Vestibulo-Ocular Reflexes of Adventitiously and Congenitally Blind Adults

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The vestibulo-ocular reflex (VOR) was measured in congenitally blind, adventitiously blind, and normally sighted adults to determine how it was affected by loss of vision. VOR gain and phase were measured in subjects rotated sinusoidally in total darkness, while concentrating on an imaginary earth-fixed target. Gain was lower in adventitiously blind subjects than in sighted subjects. The gain reduction in blind subjects was accompanied by an increase in the amount of phase lead at low frequencies. The dominant time constant was typically 3 sec for adventitiously blind subjects and 16 sec for sighted subjects. No convincing vestibulo-ocular responses were measured in congenitally blind subjects except at the highest test frequencies. These findings demonstrate that vision is necessary early in life for development of the VOR, and that vision is also necessary throughout life for ongoing maintenance of the VOR. Invest Ophthmol Vis Sci 27:1154-1159, 1986

The vestibulo-ocular reflex (VOR) is the primary mechanism for stabilizing the visual field during head rotations. Stabilization is achieved by vestibularly induced eye movements that cancel the apparent visual field motion that would accompany head movements. These eye movements are effective because they are generated with minimal delay, and with velocities that are equal but opposite to the velocities of head movements.

Two processes assure adequate VOR performance throughout life, even though it is configured as an open loop control system comprised of structures that change due to growth, aging, and disease. First, vestibulo-ocular responses, which are present at birth, develop until they are identical to those observed in adults.1-4 Thereafter, an adaptive, plastic process maintains VOR performance by calibrating the response to reduce visual field motion during head rotations.5-8

This study, measurement of the VOR in blind subjects, was designed to determine how visual experience affects VOR development and VOR maintenance. Earlier observations date back to 1918 when caloric nystagmus in the blind was described as increased.9 In later studies, it was suggested that caloric nystagmus may be absent in patients who have been blind from birth.10,11 More recently, the VOR was described as absent or significantly reduced in the congenitally blind (blind from birth) and as retained by the adventitiously blind (blind after considerable visual experience).12 Based on these findings, it was suggested that vision was important in the early years to fashion neural structures mediating the VOR.

We measured VOR gain and phase in congenitally blind, adventitiously blind, and sighted subjects. The influence of vision on VOR development was determined by comparing the responses of congenitally blind subjects who had no vision during VOR development with the responses of adventitiously blind subjects who had vision during this time and later went blind. The influence of vision on VOR maintenance was determined by comparing the responses of adventitiously blind subjects with those of normally sighted subjects.

Materials and Methods

Subjects

Vestibulo-ocular reflexes of five congenitally blind, six adventitiously blind, and three normally sighted adults were measured. In all cases, blindness was caused by anterior visual disorders; disease or injury of the eye, retina, or optic nerve. Subjects were classified as congenitally blind if they never had form vision. They were classified as adventitiously blind if they recalled visual experiences but no longer had form vision. None of the blind subjects could reliably detect the presence of light. Each subject's visual history is summarized in Table 1.
Table 1. Age, visual history, and summary of VOR characteristics for all subjects examined

<table>
<thead>
<tr>
<th>Subject</th>
<th>Group</th>
<th>Age/years of blindness</th>
<th>Diagnosis</th>
<th>Gain* (sd = 0.18)</th>
<th>Phase†</th>
<th>Voluntary saccades</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 S</td>
<td>26/0</td>
<td>Normal</td>
<td>0.9</td>
<td>18.7</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2 S</td>
<td>26/0</td>
<td>Normal</td>
<td>0.9</td>
<td>10.6</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>3 S</td>
<td>34/0</td>
<td>Normal</td>
<td>1.0</td>
<td>17.7</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>4 A</td>
<td>33/12</td>
<td>Diab retin</td>
<td>—</td>
<td>3.2</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>5 A</td>
<td>55/3</td>
<td>Diab retin</td>
<td>0.2</td>
<td>2.7</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>6 A</td>
<td>37/5</td>
<td>Diab retin</td>
<td>0.6</td>
<td>14.5</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>7 A</td>
<td>36/32</td>
<td>Detached retin</td>
<td>0.4</td>
<td>—</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>8 A</td>
<td>64/5</td>
<td>Glaucoma</td>
<td>0.2</td>
<td>1.5</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>9 A</td>
<td>67/12</td>
<td>Glaucoma</td>
<td>0.5</td>
<td>2.7</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>10 C</td>
<td>27/27</td>
<td>RLF</td>
<td>&lt;0.1</td>
<td>—</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>11 C</td>
<td>30/30</td>
<td>RLF</td>
<td>&lt;0.1</td>
<td>—</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>12 C</td>
<td>31/31</td>
<td>RLF</td>
<td>&lt;0.1</td>
<td>—</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>13 C</td>
<td>39/39</td>
<td>RLF</td>
<td>&lt;0.1</td>
<td>—</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>14 C</td>
<td>36/36</td>
<td>Opt nerve dis</td>
<td>&lt;0.1</td>
<td>—</td>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>

S = sighted, A = adventitiously blind, C = congenitally blind, Diab retin = Diabetic retinopathy, RLF = Retrolental fibroplasia, Opt nerve dis = Optic nerve disease.

* Measured at 0.2 Hz, ±25 deg/sec peak velocity. Gain for sighted subjects 1, 2, and 3 was 0.83, 0.95, and 1.03 when computed with individual rather than standard calibration factor.

† Dominant time constant (seconds) based on 45° phase lead.

Vestibulo-ocular reflexes of four additional adventitiously blind and two additional congenitally blind subjects were recorded and examined qualitatively. Their responses were consistent with the results to be presented, but they were excluded from the quantitative analysis either because non-vestibular eye movements (including nystagmus) precluded confident measurements, or because they had undergone surgery that might have affected ocular motility.

Consent statements were signed by all subjects after the experimental procedure and their rights as subjects were explained.

Procedure

Vestibular tests were conducted in total darkness using passive, whole body, sinusoidal rotations about an earth vertical axis, generated by a servo-controlled motorized chair (Contraves Goerz Model 404D, Pittsburgh, PA). Subjects were instructed and frequently reminded to concentrate on an imaginary earth-fixed target during rotations. If they lost track of this imaginary target or if it passed too far to one side, they were instructed to imagine a new one directly in front of them. Under this mental set gain is at least as large as it is when subjects perform mental arithmetic. During certain trials, subjects were asked to demonstrate voluntary control over VOR gain by alternating their concentration between an imaginary earth-fixed and an imaginary head-fixed target.

Subjects were rotated sinusoidally at 1.0, 0.5, 0.2, 0.1, 0.05, and 0.02 Hz with peak velocity equal to ±25 deg/sec. Each trial consisted of at least six cycles of rotation. Additional trials were run at 0.5 and 0.05 Hz with peak velocity equal to ±15 and ±50 deg/sec.

Eye Movement Recording and Calibration

Eye movements were recorded with infrared limbus trackers that were adjusted for maximum response and symmetry to voluntary saccades. Some subjects could not make voluntary saccades, so the eyetracker was adjusted until their resting eye movement patterns (primarily spontaneous nystagmus) were discernible in the eyetracker response. Between trials, subjects were again asked to make voluntary saccades to verify the signal from the eyetracker.

The eyetracker could not be absolutely calibrated for blind subjects, so a standard calibration factor was used to convert their eye movement recordings to degrees. Recordings from sighted subjects were converted using the same standard calibration factor, thereby increasing the probability that gain differences between the two groups were neurophysiological differences rather than calibration differences which might arise from random differences in iris pigmentation, eyetracker adjustment, or eye size. For control purposes, the eye movement recordings from sighted subjects were also converted to degrees using their individual calibration factors, which deviated from the standard by less than 8%. As another control, intersubject calibration differences were evaluated by measuring calibration factors for eight sighted subjects, with widely varying iris pigmentation and eye size, viewing targets at ±10°. The standard deviation of the calibration factors was 18%. Note that systematic differences between calibration factors of sighted and blind individuals could degrade the accuracy of the gain measurements, but the anterior reflective surfaces of our blind subjects were not different in color, clarity, or iris definition from our sighted subjects. Importantly, phase mea-
measurements are not affected by random or systematic calibration differences.

Limbus tracking was selected over two other measurement techniques: electro-oculography and magnetic search coils. Electro-oculography (EOG) was not selected because the corneo-retinal potential can be attenuated by ocular diseases associated with blindness. Search coils were not selected in order to avoid any physical contact with the eyes of blind subjects.

Eye position and chair velocity were recorded on a chart recorder (Gould, Model 220, Cleveland, OH) at high speed and high gain settings. These high resolution recordings were analyzed to obtain mean values of peak slow phase eye velocity, peak chair velocity, and the phase between them. Mean values were calculated from a nearly equal number of left and right half cycle measurements, and were based on a minimum of 6 and a maximum of 24 measurements. Some half cycles were not measurable because the maximum slope or the velocity turn around point was masked by nonvestibular eye movements and other types of noise. Chair velocity was determined from the amplitude of the recordings, and used as a measure of head velocity. Phase was determined by calculating the number of degrees of phase shift between zero eye and zero head velocity.

VOR gain (defined as the ratio between the mean value of peak slow phase eye velocity and head velocity), and VOR phase (eye relative to head) were computed for each trial and plotted versus frequency.

Results

Eye Movement Characteristics

Vestibularly induced and voluntarily generated eye movements of sighted, adventitiously blind, and congenitally blind subjects were qualitatively different (Fig. 1). The responses of sighted subjects had the largest slow phase eye velocity, and the largest number of fast phase saccades. In comparison, responses of adventitiously blind subjects were reduced in amplitude and contained fewer fast phase saccades. However, the number of random saccades (not vestibularly induced anti-compensatory saccades) was increased. No convincing vestibularly induced eye movements were observed in congenitally blind subjects (with some exceptions to be discussed). The resting eye movements of these subjects were not distinguishable from their eye movements during vestibular stimulation—both were characterized by involuntary, smooth eye movements interrupted by fast and slow phase nystagmus patterns and poor eyelid control.

Voluntary control of VOR gain was demonstrated by sighted subjects and by adventitiously blind subjects. Gain was highest when subjects concentrated on an imaginary earth-fixed target; gain was lowest when they concentrated on an imaginary head-fixed target (Fig. 2). Even a 36-yr-old subject with just 4 yr of vision demonstrated this ability. Voluntary control was observed at all test frequencies, at ±25 deg/sec peak velocity.

Five of the six adventitiously blind subjects were able to make voluntary saccades, although they had less control over the amplitude of these saccades than did sighted subjects performing the same task in total darkness. The only adventitiously blind subject who could not make voluntary saccades was the subject who had only 4 yr of vision. None of the congenitally blind subjects could move their eyes voluntarily.

VOR Gain

Blindness reduced the amplitude of vestibularly induced eye movements. Mean values of VOR gain for
Fig. 2. Vestibulo-ocular reflexes of sighted and adventitiously blind subjects concentrating on an imaginary earth-fixed target to maximize responses (left), and on an imaginary head-fixed target to suppress responses (right). Both subject groups altered the gain of their responses by altering their mental set. Peak rotational velocity was ±25 deg/sec.

Each subject show the extent of the reduction (Fig. 3). The gain curve for each sighted and each blind subject has a statistical variability due to the standard calibration factor (18% s.d.); however, absolute gain can be determined for the sighted subjects (Fig. 3, legend). Gain for low frequency, large amplitude rotations was not measurable for two of the sighted subjects because their eye movements saturated the eyetracker.

Without exception, VOR gain was lower in adventitiously blind subjects than in sighted subjects. In adventitiously blind subjects, gain ranged from 0.1–0.6, whereas it ranged from 0.65–1.1 in sighted subjects. The standard deviation of the half-cycle values from the mean, which were not dominated by asymmetries, are indicated by the error bars. The gain decrease, independent of any assumption about calibration factors, was corroborated by the decreased number and size of fast phase saccades. Sinusoidal vestibular rotations did not produce observable compensatory eye movements in the congenitally blind at frequencies below 0.5 Hz, even at peak velocities up to ±50 deg/sec. The gain plotted in Figure 3 for the congenitally blind represents the maximum gain that might exist, but could not be measured due to the overall signal to noise ratio of the recordings. Interestingly, the primary source of noise was biological noise, such as random eye movements and eyelid closure. Sinusoidal rotation at frequencies above 0.5 Hz did produce eye movements in the compensatory direction in two of the five congenitally blind subjects. In these subjects, mean values of gain at 1 Hz were 0.47 and 0.46.

VOR gain was apparently constant with respect to frequency for sighted subjects, as well as for adventitiously blind subjects. The gain decrease observed at low frequencies for both sighted and blind subjects (Fig. 3) was probably due to their inability to concentrate on an imaginary earth-fixed target during large amplitude rotations.14

Mean values of VOR gain at a specific test frequency varied across adventitiously blind subjects. At 0.5 Hz, for example, gain varied from 0.19–0.58. The variation may be due in part to random calibration variations. There was no apparent correlation between a subject's gain and age, or the cause or duration of blindness.

Fig. 3. Mean values of VOR gain and phase vs frequency for each subject, based on a standard calibration factor (±18% s.d.). Gain shown for congenitally blind is the maximum gain that would not be detected due to non-vestibular eye movements. Error bars show half cycle deviations from the mean (±1 s.d.). Absolute gain for subjects, based on his actual rather than the standard calibration factor, is 8% lower than shown. Gain for Subjects b and c are 3% and 5% higher than shown.
For example, VOR gain in a 55-yr-old subject who was blind for 3 yr due to diabetic retinopathy was consistently lower than VOR gain in a 67-yr-old subject who was blind for 12 yr due to glaucoma. An 0.5 Hz, gain for these individuals was 0.14 and 0.46, respectively. The age and visual history of individual subjects are provided in Table 1.

VOR Phase

Adventitious blindness caused an increase in VOR phase lead at low frequencies. In sighted subjects, the phase between eye rotation and oppositely directed head rotation approaches 0° for frequencies above 0.1 Hz. As the frequency of rotation decreases, phase lead appears. In this study, phase lead measured in sighted subjects was 7 ± 1° at 0.1 Hz, 15 ± 3° at 0.05 Hz, and 28 ± 3° at 0.02 Hz. In contrast, phase lead in four of the adventitiously blind subjects was 31 ± 11° at 0.1 Hz, and 50 ± 5° at 0.05 Hz. At 0.02 Hz, phase was 59 ± 24° based on measurements in three subjects. Phase measurements made at different peak velocities (± 15 and ±50 deg/sec) confirmed that the increased phase lead was not dependent on rotational velocity. Note that phase measurements are unaffected by calibration differences.

In two of the six adventitiously blind subjects, no phase lead increase was measured. One of these subjects was 37 yr old, and had been blind for less than 1 yr when examined. The other subject was 36 yr old, and had been blind for 32 yr due to detached retinas. The lowest frequency at which this subject's VOR was measured was 0.1 Hz; it is not clear whether phase lead would have increased at lower frequencies.

VOR phase can be characterized by a single, dominant time constant determined by the frequency at which 45° of phase lead develops. The time constant equals \(1/2\pi f\) where \(f\) is in Hz. The dominant VOR time constants for the three sighted subjects were 11, 18, and 19 sec. Of the four adventitiously blind subjects with increased phase lead, three had time constants of 3 sec, and one had a time constant of 1.5 sec.

Discussion

Complete loss of vision influences the vestibulo-ocular reflexes in humans. Adventitiously blind subjects who had vision and subsequently went blind retained a VOR with reduced amplitude and time constant. In contrast, congenitally blind subjects who never had vision had no vestibulo-ocular responses, with minor exceptions.

Early visual experience must influence the development of the VOR, because congenitally blind subjects had little or no responses, whereas adventitiously blind subjects had consistent, measurable responses. That is to say, visual experience must be necessary early in life for the development or preservation of permanent neural structures or connections between neural structures that underly generation of vestibularly induced eye movements. The alternative explanation, that the congenitally blind subjects had no VOR because they had been blind longer than adventitiously blind subjects, can be ruled out based on the visual histories of individual subjects. Among the subjects examined, four had nearly equivalent durations of blindness, approximately 30 yr. Of these subjects, the only one who retained consistent vestibulo-ocular responses was the subject who had normal vision during his first 4 yr of life. The remaining subjects, all of whom were blind from birth, had little or no VOR. Thus, 4 yr of vision early in life was enough to develop VOR structures that continued to generate responses after 30 yr of blindness.

An analogy can be drawn between the influence of early visual experience on VOR development and the development of binocular vision. Prior to visual experience, the cortex is primitively organized for binocular vision. However, the organization is modifiable during infancy; adequate visual experience is necessary during this period for normal development to occur. The influence of visual experience on the development of these two systems, and observations that the control system for generating voluntary eye movements also requires visual experience to develop, suggests that many neural systems have a critical period during which adequate visual information is required for the development of normal function.

Vision must also be essential throughout life for the ongoing maintenance of the VOR, since adventitious blindness results in degraded responses. In subjects with normal vision, VOR gain is greater than 0.6 and has a time constant of 16 sec when subjects perform mental arithmetic or concentrate on an imaginary earth-fixed target. In adventitiously blind subjects with previously normal vision, gain is between 0.1 and 0.6, with a time constant around 3 sec measured under the conditions which maximize their response. Even in subjects with more than 50 yr of normal vision prior to blindness, the VOR was not maintained at a level observed in sighted subjects. We stress the change in phase here, which is not affected by any assumptions about calibration.

What structures are affected by the adventitious loss of vision? The time constant decrease from 16–3 sec measured in the blind implicates two central neural structures. One structure, the velocity storage mechanism, compensates for the reduced response of the vestibular end organs at low frequencies by effectively increasing the time constant of the system to 16 sec. Decay of the velocity storage mechanism would decrease the VOR time constant to that of the semicircular canals (7 sec), but not to 3 sec as measured in
the blind. A second structure, the neural integrator, could account for this shortened VOR time constant, and could perhaps, also account for the even shorter time constants reported for the VOR in albinos with congenital nystagmus, and for the doll's head response in vegetative and unconscious patients. The neural integrator integrates eye velocity commands to eye position commands with a time constant estimated to be 25 sec. A decrease in this time constant could shorten the time constant of the VOR (measured from sinusoidal rotations or the doll's head response) to a value below that established by the velocity storage mechanism or the semicircular canals. At the same time, a subject's ability to hold an eccentric gaze would deteriorate, and the instantaneous eye velocity during each slow phase of rotatory nystagmus would show a continuous decrease, although the time constant of nystagmus would remain unchanged. We recorded these eye movements, but found them difficult to analyze because of involuntary eye movements and low gain.

The influence of vision on VOR development and maintenance has been studied in cats. One group of cats, reared in darkness from birth to age 15 months, had VOR gains around 0.3. In addition, VOR phase lead increased and became amplitude dependent. When placed in a normally lit environment for 5 months, no plastic changes (i.e., gain or phase improvements) were observed. A second group of cats, reared with normal vision to adulthood, then deprived of vision for 135 days, had normal vestibulo-ocular reflexes. Since the durations of visual deprivation and blindness were not equivalent, the changes in the cats and humans VOR cannot be fully compared and contrasted. However, it is clear that, in both cat and humans, vision is required during a critical period for development of normal vestibulo-ocular reflexes.

What emerges from studies of VOR development during infancy and childhood, studies of VOR plasticity, and studies of VOR in patients is a description of a process for stabilizing the visual field throughout life. Not surprisingly, the process includes both the development and ongoing maintenance of neural structures and/or connections between neural structures based on visual-vestibular interactions.

**Key words:** vestibulo-ocular reflex, blindness, visual loss, velocity storage, neural integrator

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**References**