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RESEARCH ARTICLE

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Vestibular and non-vestibular contributions to eye movements that compensate for head rotations during viewing of near targets

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Abstract Geometry dictates that when subjects view a near target during head rotation the eyes must rotate more than the head. The relative contribution to this compensatory response by adjustment of the vestibulo-ocular reflex gain (Gvor), visual tracking mechanisms including prediction, and convergence is debated. We studied horizontal eye movements induced by sinusoidal 0.2–2.8 Hz, en-bloc yaw rotation as ten normal humans viewed a near target that was either earth-fixed (EFT) or head-fixed (HFT). For EFT, group median gain was 1.49 at 0.2 Hz declining to 1.08 at 2.8 Hz. For HFT, group median gain was 0.03 at 0.2 Hz increasing to 0.71 at 2.8 Hz. By applying transient head perturbations (peak acceleration $>1{,}000^\circ\ \mathrm{s}^{-2}$) during sinusoidal rotation, we determined that Gvor was similar during either EFT or HFT conditions, and contributed only ~75% to the compensatory response. We confirmed that retinal image slip contributed to the compensatory response by demonstrating reduced gain during EFT viewing under strobe illumination. Gain also declined during sum-of-sines head rotations, confirming the contribution of predictive mechanisms. The gain of compensatory eye movements was similar during monocular or binocular viewing, although vergence angle was greater during binocular viewing. Comparison with previous studies indicates that mechanisms for generation of eye rotations during near viewing depend on head stimulus type (rotation or translation), waveform (transient or sinusoidal), and the species being tested.

Keywords Vestibulo-ocular reflex · Retinal image slip · Prediction · Vergence

Introduction

To see the environment clearly, images of stationary objects must be held fairly still on the retina (Carpenter 1991). During natural activity, especially locomotion, head perturbations with predominant frequencies ranging, in yaw, up to 3 Hz pose a threat to clear vision (Grossman et al. 1988; Das et al. 1995b; Crane and Demer 1997). The vestibulo-ocular reflex (VOR) generates eye rotations at short latency (<15 ms) that can compensate for such head perturbations (Maas et al. 1989; Collewijn and Smeets 2000) and thus maintain a clear and stable visual percept. Individuals who have lost vestibular function report that they cannot see their environment clearly while they are in motion (J.C. 1952). Thus, the VOR is indispensable for clear vision during natural activity (Leigh and Zee 1999). Nonetheless, other factors contribute to the generation of eye rotations that compensate for head perturbations. One factor is visually mediated eye movements, for example smooth pursuit, but it acts at longer latencies (~100 ms) than the VOR (Carl and Gellman 1987). Another factor is the predictive mechanism that acts to negate the delay inherent in visual signal processing (Dallos and Jones

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1963; Barnes 1993; Barnes et al. 2000). Hereafter, we refer to the sum of vestibular and non-vestibular contributions to eye movements that compensate for head rotations as the enhanced VOR (EVOR).

Special demands are made when subjects view a *near*, earth-fixed stationary target during head rotations (Blakemore and Donaghy 1980; Biguer and Prablanc 1981; Viirre et al. 1986; Hine and Thorn 1987; Han et al. 2001). Because the eyes do not lie on the axis of head rotation, they are displaced (translated) and rotated when the head turns. Thus, during near-viewing, to hold the gaze on the target, the eye must rotate more than the head; with the target at the subject's near point of focus, the gain of EVOR (eye velocity/head velocity) can exceed 1.5. Previous studies with the monkey (Viire et al. 1986; Snyder and King 1992) have suggested that such gain increases, which occur within 20 ms of the onset of eye movements, are because of an increment of the internal gain of the VOR (Gvor), perhaps achieved by a separate "short-latency" pathway. In humans, the gain of EVOR during viewing of a near target may occur even earlier (8–18 ms) after the onset of head rotation (Crane and Demer 1998). These studies suggest, therefore, that Gvor is preset to an appropriate value for viewing a near target before a head rotation starts. Some evidence suggests that the brain might monitor the angle of vergence and use this signal to preset Gvor (Snyder and King 1992).

The questions addressed in this study were:

1) how much does Gvor contribute to the human EVOR during viewing of a near target during sinusoidal head-and-body oscillation?
2) what non-vestibular mechanisms are used to modulate EVOR to an appropriate level?
3) how important is vergence angle in determining EVOR?

Our findings suggest that both the nature of the rotational stimulus and the viewing conditions influence the response. Preliminary results have been published as abstracts (Han et al. 2004, 2005).

Methods

Subjects

We studied 10 normal human subjects (four females, ages 24–57 years). Five subjects were naive about the purpose of the study, two were experienced in ocular motor studies, and three were aware of the purpose of the experiments. No subjects had any ocular motor abnormalities or were taking drugs with effects on the nervous system. Five subjects were myopes (corrections were −3.5D on average), but were able to see clearly the near visual stimuli without their spectacle corrections throughout the testing. All subjects gave written, informed consent in accordance with our Institutional Review Board and the tenets of the Declaration of Helsinki.

Experimental stimuli

Head and eye rotation were measured using the magnetic search-coil technique, with 6-ft (1.8 m) field coils (CNC Engineering, Seattle, WA, USA) that used a rotating magnetic field in the horizontal plane and an alternating magnetic field in the vertical plane. Each subject wore a scleral search coil (Skalar Delft, Netherlands) on each eye to measure gaze angle. Angular head rotations were measured by means of a third coil which was firmly attached to the forehead of subjects. We confirmed the reliability of the forehead coil measurement of head rotation by comparing records obtained with a coil attached to dental bite-appliance. Search coils were calibrated on a protractor device before experiments. The system was 98.5% linear over an operating range of ±20° in both horizontal and vertical planes, and the SD of system noise was <0.02°.

Angular head rotation in yaw was applied using a 30-ft-lb vestibular chair (Templin Engineering, Laytonville, CA, USA). Subjects sat in the chair in the search coil field, with their heads aligned so that the axis of chair rotations corresponded as closely as possible to the midpoint of the interaural line. They wore a modified cycle helmet that contained foam pads to ensure a snug fit for each subject. Subjects braced their heads against the headrest of the chair throughout the recording session.

Four types of *visual stimuli* were used in these experiments.

1. A far target consisting of a red laser spot subtending an angle of 0.05° projected on to a wall at a viewing distance of 3 m; it was either viewed in ambient light, or flashed at 1 Hz in an otherwise dark room—flashed far target.
2. An earth-fixed near target (EFT), consisting of a black cross (1×1 cm) on a white background, positioned at the eye level of each subject. With one of the subject's eyes patched throughout the experiment, the cross target was aligned with the viewing eye at a distance corresponding to the near point of accommodation for each subject, range 11–14 cm (median 12 cm).
3. A head-fixed near target (HFT), consisting of a similar black cross attached to a rigid plastic rod attached to the modified cycle helmet; the target was aligned with the viewing eye, at the same distance to the EFT for each subject. The EFT and HFT were viewed in ambient room light.
4. Strobe illumination—four subjects viewed the EFT under stroboscopic illumination (Monarch PB phase-strobe, Amherst, NH, USA) with 30 ms flashes at 4 Hz, in an otherwise dark room. Similar stroboscopic illumination has previously been used to eliminate retinal image slip during vestibular experiments (Melvill Jones and Mandl 1981). We repeated these experiments in two subjects with the same stroboscopic duration but a flash rate of three times the rotational head frequency; in this way the

strobe provided the same number of target fixations during each rotational cycle.

Vestibular stimuli consisted of three types of en-bloc yaw rotation.

1. Sinusoidal head rotations: at each of five test frequencies –0.2, 0.7, 1.0, 2.0, and 2.8 Hz with a constant peak velocity of 15° s^{-1}. At the beginning of each session, each subject was rotated at a frequency of 0.1 Hz with a peak velocity of 15° s^{-1} while they monocularly viewed a stationary far laser target under room light. This procedure served as a calibration check and assumed that our subjects continuously foveated on the target and generated compensatory eye movements with a gain of 1.0.
2. Transient head perturbations: to measure the dynamic internal VOR gain (Gvor) and to quantify the vestibular contributions to the overall EVOR responses under different viewing conditions, we applied transient head perturbations during sinusoidal rotations when subjects were viewing the EFT or HFT at the five test frequencies. Because the velocity of vestibular chair was controlled by a voltage signal (motor servo), we used a computer program that generated the acceleration pulses by changing the sign (representing the direction of chair rotation) of the control signal at the peak velocity. Consequently, at each perturbation the chair velocity changed from 15° s^{-1} to $-15°$ s^{-1} abruptly, or vice versa, generating measured peak head accelerations $>1{,}000°$ s^{-2}. A total of nine perturbations were applied non-predictably during a 40 s trial at each of the test frequencies.
3. Sum-of-sines stimuli (pseudorandom rotations): to investigate the contribution to the responses of predictable visual tracking eye movements, we applied sum-of-sines stimuli (pseudorandom chair rotations) in four subjects during viewing of the EFT. The component sine waves had frequencies of 0.38, 1.23, 2.08, and 2.63 Hz, with peak velocities of 3.3, 5.5, 6.0, and 15.3° s^{-1}, respectively. Thus, the velocity ratio between the highest and lowest frequency components was >4.0, which Barnes (1993) has established as a reliable strategy for preventing predictive visual tracking.

Experiments

There were eight experiments. Each trial lasted 40 s. Subjects were instructed to maintain fixation of the near stimuli using one eye (chosen by themselves); the other eye was occluded but its position was monitored by an eye coil during experiments 2 and 3. During all testing, one of the experimenters encouraged subjects to sustain fixation on the visual target.

1. *Head rotations in darkness (VOR)*: Subjects attempted to fixate the far target (a laser flashing at 1 Hz) while they were rotated sinusoidally in darkness at the five test frequencies.
2. *Head rotations while viewing the EFT*: Subjects attempted to fixate the near EFT while they were rotated sinusoidally at each of the five test frequencies in ambient room illumination.
3. *Head rotations while viewing the HFT (eye-head tracking)*: Subjects attempted to fixate the near HFT during rotation at each of the five test frequencies in ambient room illumination.
4. *Head perturbations while viewing the EFT*: Experiment 2 was repeated, during which transient head perturbations were delivered.
5. *Head perturbations while viewing the HFT*: Experiment 3 was repeated, during which transient head perturbations were delivered.
6. *Head rotations under strobe illumination*: Experiment 2 was repeated but under stroboscopic illumination in an otherwise dark room, with the strobe rate at 4 Hz (four subjects) and with the strobe rate equal to three times head rotational frequency (two subjects). Because the strobe rate determines the sampling interval of subjects' visual information, it should have a frequency that is at least twice that of the stimulus in order to avoid aliasing. We therefore tested at rotational frequencies 0.2–2.0 Hz, but not at 2.8 Hz.
7. *Sum-of-sines head rotation*: Experiment 2 was repeated using the sum-of sines stimulus in four subjects. In addition, eye responses to sinusoidal head rotations at each of the sum-of-sines component frequencies were also measured.
8. *EFT during binocular viewing*: Experiment 2 was repeated as five subjects viewed the near targets binocularly (aligned on the eye that had viewed monocularly). We positioned the near targets at the same distance during binocular or monocular viewing for each subject. Vergence angle was measured throughout experiments.

Data collection and analysis

Horizontal and vertical head and gaze (eye-in-space) signals were low-pass filtered using Krohn-Hite Butterworth filters with a bandwidth of 0–150 Hz, before digitization with 16-bit precision at 500 Hz. Portions of data contaminated by blinks or any extraneous saccades were visually identified and discarded. Eye-in-head rotations (referred to, hereafter as "eye position") were calculated by subtracting the head position signal from eye-in-space (gaze) signal. Convergence angle was obtained by subtracting right gaze from left gaze. We differentiated these signals to obtain corresponding velocity measurements, and filtered these signals with a Remez filter of bandwidth 0–40 Hz (Ramat et al. 1999). The quality of each record was reviewed before further analysis, ensuring that each subject sustained fixation on the visual target (evident by corrective saccades at high frequencies of head rotation, when smooth eye movements failed to compensate fully for head rotations). We also checked the stability of vertical head position. Before filtering, saccades were removed from the eye velocity via an interactive routine described elsewhere (Das et al. 1995a). We determined the gain of VOR or EVOR during head rotation at each frequency by calculating the ratio of power spectral density of eye and head velocity at the frequency of interest, including the sum-of-sines stimuli, using a fast-Fourier transform (FFT) method. The phase response was determined by measuring phase angle of these paired signals and recording the phase difference (phase shift) between them at the frequency of interest. A negative phase shift indicates that the eye velocity signals lag behind head velocity signals.

For transient head-perturbation stimuli, we defined the stimulus onset as when head acceleration exceeded $200° \mathrm{s}^{-2}$, and measured "onset head velocity" and "onset eye velocity" at this point. We then determined, interactively, the peak head and eye velocity values in the 80-ms period after the stimulus onset (Aw et al. 1996). The value of Gvor for each perturbation was calculated by use of Eq. 1:

$$\mathrm{Gvor} = \frac{\text{Peak eye velocity} - \text{Onset eye velocity}}{\text{Peak head velocity} - \text{Onset head velocity}} \qquad (1)$$

A total of nine head perturbations were employed at each frequency of head rotation, and from these responses we calculated the median value of Gvor for each test frequency. As a check of the reliability of this method, we also measured the median value of eye and head velocity in the 80-ms period after stimulus onset, and used these values to make a separate estimate of Gvor; similar results were obtained, and here we present estimates of Gvor based on measurements by use of Eq. 1. Paired statistical comparisons of Gvor were made between viewing of an EFT and an HFT for each subject and frequency: a *t*-test was used when data were normally distributed; otherwise, a Wilcoxon rank-sum test was used instead.

Results

General features of responses to sinusoidal rotation

Figure 1 summarizes the gain values and phase shifts of responses from all 10 subjects for experiments 1–3. In these Bode plots, gain and phase values are for eye velocity with respect to head velocity for experiment 1 (Figs. 1a, b, flashed far target in darkness), experiment 2 (Figs. 1c, d, EFT), and experiment 3 (Figs. 1e, f, HFT). During viewing of the EFT, the gain of compensatory responses (Fig. 1c) was over 50% greater than viewing the flashed far target in darkness (Fig. 1a) at lower frequencies of rotation. However, at higher frequencies, EVOR gain declined (Fig. 1c) and phase shift increased (Fig. 1d) for EFT, but changed little for the flashed far target in darkness (Figs. 1a, b). During viewing of the HFT, EVOR gain (Fig. 1e) and phase lags (Fig. 1f) were small at lower test frequencies (because the VOR was being canceled); at higher test frequencies, EVOR gain and phase increased, especially for rotational frequencies above 1 Hz.

Head perturbation: determination of the vestibular contribution to the responses

Figure 2 summarizes responses of 10 subjects to head perturbations that were applied as they were oscillated sinusoidally at each of the five test frequencies during viewing of EFT (a) or HFT (b); median values of Gvor are plotted as frequency histograms. For comparison, we also plot measurements of Gvor during rotation while viewing the flashed far target in darkness (experiment 1) in Fig. 2c. Note that for Figs. 2a and 2b Gvor values are dynamic VOR gains measured through transient head perturbations whereas Gvor in Fig. 2c are steady state gain values. The range of Gvor values was similar for the two near visual stimuli. Substantial variance of data is evident in these histograms, similar to previous studies (Collewijn and Smeets 2000). Lower values of Gvor were in myopes who habitually wore spectacle corrections, which is a recognized association (Cannon et al. 1985).

We performed paired comparisons, for each normal subject and frequency, of Gvor values for the EFT and the HFT near-viewing conditions (Fig. 2d); there were no significant differences for nine out of the 10 subjects ($P > 0.053$). One subject showed a significant greater value of Gvor during viewing of the EFT than the HFT ($P < 0.001$). In fact, there was a significant correlation of Gvor between EFT and HFT ($P < 0.001$), with a correlation coefficient of 0.72. We also compared Gvor values during the two near-viewing conditions with VOR gain values measured in darkness. For the group of subjects, a paired comparison showed that Gvor during viewing the EFT was significantly greater than VOR gain in darkness ($P = 0.007$). The median value of Gvor during EFT was 0.98 for the group of subjects (range 0.39–1.42), whereas the median value of VOR gain in darkness was 0.91 (range 0.54–1.04). However, for the group of subjects, a paired comparison of Gvor during viewing the HFT and VOR gain in darkness showed no significant difference ($P = 0.078$). The median value of Gvor during viewing of the HFT was 0.97 for the group of subjects (range 0.37–1.33).

We then estimated the percentage contribution of Gvor to the overall gain of EVOR during viewing of the EFT, as calculated by Eq. 2:

$$\text{Contribution} = \frac{\mathrm{Gvor}}{\text{EVOR gain}} \times 100\% \qquad (2)$$

For the group of subjects, Gvor contribution was fairly consistent across the range of frequencies tested. Overall, Gvor only accounted for 73% (group median) of the

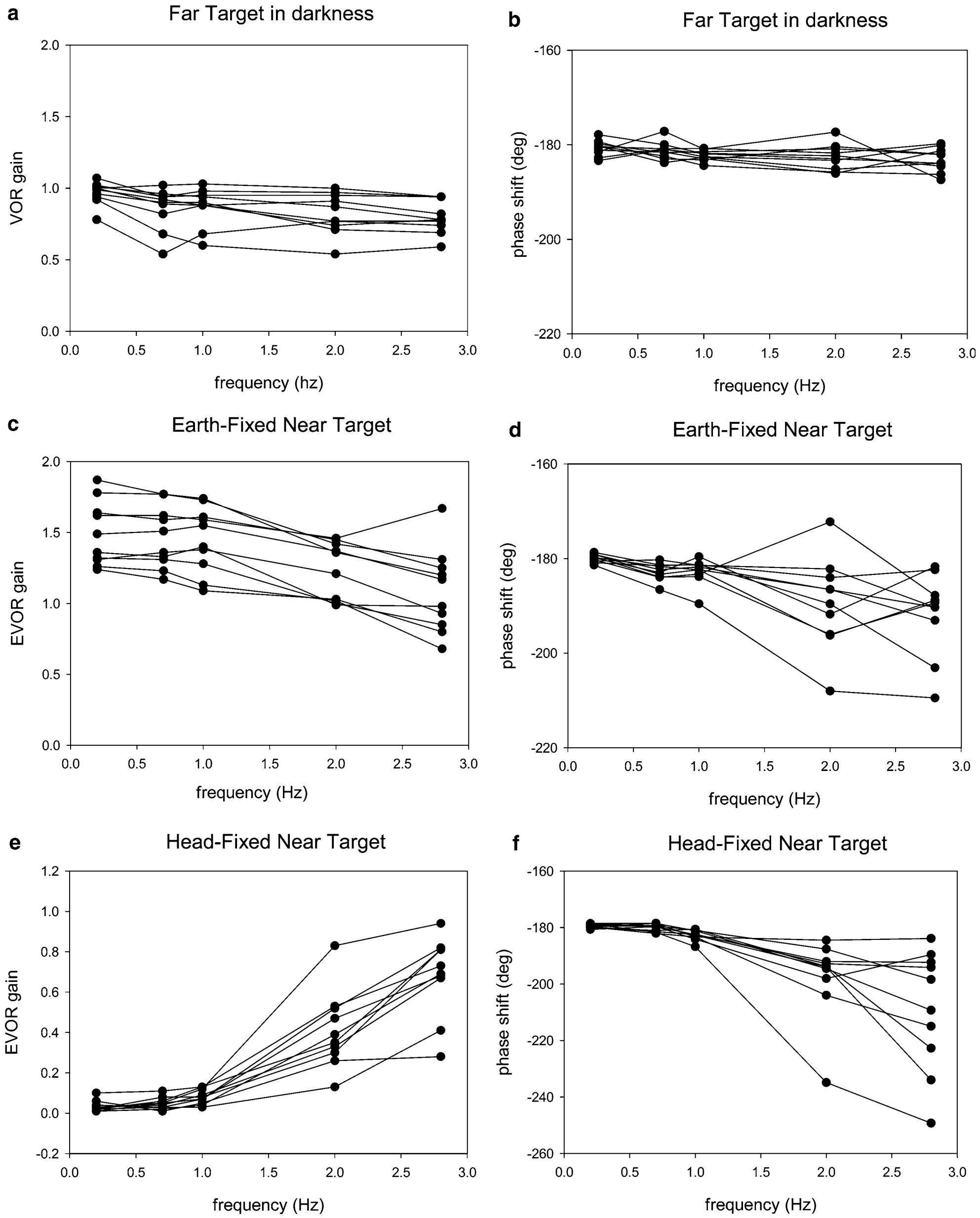

Fig. 1 Bode plots summarizing gain values and phase shifts from 10 normal subjects during en-bloc rotation (experiments 1–3) over the frequency range 0.2–2.8 Hz. **a** and **b** summarize responses during viewing the flashed far target in darkness (experiment 1). Note that VOR gain and phase shifts changed little over the range of test frequencies. **c** and **d** summarize responses while viewing the EFT (experiment 2); all subjects showed increased EVOR gain at lower frequencies, but reduced EVOR gain (**c**) and increased phase shifts (**d**) at high frequencies. **e** and **f** summarize responses while viewing the HFT (experiment 3); EVOR gain (**e**) and phase shifts (**f**) increased substantially at test frequencies above 1.0 Hz

total EVOR gain, less for greater response gains for lower frequencies, indicating that other mechanisms make a substantial contribution to EVOR gain.

Identification of non-vestibular factors

Because Gvor accounted for only about 75% of the observed behavior during EFT, we employed experiments to test three potential non-vestibular factors that could contribute to EVOR gain:

1) retinal image motion;
2) effects of the predictive nature of the stimulus motion; and
3) vergence angle.

Contribution of retinal slip to the EVOR

In four subjects, we measured the gain of EVOR during head rotations at 0.2–2.0 Hz while viewing of the EFT under strobe illumination in an otherwise dark room (experiment 6), which essentially abolished retinal image slip. Figure 3a compares the EVOR gains under strobe illumination (open symbols connected by dotted lines) with those measured under ambient room light (black symbols connected by black lines) at the test frequencies. The results indicated that, especially at frequencies of head rotation ≥1.0 Hz, each of the four subjects showed higher EVOR gain during ambient illumination (when retinal slip information was available) compared with strobe illumination. However, strobe illumination also provides position cues during each flash. Consequently, more position cues occurred during each cycle of lower-

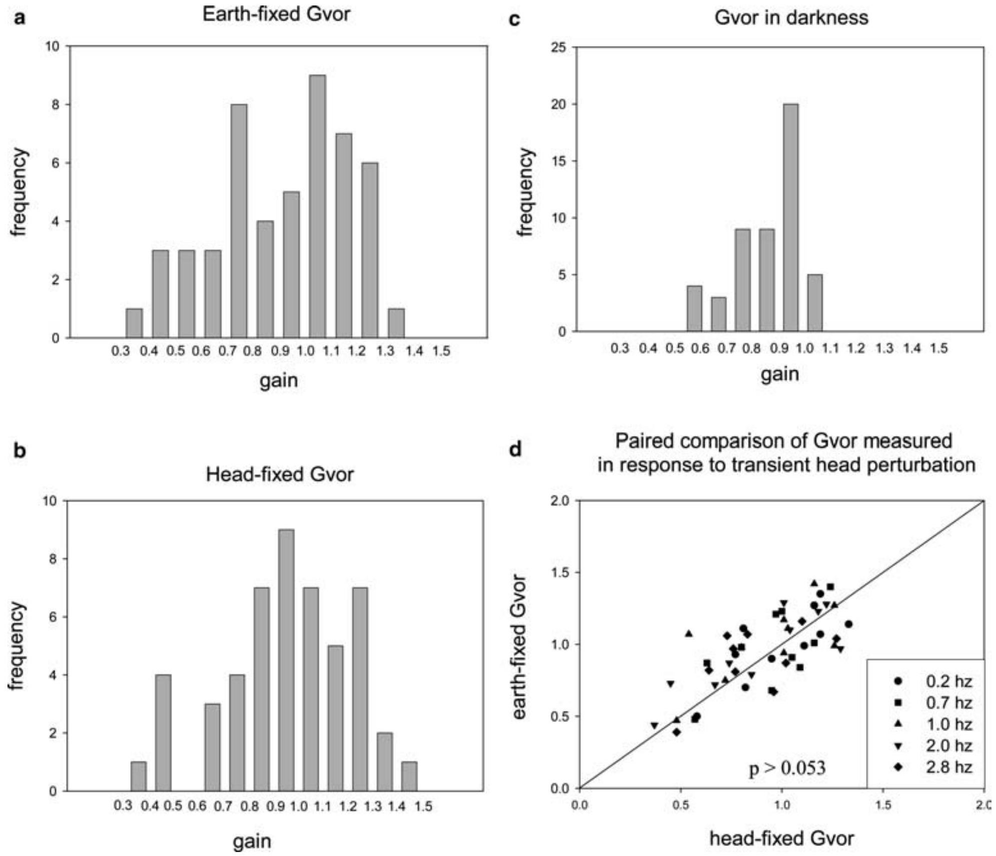

Fig. 2 Histograms summarizing distribution of Gvor for the five test frequencies and 10 normal subjects ($n = 50$) when viewing the EFT (plot **a**, experiment 4) or the HFT (plot **b**, experiment 5). Plot **c** summarizes VOR gain measured in darkness (experiment 1). Plot **d** summarizes the comparison of median Gvor values between viewing of the EFT and HFT; a paired *t*-test showed no significant difference ($P > 0.053$)

frequency versus higher-frequency rotation, with the fixed 4 Hz stroboscopic rate. To address this issue, in two subjects we repeated experiment 6 using a stroboscopic rate which was always three times the frequency of head rotation. In this way, the number of positional cues occurring in each rotational cycle was constant for all stimulus frequencies. In Fig. 3a, these data are plotted as gray symbols connected by gray lines. Both subjects showed lower gain values during this strobe than under ambient illumination. Thus, irrespective of the stroboscopic frequency, gain was reduced, suggesting that retinal image velocity is used to optimize compensatory eye movements, including at the higher rotational frequencies that we employed.

Contribution of prediction mechanisms to the EVOR

We used sum-of-sines head rotations in four subjects to minimize contributions of predictive eye movements during viewing of the EFT (experiment 7). Results were compared with responses to sinusoidal head rotations at each component frequency of sum-of-sines, as shown in Fig. 3b. All four subjects showed greater EVOR gain values for single sinusoidal stimulus than the sum-of-sines stimulus for the lower two component frequencies, at which predictive mechanisms work best ($P < 0.001$), but not at the higher two frequencies ($P = 0.383$). These results support the view that predictive mechanisms contribute to the overall EVOR gain.

Contributions of vergence angle to the EVOR during near viewing

Experiment 2 was conducted as 10 normal subjects monocularly viewed the near EFT, but wore two eye coils to monitor the angle of vergence. Figure 4a summarizes the relationship between vergence angle and EVOR gain during monocular viewing of the near EFT; multiple linear regression analysis showed a significant negative relationship between EVOR gain and stimulus frequency ($P < 0.001$), but not with vergence angle ($P = 0.15$; $R^2 = 0.35$). During monocular viewing, the main stimuli to convergence are accommodation and the perception of nearness in the viewing eye; there is no visual feedback control of vergence. Although our subjects maintained fixation of the near target, which would tend to stabilize the state of accommodation, we considered the possibility that their angles of vergence differed from during binocular viewing. Accordingly, we repeated the experiments with five subjects during binocular viewing of the near target, when vergence eye movements could be visually controlled, and made paired comparisons of vergence angle and EVOR gain under the two viewing conditions using a *t*-test. Binocular viewing (mean vergence angle 22.2°) was associated with significantly greater ($P < 0.001$) vergence angles than monocular viewing (mean vergence angle 13.2°); however, there was no significant difference in EVOR gain ($P = 0.882$) during the two viewing conditions.

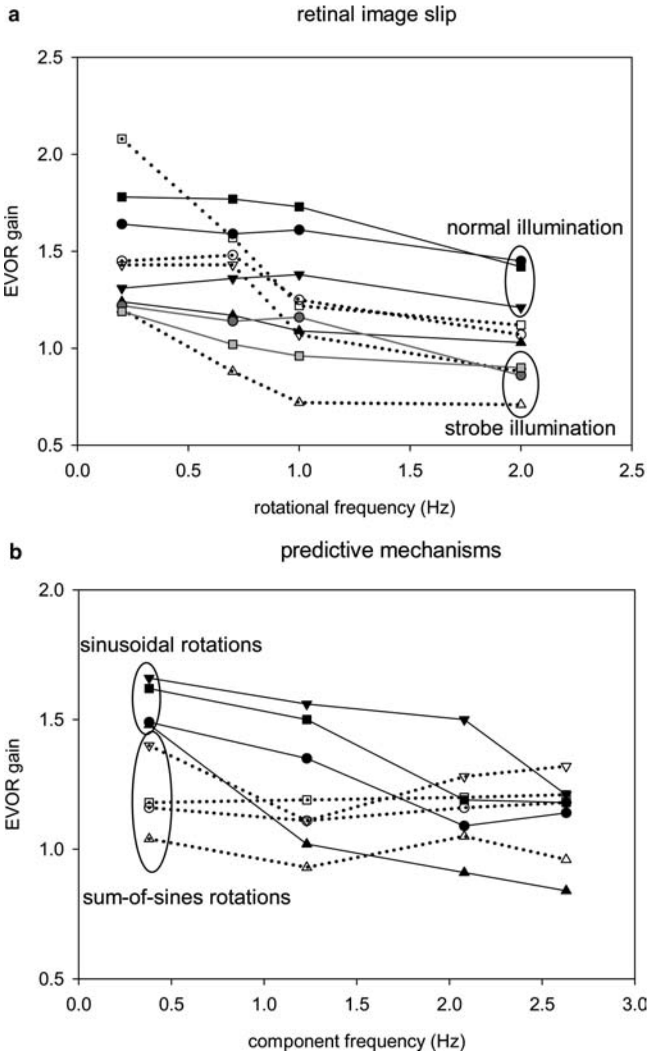

Fig. 3 Non-vestibular contributions to EVOR gain by retinal image slip and predictive mechanisms. **a** shows comparisons of EVOR gain, from four subjects, between ambient (experiment 2) and strobe illumination (experiment 6) during viewing of the EFT at the test frequencies. Each subject is coded with a distinctive symbol shape. *Black symbols connected by black lines* are responses under normal illumination; *open symbols connected by dotted lines* are during strobe illumination at 4 Hz flash rate; *gray symbols connected by gray lines* are during strobe illumination in which the flash rate is three times the rotational frequency. All subjects show higher EVOR gain under normal than both strobe illumination conditions even during high frequencies (1.0 Hz) of head rotation. **b** shows comparisons of EVOR gain, from the same four subjects, between sinusoidal and sum-of-sines head rotations at each of the component frequencies while viewing of the EFT (experiment 7). Filled *symbols connected by solid lines* are during sinusoidal head rotations; *open symbols connected by dotted lines* are during sum-of-sines rotations. All subjects show higher EVOR gain during sinusoidal versus sum-of-sines stimuli for the two lower frequency components, indicating that prediction contributes to EVOR gain

Figure 4b summarizes the relationships between EVOR gain, vergence angle, and rotational test frequency during binocular viewing for five subjects. Multiple linear regression analysis showed a significant relationship between EVOR gain and both stimulus frequency and vergence angle ($P < 0.001$; $R^2 = 0.67$); EVOR gain $= -0.176 - (0.214 \times \text{rotational frequency}) + (0.079 \times \text{vergence angle})$.

Discussion

In this study we used new experimental strategies to investigate vestibular and non-vestibular contributions to the enhanced VOR during viewing of near targets. Our main findings are:

1) during sinusoidal rotation in yaw, the internal gain of the VOR, Gvor, accounts for only about 75% of the total ocular motor response as subjects view a near EFT;
2) Gvor is similar during viewing of either an EFT or HFT;
3) both retinal image slip and predictive mechanisms contribute to the EVOR gains; and
4) vergence angle was not correlated with EVOR gain during monocular viewing, but was so during binocular viewing.

In discussing our findings, first, we summarize current evidence for the vestibular contribution to the increased gain of compensatory eye movements during near-viewing response. Second, we review the possible role played by non-vestibular mechanisms, including retinal image velocity and prediction. Third, we examine the relationship between vergence angle and EVOR. Finally, we relate our findings to performance of EVOR during natural activities.

The vestibular contribution to generation of compensatory eye movements during near viewing: dependence on stimulus properties

Previous studies have shown that target location, eye-head geometry, and axis of head rotation are important determinants of the eye response to compensate for head rotation in cats, monkeys, and humans (Blakemore and Donaghy 1980; Biguer and Prablanc 1981; Viirre et al. 1986). In this study we aligned near visual targets on the visual axis of the viewing eye and rotated subjects' heads on an axis close to the midpoint of the interaural axis; we did not set out to study the effects of eccentric head rotation.

What is the neural mechanism for the near-viewing response to head rotation? Viirre et al. (1986) demonstrated that for monkeys the gain of compensatory eye movements during near viewing was ideal even up to a frequency of 2.0 Hz. Using transient stimuli, they showed that when the animal viewed a near target, the ocular response deviated from that during viewing a far target within 20 ms of the onset of head rotation. Viirre et al. (1986) proposed that the brain uses canal and otolith inputs to generate a central estimate of target location in head coordinates, and this is followed by a transformation into eye movement commands. Snyder

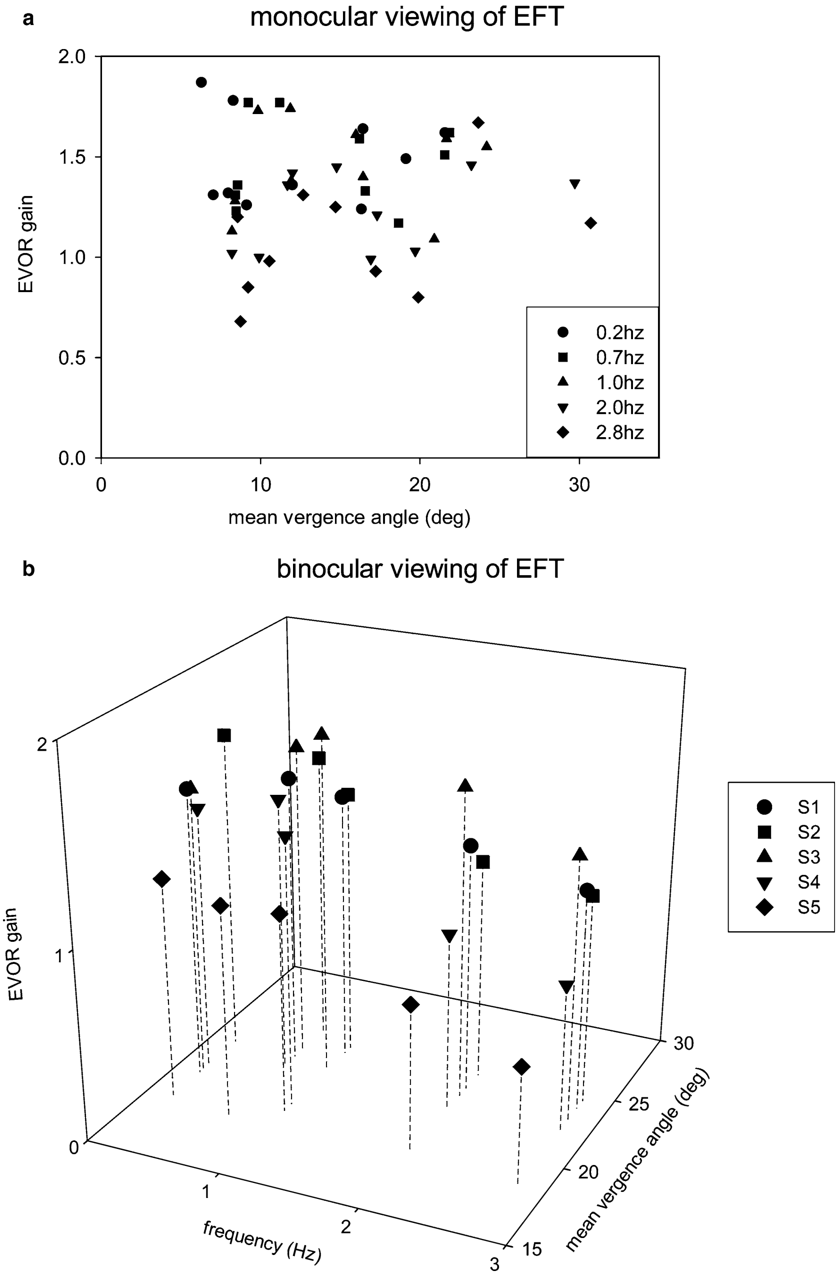

Fig. 4 Relationship between EVOR gain and vergence angle during yaw head rotations over the frequency range 0.2–2.8 Hz. **a** shows a plot of EVOR gain versus mean vergence angle at each frequency, for 10 normal subjects, during monocular viewing of the EFT (experiment 2); there is no correlation between EVOR gain and vergence angle. **b** shows a plot of EVOR gain, from five subjects, during binocular viewing of the EFT (experiment 8) as a function of rotational frequency and the mean vergence angle throughout each frequency; EVOR gain increases as vergence angle increases, and as rotational frequency decreases. See text for details

and King (1992), using transient stimuli, confirmed that the increased gain associated with near viewing became apparent ~20 ms after the onset of the stimulus, and postulated an additional short-latency pathway to account for this behavior.

In humans, Crane and Demer (1998) applied *transient head rotations* and identified a gain increase attributable to target distance within 8–18 ms after the onset of head rotations. Based on the results of gentamicin-induced hair cell lesions of the vestibular labyrinth, Migliaccio et al. (2004) suggested that the near-viewing component of the response depends on irregular vestibular nerve afferents. Thus, these results imply that, in humans, factors other than visual tracking, which acts at longer latency (Gellman et al. 1990), exist to increase Gvor during near viewing. The EVOR has also been tested in humans with *sinusoidal head rotations* during viewing of a near target. Reported results are similar to those from this study (Figs. 1c, d): the gain of EVOR is appropriately increased at lower frequencies, but declines with increasing phase shifts as test frequency increases (Hine and Thorn 1987; Crane et al. 1997). Thus, whereas responses to transient stimuli indicate an increase of Gvor as the mechanism for increased EVOR gain, responses to sinusoidal stimulation over a range 0.2–2.8 Hz suggest a non-vestibular contribution that deteriorates at higher frequencies of head rotation.

Our approach was to test Gvor with transient head perturbations *during* sinusoidal yaw rotation. We were surprised to find that Gvor did not differ during viewing of either the EFT or HFT for nine out of 10 subjects (group medians of 0.98 and 0.97, respectively). These values of Gvor during near viewing were only slightly greater than during viewing of a far target flashed in darkness (experiment 1, group median 0.91) (Fig. 2). Thus, there seems to be a difference if, on the one hand, Gvor is measured at the onset of a head rotation starting from a stationary position and, on the other hand, if Gvor is measured while the head is in motion (sinusoidal oscillations in our study). A similar phenomenon has been commented on before by Paige et al. (1998), who noted that during fixation of a HFT, if transient stimuli are used, the response gain is reduced to about 0.7 (Huebner et al. 1992) but if sinusoidal stimuli are used, no such gain decrease is apparent (Paige 1994).

Contributions by non-vestibular mechanisms to generation of compensatory eye movements

Because the contribution of the Gvor to the overall gain of compensatory eye movements during our experiments was only about 75%, which non-vestibular mechanisms could contribute? The decline in gain of compensatory eye movements during fixation of the EFT that occurs at frequencies above 1.0 Hz (Fig. 1c) suggested that visual tracking plays an important role. When smooth-pursuit eye movements are tested with sinusoidal target motion, gain decreases and phase lag increases for stimuli above 1.0 Hz (Lisberger et al. 1981; Barnes 1993). At lower frequencies, gain may be close to 1.0 and phase shift almost zero; this behavior is attributed to predictive mechanisms (Dallos and Jones 1963; Barnes et al. 2000) which the brain mobilizes to counter delays inherent in the visual system.

In this study, we used two new approaches to determine how non-vestibular mechanisms contributed to EVOR during viewing of the EFT. First, we measured compensatory eye movements under strobe illumination (experiment 6), which essentially abolishes retinal slip information (Melvill Jones and Mandl 1981), and found that the gain of the response decreased, especially at higher frequencies of head rotation (Fig. 3a). This gain decrease was also present when we used a stroboscopic rate that was a fixed multiple (three times) of head rotational frequencies, so that target position cues were similar throughout. Second, we measured compensatory eye movements using sum-of-sines chair rotations, which minimize the effects of prediction. We found that EVOR gain was reduced during sum-of-sines stimulation compared with sinusoidal rotations, especially at lower component frequencies (Fig. 3b). Prediction is known to decline at higher frequencies (Barnes 1993; Barnes et al. 2000), and the difference between sinusoidal and sum-of-sines stimulation became insignificant for the higher component frequencies. Taken together, the contributions from retinal image velocity and predictive mechanisms provided circumstantial evidence that visually mediated eye movements make an important contribution to EVOR during viewing a near target, although other non-vestibular factors may assist.

Vergence angle and the compensatory response during near viewing

During experiment 2, subjects viewed the near visual target monocularly. In this situation the main stimulus to vergence is accommodation (which is open-loop), and we found that vergence angle did not correlate with EVOR gain (Fig. 4a). Thus, all subjects were able to maintain a constant vergence angle throughout the test rotational frequencies, but EVOR gain declined as frequency increased, regardless of the vergence angle. In experiment 8, subjects viewed the target binocularly so that vergence angle was appropriate for near viewing. Under these conditions, vergence angle did correlate with EVOR gain. Although it is possible that the effects of vergence on VOR are only evident at larger angles of convergence, monocular cues can provide the visual information required to adjust VOR gain appropriately (Viirre et al. 1986). Thus, for our experiments, even though vergence angle was greater during binocular viewing, EVOR was not significantly different during monocular versus binocular viewing for each subject.

Several previous studies have suggested that vergence angle is a determinant of EVOR gain. In humans, Paige et al. (1998) found a small effect of vergence angle at their highest test frequency of 4 Hz. Snyder and King (1992) reported that for monkeys, and for head rotations around an axis lying between the otoliths, vergence angle was linearly related to the gain of compensatory movements. However, in a related study, Snyder et al. (1992) tested VOR responses *during* vergence movements, and were able to show that compensatory responses anticipated vergence movements, suggesting that a “central command signal rather than an afferent or efferent copy of vergence position was used to modulate VOR gain”. Our present studies are in accord with this interpretation. However, the role of vergence may be stimulus-dependent; for example, there is evidence that vergence angle determines response gain during sinusoidal stimulation of the translational VOR in monkeys (Wei et al. 2003).

Possible significance of present results for natural behavior

During locomotion, head perturbations have a periodicity to them because of stepping frequency (Grossman et al. 1988, 1989; Das et al. 1995b; Crane and Demer 1997). In the yaw plane, predominant frequencies are typically in the range 0.5–2.0 Hz with harmonics up to 10 Hz. Thus, the range of frequencies employed in the current study is not dissimilar to those occurring during locomotion. During walking and running it is sometimes important to view proximate objects to avoid collision; in those circumstances EVOR performance during near viewing is important. Our results suggest that in such circumstances EVOR is adequate to compensate appropriately for fundamental frequencies, and partially compensates for higher-frequency harmonics. However, some caution is required when extrapolating our results, which concern en-bloc rotation to the head-free condition of natural locomotion, because electrophysiological studies have identified vestibular nucleus neurons that behave differently during active and passive head rotation in monkey (McCRea and Luan 2003; Cullen and Roy 2004). In conclusion, future studies of mechanisms that keep the "eyes on the target" (Angelaki 2004) must take into account species, vestibular stimulus type (rotation or translation), waveform (transient or sinusoidal), and viewing condition (monocular or binocular).

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References

Angelaki DE (2004) Eyes on target: what neurons must do for the vestibuloocular reflex during linear motion. J Neurophysiol 92:20–35

Aw ST, Haslwanter T, Halmagyi GM, Curthoys IS, Yavor RA, Todd MJ (1996) Three-dimensional vector analysis of the human vestibuloocular reflex in response to high-acceleration head rotations I. Responses in normal subjects. J Neurophysiol 76:4009–4020

Barnes GR (1993) Visual-vestibular interaction in the control of head and eye movement: the role of visual feedback and predictive mechanisms. Prog Neurobiol 41:435–472

Barnes GR, Barnes DM, Chakraborti SR (2000) Ocular pursuit to repeated, single-cycle sinusoids reveals behavior compatible with predictive pursuit. J Neurophysiol 84:2340–2355

Biguer B, Prablanc C (1981) Modulation of the vestibulo-ocular reflex in eye-head orientation as a function of target distance in man. In: Fuchs AF, Becker W (eds) Progress in oculomotor research. Elsevier, Amsterdam, pp 525–530

Blakemore C, Donaghy M (1980) Co-ordination of head and eyes in the gaze changing behavior of cats. J Physiol 300:317–335

Cannon SC, Leigh RJ, Zee DS, Abel L (1985) The effect of the rotational magnification of corrective spectacles on the quantitative evaluation of the VOR. Acta Otolaryngol (Stockholm) 100:81–88

Carl JR, Gellman RS (1987) Human smooth pursuit: stimulus-dependent responses. J Neurophysiol 57:1446–1463

Carpenter RHS (1991) The visual origins of ocular motility. In: Cronly-Dillon JR (ed) Vision and visual function. MacMillan Press, London, pp 1–10

Collewijn H, Smeets JB (2000) Early components of the human vestibulo-ocular response to head rotation: latency and gain. J Neurophysiol 84:376–389

Crane BT, Demer JL (1997) Human gaze stabilization during natural activities: translation, rotation, magnification, and target distance effects. J Neurophysiol 78:2129–2144

Crane BT, Demer JL (1998) Human horizontal vestibulo-ocular reflex initiation: effects of acceleration, target distance, and unilateral deafferentation. J Neurophysiol 80:1151–1166

Crane BT, Demer JL (1999) Latency of voluntary cancellation of the human vestibulo-ocular reflex during transient yaw rotation. Exp Brain Res 127:67–74

Crane BT, Viirre ES, Demer JL (1997) The human horizontal vestibulo-ocular reflex during combined linear and angular acceleration. Exp Brain Res 114:304–320

Cullen KE, Roy JE (2004) Signal processing in the vestibular system during active versus passive head movements. J Neurophysiol 91:1919–1933

Dallos PJ, Jones RW (1963) Learning behavior of the eye fixation control system. IEEE Trans Autom Contr AC-8:218–227

Das VE, Leigh RJ, Thomas CW, Averbuch-Heller L, Zivotofsky AZ, DiScenna AO, Dell'Osso LF (1995a) Modulation of high-frequency vestibulo-ocular reflex during visual tracking in humans. J Neurophysiol 74:624–632

Das VE, Zivotofsky AZ, DiScenna AO, Leigh RJ (1995b) Head perturbations during walking while viewing a head-fixed target. Aviat Space Environ Med 66:728–732

Gellman RS, Carl JR, Miles FA (1990) Short latency ocular-following responses in man. Vis Neurosci 5:107–122

Grossman GE, Leigh RJ, Abel LA, Lanska DJ, Thurston SE (1988) Frequency and velocity of rotational head perturbations during locomotion. Exp Brain Res 70:470–476

Grossman GE, Leigh RJ, Bruce EN, Lanska DJ, Huebner WP (1989) Human vestibulo-ocular reflex during locomotion. J Neurophysiol 62:264–272

Han Y, Somers JT, Kim J-I, Kumar AN, Leigh RJ (2001) Ocular responses to head rotation during mirror-viewing. J Neurophysiol 86:2323–2329

Han Y, Kumar AN, Leigh RJ (2004) Test of a superposition model of the interaction between vestibular and vergence systems using a parameter estimation technique. Soc Neurosci Abstract 411.11

Han Y, Kumar AN, Somers JT, Reschke MF, Leigh RJ (2005) Effects of retinal image slip on modulation of visual-vestibulo-ocular reflex during near-viewing. Ann NYAcad Sci 1039:(in press)

Hine T, Thorn F (1987) Compensatory eye movements during active head rotation for near targets: effects of imagination, rapid head oscillation and vergence. Vis Res 27(9):1639–1657

Huebner WP, Leigh RJ, Seidman SH, Thomas CW, Billian C, DiScenna AO, Dell'Osso LF (1992) Experimental tests of a superposition hypothesis to explain the relationship between the vestibuloocular reflex and smooth pursuit during horizontal combined eye-head tracking in humans. J Neurophysiol 68:1775–1792

J.C. (1952) Living without a balancing mechanism. N Engl J Med 246:458–460

Leigh RJ, Zee DS (1999) The neurology of eye movements, 3rd edn. Oxford University Press, NY

Lisberger SG, Evinger C, Johanson GW, Fuchs AF (1981) Relationship between eye acceleration and retinal image velocity during foveal smooth pursuit in man and monkey. J Neurophysiol 46:229–249

Maas EF, Huebner WP, Seidman SH, Leigh RJ (1989) Behavior of human horizontal vestibulo-ocular reflex in response to high-acceleration stimuli. Brain Res 499:153–156

McCrea RA, Luan H (2003) Signal processing of semicircular canal and otolith signals in the vestibular nuclei during passive and active head movements. Ann NY Acad Sci 1004:169–182

Melvill Jones G, Mandl G (1981) Motion sickness due to vision reversal: its absence in stroboscopic light. Ann NY Acad Sci 374:303–311

Migliaccio AA, Minor LB, Carey JP (2004) Vergence-mediated modulation of the human vestibulo-ocular reflex is eliminated by a partial peripheral gentamicin lesion. Exp Brain Res 159:92–98

Paige GD (1994) Senescence of human visual-vestibular interactions: smooth pursuit, optokinetic, and vestibular control of eye movements with aging. Exp Brain Res 98:355–372

Paige GD, Telford L, Seidman SH, Barnes GR (1998) Human vestibuloocular reflex and its interactions with vision and fixation distance during linear and angular head movement. J Neurophysiol 80:2391–2404

Ramat S, Somers JT, Das VE, Leigh RJ (1999) Conjugate ocular oscillations during shifts of the direction and depth of visual fixation. Invest Ophthalmol Vis Sci 40:1681–1686

Snyder LH, King WM (1992) Effect of viewing distance and the location of the axis of rotation on the monkey's vestibulo-ocular reflex (VOR). I. Eye movement responses. J Neurophysiol 67:861–874

Snyder LH, Lawrence DW, King WM (1992) Changes in vestibulo-ocular reflex(VOR) anticipate changes in vergence angle in monkey. Vision Res 32:569–575

Viirre E, Tweed D, Milner K, Vilis T (1986) A reexamination of the gain of the vestibuloocular reflex. J Neurophysiol 56:439–450

Wei M, DeAngelis DC, Angelaki DE (2003) Do visual cues contribute to the neural estimate of viewing distance used by the oculomotor system? J Neurosci 23:8340–8350