Tuning of gravity-dependent and gravity-independent vertical angular VOR gain changes by frequency of adaptation

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Yakushin SB. Tuning of gravity-dependent and gravity-independent vertical angular VOR gain changes by frequency of adaptation. J Neurophysiol 107: 3349–3356, 2012. First published March 7, 2012; doi:10.1152/jn.01075.2011.—The gain of the vertical angular vestibulo-ocular reflex (aVOR) was adaptively increased and decreased in a side-down head orientation for 4 h in two cynomolgus monkeys. Adaptation was performed at 0.25, 1, 2, or 4 Hz. The gravity-dependent and -independent gain changes were determined over a range of head orientations from left-side-down to right-side-down at frequencies from 0.25 to 10 Hz, before and after adaptation. Gain changes vs. frequency data were fit with a Gaussian to determine the frequency at which the peak gain change occurred, as well as the tuning width. The frequency at which the peak gravity-dependent gain change occurred was approximately equal to the frequency of adaptation and the width increased monotonically with increases in the frequency of adaptation. The gravity-independent component was tuned to the adaptive frequency of 0.25 Hz but was uniformly distributed over all frequencies when the adaptation frequency was 1–4 Hz. The amplitude of the gravity-independent gain changes was larger after the aVOR gain decrease than after the gain increase across all tested frequencies. For the aVOR gain decrease, the phase lagged about 4° for frequencies below the adaptation frequency and led for frequencies above the adaptation frequency. For gain increases, the phase relationship as a function of frequency was inverted. This study demonstrates that the previously described dependence of aVOR gain adaptation on frequency is a property of the gravity-dependent component of the aVOR only. The gravity-independent component of the aVOR had a substantial tuning curve only at an adaptation frequency of 0.25 Hz.

monkey: vestibulo-ocular reflex

THE ANGULAR VESTIBULO-OCULAR REFLEX (aVOR) gain can be decreased by oscillation of the subject about the yaw or pitch axes while presenting a subject-fixed visual surround, and gain increases can be induced by rotating the visual surround out of phase with respect to the head (Gonsior and Melvill Jones 1976; Lisberger and Miles 1980; Yakushin et al. 2003c). Both changes represent an adaptation to relative motion of the surround and the subject (Ito 1972; Lisberger et al. 1984; Miles and Eighmy 1980; Robinson 1976), but the former is based on a suppression mechanism whereas the latter is based on ocular following (Hirata et al. 2002; Raymond and Lisberger 1997). Gain increases are harder to induce than gain decreases (Hirata et al. 2002; Miles and Fuller 1974), which may be due to differences in neuronal mechanisms (Boyden et al. 2006; Boyden and Raymond 2003; Hirata et al. 2002; Kimpo et al. 2005; Li et al. 1995). Changes in the aVOR gain can have both global and context-specific components. An example of context-specific adaptation is the gain differences required for subjects looking up and down when wearing bifocals (Schelhammer et al. 1992) or when viewing near and far objects, i.e., vergence (Lewis et al. 2003). Another example of context-specific adaptation is cross-axis adaptation, which alters the direction of eye rotation in response to a specific head rotation (Baker et al. 1986; Harrison et al. 1986b; Hay 1968; Schultheis and Robinson 1981).

The dependence of the aVOR gain changes on gravity (Baker et al. 1987; Tan et al. 1992; Tilliket et al. 1993; Yakushin et al. 2000a) is contextual learning, which has been investigated in more detail than any other context and has broad implication regarding global and localized learning (Schubert et al. 2008; Yakushin et al. 2003a, 2003b, 2003c, 2005a, 2005b, 2009). Specifically, when changes in the horizontal/yaw or vertical/pitch aVOR are induced in a particular head orientation, for example, in the left-side-down head position, the changes in gain will be maximal in the position of adaptation and minimal in the alternate side-down position. According to our model of gravity-dependent adaptation of the aVOR gain, there are two components of gain changes: global and local (Xiang et al. 2006). Gain changes plotted as a function of the head orientation could be well approximated by a bias and sinusoidal function where the bias represents the global (gravity independent) component. The amplitude of the sinusoidal variation represents the contextual (gravity dependent) component of aVOR gain changes. The model predicts that the aVOR gain in upright or in statically tilted forward or backward positions would be the same after gain adaptation in the side-down position. Indeed, this was observed experimentally for horizontal and vertical aVOR regardless of whether the aVOR gain was increased or decreased (Yakushin et al. 2003a, 2003c, 2005b).

The work of myself and my colleagues (Yakushin et al. 2003a, 2003b, 2005a, 2005b) on gravity-dependent adaptation has been focused on understanding the spatial aspects of the adaption and was studied at a single frequency of adaptation (0.2 or 0.5 Hz). The dependency of gravity-dependent adaptation induced by the single frequency of adaptation on the postadaptive gain as a function of frequency is not known. Such information is important because the head rotations during normal daily activity comprise frequencies of 10 Hz and higher (Armand and Minor 2001; Grossman et al. 1988). Numerous studies of the frequency dependence of adaptation have shown that when gain changes are induced and tested at the same orientation, the greatest changes occur at the frequency of adaptation (Feil et al. 2003; Harrison et al. 1986a; Hirata et al. 2002; Lisberger et al. 1983; Powell et al. 1991; Raymond and Lisberger 1996; Robinson 1976). Gravity-de-
dependent aVOR gain changes have been found in a range of frequencies when the adaptive stimulus is a superposition of four frequencies from 0.5 to 3.7 Hz (Schubert et al. 2008). Adaptation at low frequencies has been found to be more tuned to the frequency of adaptive stimulus than adaptation at high frequencies (Raymond and Lisberger 1996). It has been suggested that aVOR gain adaptation is mediated by a set of parallel channels tuned to a specific frequency band (Lisberger et al. 1983). Each channel has its own gain control elements, with partial overlap of channel bandwidth.

The purpose of this study was to determine whether frequency-dependent tuning of the vertical aVOR gain is similarly present in the gravity-dependent and -independent component of aVOR gain adaptation. I also investigated whether the frequency at which the adaptation is maximal is related to the adaptation frequency and how this is related to the tuning width. This will further elucidate the relationship between the global gravity-independent and local gravity-dependent components.

METHODS

Experiments performed on two cynomolgus monkeys (M1, M2) conformed to the Guide for the Care and Use of Laboratory Animals (National Research Council 1996) and were approved by the Mount Sinai School of Medicine Institutional Animal Care and Use Committee.

The surgical procedures used in these experiments have been described in detail (Yakushin et al. 2000b). A head mount was installed to hold the head in stereotaxic coordinates during the experiments (Sirota et al. 1988; Yakushin et al. 2000b). Eye movements were recorded with frontal (Judge et al. 1980) and torsional scleral search coils implanted into the left eye (Dai et al. 1994). During testing, animals sat in a primate chair in a multi-axis vestibular stimulator surrounded by an optokinetic drum (Contraves) (Yakushin et al. 2003c, 2005b). The axes of rotation of the animals and the optokinetic drum were collinear, and the drum rotated in light, producing full-field visual stimulation. The monkey’s head was fixed in a rigid 15-cm frame that held two sets of field coils with the left eye centered in the magnetic fields (Neurodata).

Eye velocities were calibrated by rotating the animals in light at 30°/s about the roll, pitch, and yaw axes. It was assumed that horizontal and vertical gains were unity in this condition (Raphan et al. 1979). Roll gains were assumed to be 0.6 when the rotation was around a naso-occipital axis aligned with the spatial vertical (Crawford and Vilis 1991; Henn et al. 1992). Roll, pitch, and yaw eye position as well as chair, drum, and tilt axis positions and velocities were recorded with amplifiers having a bandpass of DC to 40 Hz. The equipment was controlled and data were acquired with a computer, using data acquisition software (developed with Dmitry Ogorodnikov, Neurology Dept., Mount Sinai School of Medicine). Voltages were digitized at 1 kHz/channel with 16-bit resolution (Data Translation) and stored for future analysis. Eye position voltages were smoothed and digitally differentiated by finding the slope of the least-squares linear fit to 25 data points, corresponding to a filter with a 3-dB cutoff above 40 Hz, the cutoff frequency of the filters used for data acquisition. Saccades were eliminated with the use of a maximum likelihood ratio criterion (Singh et al. 1981). There were no significant eye velocities in the horizontal or torsional components of the aVOR in any of the applied tests, and therefore only the vertical/pitch component is considered further.

The vertical aVOR was tested by oscillating animals about their interaural axes in darkness at 0.25, 0.5, 1, 2, 4, 6, 8, and 10 Hz with a peak velocity ~60°/s for at least 10 cycles, either upright or tilted in 10° increments up to 90° in the left-side-down to right-side-down (LSD-RSD) plane. Desaccaded eye velocities and the stimulus velocity were fit with a cosine function at the stimulus frequency to compute the aVOR gains and phases. The testing frequency was randomized, and the durations of the tests were varied for different frequencies, with the longest being ~20 min (0.25 Hz) and the shortest being ~5 min (10 Hz). Because the retention of the gain changes depends on the time after testing within the first 20-30 min immediately after adaptation (Kuki et al. 2004), the first test was started ~30 min after adaptation and 5-15 min were allowed between tests. Between tests, animals sat in darkness in the upright position. Occasionally, the aVOR testing at 0.25 Hz was repeated at different times of adaptation. No significant difference was observed between tests performed at 0.5 to 2.5 h after adaptation.

The gain of the vertical aVOR was decreased or increased by sinusoidal in-phase or out-of-phase rotation of the animal and a visual surround about the animal’s interaural axis in side-down position for 4 h at 0.25, 2, and 4 Hz. Each animal was adapted once in each condition. In one experiment aVOR gain was also decreased at 1 Hz. Previous studies had demonstrated that retention of gravity-dependent gain changes could be observed for several days (Schubert et al. 2008; Yakushin et al. 2003a, 2003b); therefore, at least a week was allowed before the next adaptation session.

Gains obtained before and after adaptation were computed for each testing frequency (Fig. 1, A–C), and the percentage of gain changes relative to preadapted values was determined at each head orientation (Fig. 1, D and E). Changes were plotted as a function of head orientation and fit with a sinusoidal function and bias

\[ y = \alpha \cdot \cos(x + \beta) + \gamma \] (1)

to determine gravity-dependent (\( \alpha \)) and gravity-independent (\( \gamma \)) gain changes (Fig. 1E). Previous experiments on yaw and pitch aVOR gain adaptation indicated that the spatial phase \( \beta \), or the head orientation in which maximal gain changes were observed, is close to the position of adaptation (Yakushin et al. 2003b, 2003c, 2005a, 2005b). Because a major purpose of this study was to determine the amount of gravity-dependent and -independent gain changes as a function of frequency, it was assumed that the peak gain changes occurred in the position of adaptation in this study. Therefore, the spatial phase \( \beta \) was assumed to be 90° for adaptation RSD and ~90° for adaptation LSD.

The significance of the fit was verified by \( F \) statistic, a reduced case of ANOVA at \( P < 0.05 \) (Yakushin et al. 1998, 2011).

It should be noted that gravity-dependent changes are determined as the amplitude of the fit and according to such convention are always positive regardless of whether the aVOR gain was increased or decreased. Gravity-independent gain changes, however, are positive for gain increases and negative for gain decreases. To enable comparison of the magnitude of changes in the two components, gravity-independent gain values for gain decreases were multiplied by -1. With this convention, gravity-independent gain changes could be negative if a gain increase was observed after an attempted decrease in aVOR gain, and vice versa. Similarly for gravity-dependent gain changes, when the gain was decreased RSD as shown in Fig. 1E, changes would be positive as long as the minimum of the sinusoidal fit was observed RSD; otherwise, gravity-dependent gain changes would be negative.

To compare gravity-independent gain changes (\( \gamma \), Eq. 1), the values predicted by a least mean square fit for each head orientation \( \alpha \cdot \cos(x + \beta) \), Eq. 1) were subtracted from original values. A standard \( t \)-test was used to compare pairs of data, and ANOVA was used to compare sets of data.

To determine the spatial width or tuning of gravity-dependent and -independent gain changes to the frequency of adaptation, gain changes were fit with the sum of a bias (\( A \)) and a Gaussian, where \( B \) is the amplitude, \( C \) is the frequency at which the peak occurs, and \( D \) is the standard deviation:

\[ y = A + B \cdot \exp\left(-\left(\frac{x-C}{D}\right)^2\right) \]
were larger at 1 Hz (6.8%, head position was smaller. Gravity-dependent gain changes
frequency of adaptation, the gain decrement as a function of
circles, 0.25 Hz) or higher (Fig. 1 B, filled circles) than the
C when the gain was tested at frequencies lower (Fig. 1 B, open circles) represent the vertical gain
before adaptation, and filled circles represent the vertical gain after it was adaptively decreased at 1 Hz in RSD position. D–F: gain changes plotted as a function of head orientation were fit with bias and sinusoid to obtain gravity-dependent and -independent gain changes, Insets below are approximate head orientations during testing. G: gravity-dependent (filled squares) and -independent gain changes (open squares) as a function of testing frequency. Solid curve is a Gaussian fit through the data. Dashed line represents the average value for the bias.

The standard deviation was used as a measure of the width of tuning. If the fit was not significant at \( P < 0.05 \) as determined by the critical \( r \) value (Fisher and Yates 1953), it could not be fit by a Gaussian, the average value of the gravity-independent gain changes obtained for all tested frequencies was taken as a bias, and no spatial width was assigned to the tuning (see Tables 2 and 4, N/A).

To compare phases of the aVOR before and after adaptation, the phases of the slow phase of eye velocity with regard to the stimulus velocity were determined in every head orientation, and the average \( \pm \) SD was determined for each given frequency (see Fig. 4). The significance of the phase difference obtained before and after adaptation was determined using a \( t \)-test.

**RESULTS**

**Determining the tuning of gravity-dependent and -independent gain changes.** The vertical aVOR gain in an unadapted state was invariant for head tilts from LSD to RSD (Fig. 1, A–C, open circles), but the average gain over all head positions increased slightly as the frequency was changed from 0.25 to 1 and 10 Hz (Keller 1978). When the vertical aVOR gain was adaptively decreased at 1 Hz RSD for 4 h and then tested at 1 Hz, the largest gain decrement occurred in the position of adaptation, and the change was progressively smaller as the head was moved to LSD (Fig. 1B, filled circles). However, when the gain was tested at frequencies lower (Fig. 1A, filled circles, 0.25 Hz) or higher (Fig. 1C, filled circles) than the frequency of adaptation, the gain decrement as a function of head position was smaller. Gravity-dependent gain changes were larger at 1 Hz (6.8%, \( P < 0.05 \), \( F \) statistic) than at 0.25 and 10 Hz (3.4 and 0%, respectively; Fig. 1, D–F). The gravity-independent gain changes were comparable (12 ± 1.5 and 14.8 ± 1.4% for frequencies of 1 and 0.25 Hz, respectively), being somewhat smaller at 10 Hz (8 ± 2.0%, ANOVA, \( P < 0.001 \), Bonferroni’s adjustment).

When the amplitudes of the gravity-dependent and -independent gain changes were plotted as a function of testing frequency, the gravity-dependent gain changes (Fig. 1G, filled squares) could be approximated by a Gaussian curve (\( P < 0.05 \)) whose peak value occurred at the frequency of adaptation (black curve). The amplitude was 5.7%, and the spatial width was 0.9 Hz (Fig. 1G). It should be noted that Gaussian fit in this case does not account for the gradual decrease in the gravity-dependent component observed at frequencies above 2 Hz. The gravity-independent gain changes were 10.1 ± 2.5% but could not be fit by a Gaussian (Fig. 1G, open squares).

In every instance, the peak of the Gaussian fit for the gravity-dependent gain changes occurred close to the frequency of adaptation for adaptation at 0.25, 1, 2, and 4 Hz (0.8 ± 0.5°). For further analyses, we assumed the peak of the fit to be at the frequency of adaptation and determined the amplitude and tuning width.

**aVOR gain increase.** After the increases in aVOR gain, the Gaussian fits to the gravity-dependent gain changes at all tested frequencies were significant (\( P < 0.05 \), \( F \) statistic; Table 1). The amplitude of the fit was 6.9 ± 1.2% for adaptation performed at 0.25, 2, or 4 Hz (varying from 4.8 to 8.4%; Table 1). The spatial width of gravity-dependent gain changes increased with the frequency of adaptation in both animals (\( P < 0.05 \), \( F \) statistic), being on average 1.0, 1.7, and 2.5 Hz after adaptation at 0.25, 2, and 4 Hz, respectively. It should be noted
that spatial width represents the range of frequencies about the frequency of adaptation where gain changes are significant at ±1 SD, i.e., 0.25 ± 1.0, 2.0 ± 1.7, and 4.0 ± 2.5 Hz for adaptation at 0.25, 2, and 4 Hz, respectively. Distribution of gravity-dependent gain changes obtained after adaptation at 0.25, 2, and 4 Hz from animals M1 and M2 are shown in Figs. 2, A–C, and 3, A–C, respectively (filled squares and black curves). In every instance, maximal changes were observed at the frequency of adaptation and the spatial width of the tuning curve gradually increased. The bias of the fit (A in Eq. 2) was close to zero (0.6 ± 0.74%).

The gravity-independent gain changes could be fit by a Gaussian distribution only when the adaptive changes were induced at 0.25 Hz (Figs. 2 A and 3 A, Table 2). The tuning width was smaller compared with that of the gravity-dependent component from the same experiment (0.3 vs. 1.0 Hz; Tables 1 and 2). Gravity-independent gain changes obtained after gain increases induced at 2 and 4 Hz did not follow a Gaussian distribution (P > 0.05, F statistic; Figs. 2 and 3, B and C). These findings indicate that gravity-independent gain changes after the aVOR gain increase were widely distributed over the frequency when adapted at frequencies above 0.25 Hz. Amplitudes of the fit for gravity-dependent and -independent components after the aVOR gain increase at 0.25 Hz were comparable (7.2 vs 9.6%). Furthermore, peak changes were always observed at frequencies other than the frequency of adaptation. Interestingly, in M1, gain decreases were observed at 0.25 and 0.5 Hz after gain increases at 2 and 4 Hz (Fig. 2, B and C). At frequencies above the frequency of adaptation, however, only increases in the gravity-independent component were observed. Because of unexpected gain decreases at lower frequencies, despite the fact that the gravity-dependent and independent components were overlapped at several testing frequencies after adaptation of M1 at 4 Hz, only the gravity-dependent component followed a Gaussian distribution (Fig. 2C).

The average gravity-independent gain changes (bias) were close to zero in one animal (0.4 ± 0.7%, Table 2) but larger (4.9 ± 2.2%) in the second animal (P = 0.014). This shows that there is individual variability between the animals in the amount of gravity-independent gain increase.

Thus gravity-dependent gain changes after aVOR gain increases were tuned to the frequency of adaptation. The tuning width progressively increased with the frequency of adaptation.

aVOR gain decrease. The gravity-dependent gain changes followed Gaussian distribution in every case. The amplitude of the fit was approximately the same at all frequencies of adaptation (4.6 ± 0.81%) but was smaller than that after a gain increase (6.9 ± 1.2%, P = 0.002). The spatial width of the fit progressively increased for adaptation at higher frequencies (Table 3). This is also shown in Figs. 2, D–F, and 3, D–F (filled squares and black curves). Thus gravity-dependent gain changes after aVOR gain decreases were tuned to the frequency of adaptation, and the spatial width of tuning increased for adaptation at higher frequencies. The bias of the fit to the data obtained at all tested frequencies was small (1.4 ± 0.87%; Table 3).

Gravity-independent gain changes followed a Gaussian distribution after adaptation at 0.25 Hz (Table 4). The amplitude of the fit was 4.7%. The spatial width was 0.4 Hz, comparable

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Table 1. Gravity-dependent component of aVOR gain increase

<table>
<thead>
<tr>
<th>Frequency of Adaptation, Hz</th>
<th>Animal</th>
<th>Bias, % Gain Change</th>
<th>Amplitude, % Gain Change</th>
<th>Width, Hz</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25</td>
<td>M1</td>
<td>0.6</td>
<td>6.8</td>
<td>0.9</td>
</tr>
<tr>
<td></td>
<td>M2</td>
<td>2.0</td>
<td>7.6</td>
<td>1.1</td>
</tr>
<tr>
<td>2</td>
<td>M1</td>
<td>0.4</td>
<td>7.1</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td>M2</td>
<td>0.8</td>
<td>8.4</td>
<td>1.9</td>
</tr>
<tr>
<td>4</td>
<td>M1</td>
<td>0.1</td>
<td>4.8</td>
<td>2.5</td>
</tr>
<tr>
<td></td>
<td>M2</td>
<td>-0.1</td>
<td>6.6</td>
<td>2.4</td>
</tr>
</tbody>
</table>

aVOR, angular vestibulo-ocular reflex; M1 and M2, monkeys 1 and 2.

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Fig. 2. Gravity-dependent (filled squares) and -independent gain changes (open squares) plotted as a function of testing frequencies after the aVOR gain was increased (A–C) and decreased (D–F) at 0.25 (A and D), 2 (B and E), and 4 Hz (C and F). Data in A–F were obtained on different experimental days from 1 animal (M1). See text for details.
to that of the gravity-dependent component (0.5 Hz, \( P > 0.05 \), F statistic) after adaptation at the same frequency (Tables 3 and 4). The bias was substantial (8.8%) when the gain was decreased at 0.25 Hz. The average gravity-independent gain change for all experiments when the aVOR gain was decreased at different frequencies was 10.5\( \pm 2.9\% \), being larger than average gravity-independent gain increase obtained from the same animals over the same period of adaptation (2.6\( \pm 2.9\%, \ P = 0.0002 \)).

Thus, regardless of whether aVOR gain was increased or decreased, there was an increase in the spatial width of the Gaussian fit of the gravity-dependent gain changes as the frequency of the aVOR gain adaptation increased from 0.25 to 2 and 4 Hz. Gravity-independent gain changes were less tuned to the frequency of adaptation. Gravity-independent gain changes were significant at all tested frequencies in experiments when the aVOR gain was increased or decreased in one animal but were present only at frequencies close to the frequency of adaptation when the aVOR gain was increased in the second animal.

Changes in phases of the aVOR. There were small (2–3°) but significant changes in phases in 77% of experiments (\( P < 0.05 \)). In \( \approx 5\% \) of cases, the changes were more profound when the aVOR was tested with animals tilted toward the side in which adaptation was induced, where larger gain changes were observed. When only tilts toward the ipsi-adaptation side were considered, changes in phases after adaptation were significant in 84% of experiments (Fig. 4, black vs. gray symbols).

When the vertical aVOR gain was decreased at 0.25 (Fig. 4A), 2 (Fig. 4B), or 4 Hz (Fig. 4C), the phase of the aVOR led (positive values) that of the aVOR before adaptation for frequencies above the frequency of adaptation. It lagged (negative values) at frequencies below the frequency of adaptation. When the aVOR gain was increased, the phase lagged at frequencies above the frequency of adaptation and led at frequencies below the frequency of adaptation (Fig. 4, D–F).

**DISCUSSION**

This study demonstrates that the frequency-dependent tuning of the vertical aVOR gain adaptation induced by 4 h of visual-vestibular conflict is coded through the pathway that controls the gravity-dependent component of the aVOR and has a little to no effect on the global gravity-independent gain adaptation. The gravity-dependent gain changes peaked at the frequency of adaptation and decreased toward zero as the testing frequency deviated from the frequency of adaptation. The gain changes were narrowly tuned to the frequency of adaptation.

### Table 2. Gravity-independent component of aVOR gain increase

<table>
<thead>
<tr>
<th>Frequency of Adaptation, Hz</th>
<th>Animal</th>
<th>Bias, %Gain Change</th>
<th>Gaussian Fit</th>
<th>Amplitude, %Gain Change</th>
<th>Width, Hz</th>
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<tbody>
<tr>
<td>0.25</td>
<td>M1</td>
<td>1.2</td>
<td></td>
<td>5.9</td>
<td>0.3</td>
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<tr>
<td></td>
<td>M2</td>
<td>3.4</td>
<td></td>
<td>13.3</td>
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<tr>
<td>2</td>
<td>M1</td>
<td>0.2 ± 2.6</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>M2</td>
<td>7.4 ± 1.4</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>4</td>
<td>M1</td>
<td>−0.2 ± 3.3</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>M2</td>
<td>3.8 ± 0.8</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
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N/A, not applicable (see text for details).

### Table 3. Gravity-dependent component of aVOR gain decrease

<table>
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<th>Frequency of Adaptation, Hz</th>
<th>Animal</th>
<th>Bias, %Gain Change</th>
<th>Gaussian Fit</th>
<th>Amplitude, %Gain Change</th>
<th>Width, Hz</th>
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<tbody>
<tr>
<td>0.25</td>
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<td>1.6</td>
<td></td>
<td>4.7</td>
<td>0.5</td>
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<tr>
<td></td>
<td>M2</td>
<td>1.6</td>
<td></td>
<td>4.2</td>
<td>0.5</td>
</tr>
<tr>
<td>2</td>
<td>M1</td>
<td>1.2</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>M2</td>
<td>3.1</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>4</td>
<td>M1</td>
<td>0.8</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>M2</td>
<td>1.3</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
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Fig. 3. Gravity-dependent (filled squares) and -independent gain changes (open squares) plotted as a function of testing frequencies after the aVOR gain was increased (A–C) and decreased (D–F) at 0.25 (A and D), 2 (B and E), and 4 Hz (C and F). Data in A–F were obtained on different experimental days from 1 animal (M2). See text for details.
adaptation when induced at lower frequencies. The spatial width of the tuning increased when the adaptation was performed at higher frequencies. Changes in the gain of the gravity-independent component were uniform across all tested frequencies, and changes were larger for aVOR gain decreases than for gain increases. In previous studies of frequency-dependent adaptation, gain changes were induced and tested at the same head orientation. It was concluded that gain increases and decreases were mediated by different mechanisms (Boyden et al. 2006; Boyden and Raymond 2003; Broussard et al. 2011; Kimpo et al. 2005). Moreover, it has been shown that decreases in the aVOR gain are generalized to other frequencies more than gain increases in primates (Kimpo et al. 2005; Lisberger et al. 1983), and the tuning becomes wider for adaptation at higher frequencies (Kimpo et al. 2005; Raymond and Lisberger 1996). In the present study, the separation of global (gravity independent) and local (gravity dependent) learning demonstrated that the asymmetric effects of gain increase and gain decrease, as well as the frequency-dependent tuning, are associated only with the gravity-dependent component of the aVOR. Thus a consideration of the contextual and global components is critical for understanding the asymmetric and tuning properties of aVOR adaptation.

It is commonly accepted that the cerebellar flocculus is important for the aVOR gain adaptation (see Ito 1984 for review). Later studies demonstrated that the flocculus is most likely controlling the low frequency of the aVOR gain adaptation, whereas the adaptation of the aVOR at high frequencies may occur in flocculus-target neurons in the vestibular nuclei (Blazquez et al. 2006; Lisberger and Pavelko 1988; Lisberger et al. 1994; Miles et al. 1980). This implies that frequency tuning, at least for high frequencies, is controlled outside of the flocculus. The present study, which demonstrates that the tuning at all frequencies is implemented through the gravity-dependent component, supports the idea that frequency tuning is extrafloccular.

There is considerable evidence that eye-head velocity (EHV) neurons in VN receive floccular projections, which implement the aVOR gain adaptation (Lisberger 1994). The site of gravity dependent adaptation, which would require otolith as well as canal activation, is still not known. Some reports indicate that there is otolith information passing through the flocculus and ventral paraflocculus (Snyder and King 1996). However, neuronal firing rates of the floccular neurons do not indicate anything other than canal-related activity in the flocculus (Fukushima et al. 1996; Highstein et al. 1997; Hirata and Highstein 2000; Shojaku et al. 1990). Furthermore, there is an indication that EHV neurons, some of which are likely to be flocculus target neurons, code only the gravity-independent component, whereas the gravity-dependent component is coded in the activity of position-vestibular-pause (PVP) neurons (Kolesnikova et al. 2011).

From these findings, together with the results in this study, it appears that the flocculus most likely codes the gravity-independent component of the aVOR gain adaptation (global learning), whereas the gravity-dependent and, consequently, the frequency-dependent adaptation is coded elsewhere. This learning could be implemented through areas in the cerebellum that receive otolith information, such as the fastigial nuclei (FN), whose canal-related neurons receive a wide range of static and dynamic otolith inputs (Büttner et al. 1996; Gardner and Fuchs 1975; Shaikh et al. 2005). Recently, it has been shown that gravity-dependent adaptation is reversibly damaged after muscimol injection in the caudal FN (Kolesnikova et al. 2012). The results in this study, together with the fact that the frequency tuning of aVOR adaptation is related to the gravity-dependent component, suggest that the FN could code the

Table 4. Gravity-independent component of aVOR gain decrease

<table>
<thead>
<tr>
<th>Frequency of Adaptation, Hz</th>
<th>Animal</th>
<th>Bias, %Gain Change</th>
<th>Amplitude, %Gain Change</th>
<th>Width, Hz</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25</td>
<td>M1</td>
<td>8.8</td>
<td>4.7</td>
<td>0.4</td>
</tr>
<tr>
<td></td>
<td>M2</td>
<td>8.8</td>
<td>4.7</td>
<td>0.4</td>
</tr>
<tr>
<td>1</td>
<td>M1</td>
<td>11.8 ± 1.9</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>M2</td>
<td>15.8 ± 3.2</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>2</td>
<td>M1</td>
<td>6.8 ± 1.2</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>M2</td>
<td>10.8 ± 0.7</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>4</td>
<td>M1</td>
<td>8.7 ± 2.1</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>M2</td>
<td>10.7 ± 2.1</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Fig. 4. Phase changes observed after the aVOR gain decreases (A–C) and increases (D–F) induced at 0.25 (A and D), 2 (B and E), and 4 Hz (C and F). Dashed vertical gray line and arrow indicate the frequency at which the aVOR gain was adapted. Black symbols represent significant changes in phase (P < 0.05).
Gravity-dependent adaptation requires that patterns of otolith activation be distributed in canal-otolith convergent neurons that transmit the aVOR. It is therefore one of the few instances where a distributed neural net model whose neurons receive canal and otolith input along a particular polarization direction can be a meaningful model of this context-specific adaptation (Xiang et al. 2006). The emergence of the consequent frequency dependence was an unexpected property of this part of the aVOR adaptation and provides data for a model-based analysis of frequency dependence of the gain of the aVOR adaptation.

Phase changes observed in this study were similar to those previously reported. However, this temporal feature of gain adaption could not be differentially associated with either the gravity-dependent or gravity-independent components, which are spatial determinants. Thus the reason and mechanism for these phase changes are not clear.

In summary, this study indicates that frequency-dependent adaptation of the aVOR is another example of contextual learning and, specifically, is closely related to the gravitational tuning of the aVOR. It indicates that global learning, which separates learning of the aVOR into global gravity- and local gravity-dependent components, gives us a better understanding of the organization of the frequency characteristics of the firing rates suggest multiple convergence of primary canal afferents with different dynamics. The flocculus most likely codes the gravity-independent component of the aVOR gain adaptation (global learning) and is minimally involved in frequency tuning. The increase of the spatial width of the localized learning could simply reflect the fact that the direct vestibular pathway, which is the focus of our study, is more adaptable at higher frequencies. As a result, changes in the aVOR gain induced at higher frequencies are observed over a broader frequency range (Minor and Lasker 2009).

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REFERENCES


Sirota MG, Bahae BM, Beloozerova IN, Nyrova AN, Yakushin SB, Kozlovskaia IB. Neuronal activity of nucleus vestibularis during coordinated movement of eyes and head in microgravity. Physiologist 31: 8–9, 1988.


