The Linear Vestibulo-Ocular Reflex in Patients with Skew Deviation

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PURPOSE. The linear vestibulo-ocular reflex (LVOR) is mediated primarily by the otolith organs in the inner ear. Skew deviation is a vertical strabismus believed to be caused by imbalance of otolithic projections to ocular motor neurons (disynaptically through the medial longitudinal fasciculus in the brain stem or polysynaptically through the cerebellum). The authors postulated that if skew deviation is indeed caused by damage to these projections, patients with skew deviation would show abnormal LVOR responses.

METHODS. Six patients with skew deviation caused by brain stem or cerebellar lesions and 10 healthy subjects were recruited. All subjects underwent brief, sudden, interaural translations of the head (head heaves) using a head-sled device at an average peak acceleration of $0.42g$ (range, $0.1–1.1g$) while continuously viewing an earth-fixed target monocularly at 15 and 20 cm. LVOR sensitivity (peak rotational eye velocity to peak linear head velocity) and velocity gain (peak actual-to-ideal rotational eye velocities) were calculated for the responses within the first 100 ms after onset of head movements.

RESULTS. LVOR sensitivities and velocity gains in patients were decreased by 56% to 62% in both eyes compared with healthy subjects. This binocular reduction in LVOR responses was asymmetric—the magnitude of reduction differed between eyes by 37% to 143% for sensitivities and by 36% to 94% for velocity gains. There were no differences in response between right and left heaves.

CONCLUSIONS. The binocular, asymmetric reduction in LVOR sensitivity and velocity gain provides support that imbalance in the otolith-ocular pathway is a mechanism of skew deviation. (*Invest Ophthalmol Vis Sci.* 2009;50:168–174) DOI:10.1167/iovs.08-2254

Skew deviation is a vertical strabismus typically caused by damage to the brain stem tegmentum or cerebellum.[1–4] It is often associated with ocular torsion and head tilt, which together constitute the ocular tilt reaction (OTR).[5,6] Lesions affecting the vestibular organ or its nerve,[6–8] diseases of the vestibular nuclei (e.g., lateral medullary syndrome),[9] and lesions in the midbrain[2,10–13] or cerebellum[4] have been reported to cause skew deviation or OTR. Skew deviation has been attributed to asymmetric disruption of projections from otolith receptors to the oculomotor and trochlear nuclei,[2,5,14] largely based on results from stimulation studies and clinical observations. For example, experimental stimulation of different parts of the utricular macula evokes upward, downward, or lateral eye movements.[15] Stimulating the utricular nerve in the cat produces eye movements similar to those seen in OTR: the ipsilateral eye elevates, the contralateral eye depresses, and the upper poles of both eyes roll contralaterally.[16] A comparable reaction also occurs with stimulation of the interstitial nucleus of Cajal in monkeys[17] and humans,[18] but the elevating eye is on the opposite side of interstitial nucleus of Cajal stimulation, and the head tilts and the eyes roll toward the side of stimulation.

More than a quarter century has passed since imbalance of the otolith-ocular reflex was first proposed to be responsible for skew deviation[2] and OTR.[5] However, surprisingly few studies have quantitatively documented abnormal otolith functions in these patients.[4,19,20] The otolith organs (utricle and saccule) mediate the linear or translational vestibulo-ocular reflex (VOR) during translational motion of the head and ocular counterroll during static head tilt. We demonstrated previously that patients with cerebellar skew deviation have reduced static torsional VOR (counterroll) gains that are asymmetric, with the magnitude of reduction differing between eyes and between the direction of head roll.[4] Patients with autosomal dominant spinocerebellar ataxia have decreased LVOR sensitivity.[21] However, it is unclear whether the observed reduction in linear VOR (LVOR) response was causally related to the underlying diffuse cerebellar process or to skew deviation, which was not documented in a previous study.[21] In this study, we investigate the LVOR during brief, sudden, interaural translations of the head (head heaves) in patients with well-documented skew deviation caused by discrete lesions in the brain stem or cerebellum, or both. We postulate that if skew deviation is indeed caused by imbalance of otolithic projections to ocular motor neurons (disynaptically through the medial longitudinal fasciculus in the brain stem or polysynaptically through the cerebellum), these patients would show abnormal LVOR responses.

METHODS

Patients with skew deviation were recruited from the Neuro-Ophthalmology Unit at the University Health Network in Toronto, Canada. Detailed ophthalmic and neurologic examinations were performed. Age of onset, duration of diplopia, and associated neurologic symptoms and signs were recorded. The magnitude of vertical and horizontal strabismus was measured by the prism cover test. Ocular torsion was measured using double Maddox rods. Patients wore a prism to

neutralize their strabismus, and the near point of convergence (NPC) was measured by placing a fixation target 40 cm away from the nasion. The fixation target was then moved toward the eyes until one eye lost fixation. The NPC was recorded as the distance at which fixation loss occurred. Appropriate tests were performed to rule out ocular motor nerve palsy, myasthenia gravis, thyroid ophthalmopathy, or other orbital diseases. Axial and sagittal T1- and T_2-weighted MR images with gadolinium enhancement (slice thickness, 5 mm) were obtained.

Skew deviation was diagnosed as follows[1]: a vertical misalignment (with or without head tilt or fundus torsion), the pattern of which was inconsistent with that found in palsy of one or more cyclovertical muscles[2]; positive findings on MR imaging; and[3] presence of neurologic symptoms and signs. Patients with a history of diplopia or strabismus dating to infancy or early childhood or previous surgery for strabismus were excluded.

Six patients were recruited. Their clinical characteristics are shown in Table 1. The mean age ($\pm$ SD) was 39 $\pm$ 19 years (median, 32 years; range, 22-71 years). Five were women. The mean duration of diplopia and neurologic symptoms (at the time of eye movement recording) was 12 $\pm$ 8 months (median, 11 months; range, 2-16 months). Three had abnormal NPC (patient [P]1, P3, P5). One patient had a lesion in the brain stem (P2), one had a lesion in the cerebellum (P5), and two had lesions in both the brain stem and the cerebellum (P1, P6). Two other patients with known multiple sclerosis (P3, P4) had unilateral internuclear ophthalmoplegia, indicating lesions in the brain stem. MRI revealed multiple loci of periventricular demyelinations.

Ten healthy subjects without any vestibular, neurologic, or eye diseases participated. The mean age was 39 $\pm$ 14 years (median, 32 years; range, 20-60 years). Three were women. The mean NPC was 8.9 $\pm$ 0.9 cm. The research protocol was approved by the University Health Network Ethics Committee and adhered to the tenets of the Declaration of Helsinki. Informed consent was obtained from all subjects.

Testing of the Subjective Visual Vertical

Subjects sat in a natural upright position in the dark during monocular viewing of a dimly illuminated straight line. The line was mounted on a linear rotating potentiometer and was located 1 m away in the subject's midsagittal plane at eye level. Starting from a random nonvertical position, the examiner slowly rotated the line toward the earth-vertical and stopped when the subject perceived the line as vertical, as indicated verbally to the examiner. The signal from the potentiometer was amplified, digitized at 1 kHz, and stored for later analysis. Results of six trials were averaged.

The Head Heave Test

Viewing Condition. With one eye covered, subjects fixated monocularly on a target at two distances (15 and 20 cm) while translating along the interaural axis. The viewing distance was measured from the lateral canthi of the eyes, a landmark that approximates the location of the center of rotation of the globe. The target consisted of a single letter "e" of optotype size 3/32″ (12-point type size), which remained visible under ambient illumination throughout the trial. The experiment was repeated with the other eye covered. Binocular viewing was not performed so as to ensure that patients were fixating on the target, not on the second image that results from strabismus. The vergence angle and "effective" viewing distance were calculated trigonometrically for each subject, based on the individual's interpupillary distance and baseline positions of the eyes at a viewing distance of 2 m.

The Stimuli. Using a head-sled device we validated in a previous study,[22] head heave impulses were manually delivered to the head along the interaural axis to produce a steplike change of head position. Peak accelerations ranged from 0.1 to 1.1g. Stimuli were unpredictable in direction and timing to prevent subjects from making anticipatory eye movements. Before each trial, the head was recentered within a

window of less than 5 mm. On average, each subject underwent a total of 20 $\pm$ 6 heaves in each direction. Mean duration of head movement was 147 ms (range, 105-193 ms), and median amplitude within the first 100 ms was 17.1 mm (range, 11.2-26.3 mm).

Stimulus profiles did not differ between patient and control groups. The median amplitude of head movements within 100 ms of their onset was 2.22 cm for healthy subjects and 2.28 cm for patients ($P =$ 0.76). Mean maximum head yaw rotation was 0.28° $\pm$ 0.15° for healthy subjects and 0.26° $\pm$ 0.16° for patients ($P =$ 0.80). Mean peak acceleration of the head was significantly different ($P <$ 0.01) between healthy subjects (0.49g) and patients (0.34g). To compare LVOR responses between these two groups, a cutoff value of 0.45g was used so that the mean peak head acceleration was comparable. With this cutoff value, the mean peak head acceleration was 0.324 $\pm$ 0.108g for healthy subjects and 0.330 $\pm$ 0.099 g for patients ($P =$ 0.90).

Recording of Eye and Head Movements. Details of our recording technique have been described.[22] Briefly, angular eye and head positions were measured by magnetic search coils using a phase-angle system (CNC Engineering, Seattle, WA). Each subject wore a single-lead scleral coil in each eye (Skalar, Delft, The Netherlands) and sat in a chair while biting on a bite bar. Head rotation in the horizontal plane (yaw) was measured using a coil embedded in the bite bar. The error in angular position measurements introduced by translational coil displacement in the magnetic field was less than 0.2%. Eye and head signals were amplified and digitized at 1 kHz with 12-bit resolution. Data were analyzed using specialized software written in C++. Eye position signals were differentiated and filtered with a fourth-degree Savitzky-Golay filter (0-50 Hz) to obtain velocity traces.

Translational head position along the interaural axis was measured with a linear potentiometer (Omega; Laval, QC, Canada) attached to the sled frame and to one of the head plates. Head acceleration was recorded using a capacitive beam accelerometer (Crossbow Technology, San Jose, CA) attached to the bite bar.

Data Analysis

Heaves that contained artifacts such as saccades or blinks before the occurrence of peak head and eye velocity were identified and excluded from further analysis. Saccades were identified by their main sequence and blinks by their characteristic trajectory and time course. Only heave trials with a yaw head rotation of less than 0.64° and peak head accelerations of 0.1g or greater were analyzed. These cutoff values were chosen to prevent the yaw rotational VOR from being a potential confounder and to maximize the signal-to-noise ratio. Overall, 79% of heaves were included in the final analysis. Patient 6 was unable to tolerate the coil in her right eye; thus, only data from her hypertropic left eye were available for analysis.

To characterize the performance of the interaural translational VOR, two parameters were computed: sensitivity and velocity gain. LVOR sensitivity, expressed in degrees per centimeter, was calculated by dividing the peak rotational eye velocity (in degrees per second) by the peak linear head velocity (in centimeters per second) within the first 100 ms after head movement onset (before visual feedback). Peak head velocity was computed by integrating head acceleration signals. The velocity gain was calculated by dividing the actual peak rotational eye velocity (in degrees per second) by the peak velocity of the geometrically ideal rotational eye movement (in degrees per second) within the first 100 ms after the onset of head movement. The ideal eye position was computed based on the trigonometric requirements given by target distance and interpupillary distance and the head position signal of the linear potentiometer. Head movement onset was determined from the accelerometer signals and were defined as the first instant when acceleration consistently exceeded baseline by 3 SD.

Transducer delays relative to the accelerometer signal were measured with zero-latency in vitro experiments.[22,23] Latencies were 23 ms for the potentiometer and 2 ms for the coil signals with respect to the accelerometer traces. These values were used to correct the measured

TABLE 1. Characteristics of Patients with Skew Deviation

Patient	Age (y)/Sex	Duration of Skew Deviation	Cyclotorsion in Primary Position	Side of Hypertropia in Primary Position	Side of Head Tilt	Visual Acuity (refractive errors*)	Near Point of Convergence	Effective Viewing Distance	Subjective Visual Vertical	Clinical Features (in addition to skew deviation)	MRI Findings
1	31/F	11 mo	10° Excyclotorsion OD	LHT 12 PD (comitant)	Right	20/20 OD 20/20 OS (plano OU)	32 cm	82 cm (15- and 20-cm targets)	0.9° Left	Ataxia, left hemiplegia	Bilateral hemorrhage in brain stem and cerebellum; large hemorrhage in right cerebral peduncle
2	22/F	11 mo	5° Excyclotorsion OD	LHT 8 PD (comitant)	Right	20/40 OD 20/20 OS (plano OU)	10 cm	14 cm (15-cm target); 19 cm (20-cm target)	1.8° Left	Vertical gaze palsy, right-sided weakness and spasticity, ataxia	Left clival chordoma with residual tumor in the left cavernous sinus and Meckel cave; encephalomalacia involving the left pons and cerebellar peduncle
3	32/F	11 mo	None	LHT 6 PD (comitant)	None	20/20 OD 20/20 OS (plano OU)	Cannot perform (>40 cm)	248 cm (15- and 20-cm targets)	1.9° Right	Left internuclear ophthalmoplegia	Multiple high-signal intensities on T2 and FLAIR in periventricular white matter
4	71/M	7 wk	None	RHT 10 PD (incomitant)	None	20/25 OD 20/30 OS (plano OU)	8 cm	15 cm (15-cm target); 18 cm (20-cm target)	5.5° Left	Right internuclear ophthalmoplegia, ataxia	Multiple high-signal intensities on T2 and FLAIR in supratentorial and periventricular white matter
5	23/F	13 mo	5° Incyclotorsion OD	RHT 10 PD (comitant)	Left	20/25 OD 20/20 OS (minus 2.00 OU)	38 cm	101 cm (15- and 20-cm targets)	8.1° Left	Hypometric saccades, saccadic pursuit, gaze-evoked nystagmus, head tremor, ataxia	Left cerebellar hemispheric hemorrhage extending into mesial aspect of right cerebellar hemisphere, with mass effect on the fourth ventricle and brain stem
6	52/F	26 mo	10° Excyclotorsion OD	LHT 6 PD (comitant)	None	20/20 OD 20/20 OS (plano OU)	9 cm	15 cm (15-cm target); 20 cm (20-cm target)	8.2° Left	Right hemiparesis	Hemosiderin deposits in left perisylvian region, pons and adjacent cerebellum extending across the midline

* Measured in spherical equivalent. OD, right eye; OS, left eye; OU, both eyes; RHT, right hypertropia; LHT, left hypertropia; PD, prism diopter.

Right heave   **Left heave**
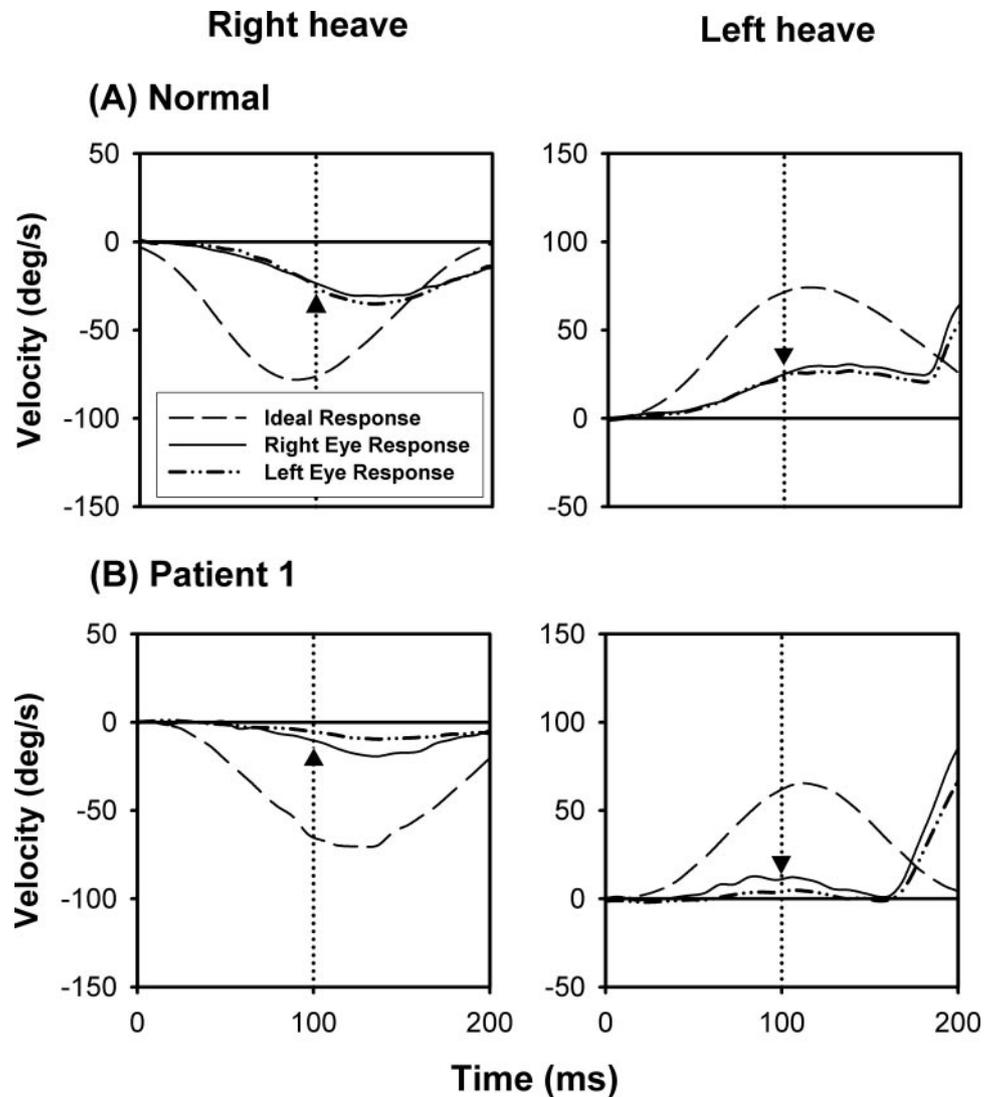
(A) Normal

(B) Patient 1

FIGURE 1. Representative velocity profiles of ideal and actual eye movements during rightward and leftward head heave within the first 200 ms after head movement onset in (**A**) a healthy subject and (**B**) patient 1. Actual eye movements that occurred after 100 ms were responses after visual feedback. *Arrowheads*: peak values of actual and ideal eye velocity in the first 100 ms (*vertical dotted line*), used to calculate the sensitivity and velocity gain. The start position of both eyes has been offset to zero.

latency values. The noise level was 0.031 mm for the potentiometer, 0.02° for the coil, and 5.5 mg for the accelerometer signals.

Statistical Analysis

To assess the effects of viewing distance (15 and 20 cm), eye (hypertropic versus hypotropic), heave direction (right versus left), and viewing eye (hypertropic versus hypotropic) on LVOR sensitivities and velocity gains between healthy subjects and patients, repeated-measures ANOVAs were performed. Significance level was set at $P < 0.05$. Any significant differences were further investigated by post hoc Tukey HSD tests. LVOR responses did not differ between right and left heaves or between right and left eye viewing; therefore, we reported herein combined data from both heave directions and both viewing eyes (during monocular viewing). In addition, LVOR did not differ significantly regardless of whether we measured the responses within the first 70, 100, and 140 ms after head movement onset. We report herein the responses within the first 100 ms. Sensitivities and velocity gains for each patient were compared with the 95% confidence interval of the healthy group mean for each viewing distance. For each patient, sensitivities and velocity gains of the hypertropic versus hypotropic eye were compared using paired *t*-tests for each viewing distance.

Mean group subjective visual vertical (SVV) was compared between healthy subjects and patients by *t*-test. SVV of each individual

patient was also compared to the 95% confidence interval of the healthy group mean.

RESULTS

Figure 1 shows the representative velocity profiles of actual and ideal eye movement responses to a single head heave in each direction from a healthy subject and P1. Normal response (Fig. 1A) to a head heave consists of a visually open-loop initial phase in which the LVOR responses in both eyes are symmetric but undercompensatory,[24–26] followed by a second phase in which gaze position error generates a corrective saccade by way of visual feedback. In contrast, LVOR responses in P1 (Fig. 1B) were reduced during both heave directions and in both eyes. This binocular reduction was asymmetric, with responses significantly lower in the left (hypertropic) eye than the right (hypotropic) eye.

Mean group sensitivities in the healthy subjects were 0.92 ± 0.36 deg/cm at 15 cm (95% confidence interval [CI], 0.69–1.15) and 0.75 ± 0.31 deg/cm at 20 cm (95% CI, 0.55–0.95; $P < 0.001$; Fig. 2). This inverse relationship between LVOR sensitivity and viewing distance is in agreement with previous reports.[23,25,27–29] In contrast, mean group sensitivities in patients failed to modulate with viewing distance, and
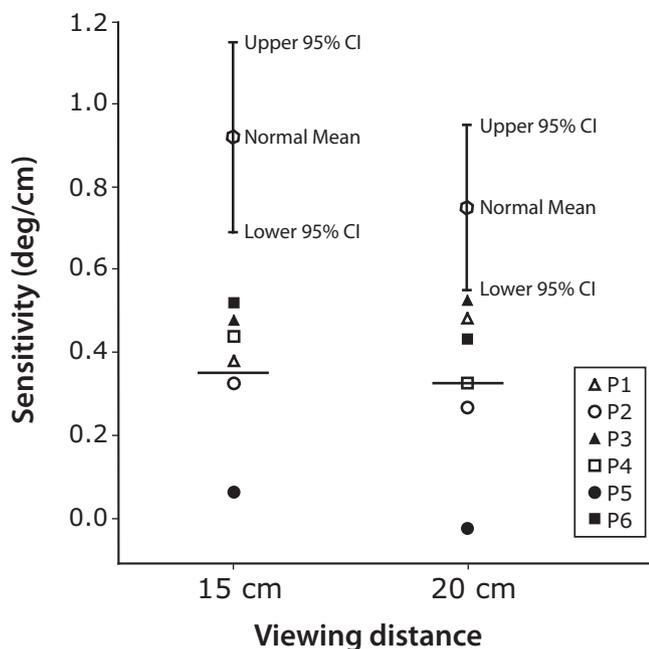
FIGURE 2. LVOR sensitivity in healthy subjects and patients during head heaves at target distances of 15 and 20 cm. Normal data are displayed to show the mean and upper and lower limits of the 95% CI. *Symbols*: LVOR sensitivities in each of the six patients; *horizontal lines*: the patient group mean. Sensitivity was significantly reduced in each patient (less than the lower limit of the 95% CI of healthy subjects). Sensitivity values shown are pooled data from both heave directions and both eyes.

they were significantly lower than those in the healthy group ($P < 0.001$); mean sensitivities in patients were 0.35 ± 0.22 deg/cm at 15 cm and 0.33 ± 0.26 deg/cm at 20 cm (Fig. 2). Sensitivities of both eyes in each of six patients were significantly reduced when compared with healthy controls (below the lower limit of 95% CI). This binocular decrease in sensitivities was asymmetric (Fig. 3)—the magnitude of reduction differed by 37% to 143% between eyes in five patients with binocular recordings ($P < 0.01$). In two patients (P1, P2), sensitivities in the hypotropic eye were higher than those in the hypertropic eye; in three other patients (P3, P4, P5), sensitivities in the hypertropic eye were higher. No consistent relationships were found between the eye with higher sensitivities and the laterality or location of brain lesions. Fixation preference did not determine which eye had higher sensitivity. No correlation was found between the magnitude of skew deviation (Table 1) and the reduction in LVOR response.

Mean group velocity gains in the healthy subjects were 0.25 ± 0.10 at 15 cm (95% CI, 0.18–0.32) and 0.27 ± 0.11 at 20 cm (95% CI, 0.19–0.35). Mean group velocity gains in patients were significantly lower ($P < 0.001$) than those in healthy subjects: 0.10 ± 0.06 at 15 cm and 0.12 ± 0.08 at 20 cm (Fig. 4). Velocity gains of both eyes in each of six patients were significantly reduced when compared with healthy controls (below the lower limit of 95% CI). Similar to the sensitivity results, binocular asymmetric reduction in velocity gains were also observed (Supplementary Fig. S1, http://www.iovs.org/cgi/content/full/50/1/168/DC1). The magnitude of reduction differed by 36% to 94% between eyes in 4 of 5 patients with binocular recordings ($P < 0.001$).

To investigate whether the reduced sensitivities and velocity gains in patients resulted from abnormal vergence, we calculated the vergence angle (Fig. 3 and Supplementary Fig. S1) and "effective" viewing distance (Table 1) for each viewing

distance. Three patients (P2, P4, P6), who had normal NPC, had normal vergence as required for a target distance of 15 and 20 cm during viewing with either eye; the other three (P1, P3, P5), who had abnormal NPC, had abnormal vergence, and their "effective" viewing distance was 4 to 12 times that of the actual target distance during viewing with either eye. Hence, the reduction of LVOR sensitivities and velocity gains in 50% of patients could not be explained by abnormal vergence.

Overall, mean group LVOR latencies did not differ between patients and healthy subjects ($P > 0.1$).

Mean group SVV was significantly higher in patients ($4.38° \pm 3.28°$) than in healthy subjects ($0.65° \pm 0.30°$; 95% CI, 0.48–0.82; $P < 0.001$). Mean SVV in each of six patients was
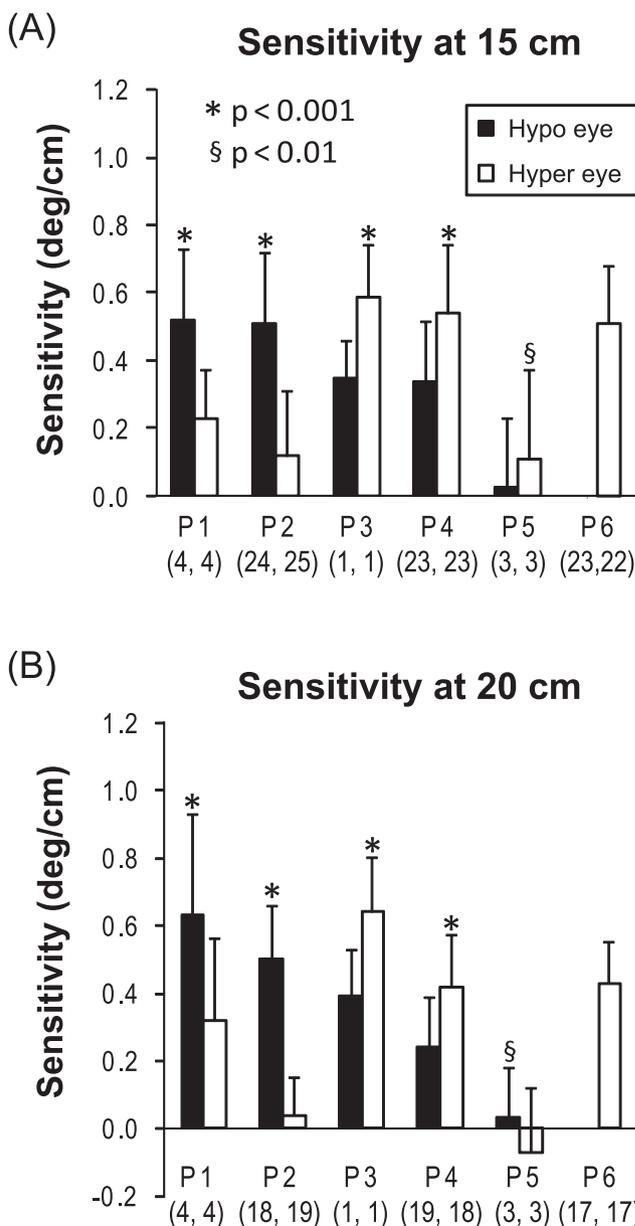

FIGURE 3. LVOR sensitivities of hypotropic and hypertropic eyes in each patient during viewing of a fixation target at (**A**) 15 cm and (**B**) 20 cm. Significant differences in sensitivities between eyes were found in each of five patients with binocular recordings. Patient 6 had monocular recording of her hypertropic eye only. Error bars indicate 1 SD. *Numbers in parentheses*: the amount of convergence during hypertropic (first number) and hypotropic (second number) eye viewing in each subject.
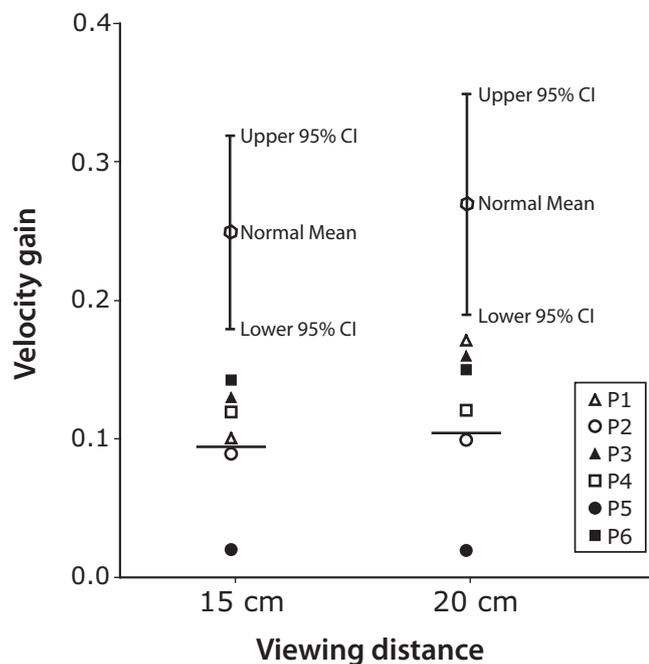
FIGURE 4. LVOR velocity gain in healthy subjects and patients during head heaves at target distances of 15 and 20 cm. Normal data are displayed to show the mean and the upper and lower limits of the 95% CI. *Symbols:* LVOR velocity gains in each of the six patients; *horizontal lines:* the patient group mean. Velocity gain was significantly reduced in each patient (less than the lower limit of the 95% CI of healthy subjects). Velocity gain values shown are pooled data from both heave directions and both eyes.

significantly greater than the upper limit of 95% CI of healthy subjects (Table 1).

DISCUSSION

Skew deviation has been attributed to an asymmetric disruption of the otolith-ocular reflex; however, few studies have investigated otolith functions in patients.[4,19,20] Patients with skew deviation caused by cerebellar lesions have reduced static torsional VOR gains that are asymmetric, with the magnitude of reduction differing between eyes and between the directions of head roll.[4] In addition, patients with skew deviation from brain stem lesions have asymmetric responses to off-vertical axis rotation, indicating that asymmetric dynamic otolith signal of the LVOR is associated with skew deviation.[20] However, because these patients[20] have primary position nystagmus, the asymmetric responses observed could be confounded by the directional bias of the underlying nystagmus. In this study, we used the head heave test to investigate otolith function in patients with skew deviation who had no primary position nystagmus. Despite the heterogeneity of the type and location of lesions in our patients, we found a marked, binocular, asymmetric reduction in LVOR sensitivity and velocity gain by 60%. To the best of our knowledge, this is the first study to demonstrate abnormal LVOR in skew deviation.

Because P3 and P4 had internuclear ophthalmoplegia on the same side as the hypertropic eye, one might expect a further decrease in LVOR responses in their hypertropic eye during adduction compared with the hypotropic eye. However, we found that the sensitivities and velocity gains in the hypertropic eye were higher than in the hypotropic eye and that the responses did not differ between right and left heaves in either eye. Thus, the presence of internuclear ophthalmoplegia in

two of our six patients could not explain the abnormal LVOR responses we observed.

Previous studies[23,25–31] indicated that target distance, target size, vergence, and relative motion (parallax) all play roles in determining LVOR responses, with target distance recently demonstrated to be a more important factor.[26] Because lesions in the otolith-ocular pathway may also damage structures that normally control vergence,[32–36] patients with brain stem or cerebellar lesions could have disrupted vergence[37,38] and, hence, abnormal LVOR. To investigate this possibility, we measured the NPC of our patients clinically, along with their vergence and "effective" viewing distance during head heaves. We found that the sensitivity was reduced by 58% and velocity gain by 63% even in patients with normal vergence. Our results are consistent with a previous report[21] that showed a loss of LVOR modulation by vergence angle and reduction in otolithic sensitivity in patients with cerebellar ataxia who had normal vergence. Taken together, our findings indicate that the decreased LVOR responses in our patients could not be attributed to abnormal vergence, thus providing additional evidence that damage to the otolith-ocular pathway is a mechanism of skew deviation.

Patients with spinocerebellar ataxia type 6 and episodic ataxia type 2 have decreased LVOR sensitivity.[21] Because these patients often have incomitant skew deviation (which was not specified in a previous study[21]), whether the decrease in LVOR sensitivity was causally related to the underlying diffuse cerebellar diseases or to skew deviation remains unclear. In the present study, all six patients had well-documented skew deviation and reduced LVOR responses; three (P2, P3, P4) had brain stem lesions without cerebellar involvement (clinically and radiographically), whereas the other three had lesions involving the cerebellum. Our findings suggest that decreased LVOR responses are associated with the presence of skew deviation, which can be caused by brain stem or cerebellar disease, or both.

The SVV has been proposed to be a sensitive test for assessing utricular function. It detects erroneous tilted perception of the true earth-vertical that might occur after a unilateral lesion to the otolith organs or their projections to the brain stem.[39] The dentate nucleus within the cerebellum has also been implicated as critical in vestibular processing, including the perception of verticality.[40] Our findings that all six patients had abnormal SVV support the notion that SVV is a sensitive test for detecting abnormal otolith function in skew deviation caused by lesions in the brain stem or cerebellum.

The asymmetric reduction in LVOR responses between eyes, but symmetric reduction between heave directions, may seem surprising at first. If skew deviation is caused by asymmetric disruption of the otolith-ocular pathway and if it is analogous to asymmetric disruption of the canal-ocular pathway (e.g., unilateral vestibular deafferentation), we might predict an asymmetric decrease in LVOR responses between heave directions in skew deviation. However, the LVOR responses after asymmetric disruption of the otolith-ocular pathway could be different for two reasons. First, the axes of polarity of the hair cells are unidirectional in the semicircular canals, whereas those in the otoliths are multidirectional, and they reverse direction across the striola. Second, the angular (rotational) VOR pathway consists of a simple three- or four-neuron arc. Although the otolith-ocular pathway has traditionally been thought to be disynaptic,[41] a more complex polysynaptic pathway that involves an extensive network within the cerebellum may play a more important role.[21,42] The symmetric reduction in LVOR responses between heave directions we found is consistent with the findings of Crane et al.,[43] who demonstrated no difference in LVOR responses between ipsilesional and contralesional directions after unilateral vestibular

deafferentation. Further investigation of the LVOR in more patients with skew deviation should clarify the mechanisms and prevalence of the LVOR abnormalities detected in our patients.

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