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Vestibulo-Ocular Reflex to Transient Surge Translation: Complex Geometric Response Ablated by Normal Aging

Jun-ru Tian^{1,3}, Eriko Mokuno⁶, and Joseph L. Demer^{1,2,3,4,5}

1 Department of Ophthalmology, University of California, Los Angeles, California

2 Department of Neurology, University of California, Los Angeles, California

3 Jules Stein Eye Institute, University of California, Los Angeles, California

4 Department of Neuroscience, University of California, Los Angeles, California

5 Department of Bioengineering Interdepartmental Programs, University of California, Los Angeles, California

6 Department of Otolaryngology, Nippon Medical School, Nippon, Japan.

Abstract

The linear vestibulo-ocular reflex (LVOR) to surge (fore-aft) translation has complex kinematics varying with target eccentricity and distance. To determine normal responses and aging changes, 9 younger [age, 28 ± 2 (SE) yr] and 11 older subjects (age, 69 ± 2 yr) underwent 0.5g whole body surge transients while wearing binocular scleral search coils. Linear chair position and head acceleration were measured with a potentiometer and accelerometer. Subjects viewed centered and 10° horizontally and vertically eccentric targets 50, 25, or 15 cm distant before unpredictable onset of randomly directed surge in darkness (LVOR) and light (V-LVOR). Response directions were kinematically appropriate to eccentricity in all subjects, but there were significantly more measurable LVOR and V-LVOR responses (63–79%) in younger than older subjects (38–44%, $P < 0.01$). Minimal LVOR latency averaged 48 ± 4 ms for younger and significantly longer at 70 ± 6 ms for older subjects. In the interval 200–300 ms after surge onset, horizontal LVOR gain (relative to ideal velocity) of younger subjects averaged over all target distances was 0.55 ± 0.04 and was significantly reduced in older subjects to 0.33 ± 0.04 . Horizontal V-LVOR gain was 0.58 ± 0.04 in younger and significantly lower at 0.35 ± 0.06 in older subjects. Vertical gains did not differ significantly between groups. Target visibility had no effect in either group during the initial 200 ms. The LVOR and V-LVOR were augmented by saccades in younger more than older subjects. Aging thus decreases LVOR velocity gain, response rate, and saccade augmentation, but prolongs latency.

INTRODUCTION

The vestibulo-ocular reflex (VOR) stabilizes gaze to reduce image motion on the retina during head movement. The angular VOR (AVOR) is mediated by the semicircular canals, sensitive to head rotation. For rotational axes approximating the eyes, the kinematic requirements for the AVOR are simple: to generate ocular rotation equal in magnitude but opposite in direction to head rotation, irrespective of target distance. Linear motion has three degrees of freedom: mediolateral (“heave,” from nautical terminology), anteroposterior (“surge”), and dorsoventral

Address for reprint requests and other correspondence: J.-R. Tian, Jules Stein Eye Inst., 100 Stein Plaza, UCLA, Los Angeles, CA 90095-7002 (E-mail: jrt@ucla.edu)..

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(“bob”). The linear VOR (LVOR) is mediated by the otolith organs, sensitive to linear head acceleration. Kinematic considerations dictate that not only head translation but also target location determine the appropriate LVOR response. Dynamics and kinematics of the LVOR have been studied in detail in monkeys (Angelaki et al. 2000a; McHenry and Angelaki 2000; Paige 1989; Paige and Tomko 1991; Schwarz and Miles 1991; Schwarz et al. 1989; Telford et al. 1996). While less studied, the human heave LVOR is known to be dependent on context, particularly the target viewed or imagined (Baloh et al. 1988; Bronstein et al. 1991; Gianna et al. 1997; Oas et al. 1992; Paige et al. 1998; Skipper and Barnes 1989; Telford et al. 1997). Most previous LVOR studies in humans have involved sinusoidal heave motion, which revealed high-pass dynamics with a cut-off frequency of ~1 Hz (Paige et al. 1998).

The surge (anteroposterior) LVOR has particularly complex kinematics and has been largely neglected in humans. Depending on initial gaze direction, kinematics dictate that there should be different horizontal and vertical responses, that these responses should differ in each eye, and that responses should be nonlinear functions of instantaneous eye position. For example, with a target centered in front of the subject (Fig. 1A), the ideal surge LVOR is a pure vergence movement whose magnitude increases with target proximity (McHenry and Angelaki 2000); the eyes converge as the head approaches the target, and diverge as the head recedes. For eccentric targets, responses also include horizontal and vertical versional (conjugate) components. During surge toward a target on the right (Fig. 1B), both eyes must rotate to the right, but the more distant left eye must rotate more than the right eye. If the target were located instead on the left, the LVOR for the same head motion would be a leftward eye rotation, greater for the right than the left eye. If the target were centered between the eyes, but displaced upward, the LVOR to forward surge would require horizontal convergence and upward rotation of both eyes. A downward LVOR would be required if the target were displaced downward. The surge LVOR has been studied in monkeys for steady-state motion and shows many of the expected geometric dependencies on target location (McHenry and Angelaki 2000; Paige and Tomko 1991; Seidman et al. 1999). Studies of the human surge LVOR have been reported to targets centered on (Ramat and Zee 2002) and laterally eccentric to (Ramat and Zee 2005) one eye during manually imposed head translation, targets centered between eyes during whole body translation (Tomlinson et al. 2000), and eccentric targets during whole-body translation (Demer and Tian 2002; Tian and Demer 2002; Tian et al. 2005). However, neither the effect on the surge LVOR of varying eccentric target locations and distances nor the effect of normal aging has so far been systematically studied.

Disynaptic connections from the otoliths to oculomotor neurons have been shown neurophysiologically (Blanks et al. 1978; Schwindt et al. 1973), and canal-related secondary vestibular neurons also receive otolith input (Chen-Huang and McCrea 1999). Despite neurophysiologic (Chen-Huang and McCrea 1999) and theoretical (Green and Galiana 1998) arguments that the same vestibular nuclear neurons participate in both AVOR and LVOR, most reports have found heave LVOR latency relatively long and variable. Using electro-oculography and heave acceleration of 0.25g, mean human LVOR latency was reported to be 38 ms (Bronstein et al. 1991), but the same investigators later found a 76-ms mean with a range up to 130 ms (Lempert et al. 1997). A more recent study from the same group used magnetic search coil recording with a peak acceleration of 0.17g, finding a LVOR latency of 45–50 ms (Gianna et al. 2000). Recent search coil recordings during manual heave of the head on neck at 0.4–1.4g showed a latency of around 20 ms (Ramat and Zee 2003), but 30–40 ms during whole body heave (Crane et al. 2003; Tian et al. 2002), and eccentric roll (Aw et al. 2003). Bob LVOR latency in monkeys was 16–18 ms during free fall (Bush and Miles 1996), much closer to AVOR latency. Even the lowest of these values is considerably longer than the 7- to 10-ms latency of the AVOR (Collewijn and Smeets 2000; Crane and Demer 1998).

Age-related degeneration has been identified in the vestibular system, including labyrinthine sensory organs, primary afferent neurons of Scarpa's ganglia, nerve fibers, secondary neurons in the vestibular nucleus complex, the cerebellum, and other CNS areas (Bergstrom 1973; Brody 1976; Engstrom et al. 1974; Hall et al. 1975; Johnsson 1971; Johnsson and Miquel 1974; Lopez et al. 1997; Richter 1980; Rosenhall 1973; Sloane et al. 1989; Torvik et al. 1986). Progressive loss of primary and secondary neurons begins at about age 40 yr (Engstrom et al. 1974; Lopez et al. 1997). Paralleling these anatomic changes, studies using sinusoidal, steady-state yaw rotation at stimulus frequencies <1.0 Hz have found a small decrease in VOR gain with age (Stefansson and Imoto 1986; Van der Laan and Oosterveld 1974; Wall et al. 1984), as well as phase leads at higher stimulus velocities (Baloh et al. 1993; Paige 1992). There are other age-related deficits in the yaw AVOR in response to high acceleration transients. Otherwise healthy older people (age, 58 – 69 yr) exhibited significantly lower gain at $2,800^\circ/\text{s}^2$ whole body acceleration (Tian et al. 2001). While all younger (age, 20 – 32 yr) subjects maintained slow phase VOR eye velocity to values $\geq 200^\circ/\text{s}$ throughout a 250-ms rotation, after 120 ms, older subjects consistently had abrupt declines in slow phase VOR velocity (Tian et al. 2001). Slow phase AVOR latencies were significantly prolonged older subjects. Late AVOR gain modulation with target distance was significantly attenuated in older subjects rotated at higher head acceleration, suggesting an age-related deficit in the otolith contribution to the LVOR (Tian et al. 2001).

Aging is associated with prolongation of latency, reduced sensitivity, and reduced saccadic augmentation of the human heave LVOR (Tian et al. 2002, 2003). However, possible corresponding age-related changes in the surge LVOR have not been studied previously. This study aimed to evaluate the geometric dependencies on horizontally and vertically eccentric target location of the human surge LVOR, as well as the effect of normal aging.

METHODS

Subjects

Consistent with data regarding loss of vestibular structure and function (Lopez et al. 1997), subjects less than age 40 yr were categorized as younger, whereas those more than age 60 yr were considered older. Nine younger and 11 older subjects were studied after giving written informed consent according to a protocol approved by the UCLA Institutional Review Board. Average age of younger subjects (5 females and 4 males) was 28 ± 7 (SD) yr (range, 19 – 37 yr), whereas the average age of older subjects (5 females and 6 males) was 69 ± 5 yr (range, 61 – 76 yr). All 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 before 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 used. 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) controlled platform that moved in surge ± 25 cm at peak acceleration of $\sim 0.5g$. Subjects were secured using multiple belts in a cushioned, nonmetallic chair mounted on the platform. 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 (Confor-foam, Aearo Specialty, Indianapolis, IN). To ensure against ocular collision with targets, subjects wore nonrefractive safety spectacles if

optical correction was not required. Trials for the 50-cm target comprised of 20 directionally randomized surges, interleaved with 10 moving forward and 10 aft. These surges, each lasting about 600 ms, were approximately evenly distributed throughout the overall duration of 66 s, with onset randomly varying from periodic by ≤ 150 ms. After acquisition, data from the directionally randomized trials were sorted by direction and aligned to onset for time locked averaging and analysis. Surge direction was always aft for 25- and 15-cm targets to avoid collision with the subject, so trials consisting of 10 surges of randomly varying onset lasted 33 s for these target distances.

Measurement apparatus

Angular eye and head position were measured with magnetic search coils, as used by other investigators and previously described in the current laboratory (Tian et al. 2002; Wiest et al. 2001). All subjects wore binocular scleral search coils embedded in an annular suction contact lens (Skalar Medical, Delft, The Netherlands) that adhered to the eyes under topical anesthesia with proparacaine 0.5% (Collewyn et al. 1975). 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). The scleral annulus worn on the right 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 the linear potentiometer in the servo loop. Head acceleration was measured using a piezoelectric linear accelerometer mounted on a bite-mold affixed to the upper teeth to faithfully record skull motion. The structure of the chair, as well as most of the subject's body, transiently deformed under the imposed acceleration so that platform position and skull acceleration did not correspond well at movement onset. This effect can be regarded as a vibration transmitted through the platform and subject at acceleration onset. The skull accelerometer was therefore considered to best reflect the time of acceleration onset. The head restraint device was robust, so that in the position domain the head could decouple only minimally from the chair and platform. At relatively long intervals after motion onset, platform and skull motions were regarded as equivalent because the small vibrations that superimposed on head acceleration ultimately cancelled and became physically insignificant relative to the gross displacement of both the platform and the skull. The platform position signal was used to compute geometrically ideal eye position for determination of gain after the response had become well developed. The skull acceleration signal was used only for determination of latency.

Measurement conditions

Each trial consisted of 10 surges in the direction or directions to be tested. For the 50-cm target distance, forward and aft surges were randomly interleaved, whereas only aft surges were used for nearer targets to avert collision with the subject. The laboratory was illuminated until 150 ms before surge onset, when it was darkened except for a luminous target 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 approached too closely by the subject. 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 level and was 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 cardboard screen attached to the light guide. Because, 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 computed actual target location from Fick angles determined from binocular search coil recordings obtained immediately before motion. Subjects were instructed to fixate the target whenever visible. Each trial was conducted with the target continuously visible [visually enhanced LVOR (V-LVOR)] and repeated with the target extinguished at random interval 30 – 60 ms immediately before motion and reilluminated after return of the chair to center (LVOR). Through the intercom, subjects were continuously reminded to maintain single vision of the target, because it was visible throughout most of the experiment except during the brief surge transients.

Data analysis

After filtering at 0 – 400 Hz by gain and phase matched eight-pole Butterworth filters (Frequency Devices, Haverhill, MA), data were sampled at 16-bit precision and 1,200 Hz using the MacEyeball data acquisition software running under LabView (National Instruments, Austin, TX) 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. Failure of binocular fixation was detected by grossly obvious loss of appropriate convergence during fixation between surges. Surges contaminated by artifacts such as saccades near surge onset or failures of binocular fixation were excluded from further analysis. On this basis 26 – 36% of total translations in younger subjects and 50 – 56% of total translations in older subjects were excluded. Consequently, mean data for varying experimental conditions were averaged from <10 of the imposed surges.

To achieve geometric symmetry for gain computation with horizontally eccentric targets, data from right eye viewing the target 10° to the left was pooled with data from the left eye viewing the target 10° to the right. For centered and vertically eccentric targets, data from the right eye only was used for analysis. Data for ab- versus adduction was considered separately only for the computation of latency to permit comparison with other studies. Data for surges from individual subjects during identical testing conditions were aligned to stimulus onset and averaged at each sampled time-point, so that all time series data shown below represent the instantaneous means of ≤ 10 repetitions. For each subject, target distance, and relative target eccentricity, only data from the one eye exhibiting the lower rate of noise and rate of artifacts were chosen to contribute the pooled gain and latency data among subjects. Data were averaged across each subject and test condition, with data points lying >2 SD outside mean values for each group being excluded in exceptional cases. This exclusion did not affect any horizontal data and removed only vertical data from one condition from each of two older subjects.

Baseline noise level was measured for each trial as its SD during the period of 50 – 100 ms before motion onset when the chair remained stationary. Eye position SD averaged $0.08 \pm 0.03^\circ$ (SD) for younger subjects and $0.04 \pm 0.03^\circ$ for older subjects before surge. There was significant intersubject variation within both the younger and older groups ($P < 0.01$), but no significant increase in noise with age. Noise was not correlated with velocity gain ($P > 0.05$). The noise level after motion onset was increased because of unavoidable vibration associated with the acceleration. Data were filtered at 50 Hz for analysis and 25 Hz only for graphic display.

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 noise by 3 SD (Angelaki and McHenry 1999). However, this method frequently exaggerated latency beyond that obtained by subjective inspection of the current data. To avoid this problem, and avert problems caused by noise, the 3 SD criterion was used merely to segment eye and head data into a baseline interval 80 ms immediately before reaching the 3 SD criterion and a response interval of 30 ms immediately after attaining the 3 SD criterion (Fig. 2). 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, whereas eye motion was determined from horizontal or vertical search coil signals. Latency was taken to be the difference between onset of head and eye motions.

Because 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 (Crane et al. 2003; Ramat and Zee 2003; Tian et al. 2002). To allow correction for signal-to-noise ratio differences and differing transducer delays, mechanically simulated data were 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. There was no slack at either the pivot or anchor points so that any chair translation rotated the mechanically rigged eye coil. When the zero-latency armature data were analyzed using the modified method of the 3 SD technique with linear fitting, an apparent latency of 20.0 ms was determined. This value was systematically subtracted from apparent latencies before reporting below. Further details of this approach can be found elsewhere (Crane et al. 2003).

Because only central and secondary target positions were used and convergence angles for each eye were $<12^\circ$, 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 three-dimensional kinematics (Yakushin et al. 1995), or torsional variations, which recordings from the right eye showed to be minimal in any case. Because fixation was verified to be stable, both eyes were assumed to foveate the targets before surge motion. Based on the angular positions of each eye, measured interpupillary distance, and measured target distance, three-dimensional linear target locations were computed for each trial. Ideal position for each eye was computed as a function of time based on platform position determined by the linear potentiometer and so reflects mechanical noise in this signal. Velocity gain of the LVOR was taken as ratio of the slope of actual eye position to the slope of ideal eye position in the interval 200–300 ms after onset of head motion (Fig. 3).

Statistical analyses were performed with the Student's *t*-test, ANOVA, and the χ^2 test. Results were considered significant at $P < 0.05$.

RESULTS

Vergence during surge LVOR

As anticipated, surge LVOR responses exhibited a prominent vergence component: converging for forward motion and diverging for aft motion. Representative vergence eye movements for the 50-cm viewing distance during forward and aft transient surge are shown for a younger subject fixing a centered, 10° right, and 10° up target (Fig. 4). As shown, observed vergence responses were directionally appropriate but were smaller than ideal in every case. This pattern was typical of both younger and older subject groups. Because ideal kinematics of the LVOR

differ for each eye depending on target location, additional data presented below emphasize the response of each eye individually, relative to its ideal response.

Transient surge LVOR responses

The conjugate LVOR of both younger and older subjects typically consisted of a compensatory VOR slow phase eye movement that depended on target location and distance.

Central and horizontally eccentric targets

Representative horizontal eye position data for central and horizontally eccentric targets from a younger subject are shown in Fig. 5 for the 50-cm target distance during forward and aft surge. With the nominally central target (Fig. 5A), the response was a convergence during forward surge and divergence during aft surge. Note that actual target location was $\sim 0.5^\circ$ to the left of center, so that actual responses were not perfectly symmetrical. The asymmetry was considered in determining ideal response. For the centered target 50 cm away, the surge LVOR closely approximated the ideal response for both eyes.

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 (Fig. 5B, *top*), and a version component to the left during aft surge (Fig. 5B, *bottom*). As expected based on geometric considerations, the forward surge LVOR was larger than the aft response. 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 left (relative to the cyclopean eye), the LVOR was dominated by a version component to the left during forward surge (Fig. 5C, *top*) and a version component to the right during aft surge (Fig. 5C, *bottom*). Once again, the forward LVOR was larger than the aft response, and the actual response was suboptimal for both directions.

Vertically eccentric targets

Representative vertical movements of both eyes of a younger subject are shown for the 50-cm target distance in the *left column* of Fig. 6. During forward surge toward a target 10° up (relative to the cyclopean eye), the LVOR was upward for both eyes. During forward surge toward a target 10° down (relative to the cyclopean eye), the LVOR was downward for both eyes. Slightly differing vertical eye positions reflect imperfect interocular target centration, which alters computed vertical angles in the Fick coordinate system. At 50 cm, the vertical LVOR was close to ideal. During aft surge receding from a target 10° up (or down), the LVOR was downward (or upward) for both eyes, but as expected based on geometric considerations, ideal and actual responses were smaller than for forward motion (Fig. 6, *right*).

Effect of target distance

As anticipated from geometric considerations, the surge LVOR was strongly dependent on target distance as well as eccentricity. This is shown in Fig. 7, illustrating the aft LVOR for a target 10° to the left of the cyclopean eye at 15-, 25-, and 50-cm distances. For the right eye, which was more eccentric from the target, the LVOR response increased progressively with target proximity, yet was always short of the ideal response. The left eye was not as eccentric as the right eye from the target and was nearly aligned to the target at the 15-cm distance. The surge LVOR response for the left eye was much smaller than for the right and was nearly absent at the 15-cm distance as geometrically appropriate. In every case, however, the LVOR was less than ideal.

Seven younger subjects completed testing at all three target distances with horizontally eccentric targets, so the effect of target distance could be assessed by ANOVA in this group. Because only three older subjects completed testing at 15 cm, the effect of target distance was

not evaluated statistically in this group. Target distance significantly influenced the velocity gain of younger subjects in both darkness (LVOR; $P < 0.05$) and light (V-LVOR; Table 1), with gain generally declining as target distance diminished. Note that while the absolute magnitude of the LVOR was smaller for remote targets during forward and aft motion, responses were a greater fraction of ideal.

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). Because trials were repeated under both conditions of target visibility, it was possible by comparison to determine the time at which the first contribution of vision was evident. LVOR and V-LVOR responses were identical until around 200 ms after surge onset, after which the V-LVOR in the light became modestly larger.

Velocity gains of the LVOR and V-LVOR were compared quantitatively to determine the effect of target visibility on the responses before 200 ms. There were no significant differences between LVOR and V-LVOR for any experimental condition or either subject group (Table 1; $P > 0.05$). This finding suggests that the LVOR is a nonvisually evoked reflex, although visual augmentation did occur after 200 ms.

Surge LVOR latency

Trials including voluntary eye movements such as saccades and blinks were excluded from determination of noise. Noise was defined as the SD of eye position during the interval 50 – 100 ms before motion onset. Noise averaged $0.08 \pm 0.03^\circ$ (SE) for younger subjects and 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 upward. To determine if this effect was prolonging latency measurements, we performed a linear regression of computed latency against LVOR magnitude at time 200 ms after onset of head motion. This regression was computed for 68 data points, each averaged from 5 to 10 surge translations, constituting data pooled from six younger subjects who could be successfully tested under a wide range of test conditions including target distances of 50, 25, and 15 cm for centered and horizontally and vertically eccentric targets. The broad range of testing conditions was designed to assure substantial physiologic variability in LVOR magnitude so that any possible dependence of latency on magnitude could be shown. Nevertheless, linear regression showed no significant correlation between LVOR latency and magnitude ($R = 0.04$, $P > 0.05$). Notwithstanding this lack of correlation, as a further precaution to avoid overestimation of latency caused by noise, latencies reported below are based on large and reliable responses.

For the 50-cm target distance where both fore and aft surge could be imposed, it was possible to compare possible effects of both surge and duction direction on LVOR latency. To obtain large amplitude LVOR responses, latencies were computed for targets contralateral to the eye under consideration (e.g., a right eccentric target for the left eye). Mean latency was 83 ± 17 and 83 ± 7 ms ($P > 0.05$), respectively, for the abducting and adducting eye during forward surge. Mean latency was 82 ± 7 and 123 ± 8 ms, respectively, for the abducting and adducting eye during aft surge ($P < 0.05$). For vertically eccentric targets, latency for the abducting eye was 147 ± 11 ms, not significantly different from the adducting eye at 103 ± 13 ms.

Reliable determination of latencies required significantly eccentric targets. Because for the two nearer target distances only aft motion could be used, and because for the nearer targets one of the eyes was nearly aligned to a horizontally eccentric target, it was not possible to perform separate analysis of abduction and adduction latencies for nearer targets. Generally there was

no significant latency difference among eccentric target locations and distances. Therefore for analysis of minimal latency, the data were pooled across target locations, and for analysis of mean latency, the data were pooled across target distances and locations.

Minimal surge LVOR latency was obtained for the 15-cm target distance, which produced the largest amplitude LVOR responses. Mean minimal LVOR latency was 48 ± 4 ms, with a range of 17–71 ms. Mean minimal V-LVOR latency was 57 ± 6 ms, with a range of 17–76 ms. There was no significant latency difference between LVOR and V-LVOR.

Horizontal and vertical pooled mean latencies are reported in Table 2 for both subject groups for LVOR and V-LVOR. There was no significant effect of target location or eccentricity on latency nor did LVOR and V-LVOR latencies differ from one another significantly ($P > 0.05$).

Surge LVOR in older subjects

TRANSIENT SURGE LVOR—Transient surge LVOR responses were less consistent and less compensatory in older than younger subjects. Horizontal data from an older subject are shown in Fig. 8, and vertical data are shown in the *right column* of Fig. 6. These records indicate smaller responses than for comparable target conditions in younger subjects (Figs. 5 and 6, *left*). Occasionally, LVOR responses in older subjects were weakly anticompensatory (e.g., center target in Fig. 8).

Older subjects had generally lower surge LVOR amplitudes, often only minimally exceeding noise. Responses distinguishable from noise were evaluated as a percentage of total surges administered for each subject and condition. A response was defined as a directionally appropriate slow phase exceeding baseline noise by ≥ 3 SD and lasting ≥ 30 ms detected by linear fitting during the first 300 ms after surge onset. Visual condition did not influence the generation of detectable responses, because there were no significant differences in the prevalence between LVOR and V-LVOR in either younger subject or older subjects. Data for LVOR and V-LVOR were pooled to compare the younger with the older subject groups. Younger subjects had detectable response rate of 63–79% for the centered, horizontally eccentric, and vertically eccentric targets. Older subjects had significantly lower detectable response rates of 32–44% for each of the three target locations ($P < 0.01$).

Velocity gain of older subjects

Horizontal surge velocity gains to horizontally eccentric targets in older subjects were significantly lower than those in younger subjects for both LVOR and V-LVOR. For surge LVOR, mean velocity gain averaged over all target distances was 0.33 ± 0.04 in older subjects, significantly lower than 0.55 ± 0.04 in younger subjects ($P < 0.01$). Corresponding horizontal values for the V-LVOR were 0.35 ± 0.06 in older subjects and 0.58 ± 0.04 for younger subjects ($P < 0.01$). However, vertical LVOR and V-LVOR velocity gains for vertically eccentric targets did not differ significantly between older and younger subjects ($P > 0.05$). Unlike younger subjects, there was no significant effect of target distance on LVOR or V-LVOR velocity gain in older subjects (Table 1). However, in the older subjects, statistical testing omitted the 15-cm target distance, for which only three older subjects could complete testing. There was no significant difference between surge LVOR and V-LVOR gains for horizontal or vertical responses to horizontally and vertically eccentric targets in either subject group ($P > 0.05$).

Latency for older subjects

In darkness (LVOR), the latency of horizontal eye movement for the horizontally eccentric target was 80 ± 6 ms in older subjects, significantly prolonged in comparison to the 65 ± 4 ms latency of younger subjects ($P < 0.05$; Table 2). In light (V-LVOR), the latency of horizontal eye movement to the horizontally eccentric target was 97 ± 9 ms, significantly prolonged in

comparison to the 61 ± 4 ms latency of younger subjects ($P < 0.05$; Table 2). However, the latency of vertical eye movements for vertical eccentric targets did not significantly differ between older and younger subjects ($P > 0.05$). Data were pooled over all target locations and distances.

Minimal latency was defined as that measured with the 15-cm target distance during aft surges, the condition evoking the largest amplitude LVOR response. Older subjects had significantly increased mean minimal LVOR latency of 70 ± 6 ms with a range of 42–113 ms compared with the value of 48 ± 4 ms for younger subjects ($P < 0.05$). Corresponding minimal V-LVOR latency in older subjects was 73 ± 6 ms with a range of 42–102 ms, significantly increased compared with 54 ± 4 ms in younger subjects ($P < 0.05$).

By all measures computed, there was no significant difference between LVOR and in V-LVOR latency in either subject group.

Vestibular catch-up saccades

Their higher velocities and accelerations easily distinguished LVOR slow phases from vestibular catch-up saccades (VCUSs). Figure 9 shows representative VCUS from a younger subject during aft surge in darkness with the target 25 cm distant and 10° to the left. The VCUSs were in the compensatory direction and augmented the slow phase. Both younger and older subjects made VCUSs in darkness for both centered and eccentric targets. VCUSs typically occurred in the interval 100–200 ms from surge onset, but occasionally <100 ms or >250 ms after onset. Amplitudes of VCUS typically ranged from 1.0 to 2.5° . Younger subjects exhibited horizontal VCUSs to horizontally eccentric targets in $19.1 \pm 2.9\%$ of surges, whereas older subjects exhibited VCUSs in $15.6 \pm 1.6\%$ of surges in darkness with horizontally eccentric targets ($P > 0.05$). For vertically eccentric targets, younger subjects exhibited vertical VCUS in $16.0 \pm 2.2\%$ of surges in darkness, whereas the rate for older subjects was VCUSs of $12.3 \pm 2.9\%$ ($P > 0.05$).

When the target was continuously visible, VCUSs occurred later compared with darkness, typically 150–250 ms from surge onset. Subjects in both groups made VCUSs at almost all target locations and target distances. The amplitude of VCUSs in light ranged from 1.5 to 3.0° . Both younger and older subjects made significantly more VCUSs in light than in darkness. For continuously visible horizontally eccentric targets, younger subjects exhibited horizontal VCUSs in $34.1 \pm 5.0\%$ of surges, whereas older subjects exhibited VCUS in $27.9 \pm 5.0\%$ of surges ($P > 0.05$). For continuously visible vertically eccentric targets, younger subjects exhibited VCUSs in $27.7 \pm 6.3\%$ of surges, whereas older subjects exhibited VCUSs in $24.3 \pm 7.0\%$ of surges ($P > 0.05$).

DISCUSSION

Dynamic kinematics of surge LVOR

The kinematic requirements for compensatory ocular responses to head translation depend on target distance and eccentricity. The surge LVOR ideally is a pure vergence movement when the target is centered between the eyes. Forward surge evokes convergence, and aft surge evokes divergence (Fig. 4), with magnitude increasing with target proximity in inverse proportion to distance. With an eccentric target, the surge LVOR includes both vergence and versional components, with the latter including both horizontal and vertical components depending on target eccentricity. The magnitude of the versional components is also inversely proportional to viewing distance. This study confirms, and extends to humans, findings in monkeys (Hess and Angelaki 2003; McHenry and Angelaki 2000).

Vestibular origin of surge LVOR

It is clear that the surge LVOR responses reported here are of vestibular origin, because they do not differ in darkness or light during the first 200 ms of motion. Nevertheless, kinematics of the surge LVOR depend qualitatively and quantitatively on location of the intended target, even if invisible, and thus correlate with the vergence angle (McHenry and Angelaki 2000). Of course, the LVOR and fast vergence could also cooperate to maintain binocular gaze stability when visual feedback is available (Miles 1993, 1998; Miles and Busetini 1992; Miles et al. 1991). Gain measurements reported here for continuously visible targets (V-LVOR) after 200 ms from surge onset include contributions from both the LVOR and from visual mechanisms. Visual information would be available to make the LVOR response more compensatory after 200 ms under many natural behavioral conditions.

Latency of normal surge LVOR

Noise level has been critical to LVOR latency determination because the weak early physiologic LVOR is difficult to discriminate from baseline noise. Special care was taken here to maximize the signal-to-noise ratio by using the most sensitive recording techniques, magnetic search coils for eye movement, and a linear accelerometer for head movement using relatively high head acceleration (0.5g) to generate a large signal and by maximizing eye movement amplitude with a near target at 15 cm. Systematic error induced by different dynamics between angular eye and linear head motion was compensated (Crane et al. 2003). Latency was determined only for large and presumably reliable LVOR responses. Nevertheless, LVOR latency was variable across subjects and target locations, yet was not correlated with LVOR magnitude. This suggests that LVOR latency may be intrinsically variable, based on physiologic factors.

This study found a mean minimal surge LVOR latency of 48 ms, with significant intersubject variability ranging from 17 to 71 ms. These results are generally concordant with the latencies of 65 ms for convergence and 33 ms for divergence reported for human surge LVOR during head-on-neck translations (Ramat and Zee 2002, 2005), although this study found no consistent latency difference between convergence and divergence. The values of human surge LVOR latency are considerably prolonged compared with the 7-ms latency reported in monkeys during forward motion (Angelaki and McHenry 1999). During aft surge, the monkey was reported to have an LVOR latency of 13 ms for the adducting and 19 ms for the abducting eye (Angelaki and McHenry 1999). The possible significance of duction-dependent variations in surge LVOR latency of monkey, and their seeming absence in humans, is unclear. The current surge LVOR latency values are similar to the mean latency of 42 ms reported for the human heave LVOR (Aw et al. 2003; Bronstein and Gresty 1988; Crane et al. 2003; Gianna et al. 1997; 2000; Tian et al. 2002). Similarity of LVOR latencies for heave and surge in humans suggests similar neural pathways for the two responses.

Magnitude of normal surge LVOR

It has been typically reported that the magnitude of the normal LVOR is suboptimal (Schwartz and Miles 1991; Schwartz et al. 1989; Telford et al. 1997). As a result, LVOR gain is much lower than unity than is the angular VOR (AVOR), typically undercompensatory in humans (Aw et al. 2003; Crane et al. 2003; Ramat and Zee 2003; Tian et al. 2002, 2003) and monkeys (Angelaki et al. 2000a; McHenry and Angelaki 2000; Paige and Tomko 1991; Schwartz and Miles 1991; Schwartz et al. 1989; Telford et al. 1997). This study confirms and extends this finding to the human surge LVOR. The surge LVOR with centered targets was more closely compensatory for ideal eye position than with eccentric targets (Fig. 5), as was the surge LVOR for more remote targets (Table 1). The surge LVOR in younger subjects was more nearly compensatory than in older subjects (Table 1). Near, eccentric targets demand the greatest amplitude surge LVOR response. However, vergence gain during surge with remote targets

has been reported to be overcompensatory during high-frequency sinusoidal translation in monkey (Angelaki and Hess 2001; McHenry and Angelaki 2000). Infinitely remote targets demand no LVOR response at all.

It remains enigmatic why the LVOR for near targets is so undercompensatory. Several explanations seem possible. Perhaps both the AVOR and LVOR are calibrated to function synergistically during natural movements that include phase-locked head translation and rotation (Crane and Demer 1997; Demer and Crane 1998, 2001; Demer and Viirre 1996; Imai et al. 2001; Moore et al. 2001; Raphan et al. 2001). The LVOR may perform better when the AVOR is simultaneously stimulated (Angelaki et al. 2002; Ramat and Zee 2003). Perhaps the LVOR is not optimized for high acceleration surge to a very near target, which after all is the situation naturally associated with imminent collision, and which arguably should evoke aversive or protective responses.

Saccades evoked during surge LVOR

VCUSs (Tian et al. 2000) were frequently observed during surge in both younger and older subjects. These VCUSs comprise saccades moving the eye toward the target and were present in both darkness and light. In view of the markedly suboptimal response of the slow phase surge LVOR, such otolith-triggered saccades seem necessary to assist stabilizing gaze. The VCUSs are of vestibular origin, because they occurred in darkness and in light within the initial 200 ms before the availability of visual feedback. The driving signals are probably based on the otolith afference in context of initial eye position, but not ongoing visual error signals. This finding is consistent with earlier studies indicating that the otoliths can drive saccades to stabilize gaze in normal subjects (Berthoz et al. 1987, 1988; Israël and Berthoz 1989) and consistent with previous findings for the heave (Ramat and Zee 2003; Tian et al. 2003) and the surge LVOR (Demer and Tian 2002; Ramat and Zee 2005; Tian and Demer 2002).

Possible neural circuits underlying surge LVOR kinematics

The neural circuits underlying the surge LVOR remain unclear, but probably include the otoliths, vestibular nuclei, and cerebellum. Eye movements and eye muscle contractions have been evoked by electrical stimulation of both the utricle and saccule (Fluur and Mellstroem 1971; Isu et al. 2000; Suzuki et al. 1969). Utricular afferents principally project into the rostral part of the descending vestibular nucleus and ventral part of the lateral vestibular nucleus (Imagawa et al. 1995). Intracellular recordings from the cat have provided evidence of monosynaptic and disynaptic connections to abducens motoneurons and both the utricles and saccules (Kushiro et al. 2000; Uchino et al. 1994, 1997). The finding of LVOR impairments in patients with cerebellar dysfunction suggests that the cerebellum participates in the LVOR (Wiest et al. 2001). Because they share a similar geometric dependence, surge LVOR circuitry may share similar structures involved in vergence and ocular following pathways such as the dorsolateral pontine nucleus, ventral paraflocculus (Gomi et al. 1998; Kawano and Shidara 1993; Kawano et al. 1990; Kobayashi et al. 1998; Shidara and Kawano 1993) and middle superior temporal cortex (MST) (Duffy 1998).

Effect of aging on surge LVOR

This study showed several age-related impairments in the human surge LVOR: fewer detectable slow phase LVOR responses, smaller amplitude responses, prolonged latencies, and reduced compensatory saccades. These deficits in older subjects are probably secondary to age-related changes in sensory and neural elements of the LVOR pathways (Bergstrom 1973; Brody 1976; Engstrom et al. 1974; Hall et al. 1975; Johnsson 1971; Johnsson and Miquel 1974; Lopez et al. 1997; Richter 1980; Rosenhall 1973; Sloane et al. 1989; Torvik et al. 1986). Morphologic studies have consistently reported attrition of peripheral vestibular neural and sensory cells as a function of age (Engstrom et al. 1974; Johnsson 1971; Richter 1980;

Rosenthal 1973; Sloane et al. 1989), including both hair cells and nerve fibers (Bergstrom 1973; Johnsson 1971; Sloane et al. 1989) beginning at about age 40 and reaching 40% by age 75 yr (Engstrom et al. 1974; Lopez et al. 1997). Lower frequency and velocity steady-state sinusoidal translations probably do not disclose these peripheral age-related changes because the influence of central processing mechanisms, including velocity storage, that could mitigate behavioral deficits. However, the findings in transient translations clearly support such aging deterioration.

Surge LVOR latency has not been previously studied in older subjects, although it has been reported in normal younger subjects (Demer and Tian 2002; Ramat and Zee 2002, 2005; Tian and Demer 2002; Tian et al. 2005; Tomlinson et al. 2000). Prolongation of LVOR latency in older subjects might have been anticipated, because older subjects consistently exhibit prolongations in AVOR (Tian et al. 2001) and heave LVOR (Tian et al. 2002, 2003) latencies, as well as in other reflexes (Moschner and Baloh 1994; Sharpe and Zackon 1987; Warabi et al. 1984, 1986). The slowings presumably reflect delays in sensory transduction, nerve conduction, and synaptic transmission. Aging is also associated with structural attrition of brain neurons and dendritic synapses (Glick and Bondareff 1979; Johnson and Miquel 1974; Nosal 1979; Rogers et al. 1984).

Another finding in this study was that older subjects were less able than younger subjects to use VCUSs for compensation during surge, despite an increase in occurrence of VCUSs when visual input was present. This finding suggests additional age-related changes of vestibular nuclei involved in saccade generation.

Possible clinical test for otolith function?

In monkeys, a relative impairment of the surge LVOR for an ipsilesional eccentric target has been reported to persist for several months after unilateral labyrinthectomy (Angelaki et al. 2000b). This finding has suggested that the surge LVOR might be a potential test to lateralize deficient otolith function. Were such a test to be developed, the potentially confounding effect of normal aging on the surge LVOR would have to be considered. The relatively weak and inconstant properties of the surge LVOR in normal older people would limit its specificity for vestibular disease.

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FIG. 1.

Kinematics of surge vestibulo-ocular reflex (LVOR). For a centered target (A), the ideal LVOR consists of a purely vergence movement greater for a near than remote target. For a horizontally eccentric target (B), the ideal LVOR consists of unequal horizontal rotations in the 2 eyes, greater for the eye more eccentric from the target, but also greater for a near than remote target.

FIG. 2.

Determination of LVOR onset. Representative data from a younger subject undergoing aft transient surge in darkness while fixing a target horizontally eccentric 10° to the left at 15 cm distance. Positive displacement represents aft surge and upward and rightward right eye rotation. Head acceleration provided the best indication of initial LVOR timing, because due to chair deformation, the platform began to move slightly before the head. Responses have been corrected for transducer dynamics. LVOR was considered to begin at time of intersection (black circle) of the baseline fit 1 (solid line) with the initial response fit 2 (broken line). A similar intersection (gray circle) indicated onset of head acceleration. Difference between onset of head and eye motions was taken to be LVOR latency. Data sampled at 1,200 Hz from onset of head translation at *time 0* and averaged over 10 trials. Dotted lines indicate $\pm$ SE. Arrow indicates when eye position exceeded baseline by 3 times the noise SD.

FIG. 3.

Determination of slow phase velocity gain. Representative data were derived from right eye of a younger subject who underwent aft transient surge in darkness while fixing a target horizontally eccentric 10° to the left at 25 cm distance. A linear regression was taken in the interval 200–300 ms after onset of head motion. Velocity gain was measured as the ratio of the slope of the 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. This method avoided significant effects from mechanical vibrations of the linear stimulator. Actual gain was 0.40 in this record. Data were sampled at 1,200 Hz from onset of head translation at *time 0* (determined by the head accelerometer) and averaged over 10 trials. Arrow indicates onset of eye movement.

FIG. 4.

Representative vergence traces from a younger subject during transient forward and aft surge in darkness while fixing a target centered (*top*), horizontally eccentric 10° to the left (*middle*), and vertically eccentric 10° up (*bottom*) for a target distance of 50 cm. Dotted gray lines indicated ideal vergence in both directions. Actual vergence is depicted by solid lines during forward surge and dashed lines for aft surge. Data sampled at 1,200 Hz from onset of head translation at *time 0* and averaged over 10 trials. Arrows indicate onset of eye movement-based head acceleration, corrected for differences in transducer dynamics.

FIG. 5.

Representative ideal (gray) and actual (black) eye positions from a younger subject fixing a 50-cm distant target centered (A) and horizontally eccentric 10° to the right (B) and left (C) during forward (top row) and aft (bottom row) surges in darkness. Data sampled at 1,200 Hz from onset of head translation at time 0, averaged over 10 trials, and filtered at 25 Hz only for graphic purposes. Dotted lines indicate $\pm$ SE. A: centered target. Observed eye position was close to ideal for forward and aft surge. Measurements show that the target was actually slightly to the left of center. Eyes converged during forward motion and diverged during aft motion. B: target 10° to the right. Actual eye position change was greater for forward than aft surge but was less than ideal. Note the disjunctive changes reflecting vergence. C: target 10° to the left. Responses mirrored those in B.

FIG. 6.

Representative actual and ideal eye position data from a younger (*left column*) and an older subject (*right column*) undergoing transient surge in darkness (LVOR) while fixing vertically eccentric 10° up (*top*) and down (*bottom*) targets 50 cm distant during forward surges. Data sampled at 1,200 Hz from onset of head translation at *time 0* and averaged over 10 trials. Data were filtered at 25 Hz only for clarity. While qualitatively similar, responses were consistently smaller in the older than younger subject.

FIG. 7.

Effect of target distance on surge LVOR. Averaged geometric ideal eye position (gray) and actual eye position (black) from right (A) and left eye (B) are plotted for the 50- (solid lines), 25- (dashed lines) and 15- (dotted lines) cm target distances during aft surges while fixing targets horizontally eccentric 10° to the left. Surge LVOR magnitude increased with decreasing target distance for the right eye, and changed little in the left eye, which was nearly aligned with the target.

FIG. 8.

Representative ideal (gray) and actual (black) eye position data from an older subject undergoing transient surge in darkness while fixing a 50-cm distant target nominally centered (A) and horizontally eccentric 10° to the right (B) and left (C) during forward (*top*) and aft (*bottom*) surges. Data sampled at 1,200 Hz from onset of head translation at *time 0* and averaged over 10 trials. Dotted lines indicate $\pm$ SE. Data were filtered at 25 Hz only for illustration. Note that responses are attenuated compared with similar Fig. 5 showing data of a younger subject.

FIG. 9.

Vestibular catch-up saccades (VCUSs, arrows) occurred during aft surge while representative younger subject fixated a target horizontally eccentric 10° to the left at 25 cm. Gray dashed line indicates ideal eye position and black solid line indicates actual eye position. Data sampled at 1,200 Hz from onset of head translation at *time 0*.

TABLE 1

Surge LVOR velocity gain

Target Distance	LVOR		V-LVOR	
	Younger	Older	Younger	Older
Fore50cm	0.75 ± 0.04	0.37 ± 0.06	0.72 ± 0.09	0.30 ± 0.03
Aft 50cm	0.57 ± 0.03	0.42 ± 0.10	0.67 ± 0.04	0.33 ± 0.10
Aft 25cm	0.55 ± 0.06	0.31 ± 0.04	0.53 ± 0.06	0.50 ± 0.15
Aft 15cm	0.32 ± 0.04	0.17 ± 0.05	0.42 ± 0.06	0.30 ± 0.10

Values are means $\pm$ SE. Means and SE of horizontal surge velocity gain for horizontally eccentric targets in darkness (LVOR) and light (V-LVOR). Gain varied significantly with target distance for younger ($P < 0.05$) subjects by ANOVA. Statistical testing for gain variation with target distance was not performed because only 3 older subjects could complete testing for 15-cm targets.

TABLE 2

Pooled mean surge LVOR latency

	Horizontally Eccentric Target, ms		Vertically Eccentric Target, ms	
	LVOR	V-LVOR	LVOR	V-LVOR
Younger	64.6 ± 4.1	60.7 ± 4.1	78.6 ± 10.6	96.1 ± 9.4
Older	80.1 ± 6.4	97.0 ± 8.7	110.8 ± 12.5	120.9 ± 12.5

Values are means ± SE Means and SE of latency for horizontally and vertically eccentric targets during surge in darkness (LVOR) and light (V-LVOR) in younger and older subjects. Data were pooled over all target locations and distances. There were significant differences between younger and older subjects for horizontal but not vertical latency both in darkness and light ($P < 0.05$).