Spatial Distribution of Gravity-Dependent Gain Changes in the Vestibuloocular Reflex


This study determined whether dependence of angular vestibuloocular reflex (aVOR) gain adaptation on gravity is a fundamental property in three dimensions. Horizontal aVOR gains were adaptively increased or decreased in two cynomolgus monkeys in upright, side down, prone, and supine positions, and aVOR gains were tested in darkness by yaw rotation with the head in a wide variety of orientations. Horizontal aVOR gain changes peaked at the head position in which the adaptation took place and gradually decreased as the head moved away from this position in any direction. The gain changes were plotted as a function of head tilt and fit with a sinusoid plus a bias to obtain the gravity-dependent (amplitude) and gravity-independent (bias) components. Peak-to-peak gravity-dependent gain changes in planes containing the position of adaptation and the magnitude of the gravity-independent components were both ~25%. We assumed that gain changes over three-dimensional space could be described by a sinusoid the amplitude of which also varied sinusoidally. Using gain changes obtained from the head position in which the gains were adapted, a three-dimensional surface was generated that was qualitatively similar to a surface obtained from the experimental data. This extends previous findings on vertical aVOR gain adaptation in one plane and introduces a conceptual framework for understanding plasticity in three dimensions: aVOR gain changes are composed of two components, one of which depends on head position relative to gravity. It is likely that this gravitational dependence optimizes the stability of retinal images during movement in three-dimensional space.

INTRODUCTION

The angular vestibuloocular reflex (aVOR) counter-rotates the eyes during angular head movement to stabilize images on the retina. If eye velocity does not match head velocity, images will slip on the retina, and over time, this disparity will produce adaptive modification of the aVOR gain (eye velocity/head velocity) (Gonshor and Melvill Jones 1973; Lisberger 1994; Miles and Eighmy 1980). Retinal image slip induced by magnifying or minifying goggles (Cohen et al. 1992), by reversing prisms (Gonshor and Melvill Jones 1973), or by rotation of the visual surround in phase or out-of-phase with the subject (Miles and Eighmy 1980) is an efficient method to modify the gain of the aVOR.

There is evidence that head position with regard to gravity is also an important context for adaptive aVOR gain changes (Baker et al. 1987a,b; Tan et al. 1992; Tiliket et al. 1993, 1994; Yakushin et al. 2000a). When the vertical aVOR was adapted in side-down positions in humans and monkeys, gain changes were maximal when the head was in the position of adaptation, i.e., with one side down, and declined as the subjects were reoriented toward the opposite side down position (Yakushin et al. 2003a–c). From this, we posited that the gain adaptation for the vertical aVOR was a superposition of two components: one gravity independent and another gravity dependent. It was not clear from the previous studies whether the gravity-dependent gain changes would apply to all components of the aVOR and whether this same organization would extend to three dimensions.

The aim of this study was to determine whether gravity dependence was inherent in adaptation of the horizontal aVOR, which generally does not interact with gravity when rotating the head about a yaw axis while upright. This would demonstrate that dependence of aVOR adaptation on gravity is a fundamental property of the aVOR and that this gravity dependence extends over every head position in three-dimensional space. It would further establish the principle that aVOR adaptation is composed of gravity-dependent and -independent components and broaden the conceptual base for studying aVOR plasticity. In the past, it has generally been assumed that aVOR gain changes only involved pathways between the semicircular canals and eye muscle motor nuclei. Demonstration that a gravity-dependent context is associated with adaptation of the gain of the aVOR in every head orientation would substantially expand the nature of the signals that are utilized in this process.

METHODS

Two cynomolgus monkeys (Macaca fascicularis) were used in these experiments. These animals were utilized in experiments on vertical aVOR gain adaptation 4 mo prior to the present experiments, but the horizontal aVOR was not studied in these animals. The work conformed to the Guide for the Care and Use of Laboratory Animals (National Research Council 1996) and was approved by the Institution Animal Care and Use Committee. During experiments, monkeys sat with their head fixed in a primate chair in a multiaxis vestibular stimulator (Yakushin et al. 2000b, 2003c). Horizontal, vertical, and torsional eye movements were recorded with two scleral search coils (Robinson 1963). Because there were no consistent modulations in vertical and torsional eye movements, only the horizontal component was studied. Eye velocity was calibrated by rotation in light at a
constant velocity of 30°/s, wherein slow phase velocity was assumed to be equal to stimulus velocity.

Horizontal aVOR gains were determined by oscillating the animals in darkness about their yaw axis at 0.5 Hz (60°/s peak velocity) before and after adaptation. The axis of rotation was either aligned with the spatial vertical or was tilted from it in 10° increments ≤90° in four different planes: frontal (tilt about naso-occipital axis, Fig. 1D, inset), sagittal (tilt about interaural axis, F, inset), and the two intermediate planes, which lay around the axes of one anterior and contralateral posterior canals. One of these is shown in Fig. 1E, inset.

Horizontal aVOR gains were decreased by in-phase and were increased by out-of-phase sinusoidal oscillation of the monkey (±14°) and optokinetic surround for 4 h at 0.2 Hz. The amplitude of the head oscillation during adaptation with the animal in the RSD position is shown by the lavender sectors in Fig. 1D, inset. Thus in some cases, animals were tilted in the plane that included the position of adaptation (Fig. 1D), whereas in other cases, the plane of tilt was rotated in yaw 45° (Fig. 1E) or 90° (F) from this plane.

The animals were adapted in one of five head orientations in each experiment: upright, left side down (LSD), right side down (RSD), prone, or supine. The test frequency (0.5 Hz) was higher than the adaptation frequency (0.2 Hz) for technical reasons. Although it is possible that observed gain changes would be bigger at the frequency of adaptation (Lisberger et al. 1983), gravity-dependent components...
of the vertical aVOR gain changes were not significantly different when tested by sinusoidal rotations from 0.2 to 4 Hz after adaptation had been done with steps of velocity (Yakushin et al. 2003c). At least 1 wk was allowed for the aVOR gain to recover before the next experiment was performed.

Eye positions were sampled at 1 kHz with 16-bit resolution and digitally differentiated using a 25-point filter (Reisine and Raphan 1992). Saccadic eye velocities were identified and removed using a maximum likelihood ratio criterion (Singh et al. 1981). The remaining slow phase eye velocities were fit with sinusoids from which the amplitude of eye velocity before and after adaptation was determined. Gains were calculated as a ratio of the amplitudes of eye and head velocity. Gain changes in each tested head orientation were expressed as a percent of the preadapted gain values and plotted as a function of head orientation. Gain values declined from a maximum of 1.2, and approached the preadapted gain of 0.8 as the head was tilted toward the opposite side.

When the animal was tilted in a peak-to-peak gravity-dependent component was 42% with head orientation in which gain had been adapted, the peak-to-peak gravity-dependent component varied between 4 and 42% in one animal and between 2 and 33% in another animal according to the angle between the plane of testing and the plane that contained the head position in which the gain had been adapted. It was maximal when the two were coincident and minimal when they were orthogonal.

Thus the bias or gravity-independent component was relatively invariant regardless of the plane in which the head was tilted. This shows that there is a gravity-independent gain change, which is distributed over all head positions. In contrast, the absolute value of the peak-to-peak gravity-dependent component varied between 4 and 42% in one animal and between 2 and 33% in another animal according to the angle between the plane of testing and the plane that contained the head position in which the gain had been adapted. It was maximal when the two were coincident and minimal when they were orthogonal.

There was no difference in the results after adaptation in the LSD and RSD positions for gain increase in the two monkeys, and these data were combined to obtain the means and SDs of the peak-to-peak gravity-dependent and -independent gain changes (Table 1). The same was true for gain decrease in the LSD and RSD positions, and the data related to these two positions were also combined. When results of the gain increase and decrease were compared, there was no statistical difference in absolute values of gravity-dependent gain changes after adaptation on side. The same was true for gravity-independent components. Thus for side-down adaptations, the peak-to-peak average gravity-dependent gain change was 31.6 ± 11.3% and gravity-independent change was 23.1 ± 6.8%.

The same dependence on head orientation in which the gain was altered was true for adaptation in prone and supine positions. Similar to the results obtained after adaptation in side-down positions, data for prone/supine adaptation were combined for gain increase and likewise for gain decrease (Table 1). There was also no difference in gravity-independent components when animals were adapted in prone or supine. The gravity-dependent gain increase, however, was larger than gain decrease (P < 0.05); the reason for this difference is not clear. The absolute value of average amplitude of the gravity-dependent peak-to-peak gain changes, however, was 20.9 ± 11.1% and average gravity-independent gain change was 31.3 ± 7.9%. Thus the general relationship described in Fig. 1, D–I, was obtained in every experiment.

These results raised the question of whether there would be a gravity-dependent component if the animals were adapted in the upright position. Furthermore, we questioned whether the gravity-dependent components would depend on the plane of tilt because every plane would include the upright position.

<table>
<thead>
<tr>
<th>Head Orientation During Testing</th>
<th>Adaptation Type</th>
<th>Gravity-Dependent Gain Changes, %</th>
<th>Gravity-Independent Gain Changes, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>LSD-RSD</td>
<td>Gain increase</td>
<td>35.4 ± 16.5</td>
<td>25.0 ± 6.8</td>
</tr>
<tr>
<td></td>
<td>Gain decrease</td>
<td>−28.4 ± 2.9</td>
<td>−21.5 ± 7.0</td>
</tr>
<tr>
<td></td>
<td>Average absolute value</td>
<td>31.6 ± 11.3</td>
<td>23.1 ± 6.8</td>
</tr>
<tr>
<td>Prone-supine</td>
<td>Gain increase</td>
<td>25.6 ± 12.3</td>
<td>31.6 ± 8.5</td>
</tr>
<tr>
<td></td>
<td>Gain decrease</td>
<td>−14.7 ± 6.3</td>
<td>−30.8 ± 8.8</td>
</tr>
<tr>
<td></td>
<td>Average absolute value</td>
<td>20.9 ± 11.1</td>
<td>31.3 ± 7.9</td>
</tr>
</tbody>
</table>

Increases and decreases in gain were tested in the plane that included head orientation in which the gain was adapted. Values are means ± SD. aVOR, angular vestibuloocular reflex; LSD-RSD, left-right side down.
The gravity-dependent components were similar regardless of the planes of tilt in both animals \((P = 0.2)\). Moreover, the gravity-independent components were equivalent for head tilt in any direction. The gravity-dependent changes were comparable when the gain was increased and decreased in M0102 \((18.1 \pm 3.7 \text{ vs. } 17.9 \pm 1.1, P = 0.92)\), whereas the gravity-independent components were bigger after gain decrease \((15.1 \pm 3.3)\) than gain increase \((6.2 \pm 1.3, P = 0.003)\). Only gain decrease was tested after adaptation in the upright position in M17115. Although both components were larger than in the other experiments, the gravity-dependent and -independent components were comparable \((-40.3 \pm 8.1 \text{ vs. } -36.0 \pm 4.7, \text{ respectively})\).

Thus both gravity-dependent and -independent components were produced after adaptation in the upright position, but in contrast to the gain changes in side-down and prone-supine positions, the gravity-dependent component was similar for every plane of tilt. These data further show that the horizontal VOR gain changes after adaptation in any position are composed of two components.

The individual gain changes in the head orientations in which the gains were determined were used to construct a surface using a spline interpolation to visualize the adaptive changes in three dimensions. After gain increase while RSD (Fig. 2A, blue arrow), the gain changes were maximal \((40\% \text{, red})\) when RSD and gradually decreased \((\text{yellow to green to blue})\) to \(0\%\) as the animal was oriented away from the RSD position. When the gain was decreased while LSD (Fig. 2B, yellow arrow), the maximal gain changes \((-40\%, \text{ blue})\) occurred with the animal in the LSD position and changes gradually decreased to \(-5\%\) as the animal was oriented away from LSD \((\text{green to yellow to red})\). Similar gain changes in three dimensions occurred after the aVOR gain was increased while prone (Fig. 2C, blue arrow) or decreased while supine (Fig. 2D, yellow arrow). In each case, the maximal gain changes occurred in the head position in which the gain was adapted, and the gain changes declined as the animal was tilted away from that position. The variation in the gain changes was relatively small when the head was tilted orthogonal to the plane that contained the position in which the gain was adapted.

Because gain changes along each of the planes of tilt closely followed a sinusoidal function (Fig. 1, D–I), we posited that they could be represented as a surface with a single peak that declined sinusoidally in any direction of movement from the head orientation at which the peak occurred. The gain change at the position of adaptation was used to predict the gain changes in all other head orientations with the assumption that the changes followed a sinusoidal function whose amplitude was also a sinusoidal function of head orientation relative to the position of adaptation. That is, the gain changes plotted as a function of tilt about a single axis would be approximated by \(y = A \cdot \cos (\alpha + B_1) + C\). When the animal was tilted about arbitrary axes in three dimensions, the changes would be approximated by \(y = A \cdot \cos (\beta + B_2) \cdot \cos (\alpha + B_3) + C\). We demonstrated previously that the peak-to-peak gravity-dependent component is of comparable magnitude to the gravity-independent component at all times during adaptation (Xiang et al. 2004). Based on this result, we simplified our model by assuming that \(A = C\).

Based on these assumptions, gain surfaces were generated (Fig. 2, E–H) that compared favorably with the corresponding surfaces generated by the spline fits to the experimental data (Fig. 2, A–D). There were local differences when the animal was tested in the prone position after adaptation while supine (Fig. 2, D and H). Overall, however, the similarities in the surfaces of the gain curves support the idea that the changes in aVOR gains declined sinusoidally as the head is moved away in any direction from the position of maximal gain change in three dimensions.

**DISCUSSION**

The major finding of this study is that a gravity-dependent component is associated with every horizontal aVOR gain change, regardless of the head orientation in which the gain was adapted. Thus signals arising in the otoliths have a considerable input to the neural structures that govern plasticity in the aVOR. Although the horizontal aVOR has been extensively studied over the last 40 years, there is little information that would suggest that input from the otolith organs plays a significant role in the amount of aVOR gain adaptation. The implication of the gravity dependence is that there must be a much broader neural organization that is called into play than simply the canal-oculomotor pathways when retinal slip signals a disparity between head and eye movements.

Our previous studies of gravity-dependent adaptation of the vertical aVOR had suggested such an organization exists, but the studies were confined to one plane (Yakushin et al. 2003a–c). The present results extend this to show that the changes in aVOR gains decline sinusoidally as the head is moved away in any direction from the position of maximal gain change regardless of the head position in which the aVOR gain was adapted. Moreover, the gravity-independent gain changes obtained for tilts in four different planes were comparable, demonstrating that they are uniformly distributed in three dimensions. Our previous studies showed that both the gravity-dependent and -independent components could be predicted in one plane if the aVOR gain was measured in the position of adaptation and the opposite head orientation (Yakushin et al. 2000a, 2003c). The present results extend this to show that it is possible to predict both components for any head orientation in three dimensions from measurements of gain in the position of adaptation.

The functional significance of gravity-dependent gain changes is of considerable interest (see Shelhamer and Zee 2003 for review). Because of the close association of the aVOR with stabilization of vision, we posit that the function of this gravity dependence is to improve stability of visual images on the retina during angular head rotation in a gravitational environment. Reorientation of the head relative to a structured visual environment would result in different amounts of retinal slip than were encountered during the adaptation process due to differences in optic flow (Miles 1997). This would require a different gain state of the aVOR for every head position to help reduce retinal slip. One strategy to achieve this would be to set the aVOR gains to be optimal for a particular head orientation and adjust them toward the unadapted state as the head was oriented away from this position. This could be accomplished by the functional relationship of gain with head position that we have demonstrated.
FIG. 2. Three-dimensional reconstructions of the experimental data (A–D) and modeling of these data (E–H). The gain was increased when RSD (A) and prone (C) or decreased when LSD (B) or supine (D). The predicted values for A–D are shown below in E–H. The dark red color and deep blue color for the experimental data and model predictions represent the maximal and minimal gain changes, respectively. The black arrows in each graph represent the positions of the head tilted 90° from the upright in LSD, RSD, prone, and supine positions. The blue arrows represent the head orientation in which the gain was increased, and the yellow arrows in which the gain was decreased. See text for details.
In a preliminary study, gravity-dependent roll gain changes were only half of those for the horizontal and vertical aVORs (Yakushin et al. 2003d). This implies that the vestibular system has a preference for supporting compensatory eye movements along the horizontal and vertical directions. This difference between horizontal and vertical versus roll is reflected in other properties of the aVOR. The unadapted gain of the roll aVOR, which is ~0.6 in humans and monkeys (Crawford and Vilis 1991; Henn et al. 1992), is substantially smaller than that of the horizontal and vertical aVOR, which are closer to unity. Similar anisotropies are also present in the visual system. Visual acuity is highest for perception of objects oriented horizontally or vertically rather than obliquely (Campbell et al. 1966; Howard and Templeton 1966). From this, we propose that the anisotropy previously shown for the visual system is global and extends to both aVOR behavior and its plasticity. That is, the aVOR gain is optimized for maintaining retinal image stability for the horizontal and vertical directions under natural conditions, and as shown here for the first time, it spatially adapts to optimize retinal stability over three-dimensional space.

GRANTS

This work was supported by National Institutes of Health Grants DC-04996, DC-05204, EY-11812, EY-04148, and EY-01867.

REFERENCES


