Oculomotor Control of Primary Eye Position Discriminates Between Translation and Tilt

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Oculomotor control of primary eye position discriminates between translation and tilt. J. Neurophysiol. 81: 394–398, 1999. We have previously shown that fast phase axis orientation and primary eye position in rhesus monkeys are dynamically controlled by otolith signals during head rotations that involve a reorientation of the head relative to gravity. Because of the inherent ambiguity associated with primary otolith afferent coding of linear accelerations during head translation and tilts, a similar organization might also underlie the vestibulo-ocular reflex (VOR) during translation. The ability of the oculomotor system to correctly distinguish translational accelerations from gravity in the dynamic control of primary eye position has been investigated here by comparing the eye movements elicited by sinusoidal lateral and fore-aft oscillations (0.5 Hz ± 40 cm, equivalent to ± 0.4 g) with those during yaw rotations (180°/s) about a vertically tilted axis (23.6°). We found a significant modulation of primary eye position as a function of linear acceleration (gravity) during rotation but not during lateral and fore-aft translation. This modulation was enhanced during the initial phase of rotation when there was concomitant semisemircular canal input. These findings suggest that control of primary eye position and fast phase axis orientation in the VOR are based on central vestibular mechanisms that discriminate between gravity and translational head acceleration.

INTRODUCTION

Static head tilt relative to gravity induces compensatory otolith-ocular reflexes. In the rabbit, these reflexes account for up to ~60% of the angle of head tilt (Baarsma and Collewijn 1975). In frontal-eyed species, such as monkeys or humans, the corresponding static otolith-ocular reflexes exhibit a much smaller gain of only ~10%. In these species, the action of static otolith-ocular reflexes in different head tilted positions is best demonstrated by the effects on the orientation of Listing’s plane, which are mediated by the saccadic system. When the head is upright and stationary, for example, the rotation axes of the eye for fixations of distant targets are confined to a single plane (Listing’s plane) when expressed relative to a common reference (von Helmholtz 1867; Tweed and Vilis 1990). Associated to this plane, a primary position can be defined as the unique reference position whose associated gaze direction is perpendicular to the plane of accessible ocular rotation axes. When the head is statically pitched or rolled, Listing’s plane of eye positions tilts or shifts in compensatory direction (Crawford and Vilis 1991; Haslwanter et al. 1992). This relatively small but consistent effect on the orientation of Listing’s plane (and primary position) suggests that it is the vector of gravity that controls this static orientation reflex by modulating the oculomotor reference. A further determinant of the orientation of Listing’s plane is the state of ocular vergence (Mok et al. 1992).

When the head dynamically rotates in space, for example, during off-vertical axis rotations, it has been shown that vestibulo-ocular reflex (VOR) fast phase eye positions also maintain a planar organization as do visually guided saccades with the head stationary. In this case, however, there is a robust and consistent gravity-dependent shift and/or tilt of fast phase displacement planes (and thus primary position), yet through angles much greater than those observed in static tilt positions (Hess and Angelaki 1997a,b). For example, during rotation of the head about its yaw axis in a tilted position, torsional and vertical primary position modulate as a function of the component of gravity along the pitch and roll axis, respectively.

Information regarding head orientation relative to gravity is presumably conveyed by primary otolith afferents that detect linear accelerations. Because the gravitational and inertial mass of the otoconia of the otolith organs are physically identical, primary otolith afferents do not discriminate between head tilt and translation (Fernández and Goldberg 1976; Loe et al. 1973). This fact raises the question whether it is gravity per se, i.e., instantaneous head orientation, or the resultant gravito-inertial acceleration, i.e., the total output of the otolith organs, that controls this remarkable gravity-dependent adjustment of the spatial orientation of saccade and VOR fast phase axes. To address this question, we compared the modulation of VOR fast phase displacement planes elicited during off-vertical axis rotation and linear translation. Preliminary results have been published in abstract form (Hess and Angelaki 1997c).

METHODS

Animal preparation and eye movement recording

Data were obtained from five juvenile rhesus monkeys (Macaca mulatta), which were chronically prepared with scleral dual-search coils for three-dimensional eye movement recording and a delrin head ring for restraining the head during the experiments. Details of fabrication and implantation of the dual-search coil have been reported elsewhere (Hess 1990). Three-dimensional eye position was measured with a two-field search coil system (CNC Engineering). The search coil signals were calibrated as described in Hess et al. (1992). In brief, an in vitro calibration prior to implantation yielded the coil sensitivities and the angle between the two search coils. The orientation of the dual coil on the eye was determined from the four coil output signals during fixations of a series of vertically arranged target lights relative to straight ahead. Horizontal, vertical, and torsional eye positions were digitized at a...
sensing a unit vector pointing along the rotation axis of the eye, and \( p \) is the angle of rotation about \( u \) (Haustein 1989).

Rotation vectors were originally expressed relative to a right-handed coordinate system, where the y-axis was aligned with the interaural (pitch) axis, whereas the z- (yaw) and x- (roll) axis were rotated upward by 18° relative to the stereotaxic horizontal plane. A positive torsional, vertical, or horizontal eye position component (\( E_{tor}, E_{ver}, E_{hor} \), respectively) corresponded to a clockwise, downward, or leftward rotation of the eye (from the subjective viewpoint). Listing’s plane and primary eye position were determined from spontaneous eye movement data in the light with the head upright and stationary.

**Experimental protocols**

During the experiments, animals were seated in a primate chair with the head restrained in a position of 18° nose-down relative to the stereotaxic horizontal (defined as “upright” position) to place the lateral semicircular canals approximately earth-horizontal. The animals were placed inside the inner frame of a superstructure consisting of two motor-driven gimbaled axes. The superstructure was mounted on a computer-controlled sled that moved on ball-bearings on a 2.0 m long earth-horizontal track. The effect of dynamic changes in linear accelerations on fast and slow eye movements was studied during either constant-velocity rotation of the animals about the head-vertical (yaw) axis or during lateral and fore-and-aft sinusoidal rotations. The experimental protocols consisted of 1) constant-velocity yaw rotations at positive or negative speeds of 180°/s about an axis tilted by 23.6° earth-vertical. This resulted in a stimulation of the otolith organs that can be described by two linear acceleration vectors oscillating in phase quadrature in the yaw plane along the x- and y-axis at 0.5 Hz (\( =180°/s \cdot 360° \)) and a constant acceleration of 0.92 g \( =1g \cdot \sin (23.6°) \) along the z-axis. Rotation started with the animal tilted toward right or left ear-down position. 2) Sinusoidal lateral translations at 0.5 Hz, \( \pm 40 \) cm (corresponding to \( \pm 0.4 \) g) along a linear earth-horizontal track with the animal in upright or supine position, and 3) sinusoidal fore-and-aft translations at 0.5 Hz, \( \pm 40 \) cm (\( \pm 0.4 \) g) with the animal in upright position.

**Data analysis**

At the beginning of each experimental session, primary position was determined with the animals upright making spontaneous eye movements while looking around in the normally lit laboratory. Primary eye position was determined by fitting a plane with minimal least squares error to these eye positions. The “thickness” of Listing’s plane was characterized by the torsional standard deviation of eye positions relative to the best-fit plane. In all VOR protocols, eye positions were expressed relative to the head-fixed coordinates \( x, y, z \) described above. Fast and slow phases of vestibular nystagmus were separated based on a semi-automated, interactive procedure that used the second derivative of the magnitude of the eye velocity vector (see also Hess & Angelaki 1997a,b). PLANAR FIT OF FAST PHASE DISPLACEMENT PLANES IN HEAD-FIXED COORDINATES. To evaluate the torsional standard deviation of VOR fast phases in head-fixed coordinates, fast phases of nystagmus were pooled from several response cycles and fitted with a planar surface according to the equation

\[
E_i = a + b E_{ver} + c E_{hor}
\]

where \( E_{ver}, E_{hor} \) are the torsional, vertical, and horizontal, respectively, components of the eye position vector \( E \). Torsional standard deviation \( (SD_{tor}) \) was estimated as

\[
SD_{tor} = \sqrt{\frac{\sum_{i=1}^{N} (E_{tor} - a - b E_{ver} - c E_{hor})^2}{N-3}}
\]

\( N \) is the total number of pooled fast phases.

GLOBAL FIT OF A GRAVITY-DEPENDENT MODULATION OF DISPLACEMENT PLANES. To test the hypothesis that 3D eye positions of VOR fast phases are organized in displacement planes that systematically change their orientation as a function of linear acceleration (Hess & Angelaki 1997b), the following analysis was performed: first, we fitted

\[
E_i = a(t) + b(t) E_{ver} + c(t) E_{hor}
\]

to fast phase eye positions, assuming the following time dependence of the coefficients \( a, b, \) and \( c \)

\[
a(t) = a_0 + a_1 \sin [\theta(t) + \alpha_1] \\
b(t) = b_0 + b_1 \sin [\theta(t) + \beta_1] + b_2 \sin [2\theta(t) + \beta_2] \\
c(t) = c_0 + c_1 \sin [\theta(t) + \gamma_1]
\]

The angle \( \theta(t) \) described the phase angle of linear acceleration, whereas \( \alpha_1, \beta_1, \beta_2, \) and \( \gamma_1 \) represented constant phase angles. The constant parameters \( a_0, b_0, \) and \( c_0 \) accounted for the static orientation of the displacement planes relative to the head-fixed coordinates \( x, y, \) and \( z \). Parameters \( a_1, b_1, \) and \( c_1 \) described the linear dependence of the time-dependent shift and tilt of the displacement plane, whereas the parameter \( b_2 \) described a second-harmonic component (for a rationale behind this choice of coefficient dependence refer to Hess and Angelaki 1997b).

For constant-velocity rotation, the phase of linear acceleration is related to the rotation velocity, \( v = 180°/s \), by

\[
\theta(t) = \omega t = 2\pi(v/360°)t
\]

For sinusoidal translation

\[
\theta(t) = 2\pi ft \text{ with } f = 0.5 \text{ Hz}
\]

In each case, the 11 parameters \( a_0, a_1, \) \( b_0, b_1, \beta_1, \) \( b_2, c_0, \) \( c_1, \) and \( \gamma_1 \) of the cyclic functions \( a(t), b(t), \) and \( c(t) \) were estimated for a given record of nystagmus by the method of minimal least squares using the Levenberg-Marquardt method.

To quantify the early versus steady-state differences in the torsional modulation of eye position, we evaluated the response cycles 2, 3, and 4 separately from the steady-state response that was reached \( \sim 1–2 \) min after rotation onset. During these early three cycles, there were about 15 fast phases, equally distributed over the stimulus cycle. Planar fits of fast phase or fast and slow phases did not yield significantly different results (Hess and Angelaki 1997b). Responses to translation were evaluated from the first full-amplitude stimulus cycle up to end of stimulation. To ensure a reasonable average density of fast phases throughout the stimulus cycle, typically 40 or more cycles had to be pooled for translational responses. This was obtained either by pooling the responses of several trials, each lasting 40–60 s, or by evaluating responses over a longer stimulus duration of up to about 90 s.

Similarly, as for Listing’s plane of visually guided saccades, fast phase displacement planes of the VOR can be associated with a uniquely defined rotation vector, \( \mathbf{P}(t) \), based on the relation

\[
\mathbf{P}(t) = [a(t), c(t), -b(t)]
\]

We have previously shown that the torsional standard deviation of 3D eye positions expressed relative to \( \mathbf{P}(t) \) or, equivalently, to gravity-dependent coordinates tends to become minimal compared with head-fixed coordinates during rotations about an off-vertical axis (Hess & Angelaki 1997b). The gravity-dependent coordinates \( x'(t), y'(t), \) and \( z'(t) \) can be defined at any moment in time by the momentary orientation of the best fit plane to VOR fast phase eye positions. Thus the \( x' \)-axis is always perpendicular to the best
fit plane, whereas the $y'$- and $z'$-axes span the plane. The momentary orientation of the mutually orthogonal $x'$-, $y'$- and $z'$-axes is determined by the rotation of the axis system relative to its orientation at time $t = 0$ (i.e., at onset of head rotation). At each point in time, this rotation is described by the vector of primary position $\mathbf{P}(t)$. Left-multiplication with the inverse primary position, i.e.,

$$E' = \mathbf{P}^{-1}E$$

transforms eye position vectors from head-fixed to gravity-dependent coordinates (Hess and Angelaki 1997b).

To compare the effects of head translation or rotation on the spatial organization of VOR fast phases, it sufficed to consider the following three quantities: 1) the modulation of the torsional component of $\mathbf{P}$, $P_{\text{tor}} = a(t)$; 2) the torsional standard deviation of 3D eye positions relative to the best-fit plane in head-fixed coordinates; and 3) the torsional standard deviation of 3D eye positions relative to the best-fit plane in gravity-dependent coordinates. A modulation of $P_{\text{tor}}$ as a function of head motion was considered significant if the torsional standard deviation of 3D eye positions was significantly reduced ($t$-test) with respect to gravity-dependent coordinates compared with head-fixed coordinates.

**RESULTS**

Constant-velocity yaw rotation about a tilted axis (23.6° from earth-vertical) induced the well known compensatory horizontal nystagmus and head position dependent torsional and vertical eye position modulation (Fig. 1A). The modulation of torsional and vertical eye position often exhibited amplitude attenuation over the first few response cycles. Off-vertical axis rotation started with the animals tilted in roll by an angle of 23.6° toward left or right ear-down. This initial roll tilt induced a counterroll of the eyes of $\sim 2\text{°}$. During the subsequent yaw rotation, torsional (and vertical) eye position remained unchanged for about 100–200 ms while a horizontal response was generated (see record before dashed vertical line in Fig. 1A). Interestingly, the modulation of torsional eye position was usually initiated with the first fast phase of nystagmus, which drove the eye into an even more eccentric torsional position (Fig. 1A dashed vertical line). During sinusoidal lateral translation mainly horizontal eye movements with little torsional modulation were generated even though the linear acceleration along the $y$-axis modulated with the same frequency and magnitude as during off-vertical axis rotation (compare Fig. 1, A and B). The same was true for fore and aft translation (not shown).

The parametric description of the 3D organization of fast phase eye positions revealed that a significant modulation of torsional primary eye position was also present during off-vertical axis rotation at the moderate axis tilt of 23.6° (Fig. 2A), as reported earlier for “barbecue spit” rotation (Angelaki and Hess 1996a; Hess and Angelaki 1997b). There was no such modulation during lateral translation (Fig. 2B).

As an independent measure of the torsional variation in 3D eye positions, we compared the torsional standard deviation of eye positions around two planes: one in head-fixed and the other in gravity-dependent coordinates (see METHODS). Similar to a significant reduction in the torsional standard deviation of responses to barbecue spit rotations when expressed in gravity-dependent coordinates, a significant decrease in torsional standard deviation was also observed here for both the initial and steady-state off-vertical axis yaw responses (Fig. 3A). The torsional standard deviation of the initial response decreased drastically from $SD_{\text{tor}} = 4.7° \pm 0.8°$ in head-fixed coordinates to $0.9° \pm 0.3°$ when expressed in gravity-dependent coordinates (Fig. 3A). During steady-state, the reduction was smaller but still significant (from $1.9° \pm 0.4°$ to $1.3° \pm 0.2°$, $P < 0.01$, $t$-test). In contrast, torsional standard deviation for translational responses during both lateral and fore-aft motion did not depend on the coordinates chosen (Fig. 3B). Even though the torsional standard deviations of fast phase eye positions were significantly larger during translation than the torsional standard deviation of visually-guided saccades with the head station-
during the first few rotation cycles and diminished gradually thereafter (compare initial versus steady-state response in Fig. 3A). This modulation was typically triggered by the first VOR fast phase that occurred at about 100–200 ms after stimulus onset (Fig. 1A dashed vertical line). This initial enhancement could suggest a facilitation by the concomitant horizontal semicircular canal input.

Contrary to rotations, no significant modulation of fast phase displacement planes occurred during translation in a lateral or fore and aft direction. Taken together, this distinct saccadic response behavior suggests the existence of a central mechanism that resolves the information about gravito-inertial accelerations conveyed by primary otolith afferents into inertial (due to translation) and gravitational components (due to head tilt).

Previous studies have proposed that central segregation of gravito-inertial signals into its components is primarily based on frequency (Paige and Tomko 1991; Telford et al. 1997). Thus, otolith signals at frequencies below \( \leq 0.5 \text{ Hz} \).
would be centrally interpreted as gravitational accelerations, whereas signals at higher frequencies would be interpreted as inertial accelerations (due to translation) with significant overlap in function. Our present findings showing appropriate tilt/translation discrimination at 0.5 Hz are not in line with this notion. Tilt/translation discrimination based on multi-sensory integration rather than frequency segregation has also been demonstrated for VOR slow phases. In fact, head angular velocity signals from the semicircular canals were shown to be crucial in the central discrimination of gravito-inertial signals for frequencies > 0.1 Hz (Angelaki et al. 1999). In the experimental paradigms used in this study, semicircular canal signals seem to enhance the discrimination effect, but do not seem to be exclusively responsible for its presence.

Theoretical analyses have suggested how angular velocity information can be used to extract the inertial (translational) and the gravitational acceleration components from otolith signals using a nonlinear filter network (Glasauer and Merfeld 1997; Vieville and Faugeras 1990). In this scheme, head velocity information originates from the semicircular canals, which are excellent rate sensors for frequencies > 0.1 Hz, albeit other sources cannot be excluded. For example, angular head velocity from centrally processed otolith signals that supplement semicircular canal function at low frequencies down to zero, i.e., constant-velocity rotation (Angelaki and Hess 1996b) may contribute as well. Our results for the steady-state responses during off-vertical axis rotation suggest that otolith-born angular velocity information might supplement the transient canal signals in the central process of resolving gravito-inertial signals.

It seems that vestibulo-ocular responses in lateral-eyed animals, such as rabbits or rats, do not discriminate head tilt from translation based on vestibular inputs alone. In rabbits, translation in darkness at frequencies up to 1 Hz generates mainly torsional and vertical eye movements that are similar to those during dynamic head tilt (Baarsma and Collewijn 1975; Barmack 1981). Rats generate horizontal as well as large vertical and/or torsional eye movements during translation; the directional characteristics of which depend on the plane of the “apparent head tilt” (Hess and Dieringer 1991). In these animals with almost panoramic vision, the static otolith-ocular reflexes exert their orienting function via the slow phase system, which tends to keep the horizontal retinal meridian with its visual streak parallel to earth-horizontal. Primates have evolved frontally placed eyes with foveal vision and explore the visual world with saccades that reorient the gaze lines every few hundred milliseconds. In these animals, the otolith-ocular reflexes subserve their orienting function by maintaining a constant relationship between the ocular rotation axes of fast eye movements and gravity, rather than by stabilizing the static orientation of the globe in space.

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