Published in final edited form as:

Exp Brain Res. 2007 February ; 176(4): 575–587.

Effect of unilateral vestibular deafferentation on the initial human vestibulo-ocular reflex to surge translation

Jun-Ru Tian, Akira Ishiyama, and Joseph L. Demer

J.-R. Tian, J. L. Demer, Department of Ophthalmology, University of California, Los Angeles, California, USA. J. L. Demer, Department of Neurology, University of California, Los Angeles, California, USA. A. Ishiyama, Department of Otolaryngology, University of California, Los Angeles, California, USA. J.-R. Tian, J. L. Demer, Jules Stein Eye Institute, David Geffen Medical School at UCLA, 100 Stein Plaza, UCLA, Los Angeles, CA 90095-7002, USA. J. L. Demer, Neuroscience Interdepartmental Program, University of California, Los Angeles, California, USA. J. L. Demer, Bioengineering Interdepartmental Program, University of California, Los Angeles, California, USA

Abstract

Transient whole-body surge (fore-aft) translation at 0.5 G peak acceleration was administered to six subjects with unilateral vestibular deafferentation (UVD), and eight age-matched controls. Subjects viewed eccentric targets to determine if linear vestibulo-ocular reflex (LVOR) asymmetry might lateralize otolith deficits. Eye rotation was measured using magnetic search coils. Immediately before surge, subjects viewed a luminous target 50 cm away, centered or displaced 10° horizontally or vertically. The target was extinguished during randomly directed surges. LVOR gain relative to ideal velocity in subjects with UVD for the contralesional horizontally eccentric target (0.59 ± 0.08 , mean $\pm$ SEM) did not differ significantly from normal (0.50 ± 0.04), but gain for the ipsilesional eccentric target (0.35 ± 0.02) was significantly less than normal (0.48 ± 0.03 , $P < 0.05$). Normal subjects had mean gain asymmetry for horizontally eccentric targets of 0.17 ± 0.03 , but asymmetry in UVD was significantly increased to 0.35 ± 0.05 ($P < 0.05$). Four of six subjects with UVD had maximum gain asymmetry outside normal 95% confidence limits. Asymmetry did not correlate with UVD duration. Gain for 10° vertically eccentric targets averaged 0.38 ± 0.14 for subjects with UVD, insignificantly lower than the normal value of 0.75 ± 0.15 ($P > 0.05$). Surge LVOR latency was symmetrical in UVD, and did not differ significantly from normal. There was no significant difference in response between dark and visible target conditions until 200 ms after surge onset. Chronic human UVD, on average, significantly impairs the surge LVOR for horizontally eccentric targets placed ipsilesionally, but this asymmetry is small relative to interindividual variation.

Keywords

Aging; Otolith; Vergence; Vestibulo-ocular reflex; Unilateral vestibular deafferentation

Introduction

The vestibulo-ocular reflex (VOR) stabilizes gaze to reduce image motion on the retina during head movement. The oculomotor field has considered three degrees of freedom for linear motion: anteroposterior (surge), dorsoventral (bob), and mediolateral (heave) (Ramat et al. 2001; Nuti et al. 2005). The linear vestibulo-ocular reflex (LVOR) is mediated by the otolith

e-mail: jrt@ucla.edu.

Grant Support: United States Public Health Service grants DC02952 and AG09693. JLD was recipient of an Unrestricted Award from Research to Prevent Blindness and is Leonard Apt Professor of Ophthalmology.

organs, sensitive to translation head acceleration. Kinematic considerations dictate that both head motion and target location determine the appropriate LVOR response. Dynamics and kinematics of the LVOR have been studied in detail in monkeys (Paige 1989; Schwarz et al. 1989; Paige and Tomko 1991; Schwarz and Miles 1991; Telford et al. 1996; Angelaki et al. 2000a; McHenry and Angelaki 2000). The human heave LVOR is strongly dependent on context, particularly the target viewed or imagined (Baloh et al. 1988; Skipper and Barnes 1989; Bronstein et al. 1991; Oas et al. 1992; Gianna et al. 1997; Telford et al. 1997; Paige et al. 1998), and exhibits high pass dynamics with a cutoff frequency of ~1 Hz (Paige et al. 1998). The surge LVOR has been studied in monkeys for steady-state motion, and exhibited geometrically appropriate dependencies on target location (McHenry and Angelaki 2000; Paige and Tomko 1991; Seidman et al. 1999). Studies of the surge LVOR have been reported in young (Demer and Tian 2002; Ramat and Zee 2002, 2005; Tian and Demer 2002; Tian et al. 2005, 2006; Tomlinson et al. 2000) and older (Tian et al. 2006) normal humans. However, the effect of unilateral vestibular deafferentation (UVD) on the surge LVOR not previously been investigated in humans.

The LVOR has been considered an intriguing possibility as a test for lateralizing otolith pathology. In both monkeys (Angelaki et al. 2000b) and humans (Bronstein et al. 1991; Aw et al. 2003; Crane et al. 2005), the LVOR in response to heave is symmetrically reduced after chronic UVD, although transient asymmetry was reported after acute UVD in humans (Lempert et al. 1998). The surge LVOR has particularly complex kinematics depending on initial gaze direction. The surge LVOR of monkeys with UVD reportedly exhibited chronic response asymmetries during viewing of horizontally eccentric targets (Angelaki et al. 2000b). The current study was conducted to determine if UVD in humans is associated with asymmetries in the surge LVOR that might indicate the laterality of the otolith deficit.

Methods

Subjects

Six subjects with UVD and eight age-matched normal subjects were studied after giving written informed consent according to a protocol approved by the UCLA Institutional Review Board. The age of subjects with UVD (two females and four males) averaged 53 ± 5 ($\pm$ SD, range 39–70) years, while the average age of normal subjects (four females and four males) was intentionally matched at 54 ± 6 (range 33–70) years. All subjects with UVD had the deficit as the result of either labyrinthectomy or neurectomy of an acoustic neuroma an average of 2.5 ± 1.2 years previously, with a range from 2 weeks to 9 years. Three subjects with UVD had facial palsy after surgery but had no evidence of cerebellar dysfunction or other neurological deficit, and no difficulty in viewing near or far targets binocularly. All normal subjects had normal hearing, and denied otological or neurological disorders. All subjects underwent ophthalmological examination to verify that they were free of ocular disease. Manifest refraction to normal corrected visual acuity of 20/20 or better was performed for each subject prior to the experiment and appropriate individual corrective lenses in plastic frames were provided as necessary for clear viewing of each target distance. Lenses included correction for presbyopia where necessary. All subjects were confirmed to have appropriate vergence for binocular fixation at the target distances employed. Subjects were instructed to omit medication on the day of the experiment.

Stimuli

Transient, whole body linear motion was provided by a pneumatically driven servo (Festo AG, Germany) controlled chair that moved in surge ± 25 cm at peak acceleration of approximately 0.5 G. Subjects were secured via multiple belts in a cushioned, nonmetallic chair mounted on the platform. In order to faithfully couple chair motion to the head, the forehead, temples, malar

regions, and chin of each subject were firmly secured to a chair-mounted head holder by pads and adjustable clamps cushioned with stiff conforming foam (Conforfoam, Aearo Specialty, Indianapolis, IN, USA). To ensure against ocular collision with targets, subjects wore nonrefractive safety spectacles if optical correction was not required. Rightward and upward eye movements were defined as positive. Trials consisted of ten forward and ten aft surges, randomly sequenced and interleaved. Subsequent data analysis was by time averaging of multiple similar trials aligned on the onset (start) of chair translation. Nevertheless, it was considered important that the translational stimuli not be predictable, because a predictable sequence of motions might have promoted anticipatory eye movements. We attempted to limit the effect of prediction on reaction time by randomly varying translation direction, and jittering the otherwise periodic onset of translations by a random interval of up to 150 ms. Each translation lasted about 600 ms and was preceded by a pause for fixation; the sequence of 20 translations for each condition had an overall duration of 66 s.

Measurement apparatus

Angular eye and head position were measured with magnetic search coils, as employed by other investigators and previously described in the current laboratory (Wiest et al. 2001; Tian et al. 2002, 2006). All normal subjects and three subjects with UVD who had normal facial nerve function and corneal sensation wore binocular scleral search coils embedded in an annular suction contact lens (Skalar Medical, Delft, The Netherlands) that adhered to the eye under topical anesthesia with proparacaine 0.5% (Collewyn et al. 1975). Surgery creating UVD frequently sacrifices the facial nerve, resulting in ipsilesional facial weakness including the orbicularis oculi muscle necessary for normal blinking and corneal protection. Three subjects with UVD were identified on ophthalmic examination to have poor blinking function and mild exposure keratopathy of the ipsilesional eye due to facial nerve paresis; these three subjects wore a search coil annulus on contralesional eye only to avoid the possibility of ipsilesional corneal injury due to corneal drying during topical anesthesia in the presence of a search coil annulus. Reference magnetic fields were generated by square wave excitation at different frequencies of two pairs of coils arranged to form sides of a rigid cube affixed to the subject chair so that the eyes were near cube center (Rommel Laboratories, Ashland, MA, USA). The scleral annulus worn on one eye contained a second winding for detection of roll, and was precalibrated on a goniometer. Angles were measured in a Fick coordinate system. Calibration of horizontal and vertical eye positions was to targets on a tangent screen 200 cm away, centered and at 15° horizontal or vertical eccentricity.

Translation of the platform supporting the chair in which subjects were seated was measured using a linear potentiometer. Head acceleration was measured using a piezoelectric linear accelerometer mounted on a bite-mold affixed to the upper teeth to accurately record the head motion. The head accelerometer was regarded as a best indicator for detecting the time of acceleration onset, giving a head acceleration signal used only for determination of LVOR latency. The head holder was mechanically sturdy to minimize decoupling of the head from the chair. The platform position signal was employed to compute geometrically ideal eye position for determination of gain after the response had become well developed between 200 and 300 ms following surge onset where the mechanical noise would not be influential. At this time, platform and head motions were considered equivalent since the small vibrations superimposed on head acceleration due to mechanical deformation of the chair and head holder became physically insignificant relative to the gross displacement of both the platform and the skull.

Measurement conditions

The laboratory was illuminated until 150 ms before surge onset, when darkened except for a luminous target 50 cm distant, formed by the proximal end of a transparent acrylic rod-shaped

light guide 8 mm in diameter, illuminated from the distal end by a red light emitting diode. The light guide was suspended from the laboratory ceiling on a low mass, adjustable, pivoting plastic suspension designed for safety to swing the target away if it approached the subject too closely. Target location was set relative to the subjects' head by reference to a temporarily-projected, low-powered red laser beam normal to the center of the 200 cm distant target screen. Head position was finely adjusted in the head holder until this beam projected at the horizontal midpoint between the eyes, and as close to the vertical mid-position as possible. The target light guide was leveled using an attached bubble indicator, and was then adjusted by reference to the projected laser beam to the height of the interocular midpoint. This position was considered the location of the theoretical "cyclopean eye". The target was either centered on, or displaced relative to the cyclopean eye either 10° horizontally or vertically. Eccentric target positions were measured by projection of the reference laser beam onto calibration marks on a tangent screen attached to the light guide. Since despite these precautions, even tiny variations in linear position of targets relative to the subject can create appreciable angular variation in initial eye position at short viewing distances, analyses determined actual target location from Fick angles determined from search coil recordings obtained immediately prior to motion.

Subjects were instructed to fixate the target whenever visible. Each trial was conducted with the target continuously visible (visually enhanced LVOR, V-LV OR), then repeated with the target extinguished at random intervals of 30–60 ms immediately prior to motion and re-illuminated after return of the chair to center (LVOR). Subjects were continuously reminded to maintain single vision of the target, as it was visible throughout most of the experiment except during the brief surge transients. Binocular fixation of a target 50 cm distant is easy and natural for most subjects, since this is double the usual reading distance.

Data analysis

After hardware filtering at 0–400 Hz by gain and phase matched 8-pole Butterworth filters (Frequency Devices, Haverhill, MA, USA), data was sampled at 16-bit precision, 1,200 Hz using MacEyeball data acquisition software running under LabView (National Instruments, Austin, TX, USA) on Macintosh computers. Analysis was performed using specialized software written in LabView. Individual surges were extracted from the data set and grouped by testing condition and direction. Occasional failures of fixation were identified during fixation periods between the translations. Failures of fixation were indicated by gross errors in eye position relative to the expected geometry, unstable eye position when no stimulus motion was present, and errors in appropriate vergence when this measure was available in all subjects but the three who had facial palsy. Trials contaminated by fixation failures or saccades near surge onset were excluded from further analysis. Trials from individual subjects were aligned to stimulus onset and averaged, so that all time series data represent the instantaneous means of up to ten repetitions. For each subject, target distance, and relative target eccentricity, only data from the eye exhibiting the lower position noise and rate of artifacts was chosen to pool among subjects.

Baseline noise was measured for each trial as its standard deviation (SD) during the interval 50–100 ms before surge onset. Eye position SD prior to surge averaged 0.06 (± 0.01 SEM) deg for normal subjects and 0.09 (± 0.02) deg for subjects with UVD. There was significant intersubject variation within both groups ($P < 0.01$). Noise was not correlated with velocity gain ($P > 0.05$). Noise after motion onset was increased because of unavoidable vibration associated with platform acceleration. Data were low pass filtered in software at 50 Hz for analysis, and 25 Hz for graphic display only.

Motion onset for head and eye were determined by a two-step technique. It is common in LVOR studies to define motion onset as that time when the signal exceeds baseline by three SD (3SD) of noise (Angelaki and McHenry 1999). However, this method frequently exaggerated latency

beyond that obtained by subjective inspection. To avoid this problem, and increase the accuracy, the 3SD criterion was used merely to segment eye and head data into a baseline interval 80 ms immediately prior to reaching the 3SD criterion, and a response interval of 30 ms immediately after attaining the 3SD criterion (Fig. 1). Linear fits were applied to both intervals, and the intersection of these fits was considered the time of motion onset. Head motion onset was determined from the bite mold accelerometer, while eye motion was determined from search coil signals. Latency was taken to be the difference between onset of head and eye motion.

Since they operate on differing physical principles, dynamic responses of the accelerometer and search coil detectors were assumed to differ. The difference was determined and compensated using mechanical simulation (Tian et al. 2002, 2006; Crane et al. 2003; Ramat and Zee 2003). To allow correction for signal-to-noise ratio differences and differing transducer delays, mechanically simulated data was collected using an armature to convert translation to rotation with zero latency. The armature placed a simulated eye search coil near the pivoting end of a rigid rod attached to the linear stimulator at the center of the reference magnetic field, with the opposite end anchored at an earth-fixed target location. Care was taken to insure there was no slack at either the pivot or anchor points so that any chair translation would rotate the mechanically rigged eye coil. When the zero-latency armature data was analyzed using the modified method of 3SD technique with linear fitting, an apparent latency of 20.0 ms was determined. This value was then subtracted from raw latencies before reporting below. Further details of this approach can be found elsewhere (Crane et al. 2003).

Since only central and secondary target positions were employed in this study, and since the required convergence angles for each eye were less than 12° for all target locations, significant kinematic interactions of horizontal, vertical, and torsional components of eye position were not anticipated. For such small angles, the Fick sequence of horizontal and vertical angular positions and velocities are very closely approximated by the search coil angles and their time derivatives without accounting for more complex 3D kinematics (Yakushin et al. 1995), or torsional variations, which recordings from one eye of several subjects demonstrated to be minimal in any case. Since fixation was verified to be stable, both eyes were assumed to foveate the targets prior to surge motion. Based on the angular positions of each eye, measured interpupillary distance, and measured target distance, 3D linear target locations were computed for each trial. Ideal position for each eye was then computed in relation to measured interpupillary distance, and actual target distance and location as a function of time based on platform position determined by the linear potentiometer. Velocity gain of the LVOR was taken as ratio of the slope of actual eye position divided by the slope of ideal eye position in the interval between 200 and 300 ms following surge onset (Fig. 2).

Statistical analyses were performed with the Student's *t* and the chi-square tests. Results were considered significant at $P < 0.05$.

Results

Vergence during surge LVOR

As anticipated, the surge LVOR exhibited a prominent vergence component, converging for forward motion, and diverging for aft motion. Representative vergence eye movements during forward surge are illustrated for a normal subject (a) and a subject with UVD (b) fixing eccentric targets 10° to the right and left (Fig. 3). Observed vergence responses were in the appropriate direction, but were smaller than ideal in every case (Fig. 3). This pattern was typical of both subject groups.

Surge LVOR responses can be considered to be composed of vergence and version components. For clarity, however, subsequent data are presented for each eye individual, since computing vergence and version components would have required subtraction of the horizontal positions of the two eyes with summation of their noise contributions. Subsequent data presented below emphasize the response of each eye relative to its geometrically ideal response.

Transient surge LVOR responses for a centered target

The surge LVOR responses of both normal subjects and subjects with UVD typically consisted of a compensatory VOR slow phase eye movement that depended on target location. With a central target, the response was a convergence during forward surge, and divergence during aft surge. Since there were no systematic differences, velocity gains for fore and aft surges were averaged. There was no significant difference between velocity gains for abduction and adduction in normal subjects, or for the contralesional and ipsilesional eye in three subjects with UVD who underwent binocular recordings. Data from all six subjects with UVD were therefore pooled. Velocity gain for centered targets was 0.29 ± 0.07 (mean $\pm$ SEM) for subjects with UVD, significantly lower than 0.58 ± 0.11 for normal subjects ($P < 0.001$).

Horizontally eccentric targets

Representative horizontal eye position data for horizontally eccentric targets from a normal subject and a subject with UVD are illustrated in Fig. 4 during forward surge. As expected based on geometric considerations, both the ideal and actual LVOR were disconjugate, with the actual response falling short of the ideal for both directions of motion. With the target 10° to the right (relative to the cyclopean eye), responses were dominated by a version component to the right during forward surge (upper panel, Fig. 4), and a version component to the left with target 10° to the left (lower panel, Fig. 4). Normal subjects did not exhibit significant nasal versus temporal asymmetry. Velocity gain averaged over all subjects with UVD was not significantly different from that in normal subjects for both ipsilesional and contralesional eccentric targets. However, within individual subjects with UVD, there was significant gain asymmetry for ipsilesionally versus contralesionally placed targets. Responses of a typical subject with right UVD are demonstrated in Fig. 4. Intra-subject variability is illustrated by error plots of $\pm$ SEM at each time point, and also for a full set of individual trials in Fig. 4b. With the target placed ipsilesionally 10° to the right, LVOR gain was 0.33 before occurrence of a catch-up saccade. Gain for left 10° , contralesionally placed target, was 0.83, not significantly different from normal.

Vestibular catch-up saccades (VCUS, Tian et al. 2000, 2003) occasionally occurred in subjects with UVD, and compensated for the deficient LVOR slow phase (indicated by arrow in Fig. 4b). Mean velocity gain was 0.48 ± 0.03 (SEM) for normal subjects, compared with 0.56 ± 0.08 for the contralesional eccentric target in UVD, and 0.35 ± 0.02 for the ipsilesional eccentric target in UVD. While gain for the ipsilesional target in UVD was significantly lower than for the contralesional target and lower than normal ($P < 0.05$), gain for the contralesional target did not differ significantly from normal ($P > 0.05$).

Gain asymmetry in UVD was defined to be the ratio of the difference in LVOR gains for ipsilesional and contralesional eccentric targets, divided by the sum of these gains. Gain asymmetry was defined in normal subjects to be the absolute value of the difference in LVOR gains for right and left eccentric targets, divided by the sum of the two gains (Fig. 5). Mean gain asymmetry was 0.17 ± 0.03 for normal subjects, significantly less than the mean gain asymmetry of 0.35 ± 0.05 subjects with UVD ($P < 0.05$).

The normal upper limit for gain asymmetry was defined to be the mean + 2SD for normal subjects (indicated by dashed line in Fig. 5). For each subject, overall gain asymmetry was

taken as the greater of the gain asymmetry measured in forward versus aft surges. Four of six subjects with UVD, but only one of eight normal subjects, had maximum gain asymmetry exceeding the normal range (Fig. 5). Despite individual variability, significantly more subjects with UVD exhibited abnormal gain asymmetry than did normal subjects (Chi-square test, $P < 0.01$). However, the degree of gain asymmetry was not correlated with the duration of UVD.

Vertically eccentric targets

Vertical targets were placed either 10° up or 10° down relative to the cyclopean eye. Representative vertical movements of the right eye are illustrated during forward surge for a normal subject (left column, Fig. 6) and for a subject with UVD (right column, Fig. 6). As expected based on geometric considerations, both the ideal and actual LVOR were disconjugate, with the actual response falling short of the ideal for both directions of motion. During forward surge toward a target 10° up, the LVOR was upward for both eyes. During forward surge toward a target 10° down, the LVOR was downward for both eyes. The vertical component of the surge LVOR with vertical eccentric targets was symmetrical even in UVD.

In both normal subjects and subjects with UVD, VCUS were occasionally observed during the surge LVOR with vertically eccentric targets. The velocity gain of the vertical component of the surge LVOR slow phase was 0.38 ± 0.14 for subjects with UVD, not significantly lower than 0.75 ± 0.15 for normal subjects ($P > 0.05$).

Effect of target visibility

Responses with a continuously visible target (V-LVOR) were qualitatively similar to those with the target extinguished immediately before surge motion (LVOR). Both responses were compared to determine the time interval when the contribution of vision became evident. In normal subjects, LVOR and V-LVOR responses were generally identical until about 200 ms after surge onset, when the V-LVOR response became modestly larger (Fig. 7a). In subjects with UVD, VCUS occurred with ipsilesional eccentric targets under both conditions (Fig. 7b).

Velocity gains of the LVOR and V-LVOR were compared quantitatively to determine the effect of target visibility 250 ms after surge onset. With horizontally eccentric targets, velocity gain of normal subjects was 0.66 ± 0.04 ($\pm$ SEM) for the V-LVOR, significantly higher than 0.48 ± 0.03 in LVOR ($P < 0.05$). In subjects with UVD, the velocity gain for ipsilesional eccentric targets was 0.39 ± 0.03 for the V-LVOR, slightly greater than the value of 0.35 ± 0.02 for the LVOR ($P > 0.05$). Velocity gain for contralesional eccentric targets was 0.59 ± 0.08 for the V-LVOR, similar to the value of 0.56 ± 0.08 for the LVOR ($P > 0.05$). There was no significant difference between LVOR and V-LVOR gains in subjects with UVD for either ipsilesional or contralesional eccentric targets ($P > 0.05$). With vertically eccentric targets, there was no significant difference between the horizontal components of the LVOR and V-LVOR in either normal subjects or subjects with UVD ($P > 0.05$). The vertical component of velocity gain with vertically eccentric targets continuously visible was 0.54 ± 0.09 for subjects with UVD, compared with 0.79 ± 0.05 for normal subjects ($P > 0.05$).

Mean gain asymmetry between right and left eccentric targets in normal subjects, and ipsi- and contralesional eccentric targets in subjects with UVD, did not significantly differ for the LVOR versus V-LVOR in either subject group ($P > 0.05$). However, fewer subjects with UVD exhibited abnormal V-LVOR than LVOR gain asymmetry. Asymmetry of the V-LVOR did not differ significantly between normal subjects and subjects with UVD ($P > 0.05$).

Latency of surge LVOR

Trials in which voluntary eye movements such as saccades and blinks occurred were excluded from determination of noise level. Noise was measured as the SD of eye position during the

interval of 50–100 ms before motion onset. Noise averaged 0.06 ± 0.01 (mean $\pm$ SEM) deg for normal subjects, and 0.09 ± 0.02 for subjects with UVD ($P > 0.05$). Noise was not significantly correlated with latency at any target distance and location ($P > 0.05$). The likely effect of noise or low LVOR response would be prolongation of computed latency, so it was assumed that artifacts would bias latency estimates toward higher values.

There was no significant difference between normal subjects and subjects with UVD in the distribution of LVOR latencies. For horizontally eccentric targets, mean LVOR latency was 67 ± 5 ms for normal subjects and 77 ± 4 ms for subjects with UVD ($P > 0.05$). For vertically eccentric targets, mean latency was 67 ± 10 ms for normal subjects, and 74 ± 10 ms for subjects with UVD ($P > 0.05$). For the center target, mean latencies were 76 ± 1 and 90 ± 7 ms, respectively, for normal and subjects with UVD ($P > 0.05$).

With the visible target, there was no significant difference in V-LVOR latency between normal and subjects with UVD. Mean V-LVOR latency for horizontally eccentric targets was 69 ± 10 ms for normal subjects, not significantly different from 84 ± 6 ms for subjects with UVD ($P > 0.05$). Mean V-LVOR latency for vertically eccentric targets was 97 ± 9 ms for normal subjects, not significantly different from 108 ± 9 ms for subjects with UVD. There were no significant latency differences between the surge LVOR and V-LVOR.

Discussion

Vestibular origin of surge LVOR

The surge LVOR theoretically is a pure vergence eye movement when the target is centered between the eyes, with forward surge inducing convergence and aft surge inducing divergence. The surge LVOR includes two components: vergence and versional when the target is displaced eccentrically. The versional movement includes both horizontal and vertical components depending on target eccentricity.

The surge LVOR responses reported here must be of vestibular rather than visual origin since they were not significantly affected by target visibility during the first 200 ms of translation. Kinematics of the surge LVOR responses depend qualitatively and quantitatively on the location of the target visually intended, even when the target is invisible. The magnitude of the surge LVOR correlates with the vergence angle even in darkness (McHenry and Angelaki 2000). However, when visual feedback is available, LVOR can be augmented by fast vergence in maintaining binocular gaze stability (Miles 1998, 1993; Miles and Busetini 1992; Miles et al. 1991).

Possible lateralization of otolith pathology

The neural circuitry underlying surge LVOR kinematics is not completely clear, but may include the otoliths, vestibular nuclei, and cerebellum. Electrical stimulation of both the utricle and saccule has been observed to induce extraocular muscle contractions and eye movements (Fluur and Mellstroem 1971; Isu et al. 2000; Suzuki et al. 1969). Utricular afferents principally project to the rostral part of the descending vestibular nucleus and ventral part of the lateral vestibular nucleus (Imagawa et al. 1995). In cat, both the utricles and saccules project to abducens motoneurons (Uchino et al. 1994, 1997a, Uchino et al. b, c; Kushiro et al. 2000). Cerebellar involvement in the LVOR is suggested by the finding of LVOR impairments in humans with cerebellar dysfunction (Wiest et al. 2001).

Neural circuitry for the AVOR is dominated by contra-lateral excitatory innervation to the contralateral abducens neurons with inhibitory connections to ipsilateral abducens neurons (Baker et al. 1969; Precht et al. 1969; Richter and Precht 1968; Schwindt et al. 1973). In contrast, the LVOR is dominated by excitatory ipsilateral connections from the otoliths to

ipsilateral abducens neurons with inhibitory connections to contralateral abducens neurons (Imagawa et al. 1995; Schwindt et al. 1973; Uchino et al. 1994, 1996, 1997b). Most eye-movement related secondary vestibular neurons are activated not only by the semi-circular canals but also the otoliths (Angelaki et al. 2001; Chen-Huang and McCrea 1999; King et al. 2003; McConville et al. 1996). Most secondary vestibular neurons projecting ipsilaterally to the abducens neurons exhibit a clear modulation during LVOR suppression (Angelaki et al. 2001; King et al. 2003; Meng and Angelaki 2003).

Existence of an ipsilateral otolith–abducens pathway provides the neuroanatomic basis for the possibility of functional lateralization of a unilateral otolith deficit. A study of the surge LVOR in labyrinthectomized monkeys showed significantly reduced gain for ipsilesional relative to contralesional targets (Angelaki 2004). The current study confirms and extends this finding to humans with chronic UVD. However, this data is difficult to interpret in context of oligosynaptic connections between the otoliths and individual extraocular muscles, whose effect of ocular rotations depends on a complex interplay of agonist contraction and antagonist relaxation.

Possible reliability for lateralization of otolith pathology

Reliability is an important consideration for a potential test lateralizing otolith pathology. Asymmetry of the human transient LVOR evoked by heave (Bronstein et al. 1991; Lempert et al. 1998; Crane et al. 2005) or transient eccentric roll (Aw et al. 2003) has not been observed in UVD. The present study demonstrated impairment of the human transient surge LVOR for ipsilesional relative to contralesional horizontal eccentric targets. Factors such as aging have been presumed to symmetrically reduce LVOR gain (Tian et al. 2006), and thus would not create directional asymmetry. The present approach of computing gain asymmetry was designed to compensate for presumably symmetrical individual factors such as aging.

Several possibilities should be considered for occasional absence of surge LVOR asymmetry in UVD. Recent studies in cat have suggested that more than half of the secondary utricular neurons receive inhibitory commissural signals (Bai et al. 2002; Uchino et al. 2001), and two-thirds of secondary saccular neurons receive inhibitory cross-striolar signals (Uchino et al. 1997c). One-third of secondary utricular neurons receive inhibitory cross-striolar signals (Ogawa et al. 2000). Redundant and converging representations of motion direction have been reported in the peripheral vestibular organ (Flock 1964; Lindeman 1969), including hair cells of opposite polarity on opposite sides of the striola (Lindeman 1969) providing excitatory innervation from only one side. This arrangement may enable one labyrinth to drive the LVOR symmetrically. Potential adaptation and compensation following chronic UVD might also reduce LVOR asymmetry. Some subjects with UVD may develop and employ alternative compensatory strategies as proposed for the AVOR (Halmagyi et al. 1990). Five of six subjects with UVD in the current study had some surge LVOR asymmetry. The only subject without surge LVOR asymmetry had UVD of 9 years duration, but there was otherwise no correlation between asymmetry and duration of lesion.

Possible basis for variation of LVOR latency

Reported latency of human LVOR is relatively long and variable. One laboratory reported latency of the human heave LVOR to be 38 ms (Bronstein and Gresty 1988; Bronstein et al. 1991), but the same laboratory reported a 76 ms mean with a range up to 130 ms in another study of subjects aged 22–49 years (Lempert et al. 1997; Gianna et al. 1997). Heave LVOR latency of 45–50 ms was reported in a more recent study by the same investigators in subjects aged 26–50 years (Gianna et al. 2000). A latency of around 20 ms was found during manual heave of the head on the neck in subjects aged 19–36 yrs (Ramat and Zee 2003), but latencies of 30–40 ms were reported in response to whole body heave in subjects aged 27–72 years

(Crane et al. 2003; Tian et al. 2002), and in response to eccentric roll in subjects aged 31–62 years (Aw et al. 2003). Mean minimal surge LVOR latency of 48 ms was reported for subjects of age ranging 19–37 years, with significant inter-subject variability ranging 17–71 ms (Tian et al. 2006). Latencies of 65 ms for convergence, and 33 ms for divergence have been reported for the LVOR during head-on-neck translations in subjects aged 23–57 years (Ramat and Zee 2002). The current study found surge LVOR latency of 67 ± 5 ms for normal subjects of ages 33–70 years, and 77 ± 4 ms for subjects with UVD of ages 39–70 years. However, monkey studies reporting much shorter LVOR latency were predominantly from juvenile monkeys. About 7 ms latency was reported for both eyes during forward surge, and 13 ms for the adducting and 19 ms for the abducting eye during aft surge (Angelaki and McHenry 1999). A latency of 16–18 ms has been reported during free fall (Bush and Miles 1996). At least some of the apparent difference in surge LVOR latency between humans and monkeys is likely to be due to aging effects.

Aging prolongs VOR latency, as consistently reported for the AVOR (Tian et al. 2001), heave LVOR (Tian et al. 2002, 2003), and surge LVOR (Tian et al. 2006). Such age-related prolongation is typical of other reflexes (Warabi et al. 1984, 1986; Sharpe and Zackon 1987; Moschner and Baloh 1994) due to delays in sensory transduction, nerve conduction, and synaptic transmission (Johnson and Miquel 1974; Glick and Bondareff 1979; Nosal 1979; Rogers et al. 1984). The current study avoided this potential confound by employing an age-matched control group.

Potential clinical test for otolith function

In monkeys, relative impairment of the surge LVOR for ipsilesional eccentric targets was reported that persisted for at least several months following unilateral labyrinthectomy (Angelaki et al. 2000b). This finding suggested that the surge LVOR might be a potential test to lateralize deficient otolith function. The current study confirms that chronic human UVD, on average, significantly impairs the surge LVOR for horizontally eccentric targets placed ipsilesionally compared with contralesionally. However, variability of this asymmetry, technical difficulty, and the potentially confounding effect on the LVOR of normal aging, may limit its value as a clinical lateralizing test for otolith function.

References

- Angelaki DE. Eyes on target: what neurons must do for the vestibulo-ocular reflex during linear motion. *J Neurophysiol* 2004;92:20–35. [PubMed: 15212435]
- Angelaki DE, McHenry MQ. Short-latency primate vestibulo-ocular responses during translation. *J Neurophysiol* 1999;82:1651–1654. [PubMed: 10482782]
- Angelaki DE, McHenry MQ, Hess BJM. Primate translational vestibulo-ocular reflexes. I. High-frequency dynamics and three-dimensional properties during lateral motion. *J Neurophysiol* 2000a;83:1637–1647. [PubMed: 10712485]
- Angelaki DE, McHenry MQ, Hess BJM. Primate translational vestibulo-ocular reflexes. IV. Changes after unilateral labyrinthectomy. *J Neurophysiol* 2000b;83:3005–3018. [PubMed: 10805696]
- Angelaki DE, Green AM, Dickman JD. Differential sensorimotor processing of vestibulo-ocular signals during rotation and translation. *J Neurosci* 2001;21:3968–3985. [PubMed: 11356885]
- Aw ST, Todd MJ, McGraive LA, Miglaccio AA, Halmagyi GM. Effect of unilateral vestibular deafferentation on the linear vestibulo-ocular reflex evoked by impulsive eccentric roll rotation. *J Neurophysiol* 2003;89:969–978. [PubMed: 12574473]
- Bai R, Meng H, Sato H, Imagawa M, Sasaki M, Uchino Y. Properties of ultricular-activated vestibular neurons that project to the contralateral vestibular nuclei in the cat. *Exp Brain Res* 2002;147:419–425. [PubMed: 12444473]
- Baker R, Mano N, Shimazu H. Postsynaptic potential in abducens motoneurons induced by vestibular stimulation. *Brain Res* 1969;15:577–580. [PubMed: 5344396]

- Baloh RW, Beykirch K, Honrubia V, Yee RD. Eye movements induced by linear acceleration on a parallel swing. *J Neurophysiol* 1988;60:2000–2013. [PubMed: 3236058]
- Bronstein AM, Gresty MA. Short latency compensatory eye movement responses to transient linear head acceleration: a specific function of the otolith-ocular reflex. *Exp Brain Res* 1988;71:406–410. [PubMed: 3169173]
- Bronstein AM, Gresty MA, Brookes GB. Compensatory otolith slow phase eye movement responses to abrupt linear head motion in the lateral direction. Findings in patients with labyrinthine and neurological lesions. *Acta Otolaryngol Suppl* 1991;481:42–64. [PubMed: 1927432]
- Bush GA, Miles FA. Short-latency compensatory eye movements associated with a brief period of free fall. *Exp Brain Res* 1996;108:337–340. [PubMed: 8815042]
- Chen-Huang C, McCrea RA. Effects of viewing distance on the responses of vestibular neurons to combined angular and linear vestibular stimulation. *J Neurophysiol* 1999;81:2538–2557. [PubMed: 10322088]
- Collewijn H, van der Mark F, Jansen TC. Precise recording of human eye movements. *Vision Res* 1975;15:447–450. [PubMed: 1136166]
- Crane BT, Tian J-R, Wiest G, Demer JL. Initiation of the human heave linear vestibulo-ocular reflex. *Exp Brain Res* 2003;148:247–255. [PubMed: 12520414]
- Crane BT, Tian J-R, Ishiyama A, Demer JL. Initiation and cancellation of the human heave linear vestibulo-ocular reflex after unilateral vestibular deafferentation. *Exp Brain Res* 2005;161:519–526. [PubMed: 15502980]
- Demer JL, Tian J-R. Human surge linear vestibulo-ocular reflex (LVOR) with vertical eccentric targets. *J Vestib Res* 2002;11:253.
- Flock A. Structure of the macula utriculi with special reference to directional interplay of sensory responses as revealed by morphological polarization. *J Cell Biol* 1964;22:413–431. [PubMed: 14203389]
- Fluur E, Mellstroem A. The otolith organs and their influence on oculomotor movements. *Exp Neurol* 1971;30:139–147. [PubMed: 5542195]
- Gianna CC, Gresty MA, Bronstein AM. Eye movements induced by lateral acceleration steps: effect of visual context and acceleration levels. *Exp Brain Res* 1997;114:124–129. [PubMed: 9125457]
- Gianna CC, Gresty MA, Bronstein AM. The human linear vestibulo-ocular reflex to transient accelerations: visual modulation of suppression and enhancement. *J Vestib Res* 2000;10:227–238. [PubMed: 11354436]
- Glick R, Bondareff W. Loss of synapses in the cerebellar cortex of the senescent rat. *J Gerontol* 1979;34:818–822. [PubMed: 512301]
- Halmagyi GM, Curthoys IS, Cremer PD, Henderson CJ, Todd MJ, Staples MJ, D'Cruz DM. The human horizontal vestibulo-ocular reflex in response to high-acceleration stimulation before and after unilateral vestibular neurectomy. *Exp Brain Res* 1990;81:479–490. [PubMed: 2226683]
- Imagawa M, Isu N, Sasaki M, Endo K, Ikegami H, Uchino Y. Axonal projections of utricular afferents to the vestibular nuclei and the abducens nucleus in cats. *Neurosci Lett* 1995;186:87–90. [PubMed: 7777205]
- Isu N, Graf W, Sato H, Kushoro M, Zakir M. Saccauloocular reflex connectivity in cats. *Exp Brain Res* 2000;131:262–268. [PubMed: 10789942]
- Johnson JE, Miquel J. Fine structural changes in the lateral vestibular nucleus of aging rats. *Mech Ageing Dev* 1974;3:203–224. [PubMed: 4374609]
- King W, Tang B, Zhou W. Translation vestibulo-ocular reflex (TVOR) signal processing by monkey vestibular neurons. *Soc Neurosci Abstr* 2003;593.21.
- Kushiro K, Zair M, Sato H, Ono S, Ogawa Y, Meng H, Zhang X, Uchino Y. Saccular and utricular inputs to single vestibular neurons in cats. *Exp Brain Res* 2000;131:406–415. [PubMed: 10803410]
- Lempert T, Gianna CC, Gresty MA, Bronstein AM. Effect of otolith dysfunction: impairment of visual acuity during linear head motion in labyrinthine defective subjects. *Brain* 1997;120:1005–1013. [PubMed: 9217684]
- Lempert T, Gianna CC, Brookes G, Bronstein AM, Gresty MA. Horizontal otolithocular responses in humans after unilateral vestibular deafferentation. *Exp Brain Res* 1998;118:533–540. [PubMed: 9504848]

- Lindeman HH. Studies on the morphology of the sensory regions of the vestibular apparatus. *Eegebnisse Der Anatomie Und Entwicklungs-geschichte* 1969;62:1–113.
- McConville K, Tomlinson RD, Na E-Q. Behavior of eye-movement-related cells in the vestibular nuclei during combined rotational and translation stimuli. *J Neurophysiol* 1996;76:3136–3148. [PubMed: 8930261]
- McHenry MQ, Angelaki DE. Primate translational vestibulo-ocular reflexes. II. Version and vergence responses to fore-aft motion. *J Neurophysiol* 2000;83:1648–1661. [PubMed: 10712486]
- Meng, H.; Angelaki, DE. Soc Neurosci Abstr. 2003. Viewing distance modulation of premotor vestibular neurons; p. 391.9
- Miles, FA. The sensing of rotational and translational optic flow by the primate optokinetic system. In: Miles, FA.; Wallman, J., editors. *Visual motion and its role in the stabilization of gaze*. Elsevier; Amsterdam: 1993. p. 393-403.
- Miles FA. The neural processing of 3-D visual information: evidence from eye movements. *Eur J Neurosci* 1998;10:811–822. [PubMed: 9753150]
- Miles FA, Busetini C. Ocular compensation for self motion: visual mechanisms. *Ann NY Acad Sci* 1992;656:220–232. [PubMed: 1599145]
- Miles, FA.; Schwarz, U.; Busetini, C. The parsing of optic flow by the primate oculomotor system. In: Gorea, A., editor. *Representations of vision: trends and tacit assumptions in vision research*. Cambridge University Press; Cambridge: 1991. p. 185-199.
- Moschner C, Baloh RW. Age-related changes in visual tracking. *J Gerontol* 1994;49:M235–M238. [PubMed: 8056943]
- Nosal G. Neuronal involution during ageing, ultrastructural study in the rat cerebellum. *Mech Ageing Dev* 1979;10:295–314. [PubMed: 480994]
- Nuti D, Mandala M, Broman AT, Zee DS. Acute vestibular neuritis: prognosis based upon bedside clinical tests (thrusts and heaves). *Ann NY Acad Sci* 2005;1039:359–367. [PubMed: 15826989]
- Oas JG, Baloh RW, Demer JL, Honrubia VL. The effect of target distance and stimulus frequency on horizontal eye movements induced by linear acceleration on a parallel swing. *Ann NY Acad Sci* 1992;656:874–876. [PubMed: 1599206]
- Ogawa Y, Kushiro K, Zakir M, Sato H, Uchino Y. Neuronal organization of the utricular macula concerned with innervation of single vestibular neurons in the cat. *Neurosci Lett* 2000;278:89–92. [PubMed: 10643808]
- Paige GD. The influence of target distance on eye movement responses during vertical linear motion. *Exp Brain Res* 1989;77:585–593. [PubMed: 2806449]
- Paige GD, Tomko DL. Eye movement responses to linear head motion in the squirrel monkey. II. Visual–vestibular interactions and kinematic considerations. *J Neurophysiol* 1991;65:1183–1196. [PubMed: 1869912]
- Paige GD, Telford L, Seidman SH, Barnes GR. Human vestibulo-ocular reflex and its interaction with vision and fixation distance during linear and angular head movement. *J Neurophysiol* 1998;80:2391–2404. [PubMed: 9819251]
- Precht W, Richter A, Grippio J. Responses of neurons in cat's abducens nuclei to horizontal angular acceleration. *Pflugers Arch* 1969;309:285–309. [PubMed: 5816077]
- Ramat S, Zee DS. Human responses to vestibular and visual stimuli moving in depth: similarities and differences. *J Vestib Res* 2002;11:297.
- Ramat S, Zee DS. Ocular motor responses to abrupt inter-aural head translation in normal humans. *J Neurophysiol* 2003;90:887–902. [PubMed: 12672783]
- Ramat S, Zee DS. Binocular coordination in fore/aft motion. *Ann NY Acad Sci* 2005;1039:36–53. [PubMed: 15826960]
- Ramat S, Zee DS, Minor LB. Translational vestibulo-ocular reflex evoked by a “head heave” stimulus. *Ann NY Acad Sci* 2001;942:95–113. [PubMed: 11710506]
- Richter A, Precht W. Inhibition of abducens motoneurons by vestibular nerve stimulation. *Brain Res* 1968;11:701–705. [PubMed: 5712019]
- Rogers J, Zornetze SF, Bloom FE. Senescent microstructural changes in rat cerebellum. *Brain Res* 1984;191:23–32. [PubMed: 6199084]

- Schwarz U, Miles FA. Ocular responses to translation and their dependence distance. I. Motion of the observer. *J Neurophysiol* 1991;66:851–864. [PubMed: 1753290]
- Schwarz U, Busetini C, Miles FA. Ocular responses to linear motion are inversely proportional to viewing distance. *Science* 1989;245:1394–1396. [PubMed: 2506641]
- Schwindt PC, Richter A, Precht W. Short latency utricular and canal input to ipsilateral abducens motoneurons. *Brain Res* 1973;60:259–262. [PubMed: 4744767]
- Seidman SH, Paige GD, Tomko DL. Adaptive plasticity in the nasooccipital linear vestibulo-ocular reflex. *Exp Brain Res* 1999;125:485–494. [PubMed: 10323295]
- Sharpe JA, Zackon DH. Senescent saccades. Effects of aging on their accuracy, latency and velocity. *Acta Otolaryngol* 1987;104:422–428. [PubMed: 3434263]
- Skipper JJ, Barnes GR. Eye movements induced by linear acceleration are modified by visualization of imaginary targets. *Acta Otolaryngol (Suppl)* 1989;468:289–293. [PubMed: 2635520]
- Suzuki JI, Tokumasu K, Goto K. Eye movements from single utricular nerve stimulation in the cat. *Acta Otolaryngol (Stockh)* 1969;68:350–392. [PubMed: 5309166]
- Telford L, Seidman SH, Paige GD. Canal–otolith interactions driving vertical and horizontal eye movements in the squirrel monkey. *Exp Brain Res* 1996;109:407–418. [PubMed: 8817271]
- Telford L, Seidman SH, Paige GD. Dynamics of squirrel monkey linear vestibulo-ocular reflex and interactions with fixation distance. *J Neurophysiol* 1997;78:1775–1790. [PubMed: 9325347]
- Tian J-R, Demer JL. Disconjugate surge linear vestibulo-ocular reflex (LVOR) with horizontal eccentric targets. *J Vestib Res* 2002;11:302.
- Tian J-R, Crane BT, Demer JL. Vestibular catch-up saccades in labyrinthine deficiency. *Exp Brain Res* 2000;131:448–457. [PubMed: 10803413]
- Tian J-R, Shubayev I, Demer JL. Impairments in the initial horizontal vestibulo-ocular reflex of older humans. *Exp Brain Res* 2001;137:448–457.
- Tian J-R, Crane BT, Wiest G, Demer JL. Effect of aging on the human initial interaural linear vestibulo-ocular reflex. *Exp Brain Res* 2002;145:142–149. [PubMed: 12110953]
- Tian J-R, Crane BT, Demer JL. Vestibular catch-up saccades augmenting the human transient heave linear vestibulo-ocular reflex. *Exp Brain Res* 2003;151:435–445. [PubMed: 12845509]
- Tian J-R, Crane BT, Demer JL. Human surge linear vestibulo-ocular reflex during tertiary gaze viewing. *Ann NY Acad Sci* 2005;1039:489–493. [PubMed: 15827006]
- Tian J-R, Mokuno E, Demer JL. The initial vestibulo-ocular reflex to surge translation: complex geometric response ablated by normal aging. *J Neurophysiol* 2006;95:2042–2054.
- Tomlinson RD, Cheung R, Blakeman A. Naso-occipital vestibulo-ocular reflex responses in normal subjects. *IEEE Eng Med Biol Mag* 2000;19:43–47. [PubMed: 10738659]
- Uchino Y, Ikegami H, Sasaki M, Endo K, Imagawa M, Isu N. Monosynaptic and disynaptic connections in the utriculo-ocular reflex arc of the cat. *J Neurophysiol* 1994;71:950–958. [PubMed: 8201435]
- Uchino Y, Sasaki M, Sato H, Imagawa M, Suwa H, Isu N. Utriculo-ocular reflex arc of the cat. *J Neurophysiol* 1996;76:1896–1903. [PubMed: 8890302]
- Uchino Y, Sasaki M, Sato H, Imagawa M, Suwa H, Isu N. Utricular input to cat extraocular motoneurons. *Acta Otolaryngol* 1997a;528:44–48.
- Uchino Y, Sato H, Sasaki M, Imagawa M, Ikegami H, Isu N, Graf W. Sacculocollic reflex arcs in cats. *J Neurophysiol* 1997b;77:3003–3012. [PubMed: 9212252]
- Uchino Y, Sato H, Suwa H. Excitatory and inhibitory inputs from saccular afferents to single vestibular neurons in the cat. *J Neurophysiol* 1997c;78:2186–2192. [PubMed: 9325385]
- Uchino Y, Sato H, Zakir M, Kushiro K, Imagawa M, Ogawa Y, Ono S, Meng H, Zhang X, Katsuta M, Isu N, Wilson VJ. Commissural effects in the otolith system. *Exp Brain Res* 2001;136:421–430. [PubMed: 11291722]
- Warabi T, Kase M, Kato T. Effect of aging on the accuracy of visually guided saccadic eye movement. *Ann Neurol* 1984;16:449–454. [PubMed: 6497354]
- Warabi T, Noda H, Kato T. Effect of aging on sensorimotor functions of eye and hand movements. *Exp Neurol* 1986;92:686–697. [PubMed: 3709742]
- Wiest G, Tian J-R, Baloh RW, Crane BT, Demer JL. Otolith function in cerebellar ataxia due to mutations in the calcium channel gene, CACNA1A. *Brain* 2001;124:2407–2416. [PubMed: 11701595]

Yakushin S, Dai M, Suzuki J, Raphan T, Cohen B. Semicircular canal contributions to the three-dimensional vestibulo-ocular reflex: a model-based approach. *J Neurophysiol* 1995;74:2722–2738. [PubMed: 8747227]

Fig. 1.

Determination of LVOR onset. Representative data from right eye of a normal subject undergoing forward surge in darkness while fixing a target 10° up. Forward surge is defined as positive. Rightward and upward eye movements are defined as positive. Head acceleration provided the best indication of initial LVOR timing, since due to chair deformation the platform began to move slightly before the head. Responses have been corrected for transducer dynamics. The LVOR was considered to begin at the time of intersection (*black circle*) of the baseline fit 1 (*solid line*) with the initial response fit 2 (*thick broken line*). A similar intersection (*gray circle*) indicated onset of head acceleration. The difference between onset of head and eye motion was taken to be LVOR latency. *Dotted lines* indicate ± 1 SEM, but error limits were too small to distinguish from measured head acceleration. Data sampled at 1,200 Hz from onset of head translation at time zero, and averaged over ten trials. The *arrow* indicates when eye position exceeded baseline by three times the noise SD marked by *thin broken line*.

Fig. 2.

Determination of LVOR velocity gain. Representative data were derived from right eye of a normal subject who underwent forward surge in darkness while fixing a target vertically eccentric 10° up. Linear regression was taken in the interval between 200 and 300 ms following surge onset. Velocity gain was computed as the ratio of the slope of actual eye position fit (*black straight line*) divided by the slope of ideal eye position (*gray straight line*) computed geometrically from chair position and target location. Actual gain was 0.64 in this record. *Dotted lines* indicate ± 1 SEM. Data sampled at 1,200 Hz from onset of head translation at time zero, and averaged over ten trials. *Arrow* indicates onset of eye movement

Fig. 3. Representative vergence traces from a normal subject (**a**) and subject with right unilateral vestibular deafferentation (UVD) (**b**) during transient forward surge in darkness while fixing a horizontally eccentric target 10° to the right (*solid line*) and to the left (*dashed line*). Ideal vergence varied among subjects, based on differences in interpupillary distance and exact starting eye position relative to the targets; these factors differed slightly between the subjects in **a** and **b**. *Gray lines*: ideal vergence. *Actual vergence*: *black lines*. *Dotted lines* indicate ± 1 SEM. Data sampled at 1,200 Hz from onset of head translation at time zero, and averaged over ten trials

Fig. 4. Representative ideal (gray) and actual (black) eye position from a normal 37-year-old man (left column, **a**, **c**) and a 39-year-old man with right UVD (right column, **b**, **d**) fixing a target 10° to the right (top row, **a**, **b**) and left (bottom row, **c**, **d**) during forward surges in darkness. For geometric symmetry, the target was always contralateral to the eye recorded. Data sampled at 1,200 Hz from onset of head translation at time zero, averaged over ten trials in **a**, **b**, and **d**, and filtered at 25 Hz only for graphic purposes. Dotted lines indicate ± 1 SEM. **a** In the normal subject, slow phase left eye position was slightly less than ideal with the target 10° to the right. **b** In the subject with right UVD, left eye LVOR slow phases were markedly less than ideal, and several vestibular catch-up saccades (VCUSs) occurred. Data for individual trials indicate variability. **c** In the normal subject, actual slow phase right eye position was slightly less than ideal with the target 10° to the left, but symmetrical with the contralateral response in **a**. **d** In the subject with right UVD, the right eye LVOR was similar to normal when the target was located contralesionally 10° to the left; there were no VCUS

Fig. 5.

Maximum gain asymmetry ratio for individual subjects. Gain asymmetry ratio was computed as gain difference divided by gain sum for targets on both sides in normal subjects, and ipsilesional versus contralesional gain in subjects with UVD. For each subject, maximum gain asymmetry was taken as the greater of asymmetries during forward and aft surges. Maximum gain asymmetry was considered abnormal if it exceeded the corresponding mean for normal subjects by two standard deviations (SD, indicated by *dashed line*). Seven out of eight normal subjects exhibited gain asymmetry within the normal range, while the majority of subjects with UVD (four out of six) had gain asymmetry significantly exceeding normal ($P < 0.01$)

Fig. 6.

Representative ideal (gray) and actual (black) eye position from the right eye of a normal 37-year-old man (left column, **a**, **c**) and a 39-year-old man with right UVD (right column, **b**, **d**) fixing a target 10° up (top row, **a**, **b**) and down (bottom row, **c**, **d**) during forward surges in darkness. Data sampled at 1,200 Hz from onset of head translation at time zero, averaged over ten trials, and filtered at 25 Hz only for graphic purposes. Dotted lines indicate ± 1 SEM. **a** In the normal subject, actual eye position was slightly less than ideal eye position with the target 10° up. **b** The LVOR slow phase was similar to normal when target located upward in the subject with UVD. **c** In the normal subject, actual eye position was slightly less than ideal eye position with the target 10° down. Note the symmetry of the response by comparison with **a**. **d** In the subject with right UVD, the LVOR slow phase had slightly smaller amplitude than normal when the target was located downward

Fig. 7.

A representative LVOR (in *dark, black*) and V-LVOR (with *visible target, gray*) response from right eye of a normal subject (**a**) and a subject with right UVD (**b**) when fixing a target 10° to the left during forward surges. In both subjects, the response in darkness (LVOR) was not significantly different from the response of a visible target (V-LVOR) until 200 ms after surge onset, when the V-LVOR became modestly larger. Data sampled at 1,200 Hz from onset of head translation at time zero, averaged over ten trials, and filtered at 25 Hz only for graphic purposes. Dotted lines indicate ± 1 SEM. **a** Normal subject. **b** Subject with right UVD