

# THE EFFECT OF OTOLITH AND SEMICIRCULAR CANAL CONVERGENCE ON THE VOR DURING ECCENTRIC ROTATION

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## INTRODUCTION

During natural locomotion the head is exposed to angular and linear acceleration. Angular acceleration is detected by the semicircular canals, linear acceleration by the otoliths. Both have to work together to achieve stabilization of gaze and stance. Convergence of canal and otolith inputs can be tested by applying eccentric rotation. Under these conditions angular stimulation remains stable independently of the eccentricity of the subject providing identical stimuli to the semicircular canals. Linear acceleration, however, depends on the distance of the subject from the center of rotation and consists of two types: *centripetal* acceleration acts along the radius and depends on angular velocity, *tangential* acceleration is dependent on angular acceleration. Variable tangential acceleration can be achieved by sinusoidal rotation at different frequencies, amplitudes and eccentricities.

It has been shown that the gain of the vestibulo-ocular reflex (VOR) is significantly enhanced during eccentric sinusoidal rotation with the nose facing outward when compared to centric rotation (5, 6, 12-15, 17). This can be explained by the additional tangential acceleration acting along the interaural axis. VOR gain, however, also depends on the target distance and eccentricity of the eyes within the head (the eyes are located anterior and lateral of the center of the head) to be fully compensatory during centric and eccentric rotations (4, 7, 9, 17, 18).

In the present study eccentricity and target distance were systematically varied while the monkey was placed in two different orientations (nose in and nose out) with respect to the rotation axis to test if the VOR gain is fully compensatory under all conditions. Most results refer to stimulation at 4 Hz, at which frequency interfering smooth pursuit eye movements play no or only a minor role (2).

## METHODS

### *Eye movement recordings*

Eye movements in the monkey (*M. mulatta*) were recorded with a scleral search coil which was implanted into the left eye under sterile conditions. Surgical procedures have been described in detail elsewhere<sup>3</sup>. Horizontal and vertical eye position signals were calibrated using fixation point calibration.

### Stimulation

The monkey was sinusoidally rotated centrally and eccentrically at different distances from the center of rotation (0-50 cm) with the nose facing inward or outward (Fig. 1). Rotational frequencies ranged from 0.25 to 4.0 Hz and amplitudes were  $\pm 0.75^\circ - 20^\circ$ . Eye movements were recorded either in complete darkness or during fixation of earth stationary lit LED targets which were located 12-180 cm in front of the monkey's eye in otherwise complete darkness.

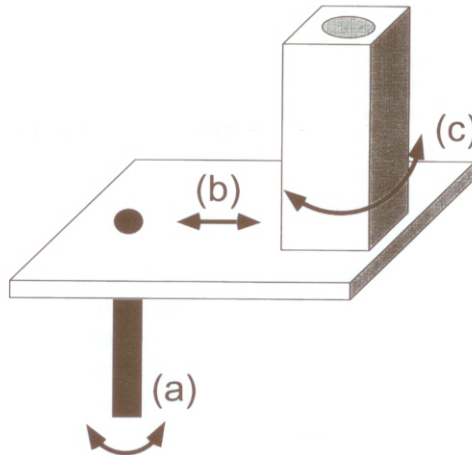


Fig. 1. - Schematic drawing of the stimulus apparatus.

The monkey is placed in a monkey chair which can be positioned at different distances (b) from the axis of rotation (a). Orientation of the monkey with respect to the center of rotation can be changed by rotating the chair on the turntable (c). The whole turntable was rotated sinusoidally around (a).

### Simulation

Compensational eye positions during rotation were calculated for different rotational paradigms, eccentricities, orientations and target distances using Matlab 5.1, The MathWorks. Eye velocity was derived from compensatory eye position. Eccentric eye position within the head has been taken into account (1.6 cm lateral from midline and 5 cm anterior from interaural line), but velocity of lateralized and cyclopean eyes did not differ significantly.

## RESULTS

Compensational VOR gain to stabilize gaze was calculated for different eccentricities, orientations and target distances (Fig. 2). When plotted with respect to the reciprocal of target distance, expected VOR gain behaves roughly linearly with an offset of 1, i.e. VOR gain should be 1 to compensate for retinal image slip irrespective of eccentricity if the target is located in the infinity. Slope of VOR gain depends on eccentricity. It is positive for eccentric rotations with the nose facing outward, i.e. the closer the target the stronger the gain enhancement. Even for centric rotation (the intersection of interaural and sagittal line is on the axis of rotation) the eyes are not centrally located, but 5 cm anterior to the rotational axis

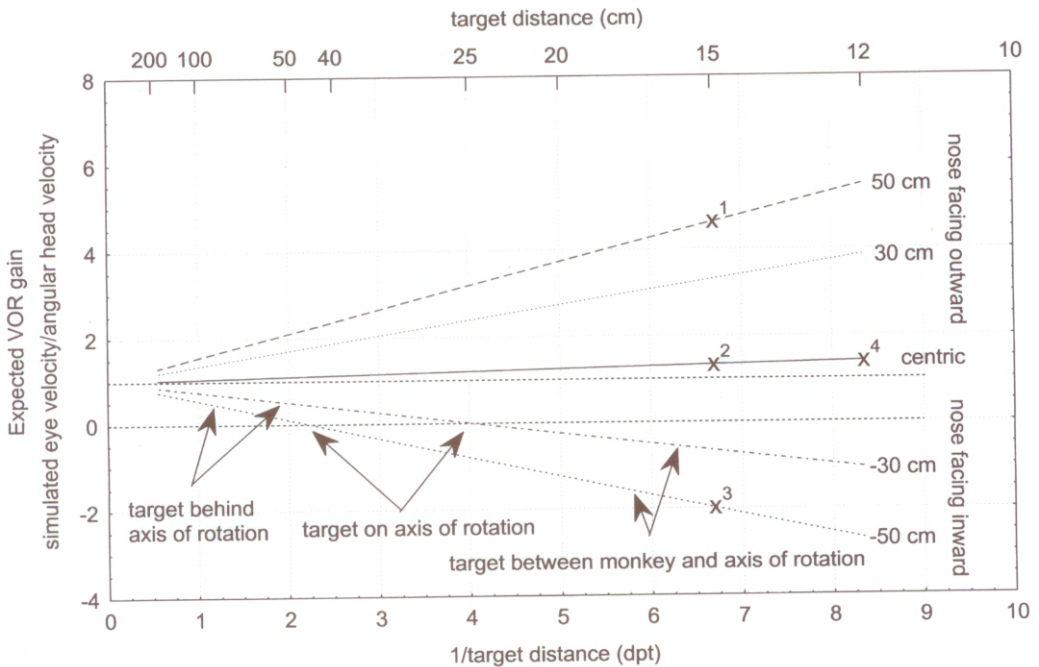


Fig. 2. - Expected VOR gain to stabilize gaze during centric and eccentric rotation with the nose facing inward or outward in response to the reciprocal of target distance (lower abscissa).

For convenience, upper abscissa displays corresponding target distances. Phase of simulated eye velocity has been shifted by  $180^\circ$ , i.e. gain is positive during centric rotation. Expected gain during centric rotation comes close to 1 only for infinite targets as eyes are eccentric within the head (see Methods). If target distance is 12 cm (= 8.3 dpt) expected gain increases to 1.39. Expected VOR gain is roughly linearly related to the reciprocal of target distance if the amplitude of sinusoidal rotation is small ( $\pm 0.75^\circ$  for this simulation). Slope is positive (i.e. gain enhancement) for eccentric rotations with the nose facing outward and negative when the nose faces inward. In the latter case gain decrement is expected while the target is behind the axis of rotation (left arrows). If the target is on the center of rotation (middle pair of arrows; e.g. 25 cm = 4 dpt in front of the eyes when the monkey is 30 cm eccentric) no eye movement is needed to stabilize the target on the retina. For targets between the monkey and the axis of rotation gain reversal should occur, i.e. the VOR gain again increases, but the phase should shift by  $180^\circ$  (right pair of arrows). Crosses indicate expected VOR gain for experiments displayed in Figure 3 (15 cm target distance; 50 cm eccentric rotation, nose facing outward (1) or inward (3); centric rotation (2)).

in the Rhesus monkey. Therefore expected VOR gain for close targets is greater than 1, e.g. 1.39 for targets 12 cm in front of the monkey (4 in Figure 2). If the nose is pointing inward the slope of VOR gain is negative, i.e. eye movements are in phase with the head movement. Three situations have to be examined differently - target behind axis/on axis/between subject and axis of rotation. In the first case gain decrement is expected for compensation (VOR gain between 0 and 1). If the target is on the rotational axis no eye movement is needed to fixate the target during rotation ("inverse VOR suppression"). For targets between the monkey and the axis of rotation gain reversal should occur, i.e. the VOR gain increases again, but the phase should shift by  $180^\circ$  (negative VOR gain).

Original recordings of centrifuge and eye velocity during sinusoidal centric and eccentric rotation at 4 Hz with a close target (target distance 15 cm) demonstrate that gain enhancement can be found in both nose in and nose out 50 cm eccentric rotation (Fig. 3). During centric rotation VOR gain is approximately 1 and phase of eye and head velocity is  $180^\circ$  apart as expected for compensation. Gain enhancement during eccentric rotation with the nose facing outward was obtained as predicted. Even gain *enhancement* for nose in eccentric rotation is in accordance with simulation if the target is closer than 20 cm (e.g. third cross in Figure 2; expected gain -2.0). In the latter case phase inversion is expected when compared to nose out eccentric rotation. Phase behavior is described in detail below.

The effect of eccentricity, orientation and target distance on the VOR gain was systematically investigated with stationary lit LED targets in otherwise complete darkness (Fig. 4). The predicted pattern of almost absent gain modulation with a VOR gain of approximately 1 during centric rotation could be confirmed experimentally (circles in Figure 4). During eccentric sinusoidal rotation VOR gain modulation strongly depended on the eccentricity and orientation of the monkey (e.g. compare group of triangles and squares in Figure 4). The third parameter which should affect VOR gain is target distance. In the nose out condition target

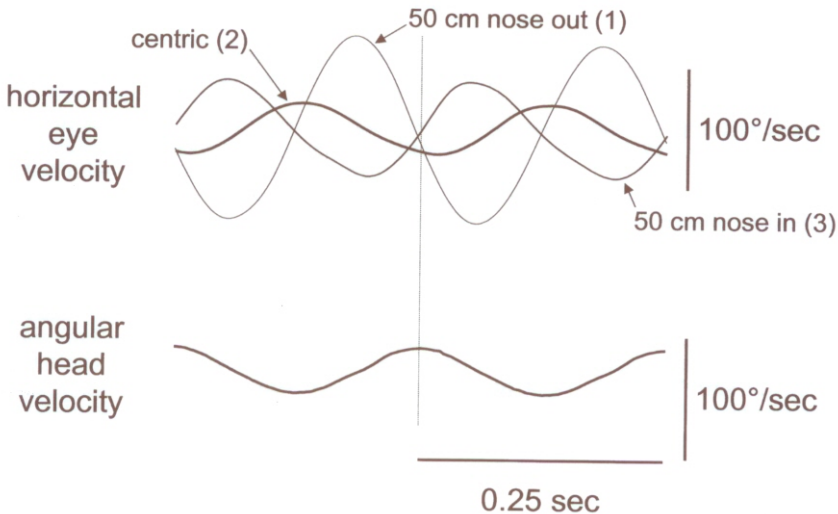


Fig. 3. - Original recordings (single trial) after filtering (using a 25 Hz gaussian low pass filter without significant phase shift) of horizontal eye velocity from centric and eccentric rotation (nose in and out).

Sections without saccadic eye movements are chosen. Sinusoidal rotation was performed at 4.0 Hz,  $\pm 0.75^\circ$ ,  $\pm 18.85^\circ/\text{sec}$ . Target distance in zero position between eyes and earth-stationary LED was 15 cm. Numbers in brackets refer to labeled crosses in Figure 2. As expected from Figure 2, VOR gain during centric rotation is approximately 1 (bold line). There is a phase shift of  $180^\circ$  when compared to head velocity. Gain enhancement is obtained for eccentric rotation both with the nose facing outward (thin line) and inward (medium line). In contrast, phase is lagging by  $80^\circ$  in the nose out and leading by  $90^\circ$  in the nose in condition inducing nearly a phase inversion between both conditions (see text for discussion).

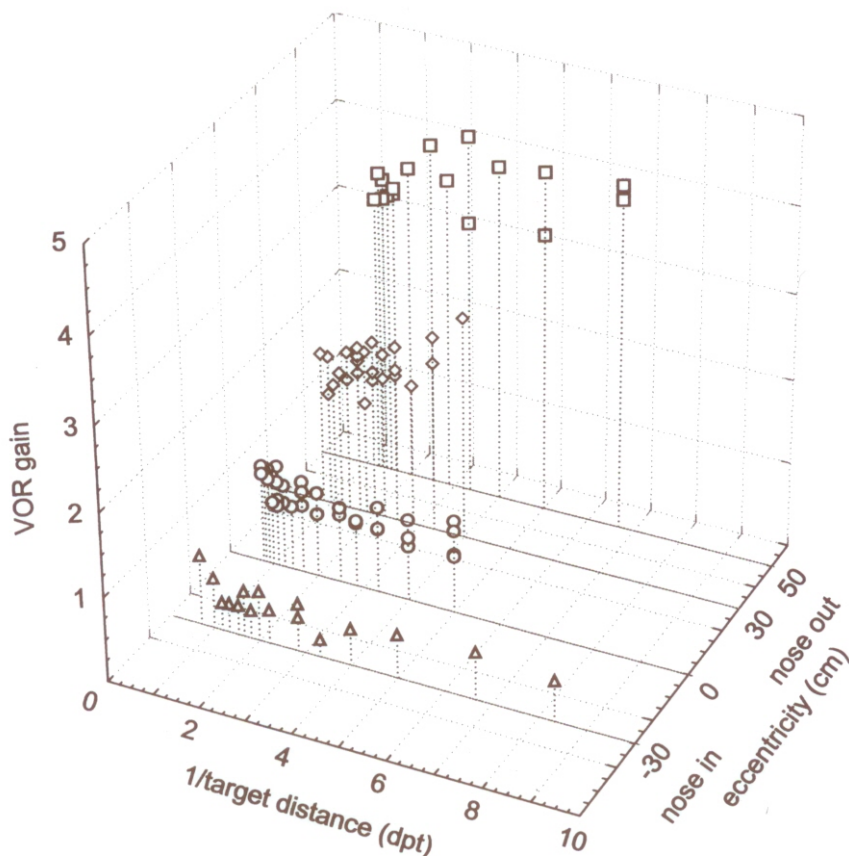


Fig. 4. - VOR gain during the same rotational paradigm as in Fig. 3 ( $4.0 \text{ Hz}, \pm 0.75^\circ$ ).

The ratio of horizontal eye velocity and angular head velocity is displayed for four different eccentricities (circles: centric rotation; rhombs: 30 cm eccentric, nose out; squares: 50 cm eccentric, nose out; triangles: -30 cm eccentric, nose in) and target distances ranging between 12 and 180 cm ( $8.3 - 0.56 \text{ dpt}$ ). A clear relationship between eccentricity and VOR gain is obvious (mean  $\pm$  standard deviation for centric rotation:  $0.91 \pm 0.16$ ; -30 cm eccentric rotation nose in:  $0.48 \pm 0.15$ ; nose out 30 cm eccentric:  $1.84 \pm 0.27$ ; nose out 50 cm eccentric:  $3.68 \pm 0.36$ ). See text for further discussion.

distance and gain enhancement are inversely related (rhombs and squares in Figure 4 and Figure 5 for a close-up). As expected, VOR gain decrement for targets that are behind the axis of rotation could be found during eccentric rotation while the nose was facing inward (triangles in Figure 4). This decrement is strongest for targets around axis of rotation (target distance 25 cm = 4 dpt), though VOR gain is not zero as predicted. For targets between the monkey and axis of rotation (target distance smaller than 25 cm equivalent to reciprocal of target distance larger than 4) there is a trend of VOR gain increase when compared to centric targets which, however, in this experiment is smaller than predicted (triangles above 4 dpt. in Figure 4).

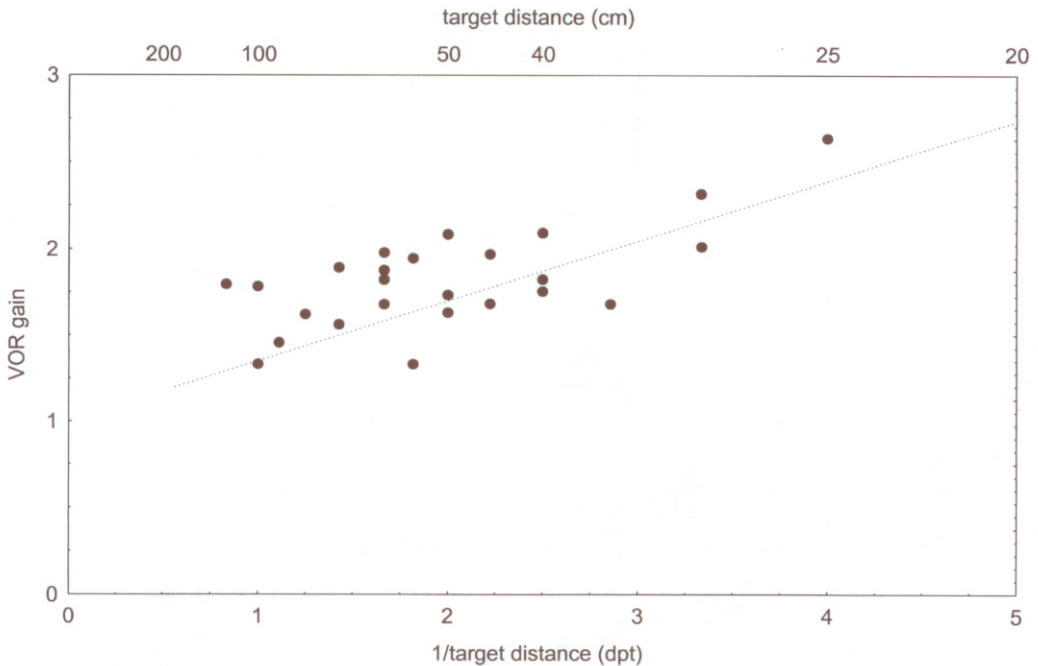


Fig. 5. - Effect of target distance on VOR gain.

Comparison between data and simulation. Parts of the data from Figure 4 are depicted (30 cm eccentric, nose facing outward; corresponding to the rhombs in Figure 4). In addition, expected VOR gain for this rotational paradigm (4 Hz,  $\pm 0.75^\circ$ ) is displayed (dotted line; equivalent to dotted line in Figure 2). For target distances larger than 25 cm experimental results align with expected data (slope: 0.35/dpt, offset: 1.0). VOR gain increases from 1.5 for target distances of 100-180 cm to 2.5 for close targets (25 cm target distance).

For better illustration experimental VOR gain during 30 cm eccentric rotation while the nose was facing outward (Figure 5, identical with rhombs in Figure 4) was directly compared with the predicted VOR gain (dots in Figure 2). Expected and experimental data align for targets farther than 25 cm demonstrating the linear relationship between reciprocal of target distance and VOR gain (slope: 0.35/dpt, offset: 1.0). Lack of cooperation of the monkey did not permit a systematic analysis of targets closer than 25 cm.

Also phase behavior was investigated for different eccentricities and target distances (Fig. 6). During centric rotation at 4 Hz phase of centrifuge and eye movements was  $180^\circ$  apart as was expected for image stabilization (mean  $\pm$  standard deviation:  $176.4^\circ \pm 3.2$ ; circles in Figure 6). However, if the monkey was rotated eccentrically, phase was shifted and did no longer meet the biological demands (Fig. 3 and 6). Phase deviation strongly depended on eccentricity with phase lead during nose in ( $-30$  cm:  $249.3^\circ \pm 13.8$ ) and phase lag during nose out eccentric rotation (30 cm:  $155.0^\circ \pm 5.4$ ; 50 cm:  $117.7^\circ \pm 9.5$ ). Target distance had no obvious effect on this phase shift in the range investigated. Even in complete

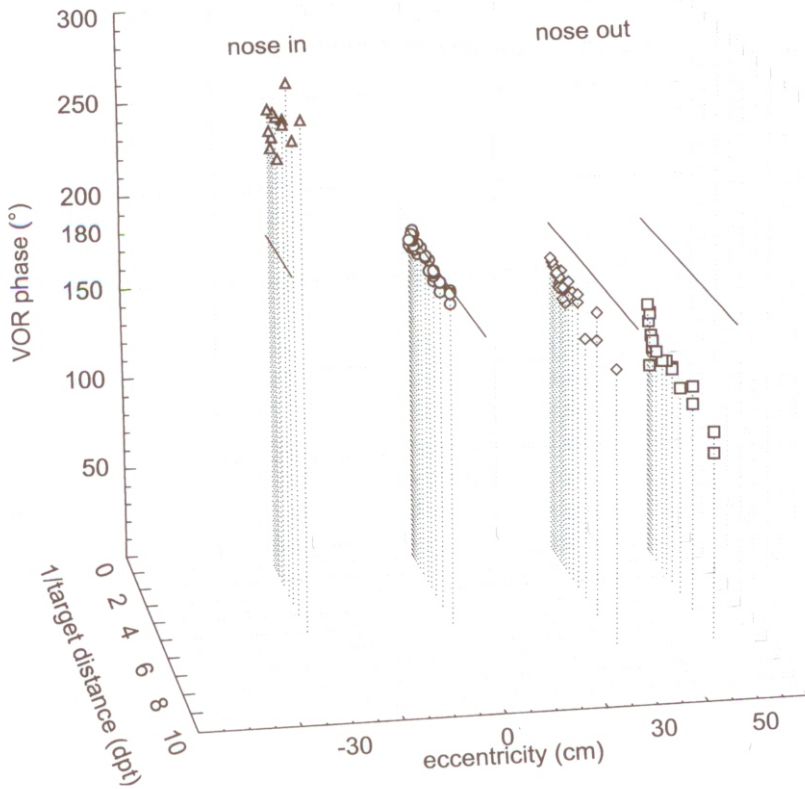


Fig. 6. - Phase shifts for the data presented in Figure 4 (4.0 Hz,  $\pm 0.75^\circ$ ).

Labels are similar as in Fig. 4. Straight lines indicate predicted phase shifts. Only for centric rotation there is a good fit between experimental and predicted values. For eccentric rotations there are systematic deviations up to  $70^\circ$ , which increase with eccentricity (compare +30 and +50 cm nose out) and in opposite directions for nose in and nose out.

darkness without any target presented to the monkey phase shifts were similar and only depended on eccentricity (not shown). During low frequency sinusoidal rotation (0.25 Hz,  $\pm 20^\circ$ ) phase deviation was not observed (no figure).

## DISCUSSION

As can be deduced from the biological demands, VOR gain modulation during eccentric rotation is of particular relevance for close targets. In contrast, expected VOR gain is 1 irrespective of eccentricity for infinite targets (Fig. 2). This stresses the need for otolith-semicircular canal convergence especially for near targets. The presence of this interaction has been previously shown (1, 4-6, 8, 11-15, 17) and could also be demonstrated in this study. There is, however, an ongoing debate if

this interaction behaves linearly (17) or originates from a synergistic enhancement of canalicular and otolithic signals (1). VOR during eccentric rotation in this study was not completely compensatory for all the paradigms tested. This is mainly caused by phase deviations leading to failure of image stabilization.

Centric rotation did not show significant gain modulation in response to target distance. This was compatible with the marginal effects expected due to the eccentric position of the eyes within the head (Figure 2 and 4, 7, 9, 17, 18). Even at high frequencies of 4 Hz when smooth pursuit mechanisms do not play a role, VOR gain and phase were almost perfectly compensatory for image displacement on the retina.

During eccentric rotation several conditions have to be differentiated.

(1) VOR gain enhancement is expected and could also be found experimentally while the monkey was oriented with the nose facing outward. This VOR gain enhancement was compensatory for most paradigms. Maximal VOR gains of up to 4.4 (in relation to the centric paradigm) could be obtained during 50 cm eccentric rotations and close targets (15 cm in front of the monkey). This demonstrates the strong influence of otolith pathways on the combined linear and angular VOR during eccentric rotation for small target distances. VOR phase during 4 Hz stimulation, however, deviated substantially from the required phase. The phase deviation increased with eccentricity causing phase lag during nose out and phase lead during nose in eccentric rotation. Target distance or illumination did not change phase behavior. In a previous study investigating the VOR in squirrel monkeys at the same stimulus frequency of 4 Hz during rotations in the centric and one eccentric position, deviations from predicted phases were also found (17). These phase deviations, however, were smaller than in our study and in the opposite direction. This point certainly needs further clarification. Although vergence angle was not controlled in our study by binocular eye position recordings, the more pronounced phase deviation cannot be solely attributed to poor cooperation of the monkey, as gain enhancement not only depended on eccentricity but also on behavioral tasks, i.e. target distance. Further experiments with systematic variations of stimulus frequency, eccentricity and target distance have to be performed while vergence angle is controlled.

To our knowledge, increasing phase deviations with eccentricity during eccentric rotations have not been described so far. VOR phase deviations during isolated high frequency linear oscillations are well-known<sup>10,16</sup>. The eccentricity depending phase deviations therefore might reflect an increasing contribution of the linear VOR to the combined linear and angular VOR during eccentric rotation.

(2) During eccentric rotation with the nose facing inward not only VOR gain but also phase should depend on target distance. There is an expected phase inversion between targets behind and in front of the axis of rotation. This range has not been investigated by us so far. In a recent study phase shifts around axis of rotation of approximately 120° at 4 Hz were obtained with vergence control (17) clearly deviating from predicted phase shifts of 180°. This can be taken as another example, in which phase deviates by a large amount from the required biological demand.



The results show that additional linear acceleration has enormous effects on the VOR induced by angular acceleration. Experimentally, the increase can be easily 4-5 fold. The knowledge of interactions between otolith and semicircular canals at the level of the VOR in combination with neuronal data from animal experiments during eccentric rotations should be introduced into clinical tests to improve the diagnostic tools for malfunctions of the otolith system.

#### SUMMARY

VOR gain modulation was systematically investigated in the Rhesus monkey (*M. mulatta*) during centric and variable eccentric (up to 50 cm) sinusoidal rotation (4 Hz,  $0.75^\circ$ ) with the nose facing in- or outward to test convergence of otolith and semicircular canal afferences. Earth-stationary lit LED-targets were placed at different distances (12 –180 cm) from the monkey. Results were compared to biological demands. During centric rotation at 4 Hz when smooth pursuit mechanisms do not play a role, VOR gain – as expected – was approximately 1 without dependence on target distance. Phase of VOR and centrifuge were shifted by about  $180^\circ$  as was predicted. If the monkey was rotated eccentrically with the nose facing outward the expected gain enhancement for close targets was obtained. Maximal experimental VOR gain during 4 Hz rotation was 4.4 which was close to demand at 50 cm eccentricity and 15 cm target distance (predicted gain: 4.6). If the nose points inward three situations have to be distinguished from simulation: (1) target behind the axis of rotation – VOR gain decrement should occur; (2) target on the axis of rotation – “inverse VOR suppression”; (3) target between monkey and axis of rotation – phase reversal. Experimentally, VOR gain decrement was obtained (situation 1). VOR gain was minimal (but not zero) for targets around the axis of rotation (situation 2). Situation 3 has not been investigated in detail so far.

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