

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

Yanning H. Han¹

Arun N. Kumar¹

Millard F. Reschke³

Jeffrey T. Somers³

Louis F. Dell'Osso^{1,2}

R. John Leigh^{1,2}

¹Departments of Biomedical Engineering and ²Neurology,
Department of Veterans Affairs Medical Center and University Hospitals,
Case Western Reserve University, Cleveland, Ohio 44106, U.S.A.

³Neuroscience Laboratory, NASA, Johnson Space Center, Houston, Texas

Running heading: VOR during near viewing

Address Correspondence to:

R. John Leigh, M. D., Department of Neurology, University Hospitals,
11100 Euclid Avenue, Cleveland, Ohio, 44106-5040.

Phone: (216)-421-3224; FAX:(216)-231-3461; E-mail: rj4@po.cwru.edu

Abstract

We studied horizontal eye movements induced by *en-bloc* yaw rotation, over a frequency range 0.2 - 2.8 Hz, in 10 normal human subjects as they monocularly viewed a target located at their near point of focus. We measured gain and phase relationships between eye-in-head velocity and head velocity when the near target was either earth-fixed or head-fixed. During viewing of the earth-fixed near target, median gain was 1.49 (range 1.24 - 1.87) at 0.2 Hz for the group of subjects, but declined at higher frequencies, so that at 2.8 Hz median gain was 1.08 (range 0.68 - 1.67). During viewing of the head-fixed near target, median gain was 0.03 (range 0.01 - 0.10) at 0.2 Hz for the group of subjects, but increased at higher frequencies, so that at 2.8 Hz median gain was 0.71 (range 0.28 - 0.94). We estimated the vestibular contribution to these responses (vestibulo-ocular reflex gain, G_{vor}) by applying transient head perturbations (peak acceleration $> 1,000 \text{ deg/s}^2$) during sinusoidal rotation under the two viewing conditions. Median G_{vor} , estimated $< 70\text{ms}$ after the onset of head perturbation, was 0.98 (range 0.39 - 1.42) while viewing the earth-fixed near target, and 0.97 (range 0.37 - 1.33) while viewing the head-fixed near target. For the group of subjects, 9 out of 10 subjects showed no significant difference of G_{vor} between the two viewing conditions ($p > 0.053$) at all test frequencies. Since G_{vor} accounted for only $\sim 73\%$ of the overall response gain during viewing of the earth-fixed target, we investigated the relative contributions of non-vestibular factors. When subjects viewed the earth-fixed target under strobe illumination, to eliminate retinal image slip information, the gain of compensatory eye movements declined compared with viewing in ambient room light. During sum-of-sine head rotations, while viewing the earth-fixed target, to

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minimize contributions from predictive mechanisms, gain also declined. Nonetheless, simple superposition of smooth-pursuit tracking of sinusoidal target motion could not fully account for the overall response at higher frequencies, suggesting other non-vestibular contributions. During binocular viewing conditions when vergence angle was significantly greater than monocular viewing ($p < 0.001$), the gain of compensatory eye movements did not show proportional change; indeed, gain could not be correlated with vergence angle during monocular or binocular viewing. We conclude that several separate factors contribute to generate eye rotations during sinusoidal yaw head rotations while viewing a near target; these include the VOR, visual-tracking eye movements that utilize retinal image motion, predictive eye movements and, possibly, other unidentified non-vestibular factors. For these experiments, vergence was not an important determinant of response gain.

INTRODUCTION

In order to see the environment clearly, images of stationary objects must be held fairly still on the retina (Carpenter 1991). During natural activities, especially locomotion, head perturbations with predominant frequencies ranging up to 5Hz pose a threat to clear vision (Grossman et al. 1988; Das et al. 1995b; Crane and Demer 1997a). 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 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

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clear vision during natural activities (Leigh and Zee 1999). Nonetheless, other factors contribute to generate eye rotations that compensate for head perturbations. One factor is visually mediated eye movements, such as smooth pursuit, that can compensate for head movements, but act at longer latencies (~100 msec) 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 1963; Barnes 1993; Barnes et al 2000). The contribution of non-vestibular factors can be demonstrated, for example, when subjects attempt to fixate the remembered location of a target in darkness during head rotations, the compensatory response is less than if they actually view the visual target (Barr et al. 1976; Das et al. 2000). In this paper, we refer to the sum of vestibular and non-vestibular factors contributing to eye movements that compensate for head rotations as the enhanced VOR (EVOR). How much non-vestibular factors contribute to EVOR appears to vary according to species and test paradigms.

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). Since the eyes do not lie on the axis of head rotation, they are displaced (translated) as well as rotated when the head turns. Thus, during the near-viewing situation, in order 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 accommodation, the gain of EVOR (eye velocity / head velocity) can exceed 1.5. Prior studies in 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 due to an increment of the internal gain of the VOR (G_{vor}). In humans,

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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). The questions addressed in the present study were: (1) How much does Gvor change during viewing of a near target? (2) what non-vestibular factors contribute to EVOR? (3) What is the behavior if subjects view a near target that is head-fixed (rather than earth-fixed)? Under this last condition, the VOR may be canceled by visual-tracking mechanisms, such as smooth pursuit (Cullen et al. 1991; Huebner et al. 1992). Preliminary results have been published as short reports (Han et al. 2003, 2005).

METHODS

Subjects

We studied 10 normal subjects (4 female, age 24 – 57 year). Five subjects were naive as to 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 - 3.5 D on average), but were able to clearly see 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 rotations were measured using the magnetic search coil technique, with 6-ft (1.8 m) field coils (CNC Engineering, Seattle, WA) that used a rotating magnetic field in the

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horizontal plane and an alternating magnetic field in the vertical plane. Each subject wore a pair of scleral search coils (Skalar Delft, Netherlands) on both eyes to measure gaze angle, and a third coil firmly attached on the forehead to measure angular head rotations. Search coils were calibrated on a protractor device before experiments. The system was 98.5% linear over an operating range of $\pm 20^\circ$ in both horizontal and vertical planes, and the SD of system noise was $< 0.02^\circ$.

Angular head rotations in yaw were applied using a vestibular chair (Templin Engineering, Laytonville, Calif). Subjects sat in a 30-ft-lb vestibular (motor driven) chair in the search coil field, with their heads aligned so that the axis of chair rotations corresponded to the axis of their natural head rotations (close to the mid-interaural point). They wore a modified cycle helmet that contained foam pads to ensure a snug fit for each subject. During the experiment, subjects braced their heads against the headrest of the chair through out the recording session.

Five 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 onto a wall at a viewing distance of 3 m; it was either viewed in ambient light, or flashed at approximately 1 Hz in an otherwise dark room. (2) An earth-fixed near target, consisting of a black cross (1cm_1cm) drawn on a small piece of white tape was attached to a piece of wood, positioned at the eye level of each subject. With one of the subject's eye patched throughout the experiment, the cross target was aligned on the viewing eye at a distance of ~ 12 cm, corresponding to the near point of accommodation for each subject. (3) A head-fixed near target, consisting of a similar black cross attached to a

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rigid plastic rod attached to the modified cycle helmet; the target was aligned on the viewing eye, at a similar distance to the earth-fixed near target. The main experiments were conducted in ambient room light. (4) In control experiments, we used strobe illumination, while four subjects viewed the earth-fixed near target. A flash rate of 4 Hz, with 30 *Fs* flash duration, was used, which has been used previously to eliminate retinal image slip during vestibular experiments (Melvill Jones and Mandl 1981). As a control experiment, we repeated these experiments with a flash frequency of 3 times the rotational head frequency and the same flash duration; in this way the same amount of target position information was available during each rotational cycle. (5) A near, horizontal smooth-pursuit target, consisting of a red laser spot (subtending an angle of 0.7E) was projected onto the black surface of a horizontally positioned board, which lay just below the subject's eye level. The zero-position of target was adjusted so that it was aligned on the viewing eye at the same distance (~ 12 cm) as the earth-fixed and head-fixed near targets. The position of the moving target was under computer control, using a X-Y mirror galvanometer (model CCX-660, General Scanning Watertown, Mass). Pursuit experiments were performed in an otherwise darkened room and subjects' heads were held still through out the testing.

Vestibular stimuli consisted of three types of *en bloc* yaw rotations: (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 deg/sec. At the beginning of each session, each subject was rotated at a frequency of 0.1 Hz with the peak velocity of 15 deg/sec while they monocularly viewed the constantly illuminated stationary laser far target. This procedure served as a calibration check

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and assumed that our subjects continuously foveated on the target and generated compensatory eye movements with a gain of 1.0. A second calibration check was made as each subject was rotated at 0.1 Hz with peak velocity of 15 deg/sec during continuously viewing of the head-fixed near target; assuming continuous foveation of this target, no eye-in-head rotations should be generated. (2) Transient head perturbations: in order to measure dynamic internal VOR level (gain – G_{vor}) and to quantify the vestibular contributions to the overall ocular responses under different viewing conditions, we applied transient head perturbations during sinusoidal rotations when subjects were viewing an earth-fixed or head-fixed near target at the five test frequencies. Since 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, left or right) of the control signal at the peak velocity. Consequently, at each perturbation the chair velocity changed from 15 deg/s to -15 deg/s abruptly, or vice versa, generating a peak acceleration $> 1,000$ deg/s/s; there were a total of nine perturbations in each 40s trial. (3) Sum-of-sines stimuli (pseudorandom rotations): in order to investigate the contribution to the responses of predictable visual tracking eye movements, we applied sum-of-sines stimuli (pseudorandom chair rotations) in 4 subjects during viewing of the earth-fixed near target. The component sine waves had frequencies of 0.38Hz, 1.23Hz, 2.08Hz and 2.63Hz, with peak velocities of 3.3, 5.5, 6.0, and 15.3 deg/sec, 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

Experimental paradigms

There were five main experiments (conducted in five sessions, in which 10 subjects participated) and four control experiments (conducted in three sessions, in which four subjects participated). Each trial lasted 40 sec. 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 Main Experiments 1 and 2. For the other experiments, only the viewing eye was wearing an eye coil, except for the vergence control experiment that required binocular viewing.

Main Experiments:

- (1) Head rotations in darkness (VOR): Subjects were asked to attempt to fixate the remembered location of the flashing far target while they were rotated sinusoidally in the vestibular chair in darkness at the five test frequencies.
- (2) Head rotations viewing the earth-fixed near target (EVOR): Subjects were rotated at each of the five test frequencies under ambient room light illumination.
- (3) Head rotations viewing the head-fixed near target (eye-head tracking EHT): Subjects were rotated at each of the five test test frequencies under ambient room light illumination.
- (4) Head perturbations during EVOR and EHT: Paradigms 2 and 3 were repeated, during which transient head accelerations were delivered.
- (5) Smooth pursuit: Subjects were asked to track the near smooth-pursuit target at each of the five test frequencies in an otherwise darkened room.

Control Experiments:

(6) EVOR under strobe illumination: Paradigm 2 was repeated but under stroboscopic illumination when the flash rate was fixed at 4 Hz for the frequency range of head rotations. In two subjects, paradigm 2 was repeated with a flash rate adjusted to 3 times the rotational head frequency.

(7) EVOR during sum-of-sines rotation: Paradigm 2 was repeated using the sum-of sines stimulus.

(8) EVOR and EHT during binocular viewing: Paradigms 2 and 3 were 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, so that we were able to compare how overall response gain changed when vergence angle differed.

Data collection and analysis

Horizontal and vertical head and gaze (eye-in-space) signals were lowpass filtered using Krohn-Hite Butterworth filters with a bandwidth of 0 - 150 Hz, prior to digitization with 16 bit precision at 465 Hz or 500 Hz. For sinusoidal head stimulations, head and gaze signals were normalized for each subject according to their response to the 0.1 Hz stimulus, based on the assumption they could continuously foveate the visual target. For near smooth pursuit, the target signal at each frequency was normalized for each subject as they followed a 0.2 Hz square wave that stepped a similar amplitude to the sinusoidal stimulus that followed. 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 (bandwidth 0- 40 Hz) (Ramat et al. 1999). Prior to filtering, saccades were removed from the eye and gaze signals via an interactive routine described elsewhere (Das et al. 1995a). We determined the gain of EVOR during head rotations for each trial by calculating the ratio of power spectral density of eye and head velocities at the frequencies of interest, including the sum-of-sines stimuli, using a fast Fourier transform (FFT) method. EHT gain during viewing of a head-fixed near target and smooth pursuit gain during tracking of a near target were calculated by taking the ratio of power spectral density of gaze and target velocities at the frequencies of interest. The phase response was determined by measuring phase angle of these paired signals and recording the phase difference between them at the frequency of interest.

For transient head perturbation stimuli, we defined stimulus onset as when head acceleration exceeded 200 deg/s/s, 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 70 ms epoch following the stimulus onset (Aw et al. 1996). The value of G_{vor} for each response was calculated by equation (1):

$$\frac{V_{eye}}{V_{head}} \quad (1)$$

There were a total of nine head perturbations employed at each frequency of head

rotation, and from these responses we calculated the median value of Gvor for each test condition. As a check of the reliability of this methodology, we also measured the median value of eye and head velocity in the 70 ms following stimulus onset, and used these values to make a separate estimate of Gvor from equation (2):

$$(2)$$

Similar results were obtained, and here we present estimates of Gvor based on measurements by equation (1). Paired statistical comparison were made between responses at each frequency and for each subject by either a paired t-test or, if the distribution of data were not normal, using a Wilcoxon rank-sum test.

RESULTS

General features of responses to sinusoidal rotation

Representative responses from one subject during the experimental conditions 1-3 are shown in Figure 1. Responses during rotation in darkness while viewing a flashing far target are shown in Figure 1A and B; at 0.2 Hz gain is 1.0 and at 2.0 Hz it is 0.9. During viewing of the earth-fixed near target, at 0.2 Hz (C), the subject was able to maintain continuous foveation of the near target, and EVOR gain was 1.49. At 2.0 Hz (D), gain declined to 1.37; thus, at this higher frequency of head rotation, eye movements did not fully compensate for head rotations. During viewing of the head-fixed target, at 0.2 Hz (E), the EVOR gain was 0.01, close to an

ideal gain of zero for this viewing situation. At 2.0 Hz (F), gain increased to 0.39, indicating that the VOR was not completely suppressed or canceled.

Figure 2 summarizes the gain values of responses from ten subjects as they viewed the far target flashed in darkness, the earth-fixed near target, or the head-fixed near target. Note that values for the head-fixed viewing condition (Figure 2 E and F) are plotted as tracking gain (corresponding to 1- EVOR gain), so that these responses can be compared directly with smooth-pursuit behavior, which is described later. At lower frequencies of rotation, the gain of compensatory responses is over 50% greater during viewing of the earth-fixed near target (Figure 2C) than the flashed far target in darkness (Figure 2A). However, at higher frequencies of head rotation, the gain and phase shift of EVOR declined during viewing of the earth-fixed near target, but changed little for the flashed far target in darkness. During viewing of the near head-fixed target, tracking gain declined and phase lags increased for rotational frequencies above 1 Hz.

Head Perturbations: Determination of the vestibular contribution to the responses

Figure 3A and B provide examples of responses to head perturbations as subjects are sinusoidally oscillated while viewing an earth-fixed or head-fixed near target. The value of G_{vor} for these two responses was similar. Figure 4 summarizes median values for ten subjects, for each of the five frequencies, that are plotted as frequency histograms. For comparison, we also plot measurements of G_{vor} during rotation in darkness (Figure 4 C); note that for A and B, G_{vor} values are dynamic VOR gains measured through transient head perturbations during

viewing of a near target, while G_{vor} in Figure 4C are steady state gain values during attempting to fixate a remembered far target in darkness. The range of values was similar for the two near-target visual stimuli, but G_{vor} values were smaller when tested in darkness. Substantial variance of data is evident in these histograms, similar to prior studies (Collewijn and Smeets 2000). In general, lower values of G_{vor} were in myopes who wore spectacle corrections, which is a recognized association (Cannon et al. 1985).

We carried out paired t-tests comparing for each subject and frequency, median gain values for the earth-fixed and the head-fixed target viewing conditions (Figure 4D); there was no significant difference in 9 out of the 10 subjects ($p > 0.053$). One subject showed a significant greater value of G_{vor} during viewing of the earth-fixed target than viewing of the head-fixed target ($p < 0.001$).

We also compared G_{vor} values based on transient head perturbations during viewing of an earth-fixed near target with G_{vor} measured in darkness; for the group of subjects, a paired t-test showed that transient perturbation G_{vor} was significantly greater than G_{vor} measured in darkness for the group of subjects ($p = 0.007$). The median value of G_{vor} during viewing of an earth-fixed target was 0.98 for the group of subjects (range 0.39 – 1.42), whereas the median value of G_{vor} measured in darkness was 0.91 (range 0.54 – 1.04). However, when we compared G_{vor} values based on transient perturbations during viewing of a head-fixed target with G_{vor} measured in darkness, a paired t-test showed no significant difference for the group of subjects ($p = 0.078$). The median value of G_{vor} during viewing of a head-fixed target was 0.97 for the group of subjects (range 0.37 – 1.33).

We made an estimate of the percentage contribution of G_{vor} to the gain of EVOR during viewing of the earth-fixed near target (Figure 5). Overall, G_{vor} only accounted for 73% of the response, less for greater response gains, indicating non-vestibular factors are critical in modulating VOR gain to an appropriate level.

Control Experiments: Identification of non-vestibular factors

Since G_{vor} did not fully account for the observed behavior, in the control experiments we tested four potential factors that could contribute to EVOR gain: retinal image motion; effects of the predictive nature of the stimulus motion; properties of visual tracking eye movements; and vergence angle.

Contribution of retinal slip to the non-vestibular component of the EVOR

In four subjects, we measured the gain of EVOR during viewing of the near earth-fixed target under strobe illumination at 4 Hz with 30 microseconds flash duration, which essentially abolished retinal slip. In Figure 6, gains during normal illumination were plotted as black symbols connected by black lines; gains during strobe illumination were plotted in open symbols connected by dotted lines. The results indicated, however, especially at frequencies of head rotation of 1.0 Hz, each of the four subjects showed higher EVOR gain during normal illumination (when retinal slip information was available) compared to strobe illumination. However, strobe illumination also provides visual cues during each flash, and this result could be explained by the fact that more position cues occurred at lower compared with higher

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rotational frequencies. To test this possibility, in two subjects, we repeated the experiment using a strobe rate which was always three times the frequency of head rotation. In this way, the number of position cues occurred in each cycle was constant for all stimulus frequencies. In Figure 6, these data are plotted as gray symbols connected by gray lines. Both subjects generally showed lower gain values during this strobe stimulus than under ambient illumination. Thus, irrespective of flash frequency, gain was reduced, suggesting that retinal image velocity is used by the brain to optimize the performance of compensatory eye movements, including the higher frequencies of head rotation that we employed.

Contribution of prediction to the non-vestibular component of the EVOR

We employed pseudorandom (sum-of-sines) head rotations in 4 subjects to minimize contributions of predictive eye movements during viewing of the earth-fixed near target. Results were compared with responses to head rotations at each component frequency of sum-of-sines. Figure 7 showed comparison of EVOR gain between sum-of-sines and sinusoidal head rotations at each of the component frequencies. All four subjects showed greater values of the gain of compensatory eye movements for single sine-wave stimuli than for corresponding components of the sum-of-sines stimulus; this was especially true for lower frequencies. These results support the view that predictive mechanisms contribute to the overall EVOR.

Comparison of smooth pursuit and the non-vestibular component of the EVOR

Since retinal image motion and prediction both appear to contribute to the non-

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vestibular component, we formally tested whether visual tracking eye movements, specifically smooth pursuit, could completely account for the non-vestibular contribution that we identified during viewing of the earth-fixed near target. We measured smooth-pursuit responses to a near target moving at same frequencies and velocities as the chair movements that we employed during viewing of the near, earth-fixed target (EVOR). We used a superposition model (Figure 8) to describe the interactions between VOR and non-VOR in accounting for the general behavior that we observed (Figures 1 and 2). Although this model does not incorporate elements to account for the dynamic characteristics of pursuit onset (Krauzlis and Lisberger 1994), we were concerned with steady-state responses to sinusoidal stimuli for both pursuit and EVOR, and assumed that predictive mechanisms would have similar influences under the two conditions. We first used a parameter estimation method implemented in the frequency domain to estimate the optimal values of the non-vestibular parameters (Das et al. 1998; Guild et al. 2001). The estimation procedure is summarized in the Appendix. For each subject we set G_{vor} at the experimentally determined value during paradigm 4 (head perturbations during viewing an earth-fixed near target). Then we estimated optimal values for non-vestibular parameters of the model using the earth-fixed near-viewing EVOR responses at each frequency of head rotations. Model fits of subjects' responses were generally good, with residual values of $< 10\%$ and parameter coefficient of variations of $< 12\%$. The optimal values of the two non-vestibular parameters, for each subject and test frequency, are summarized in Table 1. Finally we compared non-vestibular model's predictions of visual tracking with measured smooth pursuit performance for each subject and frequency. In this way, we could determine if smooth

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pursuit accounted fully for the non-vestibular factor. Figure 9 compares model predictions and measured pursuit performance to a near target in gain (A) and phase shift (B). Model predictions deviated substantially from subjects' pursuit responses at high frequencies (>1.0 Hz), with larger gain and smaller phase shift. A paired comparison of model versus experimental gain values (Figure 9A) showed substantial differences, especially at higher frequencies. This result indicated that smooth pursuit alone can not account for the non-vestibular contributions to the EVOR during viewing of the earth-fixed near target. We also compared the model's predictions of EHT during viewing of a head-fixed near target (Figure 2E and F), making paired comparisons of predicted and observed tracking gain for each frequency and each subjects. The model made much better predictions of gain for EHT (Figure 10B) than for smooth pursuit (Figure 10A), especially at higher test frequencies. Thus, the non-vestibular component differs from smooth pursuit but accounts better for EHT behavior while viewing a head-fixed target.

Experiments to determine if vergence angle is responsible for EVOR adjustment during near viewings

Our main experiments 2 and 3 were carried out as 10 subjects monocularly viewed either an earth-fixed or a head-fixed near target (12cm), but were wearing two eye coils to monitor the vergence angle. For monocular viewing, the only stimuli to convergence are accommodation and the perception of nearness for the viewing eye; there is no visual feedback control of vergence. Figure 11A and B plot the EVOR gain against vergence angle during

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monocular viewing at the two viewing conditions; no relationship between vergence angle and EVOR gain is apparent.

In addition, we repeated the experiments in 5 subjects during which subjects were viewing the earth-fixed or head-fixed near target binocularly. In this way, we were able to investigate how the gain of compensatory eye movements changed when vergence eye movements could be visually controlled. Figure 11C systematically compares the gain of compensatory responses for earth-fixed (EVOR) or head-fixed (EHT) near targets for either monocular or binocular viewing. The vertical dashed line draws the approximate boundary of vergence angle between monocular and binocular viewing. Thus, open symbols correspond to monocular viewing (left side of the vertical dashed line); gray symbols correspond to binocular viewing (right side of the vertical dashed line). The horizontal dashed line shows the approximate boundary of EVOR gain values during viewing an earth-fixed or a head-fixed target. Thus, symbols with thick edge (above the horizontal dashed line) are during viewing of an earth-fixed target; symbols with thin edge (below the horizontal dashed line) are during viewing of a head-fixed target. In general, binocular viewing was associated with greater vergence angles than monocular viewing, but there was no difference in response gain (EVOR or EHT) associated with binocular or monocular viewing. One subject was able to maintain the same vergence angle during monocular and binocular viewing at all test frequencies (data points enclosed by an ellipse indicated by arrows, close to the vertical dashed line on Figure 11C); despite this, his EVOR gain was significantly varied. Thus, our present results do not support the hypothesis that vergence angle determines the gain of eye movements to compensate for

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head rotations during viewing of a near target.

DISCUSSION

We set out to understand better vestibular and non-vestibular mechanisms contributing to eye rotations that compensate for head rotations (EVOR), while viewing a near target. Under such viewing conditions, geometry dictates that eye rotations exceed head rotations by 50% or more, depending mainly on the proximity of the target. Prior studies, especially those employing transient stimuli (Snyder and King 1992; Crane and Demer 1998), indicated that an increase of the gain of the VOR (G_{vor}) was largely responsible for eye rotations exceeding head rotations. Using sine-wave head rotations in humans, we confirmed that, at low frequencies of head rotation, the gain of EVOR was appropriately increased so as to maintain foveation of the earth-fixed near visual target (Figure 1C). However, all subjects showed a decline in gain and increased phase shift at higher rotational frequencies (Figure 2C and D). This result suggested to us that non-vestibular factors, such as visual tracking contributed to the lower frequency response but were unable to sustain their contribution at higher frequencies (Figure 9). By applying head perturbations during sinusoidal stimulation, we were able to confirm that modulation of G_{vor} could not solely account for the gain of compensatory eye movements during near-viewing (Figure 5). In control experiments, we went on to try and identify the relative contributions of vestibular and non-vestibular factors. We also investigated vestibular and non-vestibular factors when subjects viewed a near, head-fixed target, since the contribution of smooth pursuit to this eye-head tracking behavior has been previously

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investigated (Cullen et al. 1991; Huebner et al. 1992). In discussing these findings, first, we summarize current evidence for a vestibular contribution to the increased gain of compensatory eye movements during near-viewing response. Second we will review the possible role played by non-vestibular mechanisms, including visual tracking and predictive mechanisms. Third, we will examine the relationship between vergence angle and EVOR. Finally, we will discuss the relevance of our findings to performance of EVOR during natural activities.

The vestibular contribution to generation of compensatory eye movements during near-viewing

Several studies have identified the geometric factors that determine the relationship between head rotations and eye rotations that perfectly maintain the line of sight on a specified target (Blakemore and Donaghy et al. 1980; Biguer and Prablanc 1981; Virre et al. 1986). These studies also experimentally confirmed in cats, monkeys, and humans that target location, eye-head geometry, and axis of head rotation are important determinants of the response. In the present study, we aligned near visual targets on the horizontal axis of one eye and attempted to rotate subjects' heads about an axis corresponding to their natural head movements; we did not set out to study the effects of eccentric head rotation.

Having defined the geometry and behavior, subsequent research has focused on the neural mechanism for the near-viewing response to head rotation. In monkeys, Virre et al. (1986) demonstrated that the gain of compensatory eye movements during near viewing was ideal even up to frequency of 2.0 Hz. Using transient stimuli, they showed that viewing a near target caused a response that deviated from one during viewing a far target within 20 ms. Virre

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et al. proposed that the brain uses canal and otolithic inputs to generate a central estimate of target location in head coordinates, and this is followed by a transformation into eye movement commands. Snyder and King (1992) confirmed, using transient stimuli that the increased gain associated with near viewing became apparent ~20 ms after the onset of the stimulus.

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, it has been suggested that the vergence-mediated component of the response depends on irregular vestibular nerve afferents (Migliaccio et al. 2004). These results imply that G_{vor} is increased, since visual tracking eye movements act at much longer latency, even when the near target is head-fixed (Huebner et al. 1992; Johnston and Sharpe 1994; Crane and Demer 1999; Gellman et al. 1990). The EVOR has also been tested in humans with sinusoidal head rotations during viewing of a near target. Reported results are similar to the present study (Figure 2C and D): the gain of compensatory ocular responses is appropriately increased at lower frequencies, but declines with increasing phase shifts as test frequency increases (Hine and Thorn 1987; Crane et al. 1997; Paige et al. 1998). Our results of EVOR while viewing of a distant target during sinusoidal rotation (Figure 2A and B) have also been confirmed: EVOR shows little change in gain or phase shift with increasing frequency up to about 4 Hz (Kasteel-van Linge and Maas 1990; Paige et al. 1998). Taken together, these results seem to point to a paradox: responses to transient stimuli indicate an increase of G_{vor} as the mechanism for increased EVOR gain, but responses to sinusoidal stimulation suggest a non-vestibular contribution that deteriorates at

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higher frequencies of head rotation.

In the present study, we present evidence that, for human subjects who are oscillated sinusoidally, Gvor is *not* the main determinant of the increased response. Thus, estimates of Gvor made during viewing of either an earth-fixed or a head-fixed near target were not different in nine out of ten subjects (group medians of 0.98 and 0.97, respectively). The values of Gvor during near viewing were significantly greater than during viewing of a far, flashing target in darkness (group median 0.91), and the data showed variation (Figure 4). Thus, there appears to be a difference on the one hand if 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). This difference has been commented on before by Paige et al. (1998), who noted that during fixation of a head-fixed target, if transient stimuli are used, the response gain is decreased to about 0.7 (Huebner et al. 1992) but if sinusoidal stimuli are used, no such gain decreased is apparent (Paige 1994). Paige et al. (1998) go on to speculate that fixation is degraded during high frequency head rotation, with persistent image slip; they predict that if transient stimuli are applied during high-frequency oscillations, that gain would not be decreased, similar to during sinusoidal stimulation -- a result that we confirm in this study.

When we attempted to estimate the contribution of the Gvor to the overall gain of compensatory eye movements, it was typically about 73%, meaning that non-vestibular factors played a large role. We consider these factors next.

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

The decline in gain of compensatory eye movements during fixation of an earth-fixed target that occurs at higher frequencies (Figure 2C) suggested that an important non-vestibular contribution was visual tracking. Thus, it is well known that when smooth-pursuit eye movements are tested with sinusoidal target motion, gain declines and phase lag increases for stimuli above 1.0 Hz (Lisberger et al. 1981). 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. 2002), which the brain mobilizes to counter delays inherent in the visual system.

In control experiments, we applied two novel approaches to determine if smooth-pursuit mechanisms contributed to EVOR. First, we tested compensatory eye movements under strobe illumination, 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 (Figure 6). This gain decrease was also present when we used a strobe flash rate that was a fixed ratio of head rotational frequency, so that target position information was similar throughout. Second we tested compensatory eye movements using sum-of-sines chair rotations, which minimizes the effects of prediction (Figure 7). We found that the tracking gain was decreased during sum-of-sines stimulation compared with gains for rotations at component sine waves, especially those of lower frequency (Figure 7). Since prediction is known to decline at higher frequencies, the difference between sinusoidal and sum-of-sines stimulation becomes less obvious for higher component frequencies. Taken together,

these two results provided circumstantial evidence that smooth-pursuit eye movements made an important contribution to EVOR during viewing a near target. We then asked the question: Could smooth-pursuit eye movements account for the entire non-vestibular component of the overall response to head rotation?

Inspection of the Bode plots of compensatory eye movements during viewing an earth-fixed near target (Figure 2C and D) and during smooth pursuit (Figure 9A and B) suggests a qualitative difference in the decline of gain and increase of phase shift, with a more abrupt change for smooth pursuit above 1.0 Hz. We attempted to make a more quantitative determination of whether smooth-pursuit could account for all of the non-vestibular component by applying a linear model (Figure 8) and estimating optimal values of non-vestibular parameters at each frequency for each subject during EVOR. We then compared predictions of visual tracking of the non-vestibular part of the model with observed smooth-pursuit performance for the same subject and frequency (Figures 9 and 10A). We found that smooth-pursuit performance was inferior to the model's predictions, especially at higher frequencies, when observed pursuit gain was lower and phase lags greater. Interestingly, the model could predict the behavior of EHT during viewing of a near, head-fixed target better than it could predict smooth pursuit (Figure 10A and B).

What mechanism other than smooth pursuit could account for the balance of the non-vestibular contribution? One possibility is a separate "visual fixation" system, with superior tracking properties at higher test frequencies. A body of behavioral and electrophysiological work supports such a separate entity (Luebke and Robinson 1988; Lynch et al. 1977; Leigh

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and Zee 1999), which may depend on directed visual attention to a stationary target. Such systems may act at shorter latency than smooth pursuit (Gellman et al. 1990). If this is the case, then could the same fixation mechanism account for the model's ability to predict EHT behavior during viewing of a head-fixed near target (Figure 10B)? Prior studies have demonstrated that the latency to onset of EHT in humans is shorter (~ 50 ms) than for smooth pursuit eye movements (~ 100 ms), which might be an important factor (Carl and Gelman 1987; Huebner et al 1992; Johnston and Sharpe 1994; Crane and Demer 1999). An explanation for this two-fold difference in latency is lacking; however, it seems possible that the brain could harness vestibular signals, which act at a latency of < 15 ms, to generate eye movements that either track the head-fixed target (EHT) or enhance the VOR (EVOR). Such a suggestion requires electrophysiological confirmation, although recent studies have identified vestibular nucleus neurons with discharge properties that change according to gaze strategies and whether head movements are active or passive (McRea and Luan 2003; Cullen and Roy 2004).

Vergence angle and the compensatory response during near viewing

During the main experiments, subjects viewed the near visual target monocularly. In this situation, the only stimulus to vergence is accommodation (which is open-loop). We found that vergence angle did not correlate at all with EVOR gain during this testing (Figure 11A and B). In control experiments, subjects viewed the targets binocularly, so that vergence angle was appropriate for near viewing. Under these conditions, four of the subjects showed a greater vergence angle, but the gain of EVOR was not increased compared with monocular viewing. In

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one subject, the vergence angle was similar during monocular and binocular viewing and, in his case, EVOR gain was smaller during binocular viewing. Several prior studies have suggested that vergence angle is an important determinant of EVOR gain. For example, Snyder and King (1992) reported that, 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, Lawrence and King (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”. Studies in humans that have employed sinusoidal head rotations have either not compared monocular and binocular viewing conditions as we did, or have not directly measured vergence angle (Hine and Thorn 1987). Stronger evidence has been presented to indicate that vergence angle determines response gain during sinusoidal stimulation for the translational VOR in monkeys (Wei et al. 2003; Angelaki 2004). Indeed, vergence may have different effects depending on species (e.g., monkey versus human) or stimulus type (transient rotation from stationary start versus sinusoidal rotation). Based on our present study, we suggest that vergence angle is not the actual determinant of EVOR gain in humans during sinusoidal stimulation and viewing of a near target. Instead, our data indicate that monocular visual cues contain most of the information for appropriate adjustment of gain, although binocular vision of the near target may improve EVOR performance. This finding that vergence angle is not correlated with VOR gain during near viewing is consistent with our former study of visually enhanced VOR during mirror viewing (Han et al. 2001).

Possible significance of present results for natural behaviors

How relevant are our findings to natural behaviors? During locomotion, head perturbations have a periodicity to them, which is imposed by stepping frequency (Grossman et al. 1988). Fourier analysis of such head movements shows that, in the yaw plane, predominant frequencies typically in the range 0.5 - 2.0 Hz with harmonic up to 10 Hz. Thus, the range of frequencies employed in the present study are not dissimilar to those occurring during locomotion. Although we may focus our attention on distant objects during walking and running, sometimes it is important to view proximate objects, to avoid collision; under those circumstances EVOR performance during near viewing is important. Our results suggest that, under such circumstance, EVOR is adequate to compensate appropriately for fundamental frequencies, and partially compensates for higher-frequency harmonics. However, some caution is required in extrapolating our results, which concern *en bloc* rotation to the head-free condition of natural locomotion, since electrophysiological studies have identified vestibular nucleus neurons that behave differently during active than passive head rotation (McRea and Luan 2003; Cullen and Roy 2004). Further studies are needed to measure gaze stability, retinal image motion, and visual function during locomotion, as subjects view proximate objects.

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Appendix Method for estimating non-vestibular parameters

We developed a superposition model (Figure 8) to describe the interactions between vestibular and non-vestibular factors during viewing an earth-fixed near target. The non-vestibular factors include all components that could contribute to EVOR modulation during near viewing such as visual tracking and predictions. The transfer function of the model is specified in equation A1:

(A1)

In equation A1, G_{nvor} (internal gain) and T_{nvor} (time constant) are parameters representing non-vestibular factors. They are unknown parameters that need to be estimated. G_{vor} (internal gain) and T_{vor} (time constant) are parameters representing internal vestibular factor. They are known parameters: G_{vor} is measured by applying transient perturbations (acceleration > 1,000 deg/s/s) while viewing of an earth-fixed near target during sinusoidal head rotations (paradigm 4). $T_{vor} = 15$ sec (Cohen et al. 1981). $\hat{\omega}$ is the frequency spectrum, $j = \sqrt{-1}$.

and
 $\hat{\omega}_H$ and $\hat{\omega}_E$ are FFTs
of head
velocity and eye velocity, respectively. $\hat{\omega}_{E_{adj}}$ is the FFT of eye-in-orbit velocity, adjusted by
the equation of Viirre et al. (1986) for near viewing. Thus, the eye rotation (e.g., right eye,
 θ_R) required to maintain target fixation during head rotations (H) are determined by the radius

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of head rotation (R), the distance of the target from the center of head rotation ($R+D$), the interocular distance (I), and the target eccentricity (γ), as quantified by the equation A2:

(A2)

For each subject, we measured I (interocular distance) and D (target distance from the subject's viewing eye) directly.

We then optimized parameters R (radius of head rotation) and γ (target eccentricity) using equation (A2) to curve fit the EVOR responses at 0.2 Hz head rotations when subjects were able to continuously foveate on the earth-fixed near target. The optimal parameters for each subject were then used in the equation in the EVOR model ("Viire's equation" in Figure 8) to account for the retinal image motion induced by head rotation.

To find the optimal values of the non-vestibular parameters G_{nvor} and T_{nvor} , we used a nonlinear least square parameter estimation method implemented in the frequency domain (Das et al 1998). In the frequency domain, the objective function $\phi(B)$ is defined by equation A3:

(A3)

where: $\phi(B)$ is objective function;

B is the unknown parameter vector [G_{nvor} T_{nvor}];

y_i is the FFTs of the experimental data (EVOR);

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$f_i(B)$ is model outputs given by the transfer function equation (A1);

N is the number of points in FFT;

i is the harmonic number.

Each estimates was based on one trial with a total number of 5,000 data points (corresponding to 10 seconds sampling time) collected at each frequency during viewing an earth-fixed near target. Prior to running the procedure, noise and saccades were removed interactively. For each estimates, five different starting points were taken in the range of the possible values. The estimation was repeated until optimization terminated successfully. For each subject, we calculated the mean values of the estimations terminated from five initial values. In addition, we evaluated the coefficient of variation (standard deviation / mean value) for each parameter, and the results are shown in Table 1. We then identified the components of non-vestibular factor in two ways: (1) We compared the non-vestibular model predictions of smooth pursuit with the observed performance during near viewing. In this way, we could identify if smooth pursuit could fully account for the non-vestibular component. (2) We compared the non-vestibular model predictions with the observed EHT performance to identify if the same non-vestibular mechanism could account for the model's ability to predict EHT behavior while viewing of a head-fixed near target during head rotations.

Figure Legends

Figure 1. General features of EVOR responses from one subject during the main experiments 1-

3. A and B are responses during viewing of the far flashed target in an otherwise dark room.

The gain of the response is close to 1.0 at 0.2 Hz and 0.9 at 2.0 Hz. C and D are during *en-bloc*

rotation while viewing an earth-fixed near target. At low frequency (C, 0.2 Hz), the actual

EVOR gain is 1.49 which is close to the ideal gain of 1.50 (calculated from the geometry in

Appendix), indicating that the compensatory eye rotations satisfy the visual demands. At high

frequency (D, 2.0 Hz), the actual EVOR gain is 1.37 which deviates from the ideal gain 1.50 by

9% indicating that the ability to compensate for head rotations is impaired. E and F are during

en-bloc rotation while viewing a head-fixed near target (EHT). At low frequency (E, 0.2 Hz),

the actual EVOR gain is 0.01 which is close to the ideal gain of 0 indicating that VOR is

negated. At high frequency (F, 2.0 Hz), the actual EVOR gain is 0.39 indicating that VOR is

only partially suppressed.

Figure 2. Bode plots summarizing EVOR gain and phase shift, from 10 subjects, during *en-bloc*

rotation during the main experiments 1-3; head rotations are in the frequency range 0.2 – 2.8

Hz.. Plots A and B summarize responses during viewing the flashed far target in darkness.

Note that gain and phase change little over the frequency range tested. Plots C and D are

responses while viewing an earth-fixed; all subjects showed decreased gain (C) and increased

phase shift (D) at high frequencies. For viewing of the head-fixed near target (plots E and F),

tracking gain is plotted with respect to chair stimulus. Subjects showed increased gain (E) and

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increased phase shift (F) at test frequencies above 1.0 Hz.

Figure 3. Illustration of how G_{vor} was estimated from head perturbations during sinusoidal rotation. The onset of transient head perturbation is indicated by the vertical arrow in each figure. Peak velocity measurements are marked with asterisks. Plot A shows an example of the perturbation response as the subject views an earth-fixed near target; in plot B, he views a head-fixed near target. The change in head and eye velocity (inverted to aid comparisons) is similar during the two visual conditions. For plot A, G_{vor} was 1.08; for plot B, G_{vor} was 1.04.

Figure 4. Histogram summarizing distribution of median G_{vor} for each of five test frequencies and ten subjects ($n=50$) when viewing an earth-fixed (A) or a head-fixed (B) near target. Plot C summarizes G_{vor} measured in darkness. Note that for plots A and B, G_{vor} values were measured through transient head perturbations but, in plot D, G_{vor} values are based on steady-state measurements. Plot C summarizes a paired comparison of G_{vor} during viewing of either an earth-fixed or a head-fixed near target; a paired t-test showed no significant difference ($p > 0.053$).

Figure 5. G_{vor} contribution to the overall EVOR response, from 10 subjects, during viewing of an earth-fixed near target at the test frequencies. G_{vor} contribution is fairly constant at about 73% of the total behaviors. For those few points that exceed 100%, the value of G_{vor} exceeded the value of EVOR.

Figure 6. Comparisons of EVOR responses, from four subjects, between normal illumination and strobe illumination during viewing of an earth-fixed near target at the test frequency range. Black symbols connected by black line are responses under normal illumination; open symbols connected by dotted line are during strobe illumination at 4 Hz flash rate; gray symbols connected by gray line are during strobe illumination in which the flash rate is 3 times the rotational frequency. All subjects show higher EVOR gain under normal illumination than both strobe illumination conditions during high frequencies (>1.0 Hz) of head rotations.

Figure 7. Comparison of EVOR responses, from four subjects, between sines and sum-of-sines head rotations while viewing an earth-fixed near target. Filled symbols connected by solid line are during sinusoidal head rotations; open symbols connected by dotted line are during sum-of-sines rotations. All subjects show higher EVOR gain during sinusoidal versus sum-of-sines stimuli, especially at low frequency components, indicating predictions contribute to EVOR adjustment.

Figure 8. The superposition model used to describe the interaction between vestibular and non-vestibular factor when viewing of an earth-fixed near target () during *en-bloc* head rotations in the frequency range 0.2 – 2.8 Hz. The transfer function is given below the model structure. G_{nvor} (internal gain) and T_{nvor} (time constant) are parameters representing non-vestibular factor. They are unknown parameters that need to be estimated. G_{vor} (internal gain)

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and T_{vor} (time constant) are parameters representing internal vestibular system. These are known parameters: G_{vor} is measured from behaviors in darkness. $T_{vor} = 15$ sec (from previous literature). \hat{v} is the frequency spectrum. $j = \sqrt{-1}$ is the FFT of eye-in-orbit velocity (adjusted by Viirre's equation for near viewing). \hat{h} and \hat{e} are FFTs of head velocity and eye velocity, respectively. The summing junction on the left is the algebraic summation of (target velocity), \hat{v} (eye velocity) caused by head velocity \hat{h} , and \hat{e} (the proceeding eye velocity). The result is the retinal error velocity \hat{r} . The summing junction on the right represents the superposition of the internal VOR signal \hat{v}_{vor} and the internal non-VOR signal $\hat{v}_{non-vor}$ calculated by the brain to generate the final eye velocity \hat{e}_{final} .

Figure 9. Comparison between smooth pursuit tracking gain predicted by non-VOR model and the measurement from 10 subjects at each of the test frequencies. Results are summarized in Bode plots – gain (A) and phase shift (B). Experimental responses are shown in circles connected by solid line, model predictions are shown in squares connected by dotted line. Model predictions deviated from subjects' responses gain substantially at high frequencies with higher gain and smaller phase shift. Thus, smooth pursuit can not fully account for non-vestibular components that contribute to EVOR responses during viewing of an earth-fixed near target.

Figure 10. Paired comparison of predicted tracking gain for smooth pursuit (A) and EHT during viewing of the near, head-fixed target during chair rotation (B) versus experimentally

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measured near smooth pursuit responses. Each point corresponds to one test frequency for each subject. Data points that fall on the diagonal line correspond to exact predictions of behavior by the model. Note that the model predicts greater tracking gains for smooth pursuit than were observed, but that model predictions are more accurate for EHT behavior.

Figure 11. Relationship between EVOR gain and vergence angle during yaw head rotations at 0.2 – 2.8 Hz. A and B show results during monocular viewing of an earth-fixed target (A) and a head-fixed target (B), from 10 subjects. C shows the comparison of EVOR gains, from 5 subjects, between monocular and binocular viewing, as well as between earth-fixed target viewing and head-fixed target viewing. Note: in A and B, the shape of symbols codes for frequency; in C, the shape of symbols codes for subject. Also in C, open symbols are monocular viewing (left part of the vertical dashed line); gray symbols are binocular viewing (right part of the vertical dashed line). The vertical dashed line draws the approximate boundary of vergence angle between monocular and binocular viewing. Symbols with thick edge (above the horizontal dashed line) are during viewing of an earth-fixed target; symbols with thin edge (below the horizontal dashed line) are during viewing of a head-fixed target. Horizontal dashed line shows the approximate boundary of EVOR gain between viewing an earth-fixed and a head-fixed target. Note that one subject was able to keep nearly the same vergence angle during monocular and binocular viewing (data enclosed by ellipse indicated by arrow), but the EVOR gain during binocular viewing was slightly smaller.

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