Published in final edited form as:

Exp Brain Res. 2012 July ; 220(2): 165–178. doi:10.1007/s00221-012-3127-3.

Modeling spatial tuning of adaptation of the angular vestibulo-ocular reflex

Yongqing Xiang,

Department of Computer and Information Science, Brooklyn College of the City University of New York, 2900 Bedford Av & Av H, Brooklyn, NY 11210, USA

Sergei B. Yakushin, and

Department of Neurology, Mount Sinai School of Medicine, New York, NY 10029, USA

Theodore Raphan

Department of Computer and Information Science, Brooklyn College of the City University of New York, 2900 Bedford Av & Av H, Brooklyn, NY 11210, USA

Sergei B. Yakushin: sergei.yakushin@mssm.edu; Theodore Raphan: raphan@nsi.brooklyn.cuny.edu

Abstract

Gain adaptation of the yaw angular vestibular ocular reflex (aVOR) induced in side-down positions has gravity-independent (global) and -dependent (localized) components. When the head oscillation angles are small during adaptation, localized gain changes are maximal in the approximate position of adaptation. Concurrently, polarization vectors of canal–otolith vestibular neurons adapt their orientations during these small-angle adaptation paradigms. Whether there is orientation adaptation with large amplitude head oscillations, when the head is not localized to a specific position, is unknown. Yaw aVOR gains were decreased by oscillating monkeys about a yaw axis in a side-down position in a subject–stationary visual surround for 2 h. Amplitudes of head oscillation ranged from 15° to 180°. The yaw aVOR gain was tested in darkness at 0.5 Hz, with small angles of oscillation ($\pm 15^\circ$) while upright and in tilted positions. The peak value of the gain change was highly tuned for small angular oscillations during adaptation and significantly broadened with larger oscillation angles during adaptation. When the orientation of the polarization vectors associated with the gravity-dependent component of the neural network model was adapted toward the direction of gravity, it predicted the localized learning for small angles and the broadening when the orientation adaptation was diminished. The model-based analysis suggests that the otolith orientation adaptation plays an important role in the localized behavior of aVOR as a function of gravity and in regulating the relationship between global and localized adaptation.

Keywords

Adaptation; Modeling; Monkey; Vestibular; VOR

Introduction

The angular vestibulo-ocular reflex (aVOR) stabilizes gaze in space by counter-rotating the eyes in the direction that is opposite to the head rotation. Performance of the reflex is measured by its gain, which is defined as a ratio of eye velocity re head velocity. When there

is conflict between eye velocity produced by the aVOR and motion of the visual surround, there is retinal slip, which drives the aVOR to adapt its gain, so that it is in consonance with the visual surround. This adapted gain is maintained even when tested in darkness (Ito and Miyashita 1975; Gonshor and Melvill Jones 1976a; Gonshor and Melvill Jones 1976b; Miles and Lisberger 1981). This shows that the gain of the aVOR had been plastically adapted.

Adaptation of the aVOR gain has been shown to be contextual, whose adapted value is present for a specific context, but has different values in other contexts (Schultheis and Robinson 1981; Shelhamer et al. 1992; Lewis et al. 2003). Gravity serves as a context for adaptation of yaw and pitch aVOR (Baker et al. 1987a, b; Tiliket et al. 1993; Yakushin et al. 2000a, 2003a, 2005b), but to lesser extent for the roll aVOR, which already contains a gravity-dependent variation, even without adaptation (Yakushin et al. 2009). Thus, when the yaw or pitch aVOR gain is adaptively modified in a side-down position with small angles of rotation, the adaptive changes are specific for that approximate head orientation and gradually decrease as animals are oriented away from this position. The adaptation comprises two components, one that depends on gravity, localized to a specific head orientation, and one that is global, independent of gravity (Yakushin et al. 2003c).

Models of adaptation of the aVOR have largely been confined to one dimension based on a simple concept that the head and eye velocity summated with retinal slip on Purkinje cells and the error signal modified the gain of the aVOR (Ito et al. 1974; Robinson 1976; Lisberger and Fuchs 1978; Wilson and Melvill Jones 1979; Miles et al. 1980; Miles and Lisberger 1981; Lisberger 1994; Lisberger et al. 1994; Luebke and Robinson 1994; Hirata and Highstein 2001). While these models of adaptation have driven research for understanding the aVOR adaptive process for a number of years, they were not designed to shed light on global and localized learning (Kimpso et al. 2005), especially where gravity is the context (Xiang et al. 2006). This requires that aVOR learning be examined in three dimensions, and analysis and modeling methods be devised that are geared toward three-dimensional (3-D) model perspective of the aVOR and its gravitational dependence. Such 3-D modeling of aVOR gain adaptation was developed to explain cross-axis adaptation (Schultheis and Robinson 1981). In this model, cross-coupled components of an aVOR gain matrix were adapted so that a horizontal head rotation induced a vertical component of eye movement. While this model was the first forage into 3-D aspects of adaptation, it still was concerned with the global gain changes of the aVOR and did not address the contextual or localized aspects of learning.

Localized components of aVOR learning came from an understanding that gravity was an important context allowing different adapted gains for different head positions (Yakushin et al. 2000a). A model of this gravity-dependent component of adaptation considered how a distributed pattern of otolith polarization vectors might interact with canal input to generate the context for learning when there is visual-vestibular mismatch (Xiang et al. 2006). This model incorporated Hebbian learning into a 3-D neural net model, which implemented the canal and central processing of the aVOR model that we developed (Xiang et al. 2006). The feasibility of this model structure was tested against a large database of experimental data, and analysis techniques were developed to compare model predictions with the data. It is one of the few areas where distributed neural net learning models have been critical in evaluating data while maintaining a neural structure consistent with canal and otolith convergence in the central vestibular system (Xiang et al. 2006; Anastasio 2010).

The efficacy of the distributed model was its ability to predict the vertical aVOR gain distribution in 3-D after adaptation at different head positions where the gravity vector did not vary during the adaptation process (Yakushin et al. 2005a; Xiang et al. 2006). The adaptation of the horizontal aVOR with small angles of rotation, while side down, also

allows the contextual adaptation to take place (Yakushin et al. 2005b). Whether increase in the amplitude of head rotations during adaptation generates a sustained localized adaptation at some average orientation is not known. It is also not known whether the global learning is still maintained. One prediction is that when the head orientation information during adaptation is diffused over a large angle, the fusion algorithm for combining visual and orientation information for central adaptation is more widely distributed across head orientations. Accordingly, this would reduce the sharp tuning of the gravity-dependent gain changes, distributing these changes over a wider angle when the angle of head oscillation during adaptation increases.

Another explanation could be related to our recent findings that there are classes of otolith–canal convergent neurons, which adapt their polarization vectors toward the direction of gravity during side positions (Eron et al. 2008; Kolesnikova et al. 2011b) and other classes that do not (Eron et al. 2009). These neurons could provide a head fixed reference for determining the context for implementation of a specific gain. Thus, the orientation adaptation neurons could be involved in the gravity-dependent adaptation process, while the otolith-only neurons could be involved in the implementation of the context for establishing the aVOR gain. One of the few ways this could be tested is by simulating orientation adaptation, comparing model predictions and data, thereby determining whether the model required this component to explain the large amplitude adapted responses.

The purpose of this study was to model the gravity-dependent adaptation with a neural network model that considers orientation adaptation of polarization vectors and to compare its predictions with data that utilize small and large angles of head oscillations during adaptation. We previously demonstrated that the amount of gravity-dependent gain changes is similar for yaw and pitch aVOR, regardless of whether gain was increased or decreased. Thus, this study was restricted to yaw aVOR gain decrease in side-down positions and forms the basis for modeling the behavior of neurons that adapt their orientation (Eron et al. 2008; Kolesnikova et al. 2011b) and how they contribute to localized gravity-dependent adaptation.

Experimental methods

Experiments were performed on three cynomolgus monkeys (*Macaca fascicularis*, M0102, M17115, and M17088). The experiments conformed to the Guide for the Care and Use of Laboratory Animals (National Research Council 1996) and were approved by the Institutional Animal Care and Use Committee. Surgical procedures were performed in two stages under anesthesia in sterile conditions. First, a head mount was implanted on the skull to provide painless head fixation in stereotaxic coordinates during testing (Sirota et al. 1988; Yakushin et al. 2000b). At a second surgery 2 weeks later, two coils were implanted on the left eye. One coil measured the horizontal (yaw) and vertical (pitch) components of eye position (Robinson 1963; Judge et al. 1980). Another coil, placed approximately orthogonal to the frontal coil (Yakushin et al. 1995), was used to measure the torsional (roll) component of eye position.

Eye movement recordings

During experiments, animals sat in a primate chair with the head fixed to a plastic frame in a vestibular stimulator that could rotate the animal about three independent axes that go through the center of rotation of the head. There is also an optokinetic drum, which surrounds the animal and is capable of inducing full field optokinetic stimulation. The stimulator has been described in detail in previous publications (Raphan et al. 1981; Yakushin et al. 2000a). To calibrate eye movements, animals were rotated in light at constant velocity of 30°/s about a spatial vertical axis while upright for yaw, left-side-down

for pitch and prone for roll. It was assumed that horizontal and vertical gains were close to unity (Robinson 1963; Raphan et al. 1979), and torsional gains were assumed to be 0.6 (Crawford and Vilis 1991; Henn et al. 1992; Yakushin et al. 1995).

Eye position voltages and voltages related to the velocity and position of the chair oscillation as well as to the position of the spatial horizontal (gimbal) axis were recorded with amplifiers having a band pass of DC to 40 Hz. Data were acquired by computer and analyzed offline. Voltages were digitized at 1 kHz/channel with 16-bit resolution. Voltages related to eye position were digitally differentiated by finding the slope of the least squares linear fit to data points obtained over 25 ms periods. Saccades were eliminated using a maximum likelihood ratio criterion (Singh et al. 1981). The accuracy of saccade removal was monitored by visual inspection and, when necessary, was manually corrected. This correction affects less than 5 % of experimental data. Since only yaw eye velocity was induced, there were no pitch and roll components and they were not considered in the analysis.

Protocol for aVOR gain adaptation

The horizontal aVOR gain was adaptively decreased by combined in phase oscillation of the primate and optokinetic drum for 2 h with animals in a side-down position while in light. The angular amplitude of the adaptive stimulus was varied from 15° to 180°. Since it was not possible to maintain both stimulus peak velocity and frequency constant for a given amplitude, two frequencies were used. To achieve 15° amplitude, we oscillated the head at 0.25 Hz. To achieve 90°, 135° and 180° amplitudes, the head was oscillated at a lower frequency of 0.05 Hz. Both frequencies were in the range where visual-vestibular interaction would adapt the aVOR. In all cases, the gravitational vector rotated about the yaw axis of the head (a sinusoidal off vertical axis rotation, OVAR). This type of stimulus does not activate the horizontal linear vestibular ocular reflex (IVOR) at the frequencies generated by the velocities of rotation (See Raphan and Cohen 2002 for review). Moreover, the viewing distance from the animal to the visual environment (Drum) was ≈ 45 cm. For this large viewing distance, the gain of the horizontal IVOR is negligible. Vergence also was not a factor as it was the same in all conditions.

Protocol for determining gain as a function of head orientation

The gain (eye velocity/head velocity) of the horizontal aVOR before adaptation was obtained by head oscillations in yaw in darkness at 0.5 Hz ($\pm 15^\circ$ amplitude), while the animal was upright or tilted in forward–backward (F–B), left–right side-down (LSD–RSD), left anterior—right posterior (LA–RP) and right anterior—left posterior (RA–LP) canal planes in 10° increments up to 90° (Yakushin et al. 2005b). Tilt angles were not randomized to minimize the variation of gravity as the animals were tilted for testing in a given position. However, the plane of testing and directions of tilt were randomized. The average amplitude of ten cycles of head and eye velocity oscillations was used to obtain the gain.

Previous studies (Yakushin et al. 2003b, 2005a, b; Schubert et al. 2008) indicate that gravity-dependent aVOR gain changes could be observed for several days after adaptation, therefore, at least 1 week was allowed for the aVOR gain to return to the unadapted state before the next gain adaptation was induced. Yaw aVOR gain of each animal was decreased in left-side-down (LSD) or right side-down (RSD) head orientations randomly. For these two conditions, the gain reductions as a function of head orientation had mirror symmetry about the upright position. Therefore, the data were reflected about the head upright and combined. Gain changes for each head position were plotted in three dimensions and expressed as a surface using a spline interpolation (Sandwell 1987).

Statistical analysis

Depending on the type of the experiment, standard t-tests and ANOVA were used to analyze pairs or sets of data, respectively. To determine significant differences for the gravity-independent adaptation for 4 planes of tilting, the sinusoidal fits to the data were subtracted from the data values and the four residuals were compared with ANOVA. For data-model comparison, we utilized a reduced case of the analysis of variance (F statistic). These methodologies are completely described in previous publications (Yakushin et al. 1995; Kolesnikova et al. 2011b).

Results

Verification of adaptive stimulus: adaptation in the upright position

We used different frequencies of adaptation as the amplitudes were changed. This was done to maintain the accelerations at larger amplitudes to within manageable levels. Variation in frequency could be a factor in the generation of the aVOR gain changes (Yakushin 2012). We therefore performed the adaptation of the horizontal aVOR at these different frequencies and amplitudes in the upright position as a control. The result was that the gravity-independent and gravity-dependent gain changes were identical for all amplitudes and frequencies. Thus, changes that occur when animals are adapted on their sides are due to variation of gravity during adaptation.

We adapted the horizontal aVOR gain in the upright using 15°, 90°, 135°, and 180° amplitude of yaw rotation. Eye velocity relative to head velocity during suppression adaptation was the same for all amplitudes of stimulation ($p = 0.131$). The peak gain changes occurred when upright (position of adaptation) and the gain changes decreased when animals were tested when tilted toward left- and right-side-down positions (Yakushin et al. 2003c). There was no effect of the amplitude of the adaptive stimulus on either the gravity-dependent component ($7.7 \pm 2.3\%$, $p = 0.484$) or the gravity-independent component ($9.2 \pm 4.7\%$, $p = 0.147$). This shows that amplitude of the head rotation has no effect on gravity-dependent or gravity-independent components, when orientation of the head relative to gravity does not change during adaptation.

Gain decrease with small-angle head oscillation in side-down positions

Before adaptation, yaw gains were invariant as a function of head orientation re gravity (Fig. 1a, blue symbols). After adaptation in LSD (−90°), gain was minimal in the position of adaptation, but the gain approached pre-adapted values as the head was oriented toward RSD (Fig. 1a, red symbols). Gain changes relative to pre-adapted values was approximated by a sinusoid (gravity-dependent change) and a bias level (gravity-independent change) (Fig. 1b).

When the aVOR gain was decreased with small-angle oscillation amplitudes (15°) in side-down positions, the gain changes were the same as found previously (Yakushin et al. 2000a, 2003c, 2005a), although the variations among monkeys were greater than previously reported (Yakushin et al. 2005a). Regardless, the gravity-dependent gain changes were maximal in the LSD-RSD plane (6.8 %; Fig. 2a, black symbols and black fitted curve), were somewhat smaller in the LA-RP (4.7 %; Fig. 2b) and RA-LP planes (5.0 %; Fig. 2c), and were negligible in the F-B plane (0.9 %; Fig. 2d) (Table 1), but were not significantly different ($p = 0.055$, t test). The gravity-independent gain changes were $\approx -10.0\%$ in the LSD-RSD and F-B planes. The variations of data from different monkeys were greater for the RA-LP and LA-RP planes, which slightly decreased the gravity-independent bias level (-6.9% , $p < 0.05$, ANOVA).

It should be noted that with the small amplitude oscillation, there was overlap of the region covering the swing of the gravity vector in head coordinates during testing (dark shading in insets of Fig. 2) with that during adaptation (light shading in insets of Fig. 2) only when the animal was tilted LSD-RSD. Consequently, gravity-dependent gain changes in LA-RP and RA-LP are significant but smaller than the gravity-dependent changes measured in LSD-RSD. When the animals were tested F-B, the average orientation of gravity vector during adaptation is orthogonal to that during testing (Fig. 2, Inset D). Consequently, there were no gravity-dependent gain changes. The surface describing the gain changes as a function of fore-aft and side-down tilts peaked negatively at the position of adaptation (Fig. 2e).

Gain decrease with large head oscillation

Large amplitude head oscillations had a smoothing effect on the aVOR gain distribution (Figs. 3, 4, 5). The differences in average gravity-dependent gain changes for LSD-RSD, versus LA-RP and RA-LP decreased as the amplitudes increased from 90° (Fig. 3a, b, c) to 135° (Fig. 4a, b, c) (Table 1). There was also a modulation in gain changes in the F-B plane (Figs. 3d, 4d). The maximal gain decrease was observed in both prone (Forward) and supine (Back) head orientations with minimal changes close to upright head orientation. The gravity-independent component was the same ($\approx -10\%$, $p > 0.05$, ANOVA) in all planes and not affected by these amplitudes of head oscillation (Figs. 3a-d, 4a-d, dashed horizontal lines). Some decrease was observed in every head orientation although changes were smaller in the upright and RSD positions (Figs. 3e, 4e).

For adaptation with oscillations of $\pm 180^\circ$ (Fig. 5), gravity-dependent gain changes were significantly smaller than for other amplitudes of head oscillation (Fig. 5a-d; Table 1) and the gain changes were similar in virtually every head orientation (Fig. 5e). There was also now a significant increase in amplitude of the gravity-independent (bias) component ($\approx -20\%$ vs. $\approx -10\%$, $p = 0.016$, t test; Fig. 5a-d, horizontal dashed lines).

Neural network model of gravity-dependent adaptation of the aVOR

The starting point of the modeling work was the 3-D aVOR model (Raphan and Cohen 2002), which was implemented as a distributed neural net (Xiang et al. 2006). We first treated the large amplitude adaptation as learning that occurred at multiple positions. Previous results had indicated that the model was capable of learning and superposing three levels of gain at different head orientations (Xiang et al. 2006). However, as the head moved through large angles it could not predict the data for $\pm 180^\circ$ LSD adaptation (Fig. 6a). In this adaptation paradigm, the animal starts the oscillation from the -180° position which is RSD, passes the 0° (LSD) once and ends up in $+180^\circ$ position which is still RSD. This forces the original model to decrease the gain more in the RSD position than the LSD position. The model predicted a resultant adapted spatial distribution of gain changes, which had its maximal changes in the RSD position and minimal changes in LSD, which did not match the experimental data (Fig. 6a, cf red and blue symbols). The reason for this is that as the model adapts the parameters for rotation about yaw from -180° to $+180^\circ$, the RSD orientation occurs twice as frequently (both -180 and $+180$ are RSD) as for other orientations. The peak change predicted by the model expectedly occurred at RSD (Fig 6a, blue symbols). The minimal change occurred at LSD rather than where the data had its minimal change (0° -Upright) (Fig. 6a, red symbols).

This demonstrates that the model without incorporating new adaptive features cannot accurately predict the changes in aVOR gain induced by large angles of oscillation.

We considered what features of the neural learning components are necessary for fitting the data. One of the most important discoveries that could provide a basis for modeling

amplitude-dependent learning is orientation adaptation that is present in vestibular only (VO) and position-vestibular-pause (PVP) neurons (Eron et al. 2008; Kolesnikova et al. 2011b). Such orientation adaptation reconfigures the orientation of a specific group of vestibular cells, but central otolith-only units maintain their spatial orientation (Eron et al. 2009). If the orientation adapted cells would participate in the adaptation while the visual system is activated and be inactivated while testing the aVOR in darkness, it would add a new dimension to how gravity-dependent adaptation is implemented and explain the data. We now consider a model that incorporates orientation adaptation into the aVOR learning process, and relate it to our most recent physiological findings.

Conceptual modeling of gravity-dependent adaptation with orientation

adaptation—The model consists of three inputs: Head Orientation, which activates the otoliths, Head Velocity, which activates the canal system, and visual surround velocity, which is utilized in activating the weight and bias learning rules for gravity-dependent and gravity-independent adaptation. Based on our initial studies of gravity-dependent adaptation for the vertical aVOR, we postulated that the adaptation comprised two distinct processes: gravity-dependent and gravity-independent components (Yakushin et al. 2003c, 2005b). The reason for this hypothesis is that the mean of the adapted gain changes of the aVOR (bias) was approximately the same when measured for tilts in the F–B, LSD-RSD, LA-RP and RA-LP planes after adaptation with small amplitudes of rotation in a given head orientation. However, the sinusoidal variation in gain changes as a function of head orientation was largest in the plane that included the position of adaptation (LSD-RSD). There were no gain changes for tilts in an orthogonal plane. The data in this study for small amplitude adaptations confirm these findings (Fig. 2) and our hypothesis. We now have evidence that the gravity-dependent component is coded in caudal FN (Kolesnikova et al. 2012) while the gravity-independent component is coded elsewhere, probably in the flocculus, which is known to be important for aVOR gain adaptation (Ito et al. 1974; Miles and Lisberger 1981). Thus, the learned parameters (w_{ij}) for gravity-dependent adaptation in the model have been identified with the caudal FN and bias (b_{ij}) has been identified with the flocculus (Fig. 7). Orientation adaptation is hypothesized to be coded in rostral FN, utilizing an orientation estimator and input from the canal system. An important function associated with the orientation subsystem is estimation of the orientation of the head relative to gravity. This provides a frequency tuned teaching signal that helps adapt the weights, w_{ijk} in caudal FN. These weights are associated with the gain of the gravity-dependent component of the aVOR, which is adapted during visual-vestibular conflict.

It is known that the semicircular canals represent a non-orthogonal coordinate frame whose lateral canals are tipped back 30° while the vertical canals are tipped back 40° and rotated 45° relative to the head. When the head is rotated, the angular head velocity is projected along the axes of the canals and is represented in canal coordinates by a matrix, T_{can} (Yakushin et al. 1998). These head velocity components must be converted back to head coordinates to drive eye velocity. However, each component of the velocity in canal coordinates projects to a component of eye velocity with a certain gain. Thus, there are nine (9) gain values that represent the conversion of the head velocity signal to the eye velocity signal, and the complete transformation can be represented as:

$$T_{\text{head}} = \begin{bmatrix} g_{00}A & g_{01}B & g_{02}C \\ g_{10}D & g_{11}E & g_{12}F \\ g_{20}G & g_{21}H & g_{22}I \end{bmatrix} \quad (1)$$

where the elements $A, B, C, D, E, F, G, H,$ and I form the inverse of the head to canal transformation, T_{can} :

$$T_{\text{can}}^{-1} = \begin{bmatrix} A & B & C \\ D & E & F \\ G & H & I \end{bmatrix} \quad (2)$$

and the g 's are the projections from each of the three components of head velocity to the three components of eye velocity. Thus, the eye velocity vector, v_{eye} , can be represented by the stimulus head velocity vector, v_{head} :

$$v_{\text{eye}} = T_{\text{head}} \cdot (T_{\text{can}} \cdot v_{\text{head}}) \quad (3)$$

where elements of v_{eye} and v_{head} are in the order of roll, pitch, and yaw. The overall yaw gain is then calculated as:

$$v_{\text{eye}}(\text{yaw})/v_{\text{head}}(\text{yaw}) \quad (4)$$

The nine distributed gains, g_{ij} ($i = 0 \sim 2, j = 0 \sim 2$), when adapted by the artificial neural network, determine the gain matrix of the aVOR (Xiang et al. 2006).

We have hypothesized that the otolith–canal convergent neurons in the central vestibular system regulate the gravity-dependent aVOR gain adaptation (Kolesnikova et al. 2011a). Their functions are simulated as polarization vectors that have various orientations re gravity in the three canal planes. The projection of their orientation onto the axis of gravity drives the training of nine distributed aVOR gains through weights. The weights are adapted to reduce the retinal error as follows:

The gravity-dependent component is the summation of the products of the weight and a projection of the polarization vector onto the direction of the acceleration of gravity. The gravity-independent component is unrelated to the projection and is represented by a single bias value, b_{ij} . Thus, g_{ij} can be represented as:

$$g_{ij} = \sum_{l=0}^{n-1} w_{ijl} \langle \hat{\mathbf{a}}_g, \hat{\mathbf{p}}_l \rangle + b_{ij} \quad (5)$$

where n is the number of unit polarization vectors, $\langle \cdot, \cdot \rangle$ is the inner product and represents the projection of the polarization vector onto the acceleration of gravity, $\hat{\mathbf{a}}_g$. We utilized 36 polarization vectors for each canal plane for a combined number $n = 108$. These are assumed to be located in the vestibular nucleus (Fig. 7, VN). The indices $i = 0, 1, 2$ represent torsional, vertical, and horizontal VOR and $j = 0, 1, 2$ represent anterior, posterior and lateral canals, respectively. That is, g_{00} represents the gain of anterior canal activation producing the torsional VOR.

The weight values (w_{ijl}) and the bias value (b_{ij}) are trained iteratively as follows:

$$\frac{\Delta w_{ijl}}{\Delta t} = k_{ij} s_{ij} \langle \hat{\mathbf{a}}_g, \hat{\mathbf{p}}_l \rangle \frac{\Delta E_i}{\Delta t} \quad (6)$$

$$\frac{\Delta b_{ij}}{\Delta t} = h_{ij} s_{ij} \frac{\Delta E_i}{\Delta t} \quad (7)$$

where k_{ij} and h_{ij} are training speed factors for w_{ijl} and b_{ij} , respectively. ΔE_i represents the i th component of the retinal error. The vector ΔE is computed as follows:

$$\Delta E = v_{\text{eye}}^{\text{target}} - v_{\text{eye}} = g^{\text{target}} \cdot v_{\text{head}} - T_{\text{head}} \cdot T_{\text{can}} \cdot v_{\text{head}} \quad (8)$$

The parameter, g^{target} , is the measured gain of the aVOR in the position of adaptation and is the only input to the model that was experimentally determined. The s_{ij} components represent the stimulus strength from v_c^j , the rotational head velocity in the canal coordinate frames, with j representing anterior (0), posterior (1), and lateral (2) canals (See (Xiang et al. 2006) for details). They are calculated as follows:

$$S = [s_{ij}] = \begin{bmatrix} Av_c^0 & Bv_c^0 & Cv_c^0 \\ Dv_c^1 & Ev_c^1 & Fv_c^1 \\ Gv_c^2 & Hv_c^2 & Iv_c^2 \end{bmatrix} \quad (9)$$

where

$$v_c = [v_c^0 \ v_c^1 \ v_c^2]^T = T_{\text{can}} \cdot v_{\text{head}} \quad (10)$$

Model allowing orientation adaptation for the polarization vectors—To explain the large amplitude aVOR gain adaptation, we updated our model in the following way:

First, all orientations of the head during one cycle of the sinusoidal rotation were treated as adaptation sites equally and received equal amount/level of adaptation. As an example, when the animal was adapted in left-side-down (LSD) position with a $\pm 90^\circ$ rotation about the yaw axis, all positions between -90° and 90° in 10° increments are considered adaptation sites and all with the same target gain value.

In addition to modifying the weights, the polarization vectors ($\hat{p}$) were allowed to shift their orientation during the adaptation toward the direction of acceleration of gravity (Eron et al. 2008; Kolesnikova et al. 2011b). We implemented these central shifts in polarization as a summation of two vectors (Fig. 8). Each neuron received two otolith inputs, and the overall otolith response vector orientation (RVO) is the linear sum of the two with the coefficients as weights (α and $1-\alpha$). Without a loss of generalization, we assumed the otolith input less aligned with gravity is p_{lk} and is associated with α , which is initialized with a value of 0.5. As the animal's head is held close to a specific orientation, the weights, α , will be reduced adaptively, reducing this input. At the same time, an increase in the value ($1-\alpha$) will be awarded to the otolith input (p_{lq}) that is better aligned with gravity. This will shift the orientation of the polarization vector toward the gravito-inertial acceleration (GIA). Similar shifts in VO neuron were found in the RVO toward the input that is the closest to gravity (Eron et al. 2008; Kolesnikova et al. 2011b).

We also found that a feature of the model that was required to fit the data was that after adaptation, during the testing period, when there is no light, the contribution from the shifting polarization vector will be switched off during the test phase of the experiment.

In the original neural network model, it was assumed that all 36 polarization vectors ($\hat{p}$) in a canal plane were uniformly distributed over 360° , and each had initially the same weight in determining the gain. To implement orientation adaptation, we must further assume that the uniform state is adapted from a default state without gravity, which is linked to the vertical head position, and that the uniform distribution is driven by gravity in the upright position. During adaptation, the polarization vectors that change their orientation contribute to the

gravity-dependent adaptation. Following adaptation, when the animal is tested in darkness, these neurons do not contribute to the gain of the aVOR.

Comparison of experimental data with model-based predictions

The model utilizing orientation adaptation (Fig. 7) produced predictions that conform to the experimental data for the same experimental condition (Fig. 6b). The model predicted the gravity-dependent component of the experimental data for 15°, 90°, 135°, and 180° oscillation amplitudes of adaptation, respectively (Figs. 2, 3, 4, 5). The bias or gravity-independent gain changes were also accurately predicted. However, the model-predicted bias value was based on learning for the side-down position only. The small errors in bias between model and data in the LA-RP and RA-LP planes after small-angle adaptation (−10 % model prediction compared to −6.9 % for data) (Fig. 2b, c) are due to the variation of the data across animals (See above).

For the small-angle adaptation amplitude (15°), both the model and data described the same surface in 3D, showing a maximal value and sharp tuning at the LSD position (Fig. 2e, f, respectively). When the adaptation amplitude increased to 90°, the maximal value was still close to LSD, but the tuning across the surface was broader (Fig. 3e, f, blue region). For the 135° adaptation amplitude, the tuning broadened further, and the difference between maximal and minimal values was reduced (Fig. 4e, f). This trend was most prominent in the 180° amplitude of adaptation, where the surface is essentially flat, and it became hard to distinguish the point of maximal gain change (Fig. 5e). In the model prediction, all positions along the edge of the square have similar (larger) gain changes while the upright position has the smallest gain changes (Fig. 5f). These data indicate that for large adaptation angles, the localized learning (gravity-dependent gain change) of the aVOR is lost and is reduced to global (gravity-independent) learning.

Discussion

This study shows that gravity-dependent learning of the aVOR gain must have a steady orientation of gravity relative to the head during learning to effect a sharp spatial tuning of the gain changes to the position of adaptation. That is, the head should be confined to small rotational angles (< 15°) during the adaptive process in order to tune the maximal gain change at a particular head orientation. If the orientation of the head relative to gravity varies over a broad spatial range (>90°), the tuning of the learning process is distributed over a wider range of head orientations. For angles between 15° and 90°, we expect that adaptation should broaden monotonically, but this was not tested. Our original model of gravity-dependent adaptation of the aVOR (Xiang et al. 2006) could not accurately predict this phenomenon. When we incorporated otolith reorientation learning rules previously observed for central vestibular neurons (Eron et al. 2008; Kolesnikova et al. 2011b), the model simulations accurately reproduced the observed spread of the gravity-dependent gain changes as the angle of head oscillation with regard to gravity increased. Thus, the model shows that orientation adaptation is a critical feature of localized learning and helps tune the gravity-dependent component of adaptation.

Gravity-independent gain changes were approximately the same if adaptation was induced by head oscillation with amplitudes of 135° and below, indicating that ~50 % of gain changes were induced independent of gravity. The bias of the sinusoidal fit was much larger when adaptation was induced by head oscillation of 180°. The increased bias component was simulated by making the rate of adaptation of the gravity-independent component greater than the gravity-dependent component. This model prediction is consistent with data showing that the largest gravity-independent gain changes are observed after adaptation with 180° amplitude, although the rates of adaptation for the two components are not known and

this is a conjectured mechanism. Model-predicted changes, however, are more gradual as a function of angle of adaptation than experimentally observed. This suggests that the time course of the actual orientation adaptation drops more rapidly than that assumed in the model. A study of temporal aspects of otolith orientation adaptation would clarify this issue, but these data are not available.

The idea that orientation adaptation supports gravity-dependent adaptation follows from the Hebbian learning rules (Hebb 1949) that we have implemented and are assumed to drive the gravity-dependent adaptation (Xiang et al. 2006). Otolith representations in central vestibular neurons do not have a predominant orientation [See (Wilson and Melvill Jones 1979)]. Thus, when the head is in stationary orientation with regard to gravity during aVOR gain adaptation, only specific sub-groups of PVP neurons will adapt. If a unit is activated by the canal input at a head position that maximally activates the otolith-related activity, learning (increase in sensitivity) in the canal-related path (aVOR gain) is maximal. Alternatively, if orientation of the average otolith polarization vector is orthogonal to the axis of gravity in the position of adaptation or oppositely directed, then the unit may be silent during head oscillation, and therefore, learning does not occur (Eron et al. 2008; Kolesnikova et al. 2011b). Changes in polarization vectors of the convergent otolith input will, therefore, increase the number of neurons that support the learning and as a result will facilitate the learning. Consequently, when the head is oscillated with smaller amplitude, a greater number of convergent otolith polarization vectors will adapt and be better tuned to the position of adaptation than if these vectors would be spread over a greater angle. In the extreme case, when head oscillated 180°, the activation of otolith units is uniform, and therefore, only gravity-independent gain changes would occur. This is supported by the data.

The model can also be used to predict the central organization of gravity-dependent adaptation. We had previously suggested that gravity-dependent adaptation of the aVOR gain is coded in the activity of the canal–otolith neurons located in the vestibular nuclei (Yakushin et al. 2003c). Since the eye–head velocity (EHV) and position-vestibular-pause (PVP) neurons are known to be in the modifiable part of the aVOR pathway (Partsalis and Highstein 1996) and some EHV and PVP neurons receive convergent otolith inputs (McConville et al. 1996; Meng et al. 2005), they are the most likely candidates to transmit gravity-dependent changes in their firing rate to the ocular motor nuclei. Canal–otolith convergent VO neurons in this region of the medial vestibular nucleus did not specifically adapt their sensitivities, but rather adapted their orientation vectors toward the spatial vertical as animals were held in side-down positions (Eron et al. 2008). The same type of behavior was recently found for PVP, but not for EHV neurons (Kolesnikova et al. 2011b). Reorientation of the response vector orientation also did not occur for pure otolith neurons (Eron et al. 2009).

We also found that a key feature of the model that was required to fit the data was that after adaptation, during the testing period, when there is no light, the contribution from the polarization vectors that had adapted their orientation were switched off during the test phase of the experiment. A physiological finding is that pure otolith neurons do not adapt the orientation of their polarization vectors (Eron et al. 2009). This must be the case so that there is a head fixed reference frame at the end of the adaptation period. Orientation learning is only important during aVOR adaptation when vision is present. At the conclusion of the adaptation period, the light is turned off, and the only orientation information that is of importance comes from the otoliths that have not adapted their orientation. In order to maintain our original model structure with the same number of neurons, instead of implementing a separate set of neurons that do not adapt, we simply switched off the orientation adaptation at the end of the adaptive experience. If the adaptation were not

switched off, then the maximal gain changes would occur at the positions of adaptation as the old model had done (Fig. 6).

Evidence for switching off these neurons comes from the behavior of PVP neurons. These are known to be part of the aVOR's three-neuron arc (Cullen and McCrea 1993; Lisberger 1994; Roy and Cullen 2002; McCrea and Gdowski 2003; Fuchs et al. 2005), while VO neurons do not project to the oculomotor nuclei, most likely activating the vestibular nuclei on the contralateral side and providing input to the vestibulo-cerebellum (Broussard et al. 2011). Thus, it seems likely from this model-based analysis that classes of PVP and EHV are involved in the pathway that codes gravity-dependent adaptation (Kolesnikova et al. 2011a), but that orientation adaptation is coded in VO neurons and their projections through cerebellar circuits in the fastigial nucleus (Kolesnikova et al. 2012) may be activated during adaptation in light, but switched off during the testing phase in darkness.

The purpose of the neural net adaptation was to predict the three-dimensional gain distribution of the aVOR as a function of head orientation using only a single input gain change at a single orientation. The model predicts the behavior using a gravity-independent component augmented by a gravity-dependent component, which is modulated by a gravity context. The model does not simulate the dynamical processes that drive the adaptation from visual and angular and linear vestibular ocular reflexes, which is a subject for further study and beyond the scope of this study. However, some general inferences can be made from the present model adaptation equation (Eq. 8), which sheds light on central adaptive processes that govern gravity-dependent adaptation. If the ΔE in Eq. 8 is interpreted as a retinal error driving the adaptive process, then it could give us some understanding of the type of gravity-dependent adaptation that could occur following canal plugging (e.g., Yakushin et al. 1998). In the canal-plugged condition, v_{eye} is reduced at 0.5 Hz (gain ≈ 0.15), due to a shortened canal time constant, but is normal at higher frequencies (Yakushin et al. 1998). The gravity-independent and -dependent gain changes were approximately the same as the normal animal (Yakushin et al. 2000c; 0.5 Hz). A simulation at a frequency of 0.5 Hz using these reduced gains gave the same results as in normal, consistent with our predictions (not shown). At low frequencies, canal plugging eliminates the input from the canals, and the input could be set to zero. Therefore, the model predicts that any output after adaptation for a canal-plugged condition at low frequencies (0.05 Hz) will be zero. The otolith contribution in this model is to condition the canal input and not as driver for generating gravity-dependent adaptation.

Thus, this study supports our previous hypotheses that gravity-dependent adaptation is coded in the activity of central canal-otolith convergent neurons (Yakushin et al. 2003c, 2005a, b; Xiang et al. 2006). It also demonstrates that previously observed reorientation of RVO (Eron et al. 2008; Kolesnikova et al. 2011b) could be responsible for changes in the distribution of the gravity-dependent gain changes and proposes a specific mechanism for accomplishing this. This mechanism may be implemented in the neural organization of the fastigial nucleus.

Acknowledgments

We thank Dimitry Ogorodnikov for developing data analyses program, Olga Storozh for help with data processing, and Dr. Bernard Cohen for helpful suggestions and reading of manuscript. Supported by US Public Health Service Grants, DC04996, DC05204.

References

Anastasio, TJ. Tutorial on neural systems modeling. Sunderland: Sinauer Associates, Inc; 2010. p. 542

- Baker J, Wickland C, Peterson B. Dependence of cat vestibulo-ocular reflex direction adaptation on animal orientation during adaptation and rotation in darkness. *Brain Res.* 1987a; 408:339–343. [PubMed: 3594223]
- Baker JF, Perlmuter SI, Peterson BW, Rude SA, Robinson FR. Simultaneous opposing adaptive changes in cat vestibulo-ocular reflex direction for two body orientations. *Exp Brain Res.* 1987b; 69:220–224. [PubMed: 3436390]
- Broussard DM, Titley HK, Antflick J, Hampson DR. Motor learning in the VOR: the cerebellar component. *Exp Brain Res.* 2011; 210:451–463. [PubMed: 21336828]
- Crawford JD, Vilis T. Axes of eye rotation and Listing's law during rotations of the head. *J Neurophysiol.* 1991; 65:407–423. [PubMed: 2051188]
- Cullen KE, McCrea RA. Firing behavior of brain stem neurons during voluntary cancellation of the horizontal vestibuloocular reflex. I. Secondary vestibular neurons. *J Neurophysiol.* 1993; 70:828–843. [PubMed: 8410175]
- Eron JN, Cohen B, Raphan T, Yakushin SB. Adaptation of orientation vectors of otolith-related central vestibular neurons to gravity. *J Neurophysiol.* 2008; 100:1686–1690. [PubMed: 18497367]
- Eron JN, Cohen B, Raphan T, Yakushin SB. Adaptation of orientation of central otolith-only neurons. *Ann N Y Acad Sci.* 2009; 1164:367–371. [PubMed: 19645928]
- Fuchs AF, Ling L, Phillips JO. Behavior of the position vestibular pause (PVP) interneurons of the vestibuloocular reflex during head-free gaze shifts in the monkey. *J Neurophysiol.* 2005; 94:4481–4490. [PubMed: 16120671]
- Gonshor A, Melvill Jones G. Extreme vestibulo-ocular adaptation induced by prolonged optical reversal of vision. *J Physiol (L).* 1976a; 256:381–414.
- Gonshor A, Melvill Jones G. Short-term adaptive changes in the human vestibulo-ocular reflex arc. *J Physiol (L).* 1976b; 256:361–379.
- Hebb, O. *Organization of behavior.* New York: Wiley; 1949.
- Henn V, Straumann D, Hess BJM, Haslwanter T, Iida N. Three-dimensional transformations from vestibular and visual input to oculomotor output. *Ann N Y Acad Sci.* 1992; 656:166–180. [PubMed: 1599141]
- Hirata Y, Highstein SM. Acute adaptation of the vestibuloocular reflex: signal processing by floccular and ventral parafloccular purkinje cells. *J Neurophysiol.* 2001; 85:2267–2288. [PubMed: 11353040]
- Ito M, Miyashita Y. The efferens of chronic destruction of the inferior olive upon visual modification of the horizontal vestibulo-ocular reflex of rabbits. *Proc Japan Acad.* 1975; 51:716–720.
- Ito M, Shiida T, Yagi N, Yamamoto M. Visual influence on rabbit horizontal vestibulo-ocular reflex presumably effected via the cerebellar flocculus. *Brain Res.* 1974; 65:170–174. [PubMed: 4810171]
- Judge SJ, Richmond BJ, Chu FC. Implantation of magnetic search coils for measurement of eye position: an improved method. *Vision Res.* 1980; 20:535–538. [PubMed: 6776685]
- Kimpo RR, Boyden ES, Katoh A, Ke MC, Raymond JL. Distinct patterns of stimulus generalization of increases and decreases in VOR gain. *J Neurophysiol.* 2005; 94:3092–3100. [PubMed: 16033945]
- Kolesnikova, OV.; Raphan, T.; Cohen, B.; Yakushin, SB. Coding of gravity-dependent and -independent adaptation of the angular vestibulo-ocular reflex (aVOR) by central vestibular eye movement-related neurons. Vol. vol 34. Baltimore: ARO; 2011a Feb 19–23. p. 337#998
- Kolesnikova OV, Raphan T, Cohen B, Yakushin SB. Orientation adaptation of eye movement-related vestibular neurons due to prolonged head tilt. *Ann N Y Acad Sci.* 2011b; 1233:214–218. [PubMed: 21950996]
- Kolesnikova, OV.; Raphan, T.; Cohen, B.; Yakushin, SB. Gravity-dependent adaptation of the angular vestibulo-ocular reflex (aVOR) is coded in the fastigial nucleus (FN). Vol. vol 35. San Diego, California, USA: ARO; 2012 Feb 25–28. p. 18#52
- Lewis RF, Clendaniel RA, Zee DS. Vergence-dependent adaptation of the vestibulo-ocular reflex. *Exp Brain Res.* 2003; 152:335–340. [PubMed: 12879175]
- Lisberger SG. Neural basis for motor learning in the vestibuloocular reflex of primates. III. Computational and behavioral analysis of the sites of learning. *J Neurophysiol.* 1994; 72:974–998. [PubMed: 7983549]

- Lisberger SG, Fuchs AF. Role of primate flocculus during rapid behavioral modification of vestibuloocular reflex. I. Purkinje cell activity during visually guided horizontal smooth-pursuit eye movements and passive head rotation. *J Neurophysiol.* 1978; 41:733–763. [PubMed: 96225]
- Lisberger SG, Pavelko TA, Bronte-Stewart HM, Stone LS. Neural basis for motor learning in the vestibuloocular reflex of primates. II. Changes in the responses of horizontal gaze velocity Purkinje cells in the cerebellar flocculus and ventral paraflocculus. *J Neurophysiol.* 1994; 72:954–973. [PubMed: 7983548]
- Luebke AE, Robinson DA. Gain changes of the cat's vestibulo-ocular reflex after flocculus deactivation. *Exp Brain Res.* 1994; 98:379–390. [PubMed: 8056061]
- McConville KM, Tomlinson RD, Na EQ. Behavior of eye-movement-related cells in the vestibular nuclei during combined rotational and translational stimuli. *J Neurophysiol.* 1996; 76:3136–3148. [PubMed: 8930261]
- McCrea RA, Gdowski GT. Firing behaviour of squirrel monkey eye movement-related vestibular nucleus neurons during gaze saccades. *J Physiol.* 2003; 546:207–224. [PubMed: 12509489]
- Meng H, Green AM, Dickman JD, Angelaki DE. Pursuit-vestibular interactions in brain stem neurons during rotation and translation. *J Neurophysiol.* 2005; 93:3418–3433. [PubMed: 15647394]
- Miles FA, Lisberger SG. Plasticity in the vestibulo-ocular reflex: a new hypothesis. *Ann Rev Neurosci.* 1981; 4:273–299. [PubMed: 6784658]
- Miles FA, Fuller JH, Braitman DJ, Dow BM. Long-term adaptive changes in primate vestibuloocular reflex. IV. Electrophysiological observations in flocculus of adapted monkeys. *J Neurophysiol.* 1980; 43:1477–1493. [PubMed: 6768854]
- National Research Council. Guide for the care and use of laboratory animals. Washington, DC: National Academy Press; 1996.
- Partsalis AM, Highstein SM. Role of the Y group of the vestibular nuclei in motor learning or plasticity of the vestibulo-ocular reflex in the squirrel monkey. *Ann N Y Acad Sci.* 1996; 781:513–524. [PubMed: 8694440]
- Raphan T, Cohen B. The vestibulo-ocular reflex in three dimensions. *Exp Brain Res.* 2002; 145:1–27. [PubMed: 12070741]
- Raphan T, Matsuo V, Cohen B. Velocity storage in the vestibulo-ocular reflex arc (VOR). *Exp Brain Res.* 1979; 35:229–248. [PubMed: 108122]
- Raphan T, Cohen B, Henn V. Effects of gravity on rotatory nystagmus in monkeys. *Ann N Y Acad Sci.* 1981; 374:44–55. [PubMed: 6978641]
- Robinson DA. A method of measuring eye movement using a scleral search coil in a magnetic field. *IEEE Trans Bio Med Electr.* 1963; 10:137–145.
- Robinson DA. Adaptive gain control of vestibuloocular reflex by the cerebellum. *J Neurophysiol.* 1976; 39:954–969. [PubMed: 1086347]
- Roy JE, Cullen KE. Vestibuloocular reflex signal modulation during voluntary and passive head movements. *J Neurophysiol.* 2002; 87:2337–2357. [PubMed: 11976372]
- Sandwell DT. Biharmonic spline interpolation of GEOS-3 and SEASAT altimeter data. *Geophys Res Lett.* 1987; 2:139–142.
- Schubert MC, Migliaccio AA, Minor LB, Clendaniel RA. Retention of VOR gain following short-term VOR adaptation. *Exp Brain Res.* 2008; 187:117–127. [PubMed: 18231780]
- Schultheis L, Robinson DA. Directional plasticity of the vestibulo-ocular reflex in the cat. *Ann N Y Acad Sci.* 1981; 374:504–512. [PubMed: 6951449]
- Shelhamer M, Robinson DA, Tan HS. Context-specific adaptation of the gain of the vestibulo-ocular reflex in humans. *J Vestib Res.* 1992; 2:89–96. [PubMed: 1342386]
- Singh, A.; Thau, GE.; Raphan, T.; Cohen, B. Detection of saccades by a maximum likelihood ratio criterion. *Proceeding of the 34th Annual Conference on Engineering and Biology*; Houston, TX. 1981. p. 136
- Sirota MG, Babaev BM, Beloozerova IN, Nyrova AN, Yakushin SB, Kozlovskaya IB. Neuronal activity of nucleus vestibularis during coordinated movement of eyes and head in microgravitation. *Physiologist.* 1988; 31:8–9.

- Tiliket C, Shelhamer M, Tan HS, Zee DS. Adaptation of the vestibulo-ocular reflex with the head in different orientations and positions relative to the axis of body rotation. *J Vestib Res.* 1993; 3:181–195. [PubMed: 8275253]
- Wilson, VJ.; Melvill Jones, G. Mammalian vestibular physiology. New York: Plenum; 1979.
- Xiang Y, Yakushin SB, Cohen B, Raphan T. Modeling gravity-dependent plasticity of the angular vestibulo-ocular reflex (aVOR) with a physiologically-based neural network. *J Neurophysiol.* 2006; 96:3349–3361. [PubMed: 16971684]
- Yakushin SB. Tuning of gravity-dependent and gravity-independent vertical angular VOR gain changes by frequency of adaptation. *J Neurophysiol.* 2012
- Yakushin SB, Dai M, Suzuki J-I, Raphan T, Cohen B. Semicircular canal contributions to the three-dimensional vestibuloocular reflex: a model-based approach. *J Neurophysiol.* 1995; 74:2722–2738. [PubMed: 8747227]
- Yakushin SB, Raphan T, Suzuki J-I, Arai Y, Cohen B. Dynamics and kinematics of the angular vestibulo-ocular reflex in monkey: effects of canal plugging. *J Neurophysiol.* 1998; 80:3077–3099. [PubMed: 9862907]
- Yakushin SB, Raphan T, Cohen B. Context-specific adaptation of the vertical vestibuloocular reflex with regard to gravity. *J Neurophysiol.* 2000a; 84:3067–3071. [PubMed: 11110833]
- Yakushin SB, Reisine H, Büttner-Ennever J, Raphan T, Cohen B. Functions of the nucleus of the optic tract (NOT). I. Adaptation of the gain of the horizontal vestibulo-ocular reflex. *Exp Brain Res.* 2000b; 131:416–432. [PubMed: 10803411]
- Yakushin, SB.; Raphan, T.; Suzuki, J-I.; Arai, Y.; Cohen, B. *Ass Res Otolaryngol.* Vol. 20–24. Beach, Florida: St.Petersburg; 2000c Feb 23. Can the gain of the angular vestibulo-ocular reflex (aVOR) be adapted after semicircular canal plugging or lateral canal nerve section?; p. 21#77
- Yakushin SB, Bukharina SE, Raphan T, Büttner-Ennever J, Cohen B. Adaptive changes in the angular VOR: Duration of gain changes and lack of effect of nodulo-uvulectomy. *Ann N Y Acad Sci.* 2003a; 1004:78–93. [PubMed: 14662450]
- Yakushin SB, Palla A, Haslwanter T, Bockisch CJ, Straumann D. Dependence of adaptation of the human vertical angular vestibulo-ocular reflex on gravity. *Exp Brain Res.* 2003b; 152:137–142. [PubMed: 12879171]
- Yakushin SB, Raphan T, Cohen B. Gravity specific adaptation of the vertical angular vestibulo-ocular reflex; dependence on head orientation with regard to gravity. *J Neurophysiol.* 2003c; 89:571–586. [PubMed: 12522203]
- Yakushin SB, Xiang Y, Raphan T, Cohen B. The role of gravity in adaptation of the vertical angular vestibulo-ocular reflex. *Ann N Y Acad Sci.* 2005a; 1039:97–110. [PubMed: 15826965]
- Yakushin SB, Xiang Y, Raphan T, Cohen B. Spatial distribution of gravity dependent gain changes in the vestibulo-ocular reflex. *J Neurophysiol.* 2005b; 93:3693–3698. [PubMed: 15689386]
- Yakushin SB, Xiang Y, Cohen B, Raphan T. Dependence of the roll angular vestibuloocular reflex (aVOR) on gravity. *J Neurophysiol.* 2009; 102:2616–2626. [PubMed: 19692515]

Fig. 1.

Determining gravity-dependent gain changes. **a** Gains of the yaw aVOR obtained before (*blue symbols*) and after yaw aVOR gain was decreased by LSD (*red symbols*). **b** The gain changes expressed as a percentage of pre-adapted values (*diamonds*) and plotted as a function of head orientation. Gain changes were fit by a sinusoid with bias, where the amplitude of the sinusoid and the bias represent the gravity-dependent and gravity-independent gain changes, respectively.

Fig. 2. Percent gain decrease induced by head oscillation of 15° amplitude in LSD position. **a–d** Following adaptation, changes in gain were measured at 19 head orientations in LSD-RSD (a), LA-RP (b), RA-LP (c), and F–B (d) planes. *Gray lines* are data from individual experiments. *Black symbols* are average experimental values from the different experiments. *Black curves* are a sine fit through the average data. *Red curves* are the model predictions. The *light shaded* region shows the head angular excursion during adaptation. The *dark shaded* region is the head angular excursion during testing. **e** The surface describing the three-dimensional gain changes obtained from average experimental data. **f** The surface describing the three-dimensional gain changes predicted from the model. Each graph is *color coded* for relative gains. *Dark red* indicates minimal changes and *dark blue* represents maximal gain decreases for each graph

Fig. 3.

Gain decrease evoked by oscillation of the animal about LSD position with amplitude of 90°. **a–d** Gain changes were measured at 19 head orientations in LSD-RSD (**a**), LA-RP (**b**), RA-LP (**c**), and F-B (**d**) planes. See Fig. 2 for a description of the Figure meaning

Fig. 4.

Gain decrease evoked by oscillation of animal about LSD position with amplitude of 135° .

a-d Gain changes were measured at 19 head orientations in LSD-RSD (**a**), LA-RP (**b**), RA-LP (**c**), and F-B (**d**) planes. See Fig. 2 for a description of the Figure meaning

Fig. 5.

Gain decrease evoked by oscillation of animal about LSD position with amplitude of 180°.

a-d Gain changes were measured at 19 head orientations in LSD-RSD (**a**), LA-RP (**b**), RA-LP (**c**), and F-B (**d**) planes. See Fig. 2 for a description of the Figure meaning

Fig. 6.

Yaw gain changes obtained at 19 positions from LSD to RSD, following gain decrease adaptation during yaw head oscillation of $\pm 180^\circ$, starting in LSD position. **a** Filled *red circles* are the data and blue are the previous model (Xiang et al. 2006) fits to the data. The data had a minimal gain decrease in the upright position (0°) and maximal gain changes in LSD and RSD (*red symbols*). The previous model predicted maximal changes in RSD and minimal changes in LSD (*blue symbols*). **b** When orientation adaptation was incorporated into the model, it predicted that a minimal gain change could be obtained in the upright position during this kind of large amplitude adaptation stimulus (*red and blue symbols*). See text for complete description

Fig. 7. Block diagram of signal processing for coding of orientation adaption and the gravity-dependent adaptation of the aVOR. See text for complete description

Fig. 8.

Model predictions and simulations of changes in otolith polarization vector as the sum of two polarization vectors. **a–b** The orientation of the summated vector before (*blue*) and after (*red*) adaptation. The total polarization is $\hat{p}_l = \alpha\hat{p}_{lk} + (1 - \alpha)\hat{p}_{lq}$ where α is initially 0.5 and then adapts toward zero, causing the vector further away from gravity, $\hat{p}_{lk}$, to have less influence on the net orientation. This results in a net shift of the orientation toward gravity, which influences the gravity-dependent gain of the aVOR following adaptation (See text for description)

Table 1

Average gravity-dependent gain changes measured in four planes after aVOR gain was decreased about LSD head orientation with four amplitudes of head oscillation: 6°/15°, 90°, 135° and 180°

Adaptive stimulus	Tilt direction during testing			
	LSD-RSD	LA-RP	RA-LP	F-B
15°	6.6 ± 1.3	5.2 ± 2.1	5.4 ± 1.5	0.9 ± 2.1
90°	6.0 ± 3.3	6.1 ± 1.9	6.2 ± 3.2	9.8 ± 3.6
135°	3.3 ± 6.4	-8.2 ± 3.8	-3.3 ± 6.0	6.5 ± 4.4
180°	0.9 ± 5.8	-0.1 ± 8.5	1.5 ± 6.0	5.9 ± 1.2

Negative values indicate that while gain was decreased about LSD head position, maximal changes were observed with right anterior, posterior or right-side-down head tilts. See text for more details