velocity profiles during facing and back to motion centrifugation. Instead, it was necessary to consider the effects of GIA tilts on velocity storage before attempting to estimate the horizontal IVOR. In each monkey, the horizontal time constant of optokinetic after-nystagmus (OKAN) was reduced as a function of increasing head tilt with respect to gravity. When variations in horizontal time constant as a function of GIA tilt were included in the aVOR model, the rising and falling phases of horizontal eye velocity during facing and back to motion centrifugation were closely predicted, and the estimated contribution of the compensatory IVOR was negligible. Beating fields of horizontal eye position were unaffected by the presence or magnitude of linear acceleration during centrifugation. These conclusions were evaluated in animals in which the low-frequency aVOR was abolished by canal plugging, isolating the contribution of the IVOR. Postoperatively, the animals had normal ocular counterrolling and horizontal eye velocity modulation during off-vertical axis rotation (OVAR), suggesting that the otoliths were intact. No measurable horizontal eye velocity was elicited by centrifugation with angular accelerations ≤40°/s² and angular velocities ≤400°/s. We conclude that in rhesus and cynomolgus monkeys, differences between horizontal eye velocities recorded during facing and back to motion constant velocity centrifugation can be explained by orienting effects of the GIA tilt on the time constants of the horizontal aVOR and not by a superposed IVOR.

INTRODUCTION

Movement in a gravitational environment induces combined linear and angular accelerations of the head in space, concurrently activating the linear and angular vestibuloocular reflexes (IVOR and aVOR). Off-axis rotation, or centrifugation, which induces concomitant centripetal and angular accelerations, has been used extensively to study aVOR and IVOR interaction (Angelaki and Anderson 1991a,b; Angelaki et al. 1991; Crampton 1966; Curthoys et al. 1992; Lansberg et al. 1965; Merfeld 1990, 1995; Merfeld and Young 1995; Merfeld et al. 1991, 1993; Sargent and Paige 1991; Wearne 1993; Young 1967). Sargent and Paige (1991) tested monkeys with sinusoidal centrifugation to determine whether the aVOR and IVOR responses superpose. At frequencies between 1 and 4 Hz, which induced minimal tilts of the gravito-inertial acceleration (GIA), responses of the horizontal IVOR summed with those of the horizontal aVOR when the animals were upright. In the supine position, the aVOR was in the roll direction, but the IVOR was still horizontal. The horizontal IVOR, estimated by subtracting the aVOR from the overall response when the animals were upright, was the same as that measured directly when they were supine, supporting the superposition hypothesis at these frequencies.

In other studies, low-frequency and constant-velocity centrifugation has been used to extract the IVOR component of eye velocity. We use the term ‘‘constant-velocity centrifugation’’ to refer to a stimulus that has a small angular acceleration (10–40°/s²) up to a constant velocity, which is maintained for a long duration. In these studies, the horizontal eye velocity trace obtained when subjects had their backs to the direction of motion was subtracted from that when they faced the motion (Benson 1974; Merfeld 1990; Merfeld and Young 1995; Wearne 1993; Young 1967). Because the centripetal acceleration was identical in both conditions, the subtraction was assumed to cancel the aVOR responses, while summing the IVOR responses. One-half of the difference trace then should represent the IVOR response. Whether superposition holds at low frequencies and large GIA tilt angles, such as during constant velocity centrifugation, has not been determined independently. This is primarily because the low gain of the IVOR at frequencies <0.5 Hz (Paige et al. 1996; Paige and Tomko 1991a,b; Telford et al. 1997) makes its contribution to the combined response difficult to evaluate.

Studies of the spatial organization of optokinetic after-nystagmus (OKAN) in rhesus and cynomolgus monkeys (Dai et al. 1991, 1992) have shown that eye velocity responses to linear acceleration due to gravity, and to angular motion of the visual field do not necessarily superpose but interact through velocity storage. Specifically, the spatial orientation properties of velocity storage, reflected in the time constant of horizontal OKAN, vary in monkeys in side down positions depending on...
whether the eye velocity is directed toward or away from gravity. The time constant is generally longer during head tilts, which induce downward than upward cross-coupled components (Dai et al. 1991). Because velocity storage is common to OKAN and the aVOR (Raphan et al. 1979), the orientation changes that are present during OKAN also are present during postrotatory responses with the head tilted (Angelaki and Hess 1995; Harris and Barnes 1987; Raphan et al. 1992). Asymmetries in aVOR time constants also have been observed for leftward or rightward GIA tilts with respect to the head during postrotatory nystagmus (Schrader et al. 1985a,b) and during centrifugation in monkeys (Wearn et al. 1994). Because the angle of GIA tilt increases monotonically during the angular acceleration phase, reaching a maximum tilt angle at constant angular velocity, any asymmetries in the dependence of the horizontal time constant on GIA tilt during facing and back to motion centrifugation will modify the difference trace, invalidating its use as an index of the compensatory IVOR. If the functional relationship between the time-varying GIA tilt during centrifugation and the aVOR time constant were the same as that determined from a series of static head tilts with respect to the GIA, this could explain the character and shape of the difference traces observed during facing and back to motion centrifugation.

The purpose of this study was to investigate the interaction of the horizontal aVOR and IVOR during constant velocity centrifugation. In particular, we determined the relative contributions made by dynamic changes in the aVOR time constants produced by a continuously changing GIA vector, and the compensatory IVOR, to the overall response. We also investigated whether the orientation properties of velocity storage determined from OKAN were sufficient to predict the horizontal eye velocity responses during constant velocity centrifugation.

METHODS

One juvenile rhesus (Macaca mulatta; M9303) and six cynomolgus monkeys (M. fascicularis; M9307, M9306, M9308, M9223, M9351, and M9357) were used in these studies. We have not found differences between rhesus and cynomolgus monkeys in oculomotor or vestibular characteristics in previous studies. In particular, the spatial orientation properties and the dynamic characteristics of the aVOR are very similar for the two species. For this reason, findings from the two species have been used interchangeably in this report. Two of the cynomolgus monkeys (M9308 and M9351) were tested before and after their six semicircular canals were plugged. One cynomolgus monkey (M9357) was tested before and after both lateral canals were plugged. The surgical and experimental procedures conformed to the Principles of Laboratory Animal Care (National Institutes of Health Public 85–23, revised 1985) and were approved by the Institutional Animal Care and Use Committee (IACUC).

Surgical procedures

Animals were prepared at sterile surgery under anesthesia with two three-turn search coils to record the orientation of one eye in three dimensions. A frontal coil of 16 mm diam in rhesus monkeys and 14 mm diam in cynomolgus monkeys was sutured to the sclera under the conjunctiva (Judge et al. 1980). This coil was concentric with the iris, and its normal was aligned with the optic axis. A second coil of 11 mm diam was wound under the superior rectus in the horizontal plane of the same eye (Dai et al. 1994; Robinson 1963; Yakushin et al. 1995) such that its normal was approximately orthogonal to that of the frontal coil. Voltages proportional to the horizontal and vertical components of eye orientation were transduced by the frontal coil; voltages proportional to the torsional component of eye orientation were transduced by the top (roll) coil. Two head bolts were implanted in dental acrylic on the skull to provide painless head stabilization in stereotaxic coordinates during experiments. Animals received analgesics and antibiotics (morphine sulfate 2 mg im; cephalorulin 0.1 g im) after surgery to alleviate pain and counter infection.

At separate surgery, all six semicircular canals were plugged in two cynomolgus monkeys (M9308 and M9351). The animals were anesthetized and the middle ear approached posteriorly. The canals were identified under an operating microscope. Plugging was accomplished by grinding across each canal with a diamond burr until the membranous canal was interrupted. The region of the canal was packed with bone and covered with a small piece of muscle (see Yakushin et al. 1995, for details). Inactivation of the semicircular canals was verified by the absence of response to 0.2-Hz sinusoids of angular velocity (peak velocity 60°/s) in any spatial plane for the six canal plugged animals. The lateral canal plugged animal had no response when tilted ~40° nose down, so that the vector sum of the normals to the vertical canals was orthogonal to the rotation axis. Ocular counterrolling was normal in these animals, and the response to z-axis off-vertical axis rotation (OVAR) was the same as in other canal-plugged animals (Cohen et al. 1983; Correa and Money 1970; Yakushin et al. 1992), indicating that the otoliths were intact. Postoperative data reported in this study were obtained 6 and 2 mo after surgery in M9351 and M9308, respectively.

Stimulation apparatus

The stimulator is shown schematically in Fig. 1A (Neurokinetics, Pittsburgh) (see also Dai et al. 1994). It was computer controlled and had three gimbaled axes of rotation: an outer horizontal axis (A), a nested yaw axis (B), and a doubly nested inner pitch-roll axis (C). The yaw and pitch-roll axes were enclosed in a light-tight, optokinetic sphere (OKN drum), 109 cm in diameter, with 10° vertical black and white stripes on the inside. The axis of the OKN drum (D) was collinear with the yaw axis (B). When the OKN sphere rotated, driven by the OKN motor (d), it produced full-field motion that induced OKN and OKAN. The horizontal and pitch-roll axes were controlled by position servos, and the yaw and optokinetic axes by position and velocity servos. The circular spine, which was the gimbal for the horizontal axis (A), was driven by the horizontal axis motor (a). It moved over approximately ±180° with a maximum acceleration of 60°/s². The nested yaw axis (B) driven by motor (b) through the yaw axis gimbal, carried the primate chair and field coils, the centrifuge arm and the pitch-roll axis motor (c). The maximum acceleration and deceleration of the yaw axis (B) was 200°/s², and the maximum velocity was 400°/s. The pitch-roll axis (C) was driven by motor c, and moved over ±90° of excursion at a maximum acceleration of 600°/s².

Monkeys were seated in a primate chair, shown centered with respect to each rotation axis in the diagram of Fig. 1A. The chair was composed of 1.25 cm lexan, which did not flex during rotation. Velocity steps in yaw about a vertical axis were given in this on-axis position. The chair could be repositioned by 90° along the pitch-roll axis to give the animals velocity steps in pitch or roll about a spatial vertical axis. By tilting the circular spine about the horizontal axis (A) and rotating the animal around the centered yaw axis (b), the animal received OVAR. The chair could be displaced to the end of the centrifuge arms, positioning the monkey’s head 25 cm from the center of rotation. The primate chair could be positioned in 90° increments when displaced so that centripetal acceleration was directed along either the interaural or nasooccipital axis during constant velocity yaw axis centrifugation. The terms ‘‘centered’’ and ‘‘on-axis’’ rotation will be used interchangeably as will the terms ‘‘centrifugation’’ and ‘‘off-axis’’ rotation.
Recording and calibration of three-dimensional eye orientation and velocity

Two orthogonal field coils, 33 cm on a side and driven at frequencies of 24.7 kHz, were fixed to the primate chair. The head bolts were attached to a lexan ring, which fixed the head to the chair so that the head remained in the same orientation with respect to the coordinate frame defined by the field coils. With the monkey erect, the yaw axis was aligned with gravity, and the horizontal stereotaxic plane was aligned with the gravitational horizontal. Thus the lateral semicircular canals were tilted up ~30° from the earth horizontal plane (Blanks et al. 1985; Yakushin et al. 1995). The search coils were centered with regard to the field coils. Voltages proportional to the projections of the search coils onto the magnetic fields were recorded with three phase detectors (Neurodata). If the voltages from the two search coils were not orthogonal, a portion of the horizontal voltage was fed back and subtracted from the roll voltage, removing cross talk in the roll signal when the upright animal was rotated around a spatial vertical axis. This method electronically orthogonalized the search coil axes so that the effective normal to the top coil was aligned with an axis from the bottom to the top pole of the eye. Studies on monkeys have shown that there is a small nonorthogonal relationship between the maximum direction for roll and yaw (Crawford and Vilis 1991), but the angles are within the error bounds of the data reported in the study.

To calibrate yaw, pitch, and roll axis eye movements, animals were rotated about a spatial vertical axis at 30°/s in the presence of a lighted, textured visual surround in upright, side down, and prone positions. It was assumed that horizontal and vertical gains were close to unity in this condition (Crawford and Vilis 1991; Raphan et al. 1985; Yakushin et al. 1995). In brief, eye position and velocity vectors were referenced to a right-handed coordinate frame (Fig. 1B). Eye orientation is represented as Euler angles in the Fick rotation convention, with φ, θ, and ψ corresponding to rotations about the z axis, the rotated x axis, and the doubly rotated y axis. These angular deviations from the reference will be referred to as the yaw, pitch, and roll or horizontal, vertical, and torsional eye positions, respectively. Eye velocities were determined as vector components along the head-based coordinate frame (Fig. 1B). Horizontal, vertical, and torsional components of the eye velocity vector are represented as (ωx, ωy, ωz), respectively. The circular arrows correspond to the direction of rotation for a velocity component along the positive axis, according to a right-hand rule. Leftward, downward, and counterclockwise rotations (from the animal’s point of view) are represented in the figures by upward deflections in the eye position and eye velocity traces.

To validate the calibration procedure, we compared Listing’s planes during spontaneous eye movements with those found in the literature. We assumed that the average coil voltages during spontaneous positions of fixation while the animal made saccades for 15–30 s in light, correspond to the straight-ahead eye position with zero roll. This assumption is consistent with data obtained in trained and calibrated monkeys for a large range of saccades in light and dark (van Opstal et al’s point of view) are represented in the figures by upward deflections in the eye position and eye velocity traces.

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al. 1995). These average coil voltages defined the reference head coordinate frame. With the eye in this orientation, the visual axis coincides with the roll axis of the head frame. To a good approximation, this aligns with the stereotaxic coordinate frame of the head, which we physically aligned with the axes of the horizontal and vertical field coils. We then used Listing’s law to determine the ‘displacement plane’ (Helmholz 1867; Tweed and Vilis 1990), which approximately contains all axes of rotation from this reference position during saccades. The unit vector normal to the displacement plane and its angle with respect to the reference were determined. We then determined primary position as the eye position for which the visual axis is normal to the displacement plane, i.e., Listing’s plane. This corresponded to a rotation of twice the angle between the roll axis and the normal to Listing’s plane, about an axis given by their cross-product (Helmholz 1867). Computed rotation angles were generally within 15°, and the rotation axes were confined to a single plane, in accordance with Listing’s law (Crawford and Vilis 1991; Haslwanter et al. 1992). The accuracy of the technique for estimating primary position was determined by comparing displacement planes and reference positions from the monkey eye movements with those obtained from a gimbal-mounted search coil system, the reference system of which could be set arbitrarily. For a given displacement plane, the reference positions computed from the monkey or gimbal data were the same.

**Experimental protocol**

Alertness was maintained by administration of amphetamine sulfate (0.3 mg/kg) intramuscularly, 30 min before testing. Before data collection, vestibular and optokinetic time constants were habituated by repeatedly rotating the animals to each side about all axes (Cohen et al. 1992), minimizing the effects of further habituation. In consequence, the time constants and initial gains of OKAN for the upright position did not habituate further during the period of testing.

Eye movements were induced in three stimulus paradigms. Optokinetic stimulation was given in the upright position or statically tilted left ear down (LED) or right ear down (RED) with regard to gravity at angles of 0, 17, 36, 45, 52, and 90°. Velocity steps of 60 and 90°/s, lasting 30 s, were used to induce OKAN (Cohen et al. 1977; Raphan et al. 1979; Waespe et al. 1983). OVAR was given by tilting the axis of rotation 90° with respect to gravity and rotating the animal about its yaw axis at 60°/s. Peak interaural linear acceleration was 1 g for 90° tilts.

Combined linear and angular accelerations were delivered by eccentric rotation on a centrifuge, either facing the direction of motion (Fig. 1C) or with back to the motion (Fig. 1E). The direction of gravitational acceleration with respect to the head is indicated as $A_g$. The direction of head rotation during vestibular stimulation also is indicated by a circular arrow and is denoted $A_{rz}$. Animals also were rotated about a centered axis (Fig. 1D). For $+z$ rotation, animals were right ear out (REO) when facing motion (Fig. 1C) and left ear out (LEO) when back to motion (Fig. 1E). For $-z$ rotation, these conventions were reversed. The centrifuge was accelerated at 40°/s² to a final angular velocity of 400°/s. The final stimulus velocity was maintained for $\geq 120$ s. We term this stimulus constant velocity centrifugation.

During centrifugation with constant angular acceleration, gravitational ($A_g$) and centripetal ($A_c$) accelerations sum, producing GIA. At the onset of rotation, the GIA vector rotates in three dimensions, reaching a steady state position in the $xz$ (roll) plane of the head during the period of constant centrifuge velocity. For the angular accelerations used in this study (10 and 40°/s²), a small constant tangential acceleration ($<0.02 \, g$) was present throughout the angular acceleration period. Because its magnitude in relation to the centripetal acceleration (1.24 g) was small, its effect on the change in horizontal time constant was neglected. Thus only the effects of GIA tilt in the $xz$ plane on the horizontal time constant were considered.

At a final angular velocity of 400°/s, the GIA was tilted by 52° in the animal’s roll plane. For facing and back to motion centrifugation, $A_c$ was directed along the interaural axis ($C_g$), and the GIA tilted dynamically in the roll plane of the head, through an angle $\theta_s$ that increased with the angular velocity of the centrifuge. Cross-coupled components of eye velocity appeared when the GIA was tilted with regard to the head. Changes in eye position and eye velocity were examined during all of these motions to determine the effects of interaural linear acceleration on the horizontal component of eye movement.

The respective directions of compensatory linear (black arrows) and angular (white arrows) VORs during facing and back to motion centrifugation are indicated in Fig. 1, C and E. Regardless of whether the animal is LEO or REO, the compensatory horizontal IVOR is always in the centrifugal direction. That is, when the right ear is out, the direction of the compensatory IVOR should be rightward ($-z$; Fig. 1C), and when the left ear is out, the compensatory IVOR should be leftward ($+z$; Fig. 1E).

**Data acquisition and processing**

Eye position data and photocell voltages, measuring the state of the light and the passage of stripes, were sampled at a rate of 600 Hz per channel using the DAOS data acquisition system (Mycon Technology) running on a 386-based digital computer. Before sampling, eye position data were prefiltered by an eight-pole Butterworth filter with a corner frequency of 30 Hz. Slow phase eye velocity was obtained by transforming the eye velocity vector to head coordinates and removing saccades with an order statistic filter (Engelken and Stevens 1990, 1991).

Programes were written using C/C++ and Matlab (MathWorks) to analyze pitch, roll, and yaw slow phase eye velocities. Eye velocity was analyzed from the onset of OKAN to the point where the horizontal component decayed to zero. OKAN time constants were estimated by fitting a single exponential to the decaying portion of eye velocity, 1–2 s after the light was extinguished, indicating offset of the OKN stimulus. Horizontal VOR time constants were estimated by fitting a sum of two exponential functions, representing the cupula and velocity storage modes, following angular velocity steps of 60°/s. The cupula time constant was constrained to 4 s (Büttner and Waespe 1981; Fernández and Goldberg 1971), and the initiator integral state was constrained to be zero. The time constant of velocity storage was estimated from a constrained fit to the data with only the integrator time constant allowed to vary. This technique gives a better estimate of the dynamics of the VOR than if a single exponential was fitted.

During the angular acceleration at the onset of centrifugation, a number of processes complicate the estimation of velocity storage time constants. The input signal driving the aVOR is a ramp of angular velocity producing a parabolic increase in centripetal acceleration. This is accompanied by a continuous tilt of the GIA from the spatial vertical, which induces a corresponding reduction in the horizontal aVOR velocity storage time constant. In addition, both the cupula deflection and the induced velocity storage response increase slowly, producing nonzero initial conditions for the internal states of the system at the onset of constant angular velocity. Because the states cannot be measured, they are unconstrained in exponential fits to the decaying portion of eye velocity. Such unconstrained fits can lead to widely fluctuating estimates of the system time constants, depending on the choice of initial states. During centrifugation therefore, aVOR velocity storage time constants cannot be estimated by fitting a sum of exponential functions to eye velocity, as they can for steps of head velocity during centered rotation (Raphan et al. 1979).

The dynamical system representation allowed us to simulate changes in the time constants as a function of GIA tilt angle, which varied with time during centrifugation (see section on model implementation and parameter identification). The aVOR model (Eqs. 1 and 2) was used to estimate system parameters ($h_1$, $h_2$, $g_{c1}$, $g_{c2}$, and $g_{s1}$) for each monkey by fitting the centered rotation data. The best-fitting parameters then were held constant, and the decline in horizontal time...
constant as a function of GIA tilt (Eq. 4), derived from OKAN data with the head statically tilted (Eq. 3), was introduced into the model to predict facing and back to motion centrifugation traces. A second estimate of velocity storage time constants during centered rotation and centrifugation also was obtained by fitting a single exponential function to the decay of eye velocity, starting \( \pm 10 \) s after the onset of constant angular velocity, to avoid the initial period when both cupula and velocity storage contribute to eye velocity. Assuming a cupula time constant of \( 4 \) s, the contribution of the cupula mode will be negligible after \( 2.5 \) time constants, and eye velocity should decay with the time constant of velocity storage. Because our method used only the tail portion of the eye velocity time series, we term it the “tail-fit time constant.” The two methods gave similar values, and the tail-fit was used as an initial estimate of the velocity storage time constant when searching for the best-fitting parameters for the model simulations.

**Experimental design and statistical analysis**

The order of presentation of experimental trials was randomized to avoid systematic order effects. Repeated measures were performed in all experimental conditions: each monkey was tested at least twice in each condition, but not all monkeys were exposed to every experimental paradigm.

Differences in time constants\(^2\) between experimental conditions were evaluated statistically using planned contrasts, evaluated with the \( t \)-statistic for dependent samples (Winer et al. 1991). This method minimized the effects of habituation of time constants on the variance estimate. Intrablock variability was assessed both graphically and analytically. Position and desaccaded eye velocity traces from repeated trials were overlaid, and subject means \( \pm 1 \) SD or \( \pm 2 \) SDs were computed and graphed using programs written in MATLAB (The Mathworks). This method provides a clear graphic indication of subject trends and their variability. Deviations of the model simulations from the data then could be evaluated graphically.

The time constant of the velocity storage integrator during centrifugation was estimated from optimal first-order fits to data obtained during OKAN. The other parameters were estimated from responses to centered rotation. Simulations were done to assess the model’s ability to predict the responses to OKN, OKAN, centered rotation, and centrifugation with a single set of parameters. Because the functions relating eye velocity to the various stimulus components cannot be represented in analytic form in terms of the system parameters to allow their optimization, no figure-of-merit function of individual responses was calculated. Goodness of fit was assessed by determining the extent to which the simulated response fell within 95% confidence intervals of overlayed eye velocity responses.

**Results**

**Effects of combined linear and angular accelerations during centrifugation**

Centered rotation about the spatial vertical at an angular acceleration of \( 40^\circ / s^2 \) to a constant angular velocity of \( 400^\circ / s \) increased horizontal eye velocity (\( \omega_y \)) during the period of angular acceleration to a peak value of close to \( 200^\circ / s \) (198^\circ /s, Fig. 2A). The GIA remained aligned with the animal’s \( z \) axis for the duration of rotation. During the constant velocity period, horizontal eye velocity decayed with a time constant of \( 12.8 \) s. Vertical and roll components of eye velocity (\( \omega_x \) and \( \omega_z \)) were close to zero throughout the stimulus. Eccentric rotation on the centrifuge changed the direction of the GIA vector with respect to the head and increased its magnitude. When facing the direction of centrifuge motion (Fig. 2B), horizontal slow phase velocity (\( \omega_y \)) rose approximately exponentially approaching a lower peak velocity (165^\circ /s) than when centered (198^\circ /s; compare Fig. 2, A and B). Upward vertical (\(- \omega_z \), arrow B) and counterclockwise roll (\(+ \omega_\theta \)) components of eye velocity appeared during the acceleration period (Fig. 2B). Vertical and roll eye velocities built slowly with the tilt of the GIA. Their maxima were considerably delayed, relative to the tilt of the GIA (Fig. 2B). Horizontal eye position (\( \phi \)) moved into the slow phase direction. Average vertical eye position (\( \theta \)) remained close to the reference position while the eyes tilted (\( \phi \)) in the direction of GIA rotation (Fig. 2B). During the constant velocity period, horizontal eye velocity decayed to zero and was followed by an oppositely directed secondary nystagmus. The horizontal velocity storage time constant measured by the tail-fit method (see methods) was shorter when facing motion (5.2 s) than during centered rotation (12.8 s, Fig. 2A). Vertical eye velocity decayed slowly (arrow B, Fig. 2B), whereas the roll component decayed more rapidly. Ocular torsion was maintained at \( \pm 5^\circ \) during the constant velocity period while the GIA was tilted (arrow A, Fig. 2B).

When monkeys were oriented with their backs to the motion (Fig. 2C), horizontal eye velocity rose exponentially during the angular acceleration, reaching a higher peak velocity (175^\circ /s) than when facing the motion (Fig. 2B). The horizontal time constant (7.4 s) was shorter than during centered rotation, but was longer than when facing the motion. Downward vertical and clockwise roll eye velocity components were generated. Torsional eye position (\( \psi \)) rotated in a counterclockwise direction, following the tilt of the GIA, to reach a steady-state value of \( 7^\circ \)–\( 8^\circ \) during the period of steady-state GIA tilt (arrow A, Fig. 2C).

Differences between horizontal eye velocity profiles during facing and back to motion centrifugation were determined from overlaid traces of desaccaded horizontal eye velocity. In five separate tests in a second monkey (M9307), there was little variability (Fig. 3, A and C). Horizontal velocity storage time constants, measured by the tail-fit method and averaged over leftward and rightward traces, were smaller when the monkey was rotated off-axis (Fig. 3A, mean facing motion \( T_c = 5.1 \pm 0.6 \) s; Fig. 3C, mean back motion \( T_c = 6.2 \pm 0.58 \) s), than during centered rotation (Fig. 3B, mean centered \( T_c = 8.5 \) s).

Average horizontal eye position traces during the nystagmus, comprising both slow and quick phase were plotted for the corresponding leftward and rightward eye velocities shown in Fig. 3, D–I (leftward: Fig. 3, D–F; rightward: Fig. 3, G–I). The eyes tended to beat across the midline during rotation regardless of the direction of the GIA vector with a slight bias toward the quick phase side during the period of angular acceleration (Chun and Robinson 1978; Hood 1967). This was followed by a gradual decay toward the slow phase side. The beating fields during centrifugation (Fig. 3, D, F, G, and I) were not appreciably different from those during centered rotation (Fig. 3, E and H).

Because the interaural linear acceleration was centripetal, any compensatory horizontal IVOR should rotate the eyes in the centrifugal direction whether REO or LEO (Fig. 1, C and E, black arrows). This produces a compensatory horizontal IVOR and aVOR in the same direction whenever the animal is facing the motion. Conversely, the IVOR is always opposite to the aVOR when back to motion (Fig. 1, C and E; compare

\(^2\) The time constants and peak eye velocity value quoted in Figs. 1 and 2 were measured from the traces in these figures. Variability within animals was small and is indicated by plotting means \( \pm 2 \) SD for desaccaded eye velocity traces in Figs. 3, 4, and 7.
If the aVOR and lVOR superpose (Merfeld and Young 1995; Young 1967), subtraction of the back-to-motion response from the facing-motion response (F-B) should cancel the aVOR and double the lVOR. Division by two then would give an estimate of the average interaural lVOR. This should be in the direction of the aVOR eye velocity when facing the motion. That is, for leftward eye velocities (Fig. 4, left column), the (F-B)/2 difference traces should be leftward (+z). For rightward eye velocities (Fig. 4, right column), the difference traces should be rightward (−z).

To assess the aVOR-lVOR superposition hypothesis, difference traces were computed for each monkey (Fig. 4) and compared with predictions based on this hypothesis for each monkey. Although each animal’s data were internally consistent, intersubject variability was considerable. For M9307, the difference trace for leftward aVOR eye velocities was in the
(-z) direction (Fig. 4C), whereas the difference trace for rightward aVOR eye velocities was in the (+z) direction (Fig. 4D). These directions are opposite to the prediction of the superposition hypothesis. The same response pattern was found in two other monkeys (M9306 and M9308, Fig. 4, E–H). Patterns were inconsistent in the last two monkeys (M9223 and M9303, Fig. 4, I–L). M9303 showed little difference between facing and back to motion responses for leftward eye velocities (Fig. 4K) but had a (-z) difference response, opposite to the trend in the other four animals, for rightward eye velocities (Fig. 4L). M9223 had a significant (+z) response for both leftward and rightward eye velocities (Fig. 4, I and J). Thus the prediction of the superposition hypothesis, that the \((F - B)/2\) difference traces should be leftward for rightward eye velocities and rightward for leftward eye velocities, was not supported by the data in general and directly contradicted by the data of three monkeys.

Our alternative hypothesis was that linear acceleration affects the orientation properties of the velocity storage system, differentially modifying its time constants according to the direction of GIA tilt. According to this hypothesis, the difference between facing and back to motion eye velocities represents a difference between two waveforms with different time constants at each instant of time. To test this hypothesis, we compared each monkey’s responses to OKAN, centrifugation, and centered rotation with simulations using our one-dimensional system model of IVOR-aVOR interaction (Fig. 5), with a single set of parameters for each monkey in all three paradigms.

Model-data comparisons

The one-dimensional model of IVOR/aVOR interaction includes cascaded dynamical subsystems. These generate the velocity command from the angular VOR, the effects of GIA on velocity storage, the velocity-position transformation that drives the motoneurons, and the contribution of the compensatory linear VOR (lVOR). The block labeled ‘‘otolith afferent processing’’ comprises subblocks of otolith sensory afferent neurons with discharge regularities range from regular (REG) through intermediate (INT) to irregular (IRREG) and with corresponding ranges of response dynamics (Fernández and Goldberg 1976). These afferents are activated by linear acceleration of the head in space, which is an inertial frame. This acceleration is converted into the head frame because the afferents are fixed to the head. This implicit transformation is represented by the box ‘‘space-head transf.’’ The afferents combine to generate the compensatory IVOR response (‘‘compensatory IVOR system’’). Another system (‘‘orienting IVOR system’’), the output of which is denoted by a heavy line (Fig. 5) is responsible for modifying the spatial orientation properties of velocity storage and the subsequent orientation and time
constants of the eye velocity vector. The system implementing the aVOR, incorporating velocity storage has been adapted from previous work (Raphan and Sturm 1991; Raphan et al. 1979). The output of velocity storage and the direct aVOR path, \(y_{sz}\) sums with the output of the compensatory lVOR system, \(y_{cz}\). The summed signal is input to the velocity position integrator and its direct path to drive the oculomotor plant.

The effect of the orienting system on the aVOR was modeled as a parametric modification of the velocity storage time constant, \(1/h_{33}\), shown by the heavy arrow through “nodulus/uvula” to \(h_{33}\). The time constant was varied as a function of GIA tilt relative to the head in accordance with data obtained from OKAN with monkeys in tilted positions (Dai et al. 1991). The model then was implemented as a dynamical system, using the regression fits obtained from the OKAN data. The model simulations during centered, and facing and back to motion centrifugation were compared with the actual data (see METHODS).

MODEL IMPLEMENTATION AND PARAMETER IDENTIFICATION.

The state equations describing the one-dimensional angular acceleration transduction performed by the semicircular canals were approximated as a first-order system (Fig. 5, \(H_{ac}\)) and implemented as follows:

\[
\dot{x}_{cz} = h_{33} x_{cz} + g_{s0} a_z
\]

\[
y_{sz} = x_{cz} + g_{s1} r_{sz}
\]

The variable \(a_z\) represents yaw axis angular acceleration, \(x_{cz}\) represents the horizontal state of the cupula, \(h_{33}\) is the yaw axis eigenvalue of the cupula dynamics, equivalent to the negative reciprocal of the dominant cupula time constant (\(\approx 4\) s). The parameter \(g_{s0}\) is the coupling gain from angular acceleration to the cupula state. The signal \(r_{sz}\) is the neural signal carried by primary canal afferents, which drives the velocity storage integrator and direct pathway during yaw axis angular acceleration.

The velocity storage integrator and direct vestibular pathway are represented by state equations given by

\[
\dot{x}_{sz} = h_{33} x_{sz} + g_{s0} r_{sz}
\]

\[
y_{sz} = x_{sz} + g_{s1} r_{sz}
\]

(Raphan et al. 1979; Waespe and Cohen 1983), where \(x_{sz}\) is the state of velocity storage, \(h_{33}\) is the yaw axis eigenvalue of the velocity storage dynamical system and is equivalent to the negative reciprocal of the dominant time constant of horizontal eye velocity during OKAN and during rotation in yaw, \(g_{s1}\) is the gain of the direct vestibular pathway, and \(g_{s0}\) is the coupling gain from angular acceleration to the cupula state.
pling of the neural signal to velocity storage. The signal $y_{sz}$ represents a horizontal neural command, which superposes the state of velocity storage with the direct pathway around it. The neural command from the summed regular and irregular otolith afferents $y_{cz}$, sums with the neural command from the angular system, $y_{sz}$, to generate the signal $y_{vz}$, which drives the velocity-position integrator and the direct pathway around it. The motoneuron signal $y_{pz}$ activates the muscles, $M$, to produce a component of torque, $m_z$, which in combination with the dynamics of the plant, determines the horizontal component of eye orientation, $\Phi_n z$ (Fig. 5).

IMPLEMENTATION OF EFFECT OF GIA TILT ON HORIZONTAL TIME CONSTANT; OKAN TIME CONSTANTS AS A FUNCTION OF STATIC HEAD TILT. The function relating the horizontal time constant to the angle of GIA tilt with respect to the head $z$ axis was estimated for each monkey during OKAN with the head statically tilted in roll, either LED or RED, through angles ranging from 17 to 90°. An example is shown for M9307 (Fig. 6). For the upright condition, the time constant of leftward horizontal eye velocity ($+\omega_x$) was 7.1 s (Fig. 6A). For a 90° tilt left ear down (LED), an upward eye velocity ($-\omega_x$) was induced, and the horizontal time constant fell to 1.8 s (Fig. 6B). The rate of decrease of the horizontal time constant during OKAN with the head tilted LED, as a function of tilt angle, shown by open circle in Fig. 7A, 1 and 2, could be approximated by a straight line with negative slope. The GIA tilt induced under this condition was analogous to tilt experienced during centrifugation while facing motion with the left ear out (Fig. 2A). In each case, the GIA tilted toward the right ear, and an upward cross-coupled component of eye velocity was induced.

For a 90° tilt right ear down, a weaker downward ($-\omega_x$) vertical eye velocity was induced, and the horizontal time constant fell to 4.2 s (Fig. 6C). This condition corresponds to centrifugation with back to motion, right ear out (Fig. 2B). The relationship between the horizontal time constant of OKAN and the direction of the GIA, for any angle of head tilt, was fit with a first-order regression curve (open circles, Fig. 7A, 1 and 2), given by

$$T_{33D} = T_{33D} + f\theta_k$$

where $T_{33D}$ is the horizontal time constant for a particular head tilt angle relative to the GIA ($\theta_k$) and a particular direction ($D$), either leftward (L) or rightward (R), of eye velocity. The parameter, $h_{33D}$, is the horizontal eigenvalue for a particular direction and is equal to the inverse of the horizontal time constant. The subscript 33 indicates that the horizontal eigenvalue is the (3,3) element of the velocity storage system matrix,
The reduction in horizontal time constant as a function of tilt angles from 0 to 90° for leftward OKAN eye velocities in M9307 is shown in Fig. 7A1. Data were fit by a first-order linear regression, and the squares of the correlation coefficients ($r^2$) were calculated for each fit. The horizontal time constant was longer and declined more slowly with tilt angle during OKAN associated with downward cross-coupling (filled triangle; slope = −0.04; $r^2 = 0.94$), than during OKAN associated with upward cross-coupling (open circle; slope = −0.06; $r^2 = 0.98$). For rightward eye velocity, ($-\omega_y$), the horizontal time constants associated with upward and downward cross-coupling had similar differences in slope (Fig. 7A2). During upward cross-coupling, the horizontal time constant declined more rapidly (open circle; slope = −0.08; $r^2 = 0.98$) than during downward cross-coupling (filled triangle; slope = −0.07; $r^2 = 0.94$). Thus for M9307, the horizontal time constants associated with upward coupling were shorter than those associated with downward coupling, corresponding to shorter horizontal time constants during centrifugation when facing the motion than when back to motion. Good fits also were obtained for M9303 (Fig. 7B, 1 and 2). For leftward eye velocities, the reduction of horizontal time constant with tilt angle was the same for both downward (Fig. 7B1, filled triangle, slope = −0.06; $r^2 = 0.96$) and upward cross coupling (Fig. 7B1, open circle, slope = −0.06; $r^2 = 0.87$). For rightward eye velocities, the horizontal time constant declined more rapidly during downward coupling (Fig. 7B2, filled triangle, slope = −0.1, $r^2 = 0.96$) than during upward coupling (Fig. 7B2, open circle, slope = −0.08, $r^2 = 0.99$). The data of M9306 exhibited a similar pattern of asymmetric reduction of horizontal time constant with tilt angle for upward and downward coupling. For leftward eye velocities (Fig. 7C1), the reduction of horizontal time constant with tilt angle was greater during upward coupling (Fig. 7C1, open circle, slope = −0.09, $r^2 = 0.92$) than during downward coupling (Fig. 7C1, filled triangle, slope = −0.04, $r^2 = 0.99$). A similar pattern was present for rightward eye velocities. The horizontal time constant again declined more during upward coupling (Fig. 7C2, open circle, slope = −0.1, $r^2 = 0.77$) than during downward coupling (Fig. 7C2, filled triangle, slope = −0.04, $r^2 = 0.83$).

The generally high values for the square of the correlation coefficient ($r^2$) demonstrate that the monotonic decline in time constant as a function of tilt angle could be adequately approximated by a straight line, validating its use in modeling the differences between facing and back to motion centrifugation. The upright time constant was incorporated into the aVOR model, and parameters, $g_{s0}$ and $g_{s2}$ (Eq. 2) were determined to best fit the data during centered rotation. The simulated data (heavy lines) were superimposed on means ± 1 SD of repeated trials (gray shading) (Fig. 7, A–C, 3–5). The parameter $g_{s1}$ is the direct path gain, and determines the slope of the initial rise in eye velocity, and its peak value. The parameter $g_{s0}$ represents the strength of coupling to the velocity storage integrator and determines the shape of the rising and the initial falling characteristics of eye velocity. In accordance with the left/right asymmetries due to up/down cross-coupling asymmetries, these parameters were determined independently for leftward and rightward eye velocities in each monkey. The OKAN time constants were determined from data obtained using a stimulus velocity of 60°/s whereas the peak angular velocity of the centrifuge reached 400°/s. However, because upright OKAN and vestibular time constants decline as a function of stimulus...
velocity (Raphan et al. 1979), the upright OKAN time constant ($T_{33UD}$) shown on the intercept was adjusted to account for the high eye velocities achieved during centrifugation ($\approx 200°/s$). The value of this single exponential time constant, obtained from responses to centered rotation at 400°/s, is shown above and below the centered data (Fig. 7, A–C, 4). This adjustment shifted the regression lines downward but left the slopes unchanged.

The model parameters determined from fitting the data during centered rotation (Fig. 7, A–C, 4), were combined
with the slope of the regression of the horizontal time constant on GIA tilt, obtained from OKAN. The model then was used to determine whether the simulated responses for centrifugation were within 1 SD of overlaid eye velocity traces (Fig. 7, A–C, 3 and 5, solid line). When monkeys faced the motion (Fig. 7, A–C, 3), an upward vertical cross-coupled component was induced, and the accompanying change in the horizontal time constant was described by Eq. 3. When monkeys were rotated with backs to the motion (Fig. 7, A–C, 5), a downward cross-coupled component was induced and the change in the horizontal time constant was described by Eq. 4. The simulated data (heavy lines) were superimposed on means ± SD of repeated trials (gray shading). The simulations were within or close to ± SD of the eye velocity responses during facing and back to motion centrifugation. Thus the eye velocity responses to facing and backward centrifugation M9307, M9303, and M9306 were fitted closely by the time constants obtained from OKAN as a function of tilt angle and from centered rotation for each animal. This strongly suggests that modulation of the horizontal time constant by GIA tilt was the dominant factor in explaining the differences in eye velocity responses to facing and back to motion centrifugation in these monkeys.

Further evidence for this conclusion was obtained by simulating the data from M9307 at different angular accelerations, using the same parameters as were used to fit the data in Fig. 7A, 3–5. Two different values of angular acceleration: high (40°/s² for 10 s) and low (10°/s² for 40 s) were used to reach a steady-state angular velocity of 400°/s in each case. The data are shown in Fig. 8A and the simulations in Fig. 8B. The asymptotic level of the aVOR velocity response to a step of angular acceleration is an increasing function of the horizontal time constant and is approximately proportional to the product of the time constant and the angular acceleration (see APPENDIX for details). For this monkey, horizontal eye velocity during centered rotation (Fig. 8, center) should reach 95% of its steady-state value after three time constants or ~25 s of constant angular acceleration. This asymptotic behavior is only apparent during long-duration acceleration steps and can be seen at 10°/s² in both the data (Fig. 8A, heavy traces, arrow A) and simulations (Fig. 8B, heavy traces, arrow A) but not at 40°/s² (Fig. 8, A and B, light traces). During centrifugation, the horizontal velocity storage time constant becomes shortened as the centrifuge accelerates and the GIA tilt increases. The shorter time constant should cause the eye velocity response to asymptote earlier and at a lower level. This effect was seen in both the data (Fig. 8A, left and right, heavy traces) and the simulations (Fig. 8B, left and right, heavy traces). Because the horizontal time constant was shorter and decreased more rapidly during facing than back to motion centrifugation in M9307, the asymptote was lower when facing motion (arrow B, Fig. 8, A and B) than when back to motion. The model further predicted a decline in the steady-state eye velocity if the horizontal time constant becomes shorter after the integrator has reached a steady-state level (APPENDIX). This occurred during centrifugation with low angular accelerations of long duration and is apparent in both the data and simulations during facing motion centrifugation at 10°/s² (arrow B, Fig. 8, A and B).

CENTRIFUGATION AFTER INACTIVATION OF THE SEMICIRCULAR CANALS. The foregoing results indicate that the contribution of the compensatory IVOR to horizontal eye velocity during constant velocity centrifugation is small. To support this conclusion, we compared responses to centrifugation before and after inactivation of the aVOR. We reasoned that any nystagmus after the canals were inactivated could be attributed to the intact IVOR. Canal plugging was performed in three animals, two of which had all six canals plugged (M9308 and M9357) and a third in which the lateral canals were plugged (M9351). The lateral canal plugged monkey was tilted forward 40° during testing so that the vertical canals were not activated by the rotation around a spatial vertical axis (Yakushin et al. 1995). In this position, this monkey’s responses were equivalent to those of the six-canal plugged animals.

The response in M9308 after all six canals were plugged is typical of this group. Before plugging, M9308 had characteristic responses to centrifugation, including ocular counterrolling, which were similar to those shown for M9306 in Fig. 2 (arrows, Fig. 9A). After plugging, there was no compensatory eye velocity during on-axis rotation at the accelerations that were used. During centrifugation, ocular counterrolling was intact (arrows, Fig. 9B), demonstrating that the otolith organs were functional. No horizontal or vertical eye velocity was induced by centrifugation (Fig. 9B). This indicates that the IVOR was either of such low gain that it produced no measurable response or was absent. The same was true for the other two canal-plugged animals. These data confirm that in rhesus and cynomolgus monkeys, the primary effect of linear acceleration during constant velocity centrifugation is to induce orienting responses.
This study shows that during constant velocity centrifugation the effect of spatial orientation on the dominant time constants of the aVOR is the primary factor in determining horizontal eye velocity in rhesus and cynomolgus monkeys. The compensatory IVOR contributes little to the response. This was demonstrated by the finding that the differences between horizontal eye velocity when facing and back to motion were in the direction opposite to that predicted by the superposition hypothesis in three monkeys. Data were inconsistent in the other two monkeys, being in the direction predicted by the hypothesis for eye velocity in one direction and opposite to it the other direction. This conclusion was verified by a model-based technique in which eye velocity data obtained during centrifugation were fit by simulations using data from the same monkeys obtained during OKAN with head tilts and on-center rotation. Simulations using the same set of parameters predicted the responses at low and high values of angular acceleration. Confirmation of this conclusion was obtained in canal-plugged animals.

This conclusion is consistent with studies describing the frequency characteristics of the IVOR (Telford et al. 1997) but contradicts conclusions drawn previously from studies of IVOR-aVOR interaction using constant velocity centrifugation in which it was assumed that the IVOR and aVOR superposed (Wearne 1993; Young 1967). Characteristics of the IVOR in squirrel monkeys have been inferred from difference traces during constant velocity centrifugation (Merfeld 1990; Merfeld and Young 1995; Merfeld et al. 1993), using a three-dimensional model (Merfeld 1995). Again, it was assumed that differences between facing and back to motion centrifugation are due solely to a superposition of the compensatory IVOR and aVOR. Two inputs to a system are considered to superpose if the sum of the individual responses to each is equal to the response when both inputs are applied together. In the context of centrifugation, this means that the sum of the eye velocity responses to centered rotation and to constant linear acceleration on a sled should equal the response during constant velocity centrifugation. When the orientation effects on velocity storage are negligible, such as during high-frequency sinusoidal centrifugation when the GIA tilt is minimal, near-superposition of aVOR and IVOR holds. There also may be a contribution during OVAR where there is a sinusoidally varying compensatory IVOR, generated by the interaural projection of the rotating GIA vector. This study shows, however, that a tilted GIA during constant velocity centrifugation induces ori-
entation effects that shorten the time constant of the aVOR. Thus superposition as defined earlier cannot hold.

Central to modeling eye velocities during constant velocity centrifugation was the ability to describe dynamic changes in the horizontal time constant when the direction of the GIA was continuously changing. At the onset of rotation, there is a small centripetal acceleration and a larger tangential acceleration. The tangential acceleration dies rapidly as the centripetal acceleration builds. At every instant, the centripetal and tangential linear accelerations are combined with the gravitational acceleration. Thus there is a complex changing linear acceleration vector during the initial stages of rotation until the subject reaches a constant angular acceleration.

Despite this dynamically changing linear acceleration stimulus, the direction and approximate magnitude of the difference traces could be predicted for each animal from asymmetric reductions in the horizontal OKAN time constant as a function of head tilt. In both M9306 and M9307, the horizontal time constant was shorter at 52° GIA tilt during upward than downward cross-coupling, corresponding to a shorter horizontal time constant during facing than back to motion centrifugation. In accordance with the data, this OKAN time constant asymmetry predicted that the \((F - B)/2\) difference trace would be negative during leftward (+z) eye velocities (Fig. 4, C and E) and positive during rightward (−z) eye velocities (Fig. 4, D and F). Importantly, the temporal pattern of the difference traces was opposite to that predicted by the IVOR superposition hypothesis. Although the pattern of OKAN time constant asymmetries in M9303 differed from the other two monkeys, its centrifugation data differed nonetheless predictable from its corresponding OKAN time constants. For leftward eye velocity during OKAN, no up-down related asymmetry was present. Accordingly, the difference traces for leftward eye velocities in this monkey were close to zero (Fig. 4K). For rightward eye velocity during OKAN, the horizontal time constant was longer for upward than downward cross-coupling, opposite to the trends in the other two monkeys. The difference traces for rightward eye velocity were correspondingly negative-going, opposite to those of the other four monkeys (Fig. 4L).

The shape of the difference traces provides further evidence that they are not produced by the compensatory IVOR in the monkeys that were tested. In all cases, the difference traces rose slowly to a peak value then decayed to zero with a time constant of \(~6\) s (Fig. 4). These dynamics are characteristic of a difference between two exponential modes with different time constants. They would not be produced by the low-frequency characteristics of the compensatory IVOR (Paige and Tomko 1991a,b; Paige et al. 1996; Raphan et al. 1996; Telford et al. 1997). The dynamic changes in time constant adequately describe the differences between horizontal eye velocities during centrifugation when facing and back to motion. Moreover, in contrast with the large variations observed in humans (Wearne 1993), the beating field of horizontal eye position was not appreciably affected by the presence or magnitude of linear acceleration during centrifugation (Fig. 3). Finally, the absence of any measurable IVOR during centrifugation after inactivation of the semicircular canals by canal plugging, in the presence of a robust otolith counterrolling response, argues strongly that the observed facing-back differences are generated by the canals and not the otoliths. We conclude that it is not possible to estimate the IVOR during constant velocity centrifugation simply by subtracting the responses during facing and back to motion. Rather in rhesus and cynomolgus monkeys, these difference traces are dominated by asymmetries in dynamic modification of the horizontal time constant, which depend on the direction of vertical cross-coupled components induced by the tilted GIA.

We considered whether the squirrel monkey might have a characteristically different IVOR response from that of the rhesus or cynomolgus, which could explain the different conclusions. This seems unlikely because constant velocity centrifugation with low initial angular acceleration (Merfeld 1995; Merfeld and Young 1995) is a low-frequency stimulus. The sensitivity of the IVOR at these low frequencies is \(<0.05° \cdot \text{cm}^{-1} \cdot \text{m}^{-1}\) (Telford et al. 1997). The facing-back to motion difference traces, which were attributed to the IVOR, contained large transients (Merfeld 1995; Merfeld and Young 1995) the amplitude and temporal characteristics of which are not consistent with the IVOR at these frequencies. Whether time constant asymmetries might be responsible for generating difference responses attributed to the IVOR during facing and back to motion centrifugation in the squirrel monkey is not known because the time constants of OKAN were not measured as a function of head tilt.

Another difference between this study and those done in squirrel monkeys is that the radius arm of our centrifuge was smaller. We considered whether this could explain differences between our data and those of previous studies where the acceleration gradient was smaller (Lansberg et al. 1965; Merfeld and Young 1995). If it is assumed that there is a 5-cm difference between the two otoliths, a radius of 25 cm and off-center rotation at 400°/s to produce a centripetal acceleration of 1 g, the short arm centrifugation used in this study creates a gradient of linear acceleration between the two ears of \(~0.25\) g. This gradient is \(~25\)% of the centripetal acceleration and would cause the tilt of the GIA to be slightly different between the two ears. At the center of the head, the tilt of the GIA would be \(~52\)°. On the inboard side, the tilt would be 48°, and on the outboard side it would be 53°. Changes in time constant over these angles are small and would fall within the resolution of our time constant measurements for the aVOR and for OKAN (Fig. 7). The centripetal acceleration gradient was the same whether animals were moving forward or back and also could not have been responsible for the time constant asymmetries that were observed in this study. Moreover, the asymmetries in horizontal time constant as measured during OKAN, where there is no acceleration gradient between the two ears, adequately explained the centrifugation data for both 10 and 40°/s² (Fig. 8). Therefore the linear acceleration gradient across the two ears could not have been responsible for the differences between our conclusions and those reported in earlier studies.

The IVOR gain is reduced as fixation distance increases, and in this, as in the previous studies that used constant velocity centrifugation, viewing distance was not controlled (Merfeld and Young 1995; Young 1967). Considering the low gain of the IVOR during stimulation at constant velocity (zero frequency), it is unlikely that the viewing distance could have been close enough to generate a significant IVOR in any study where it was not controlled. As Paige et al. (1996) have shown,
it is not possible to maintain near fixation in darkness for even short periods (30 s to 1 min) while viewing an imagined target. The minimal contribution of the compensatory IVOR during constant velocity centrifugation in rhesus and cynomolgus monkeys contrasts with that found in humans. Humans generate stronger compensatory responses to the centripetal acceleration and correspondingly stronger shifts in the beating field (Weare 1993; Weare et al. 1994). These shifts appear to affect eye velocity by clamping the response during facing motion and enhancing the response during back to motion centrifugation (Raphan et al. 1996). This may, however, be an ancillary effect of a mechanism that causes a change in the beating field rather than a difference in the way the aVOR and IVOR combine to generate the velocity command to the oculomotor system (Raphan et al. 1996). Different frequency characteristics during sinusoidal linear acceleration and different weightings given to sensory context (Paige 1996) also could explain the more prominent role for the compensatory IVOR during centrifugation in humans (Raphan et al. 1996). Because OKAN is weak in humans, it will be difficult to assess the effect of a tilted GIA on the horizontal time constant using this technique. Such information is critical, however, for assessing the contribution of the IVOR to constant velocity centrifugation.

In summary, the results are consistent with the hypothesis that the compensatory IVOR contributes minimally during constant velocity centrifugation in rhesus and cynomolgus monkeys. The dominant effects of the IVOR are the orientation changes manifest as ocular counterrolling, shifts of the axis of eye velocity, and changes in the time constants of the aVOR. The orientation-induced changes during centrifugation, OKN and OKAN, can be related quantitatively to spatial orientation properties of velocity storage. Thus while quantitative aspects of low-frequency IVOR behavior remain speculative, the proposed model of aVOR-IVOR interaction captures the salient features of the IVOR-aVOR interaction at low frequencies in rhesus and cynomolgus monkeys and provides a basis for comparison with the human response.

APPENDIX

The asymptotic behavior of the aVOR eye velocity in response to a constant angular acceleration can be computed from the state equations for the cupula (Eq. 1) and velocity storage (Eq. 2) systems, when the states are no longer changing, i.e., when \( \dot{x}_c = 0 \) and \( \dot{x}_{ss} = 0 \). Under these conditions

\[
x_{ss} = \left( -\frac{g_0}{h_{c2}} \right) \alpha_x \tag{A1}
\]

\[
r_{ss} = \left( -\frac{g_0}{h_{c1}} + g_{a1} \right) \alpha_x \tag{A2}
\]

\[
x_{ss} = \left( -\frac{g_0}{h_{s3}} \right) r_{ss} \tag{A3}
\]

\[
y_{ss} = x_{ss} + g_{a1}(r_{ss}) \tag{A4}
\]

where \( x_{ss} \) is the asymptotic state of the cupula system, \( r_{ss} \) is the asymptotic state of the velocity storage system, \( r_x \) is the asymptotic level of the afferent input for a constant angular acceleration, and \( y_a \) is the asymptotic level of the neural eye velocity command. All other parameters are as defined in the text.

Substituting Eqs. A1–A3 into Eq. A4 gives the neural eye velocity command, \( y_{ss} \) in terms of the angular acceleration

\[
y_{ss} = \left( -\frac{g_0}{h_{c2}} \right) \alpha_x + g_{a1} \tag{A5}
\]

Thus the aVOR eye velocity command in the steady state, \( y_{ss} \), is proportional to the angular acceleration, \( \alpha_x \). It is also an incrementally linear function of the horizontal time constant, \( 1/h_{s3} \). If the horizontal time constant becomes smaller, such as occurs during centrifugation, \( y_{ss} \) decreases for constant angular accelerations.

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