

Video Article

# Three Dimensional Vestibular Ocular Reflex Testing Using a Six Degrees of Freedom Motion Platform

Joyce Dits<sup>1</sup>, Mark M.J. Houben<sup>2</sup>, Johannes van der Steen<sup>1</sup>

<sup>1</sup>Department of Neuroscience, Erasmus MC

<sup>2</sup>TNO Human Factors

Correspondence to: Johannes van der Steen at [J.vandersteen@erasmusmc.nl](mailto:J.vandersteen@erasmusmc.nl)

URL: <https://www.jove.com/video/4144>

DOI: [doi:10.3791/4144](https://doi.org/10.3791/4144)

Keywords: Neurobiology, Issue 75, Neuroscience, Medicine, Anatomy, Physiology, Biomedical Engineering, Ophthalmology, vestibulo ocular reflex, eye movements, torsion, balance disorders, rotation translation, equilibrium, eye rotation, motion, body rotation, vestibular organ, clinical techniques

Date Published: 5/23/2013

Citation: Dits, J., Houben, M.M., van der Steen, J. Three Dimensional Vestibular Ocular Reflex Testing Using a Six Degrees of Freedom Motion Platform. *J. Vis. Exp.* (75), e4144, doi:10.3791/4144 (2013).

## Abstract

The vestibular organ is a sensor that measures angular and linear accelerations with six degrees of freedom (6DF). Complete or partial defects in the vestibular organ results in mild to severe equilibrium problems, such as vertigo, dizziness, oscillopsia, gait unsteadiness nausea and/or vomiting. A good and frequently used measure to quantify gaze stabilization is the gain, which is defined as the magnitude of compensatory eye movements with respect to imposed head movements. To test vestibular function more fully one has to realize that 3D VOR ideally generates compensatory ocular rotations not only with a magnitude (gain) equal and opposite to the head rotation but also about an axis that is co-linear with the head rotation axis (alignment). Abnormal vestibular function thus results in changes in gain and changes in alignment of the 3D VOR response.

Here we describe a method to measure 3D VOR using whole body rotation on a 6DF motion platform. Although the method also allows testing translation VOR responses<sup>1</sup>, we limit ourselves to a discussion of the method to measure 3D angular VOR. In addition, we restrict ourselves here to description of data collected in healthy subjects in response to angular sinusoidal and impulse stimulation.

Subjects are sitting upright and receive whole-body small amplitude sinusoidal and constant acceleration impulses. Sinusoidal stimuli ( $f = 1$  Hz,  $A = 4^\circ$ ) were delivered about the vertical axis and about axes in the horizontal plane varying between roll and pitch at increments of  $22.5^\circ$  in azimuth. Impulses were delivered in yaw, roll and pitch and in the vertical canal planes. Eye movements were measured using the scleral search coil technique<sup>2</sup>. Search coil signals were sampled at a frequency of 1 kHz.

The input-output ratio (gain) and misalignment (co-linearity) of the 3D VOR were calculated from the eye coil signals<sup>3</sup>.

Gain and co-linearity of 3D VOR depended on the orientation of the stimulus axis. Systematic deviations were found in particular during horizontal axis stimulation. In the light the eye rotation axis was properly aligned with the stimulus axis at orientations  $0^\circ$  and  $90^\circ$  azimuth, but gradually deviated more and more towards  $45^\circ$  azimuth.

The systematic deviations in misalignment for intermediate axes can be explained by a low gain for torsion (X-axis or roll-axis rotation) and a high gain for vertical eye movements (Y-axis or pitch-axis rotation (see **Figure 2**). Because intermediate axis stimulation leads a compensatory response based on vector summation of the individual eye rotation components, the net response axis will deviate because the gain for X- and Y-axis are different.

In darkness the gain of all eye rotation components had lower values. The result was that the misalignment in darkness and for impulses had different peaks and troughs than in the light: its minimum value was reached for pitch axis stimulation and its maximum for roll axis stimulation.

## Case Presentation

Nine subjects participated in the experiment. All subjects gave their informed consent. The experimental procedure was approved by the Medical Ethics Committee of Erasmus University Medical Center and adhered to the Declaration of Helsinki for research involving human subjects.

Six subjects served as controls. Three subjects had a unilateral vestibular impairment due to a vestibular schwannoma. The age of control subjects (six males and three females) ranged from 22 to 55 years. None of the controls had visual or vestibular complaints due to neurological, cardio vascular and ophthalmic disorders.

The age of the patients with schwannoma varied between 44 and 64 years (two males and one female). All schwannoma subjects were under medical surveillance and/or had received treatment by a multidisciplinary team consisting of an otorhinolaryngologist and a neurosurgeon of the Erasmus University Medical Center. Tested patients all had a right side vestibular schwannoma and underwent a wait and watch policy (**Table 1**; subjects N1-N3) after being diagnosed with vestibular schwannoma. Their tumors had been stable for over 8-10 years on magnetic resonance imaging.

## Video Link

The video component of this article can be found at <https://www.jove.com/video/4144/>

## Protocol

### 1. 6DF Motion Platform

Vestibular stimuli were delivered with a motion platform (see **Figure 1**) capable of generating angular and translational stimuli at a total of six degrees of freedom (FCS-MOOG, Nieuw-Vennep, The Netherlands). The platform is moved by six electro-mechanical actuators connected to a personal computer with dedicated control software. It generates accurate movements with six degrees of freedom. Sensors placed in the actuators continuously monitored the platform motion profile. The device has <0.5 mm precision for linear and <0.05° for angular movements. Vibrations during stimulation were 0.02°. Resonance frequency of the device was >75 Hz. Platform motion profile was reconstructed from the sensor information in the actuators using inverse dynamics and sent to the data collection computer. To synchronize platform and eye movement data, a laser beam was mounted at the backside of the platform and projected onto a small photocell (1 mm, reaction time 10 µsec). The output voltage of the photocell was sampled at a rate of 1 KHz together with the eye movement data and provided a real time indicator of motion onset with 1 msec accuracy. During the offline analysis using Matlab (Mathworks, Natick, MA), the reconstructed motion profile of the platform based on the sensor information of the actuators in the platform was precisely aligned with the onset of platform motion.

### 2. Subjects

#### A. Seating

The subjects are seated on a chair mounted at the center of the platform (**Figure 2**). The subject's body was restrained with a four-point seatbelt as used in racing cars. The seatbelts were anchored to the base of the motion platform. The chair was surrounded by a PVC cubic frame and served as a support for the field coils. The field coil system was adjustable in height, such that the subject's eyes were in the center of the magnetic field.

#### B. Head fixation

The head is immobilized using an individually moulded dental-impression bite board, which was attached to the cubic frame via a rigid bar. A vacuum pillow folded around the neck and an annulus attached to the chair further ensured fixation of the subject (**Figure 1**). In addition, to monitor spurious head movements during the stimulation, we attached two 3D sensors (Analog Devices Inc, Norwood, MA) directly to the bite board, one for angular and one for linear accelerations.

### 3. Coordinate System

Eye rotations are defined in a head-fixed right-handed coordinate system (**Figure 3**). In this system from the subject's point of view a leftward rotation about the Z-axis (yaw), a downward rotation about the Y-axis (pitch) and rightward rotation about the X-axis (roll) are defined as positive. The planes orthogonal to the X, Y and Z rotation axes are respectively the roll, pitch and yaw planes (**Figure 3**).

### 4. Eye Movement Recordings

Eye movements of both eyes were recorded with 3D scleral search coils (Skalar, Delft, The Netherlands)<sup>4</sup> using a standard 25 kHz two field coil system based on the amplitude detection method of Robinson (Model EMP3020, Skalar Medical, Delft, The Netherlands)<sup>5</sup>. The coil signals were passed through an analogue low-pass filter with cut-off frequency of 500 Hz and sampled on-line and stored to hard disk at a frequency of 1 kHz with 16 bit precision (CED system running Spike2 v6, Cambridge Electronic Design, Cambridge).

### 5. Search Coil Calibration

Prior to the experiments, the sensitivity and non-orthogonality of direction and torsion coils was verified *in-vitro* by mounting the coil on a Fick gimbal system placed in the center of the magnetic field. By rotating the gimbal system about all cardinal axes we verified that all coils used in the experiments were symmetrical for all directions within 2%.

*In vivo*, the horizontal and vertical signals of both coils were individually calibrated by instructing the subject to successively fixate a series of five targets (central target and a target at 10 degrees left, right, up and down) for five seconds each. Calibration targets were projected onto a translucent screen at 186 cm distance. Post experiment analysis of the calibration data resulted in sensitivity and offset values for the each search coils. These values were then used in the analysis procedures written in Matlab<sup>3</sup>.

## 6 Stimulation

### A. Sinusoidal stimulation

The platform delivered whole-body sinusoidal rotations (1 Hz,  $A = 4^\circ$ ) about the three cardinal axes: The rostral-caudal or vertical axis (yaw), the interaural axis (pitch) and the nasal-occipital axis (roll), and about intermediate horizontal axes incremented in steps of  $22.5^\circ$  between roll and pitch.

Sinusoidal stimuli were delivered in light and darkness. In the light, subjects fixated on a continuously lit visual target (a red LED, 2 mm diameter) located 177 cm in front of the subject at eye level (**Figure 1C** left panel). Head was positioned such that Reid's line was base (the imaginary line connecting the meatus externa with the lower orbital cantus) was within 6 degrees from earth-horizontal). During sinusoidal stimulation in the dark, the visual target was briefly presented (2 sec) when the platform was stationary during each interval between two consecutive stimuli. To avoid spontaneous eye movements during the stimulation, subjects were instructed to fixate the imaginary location of the space fixed target during sinusoidal stimulation after the target had been switched off just prior to motion onset. We verified that the type of instruction mainly reduced the eye movements made in darkness, and had only a small effect on gain ( $<10\%$ ). This variability occurred in all components (horizontal, vertical and torsion) simultaneously.

### B. Impulse stimulation

Short duration whole body impulses were delivered in a dimly lit environment. The only visible stimulus available to the subject was a visual target located at 177 cm in front of the subject at eye level. Each impulse was repeated six times and delivered in random order and with random timing of motion onset (intervals varied between 2.5 and 3.5 sec). The profile of the impulses was a constant acceleration of  $100^\circ \text{ sec}^{-2}$  during the first 100 msec of the impulse, followed by a gradual linear decrease in acceleration. This stimulus resulted in a linear increase in velocity reaching a velocity of  $10^\circ \text{ sec}^{-1}$  after 100 msec. Aberrant head movements during vestibular stimulation measured by the angular rate and linear acceleration devices were less than 4% of stimulus amplitude. Peak velocity of the eye movements in response to these impulses was 100 times above the noise level of the coil signals.

## 7. Data Analysis

Coil signals were converted into Fick angles and then expressed as rotation vectors<sup>6,7</sup>. From the fixation data of the target straight ahead we determined the misalignment of the coil in the eye relative to the orthogonal primary magnetic field coils. Signals were corrected for this offset misalignment by three-dimensional counter rotation. It was also verified that no coil slippage had occurred during the experiment by verifying the position output during fixation of the target prior to each motion onset.

To express 3D eye movements in the velocity domain, we converted rotation vector data back into angular velocity. Before conversion of rotation vector to angular velocity, we smoothed the data by zero-phase with a forward and reverse digital filter with a 20-point Gaussian window (length 20 msec).

## 8. Sinusoidal Responses

**A Gain.** The gain of each component and 3D eye velocity gain was calculated by fitting a sinusoid with a frequency equal to the platform frequency through the horizontal, vertical and torsion angular velocity components. The gain for each component defined as the ratio between eye component peak velocity and platform peak velocity was calculated separately for each eye.

**B Misalignment.** The misalignment between the 3D eye velocity axis and head velocity axis was calculated using the approach of Aw and colleagues<sup>8,9</sup>. From the scalar product of two vectors the misalignment was calculated as the instantaneous angle in three dimensions between the inverse of the eye velocity axis and the head velocity axis. The 3D angular velocity gain and misalignment for each azimuthal orientation were compared to the gain and misalignment predicted from vector summation of the  $0^\circ$  (roll) and  $90^\circ$  (pitch) azimuth components<sup>10</sup>. From this vector summation it follows that when velocity gains for roll and pitch are equal, the orientation of the eye rotation axis aligns with the head rotation axis, when the two are different, the maximum deviation between stimulus and eye rotation axis is expected at  $45^\circ$  azimuth.

## 9. Impulse Responses

Left and right eye data traces of six presentations for each motion direction were separately analysed. Because left and right eye values were almost identical, the data from left and right eye were averaged to determine the gain of eye velocity in response to impulse stimulation. All traces were individually inspected on the computer screen. When the subject made a blink or saccade during the impulse that trace was manually discarded. Angular velocity components ( $N = 5$  to 6) during the first 100 msec after onset of the movement were averaged in time bins of 20 msec (providing an effective low pass filtering) and plotted as function of platform velocity<sup>11,12</sup>.

## Representative Results

### Sinusoidal stimulation light

**Figure 4** (top panel) shows for the control group the mean gain of the horizontal, vertical and torsion angular velocity components for all tested sinusoidal stimulations in the horizontal plane in the light. Torsion was maximal at  $0^\circ$  azimuth, whereas vertical had its maximum at  $90^\circ$ . **Figure 5** shows the 3D eye velocity gain in the light. Gain varied between  $0.99 \pm 0.12$  (pitch) and  $0.54 \pm 0.16$  (roll). The measured data closely correspond to the predicted values calculated from the vector sum of torsion and vertical components (dashed line of **Figure 5**).

The mean misalignment between stimulus and response axis averaged over six subjects is shown in **Figure 6**. In the light misalignment between stimulus and response axis was smallest ( $5.25^\circ$ ) during pitch and gradually increased towards roll until the orientation of the stimulus axis was oriented at  $22.5^\circ$  azimuth (maximum misalignment:  $17.33^\circ$ ) and decreased towards the roll axis. These values for each horizontal stimulus angle correspond closely to what one would predict from linear vector summation of roll and pitch contributions (dashed line in **Figure 6**).

### Sinusoidal stimulation darkness

In darkness the maximum gain of both the vertical and torsion components was significantly lower (t-test  $P < 0.001$ ) than in the light (vertical:  $0.72 \pm 0.19$  torsion:  $0.37 \pm 0.09$ ) (**Figure 7**). Also the 3D eye velocity gain was significantly (t-test  $P < 0.001$ ) lower than in the light (**Figure 8**). Gain was slightly higher than predicted from the vertical and torsion components alone (dashed line in **Figure 8**). In the dark the misalignment was minimal at  $90^\circ$  (pitch) and gradually increased to a peak around the  $0^\circ$  axis (roll). Due to the presence of a small horizontal component, the pattern of misalignment in the dark did not correspond to what one would predict from linear vector summation of only roll and pitch components (see **Figure 9**).

### Impulse stimulation

Whole body impulses about the interaural axis (pitch) resulted in near unity gain for head up and a gain about 0.8 for head down impulses. Differences were significant ( $P < 0.05$ ).

Horizontal, vertical and torsional gain components during impulse stimulation are shown in **Figure 10**. Maximum mean gain for the vertical component alone was 0.85 for pitch ( $90^\circ$  azimuth). Maximum gain for torsion was 0.42 for roll ( $0^\circ$  azimuth). Vector gain is shown in **Figure 11**. 3D eye velocity gain varied between  $1.04 \pm 0.18$  for pitch to  $0.52 \pm 0.16$  for roll. Misalignment varied between  $28.2^\circ \pm 0.18$  for roll, to  $11.53^\circ \pm 0.51$  for pitch.

In conclusion, although impulse stimulation causes only a very brief (100 msec) disruption of visual information, the gain and misalignment of eye movements have a qualitatively similar pattern as those in response to sinusoidal stimulation in darkness. In both instances the largest misalignment between 3D head and eye rotation axis occurs during roll stimulation.

## Patients

### 3D VOR in non-operated patients

**Figure 13** shows the location and the size of the tumor on MRI scans for the three non-operated subjects (see also **Table 1** in method section). The tumor was in all three cases on the right sided. Subjective complaints of dizziness of these three subjects varied. Subject N1 had an intracranial tumor with the smallest size. He presented himself with unilateral hearing problems and no complaints of vertigo. Subjects N2 and N3 did report complaints of vertigo, although neither had complete disorientation problems or vegetative problems.

**Figure 14** shows eye position traces for the three non-operated subjects in response to sinusoidal stimulation about a horizontal axis  $45^\circ$  azimuth. Ideally, this stimulus evokes only a combination of vertical and torsional eye movement components and no horizontal eye movements. During stimulation in the light there were few signs of horizontal ocular drift in subjects N1 and N2, whereas subject N3 had a horizontal leftward nystagmus (slow phase to the right) and a CW torsional nystagmus (slow phase CCW). In the dark subject N1 had little or no drift, whereas for subjects N2 and N3 instabilities appeared in the horizontal, vertical and torsional traces. The only weak sign of instability in subject N1 is in torsion, where small corrective torsional saccades were observed that were consistently in CW direction. In subjects N2 and N3 torsional instabilities were larger.

To demonstrate the changes in 3D stability in Schwannoma patients we present for subject N2 in **Figure 15** the horizontal, vertical and torsional eye velocity gain components (top panel), the 3D gain (center panel) and misalignment (lower panel). The changes in gain of the individual components have a direct impact on 3D vectorial eye velocity gain and misalignment. The close correspondence between predicted and measured 3D eye velocity and alignment as found in the control subjects no longer holds for Schwannoma patients.

In particular in subjects N2 and N3 the 3D eye velocity gain in darkness was affected. In subject N2 the overall 3D eye velocity gain was lower, which can be explained by the decrease in torsional gain (**Figure 15**). Also in subject N3 the torsion component was affected. His torsional eye velocity gains responses were asymmetric. This resulted in an up to two-fold increase in misalignment.



Figure 1. Experimental setup with the 6DF motion platform.

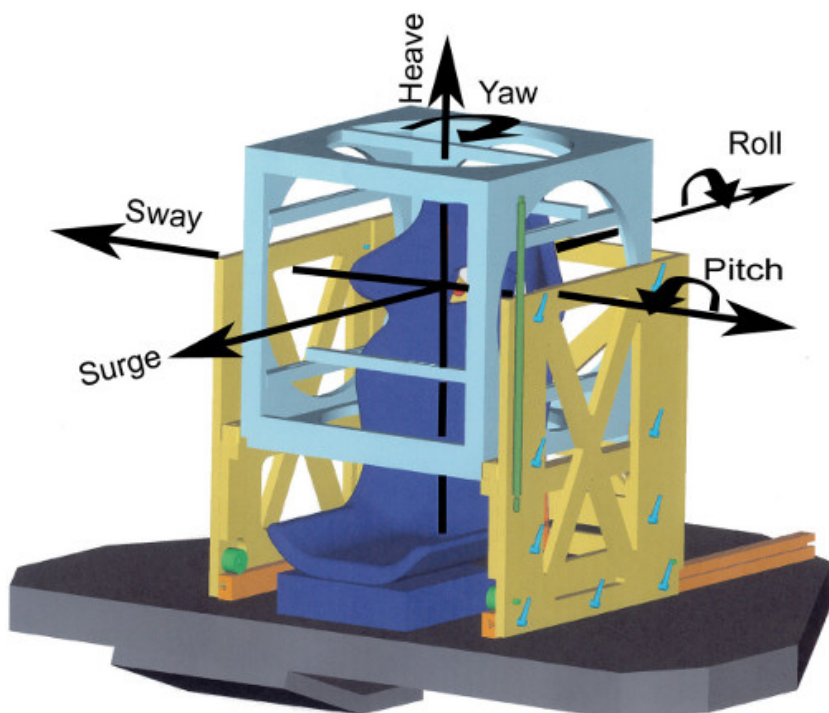


Figure 2. Schematic drawing of the electro magnetic field coil system surrounding the chair mounted on the 6DF motion platform. Arrows indicate the possible axes of rotation and translation of the platform.

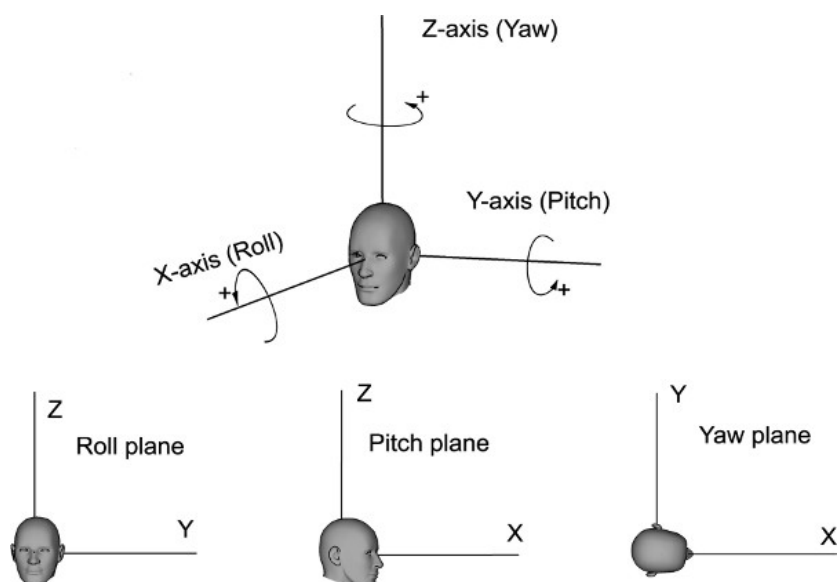


Figure 3. Directions of rotations around the cardinal axes according to the right hand rule. Bottom panels show the yaw, roll and pitch projection planes.

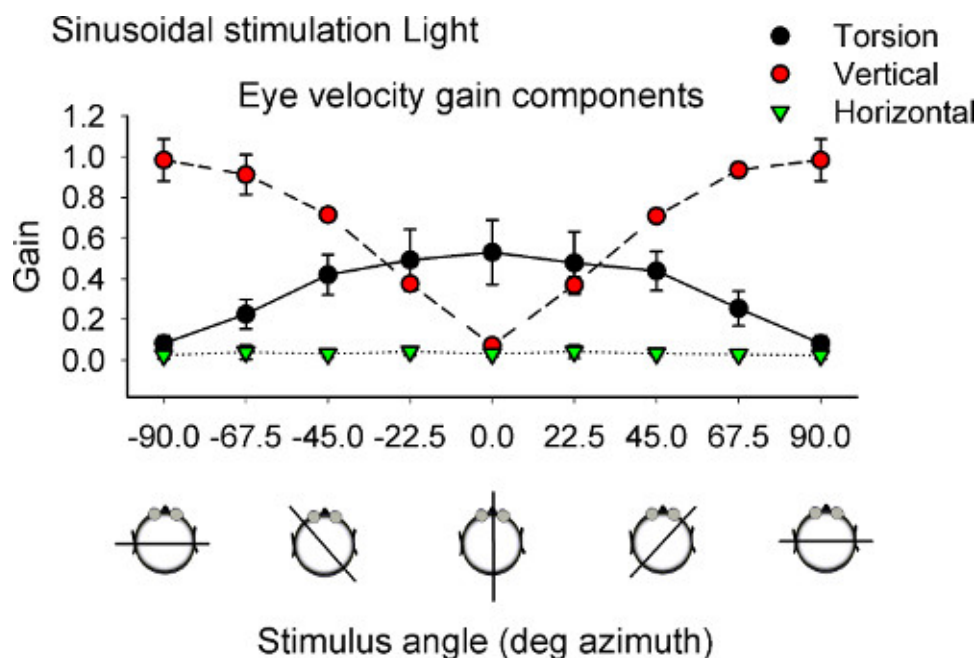
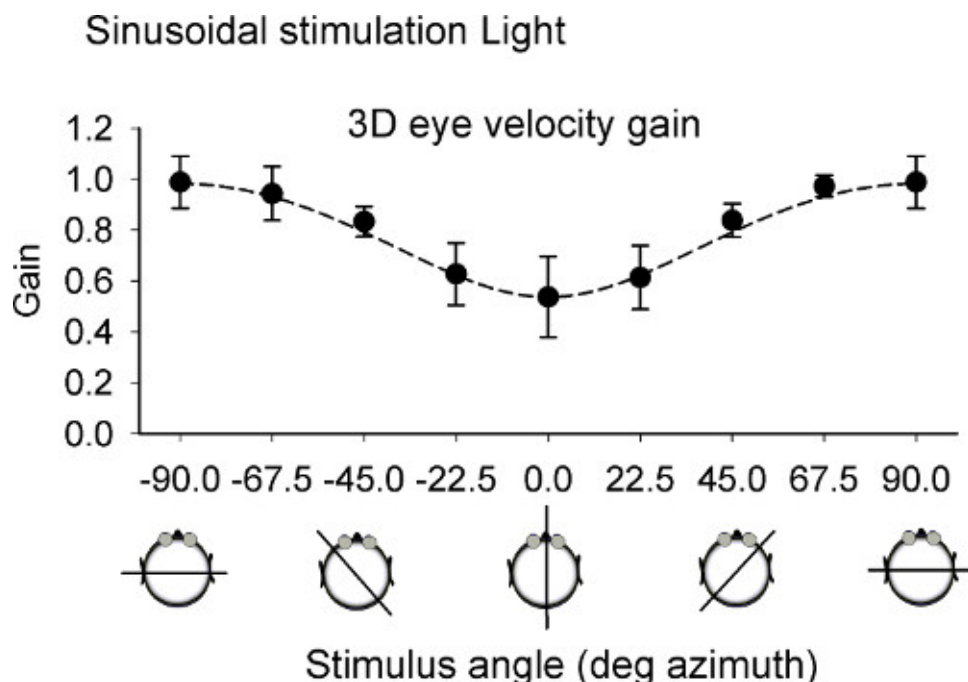
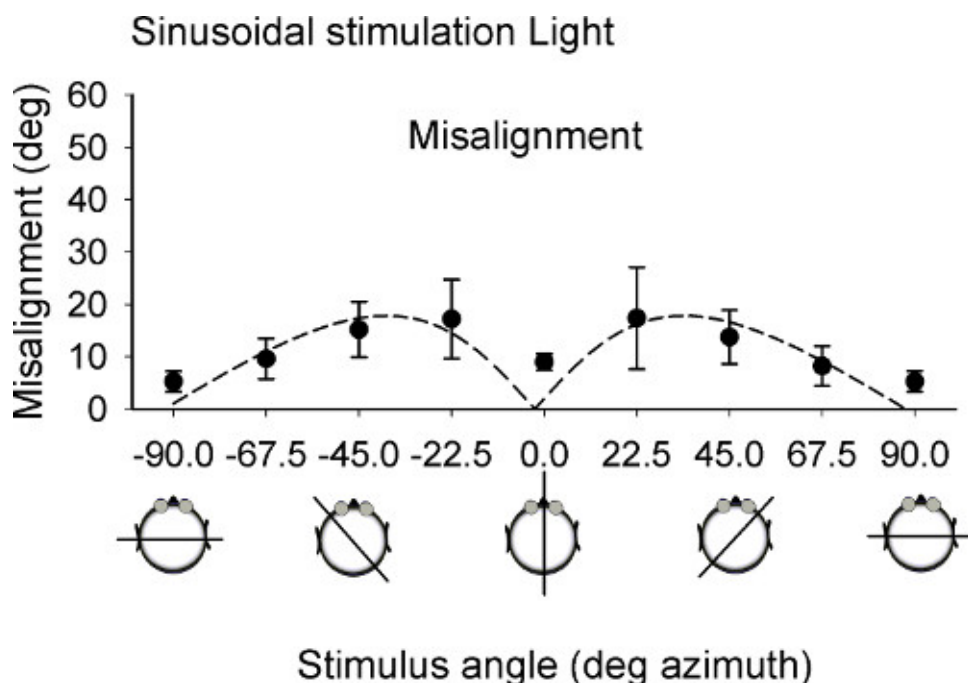


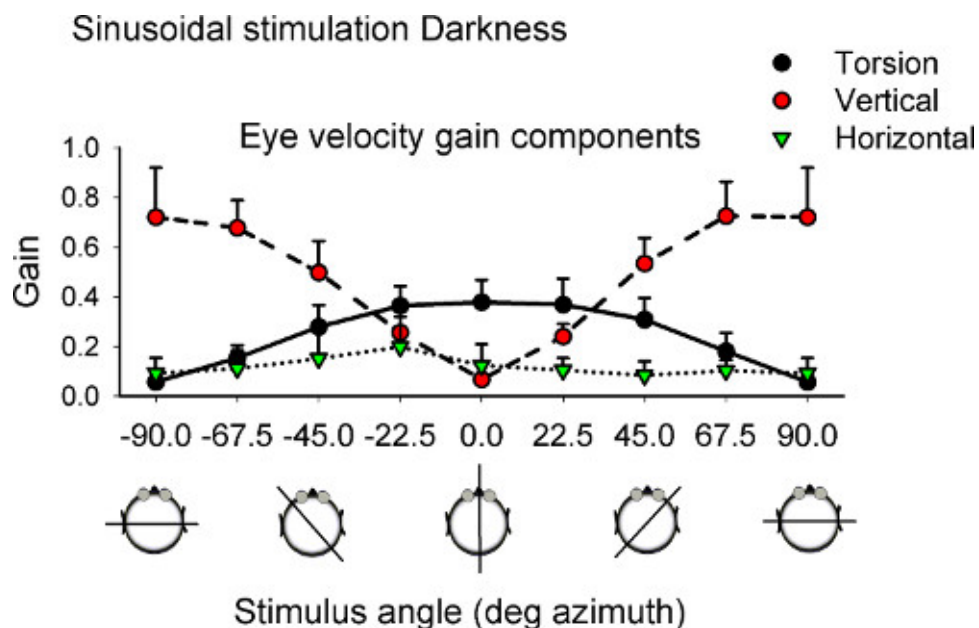
Figure 4. Mean gain of the horizontal, vertical and torsion eye velocity components. Results of horizontal axis sinusoidal stimulation for all tested horizontal stimulus axes averaged over all subjects (N = 6) in the light. Cartoons underneath give a top view of the orientation of the stimulus axis with respect to the head.



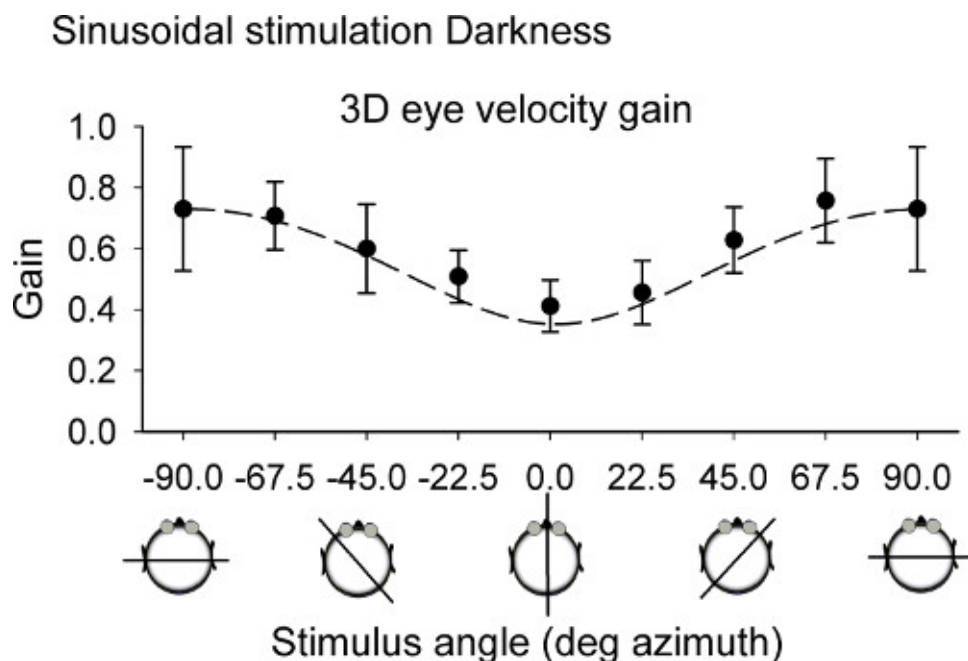
**Figure 5.** Mean 3D eye velocity gain for all tested horizontal stimulus axes averaged over all subjects (N = 6) in the light. Dashed line is the vector eye velocity gain response predicted from the vertical and torsion components. Cartoons underneath give a top view of the orientation of the stimulus axis with respect to the head.



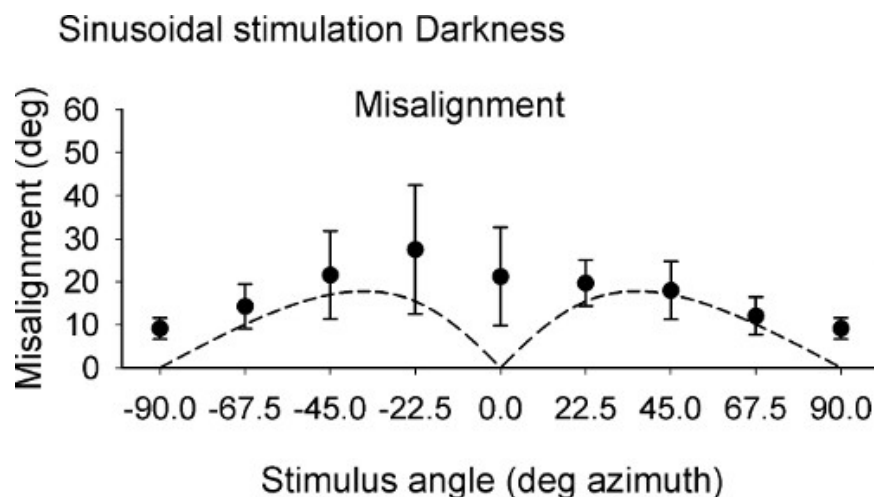
**Figure 6.** Misalignment of the response axis with respect to the stimulus axis during sinusoidal stimulation in the light. The dashed line in the lower panel represents the predicted misalignment calculated from the vector sum of only vertical and torsion eye velocity components in response to pure pitch and pure roll stimulation, respectively. Error bars indicate one standard deviation.



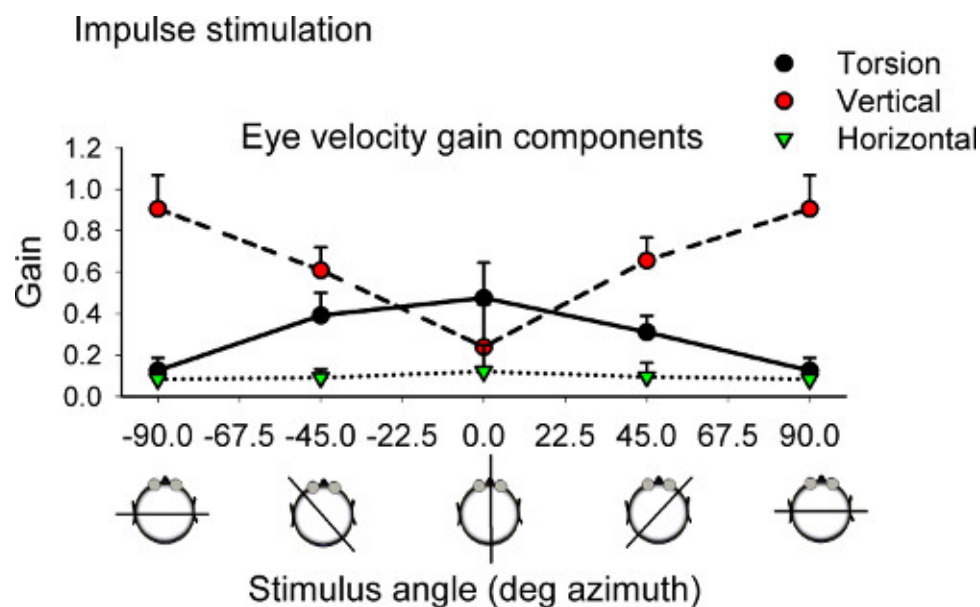
**Figure 7. Mean gain of the horizontal, vertical and torsion eye velocity components.** Results of horizontal axis sinusoidal stimulation for all tested horizontal stimulus axes averaged over all subjects ( $N = 6$ ) in darkness. Cartoons underneath give a top view of the orientation of the stimulus axis with respect to the head.



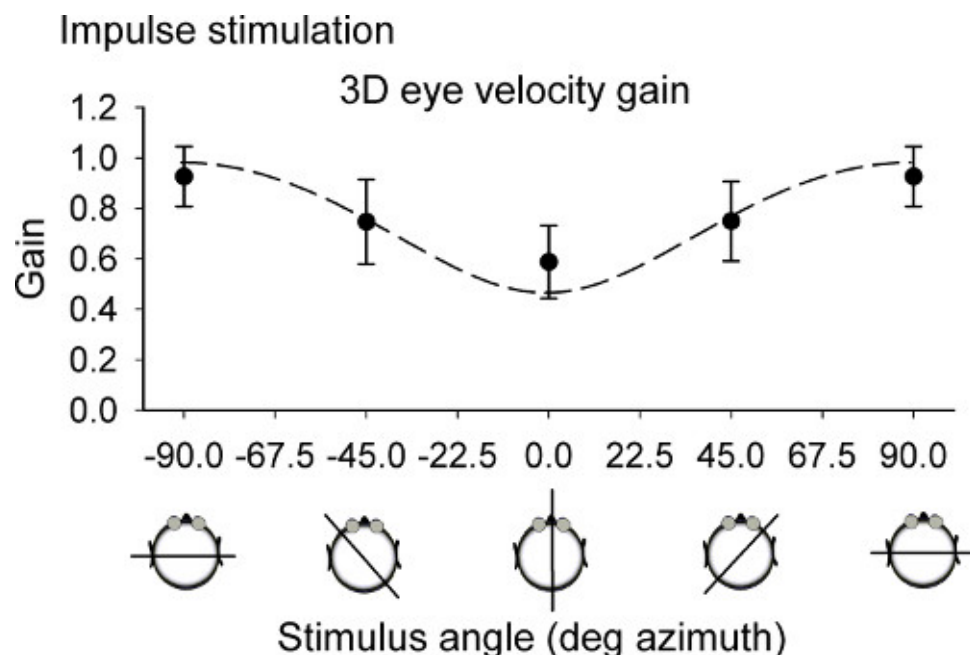
**Figure 8. Mean 3D eye velocity gain for all tested horizontal stimulus axes averaged over all subjects ( $N = 6$ ) in darkness.** Dashed line is the vector eye velocity gain response predicted from the vertical and torsion components. Cartoons underneath give a top view of the orientation of the stimulus axis with respect to the head.



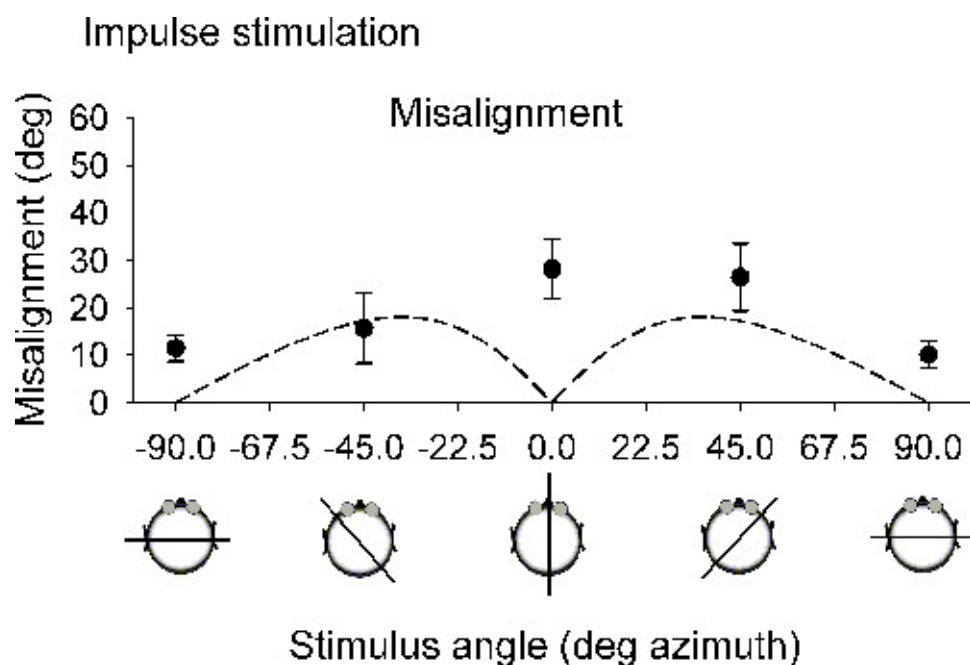
**Figure 9. Misalignment of the response axis with respect to the stimulus axis during sinusoidal stimulation in darkness.** The dashed line in the lower panel represents the predicted misalignment calculated from the vector sum of only vertical and torsion eye velocity components in response to pure pitch and pure roll stimulation, respectively. Error bars indicate one standard deviation.



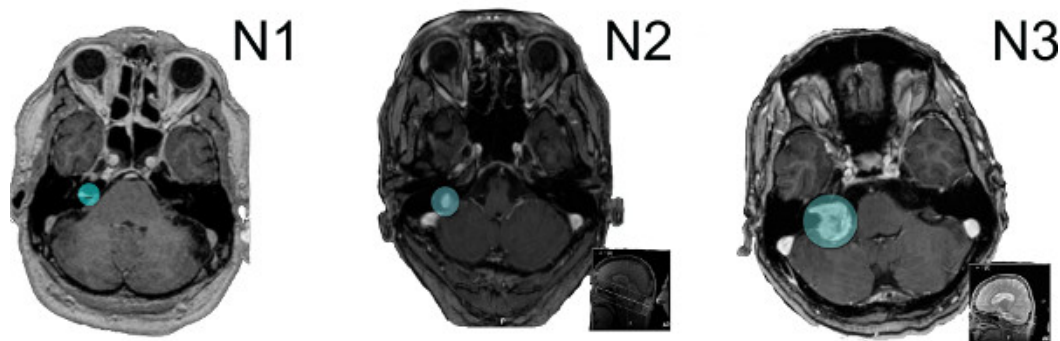
**Figure 10. Mean gain of the horizontal, vertical and torsion eye velocity components in response to horizontal axis impulse stimulation.** Responses are given for horizontal stimulus axes at 45 degrees intervals averaged over all subjects (N = 6). Cartoons underneath give a top view of the orientation of the stimulus axis with respect to the head.



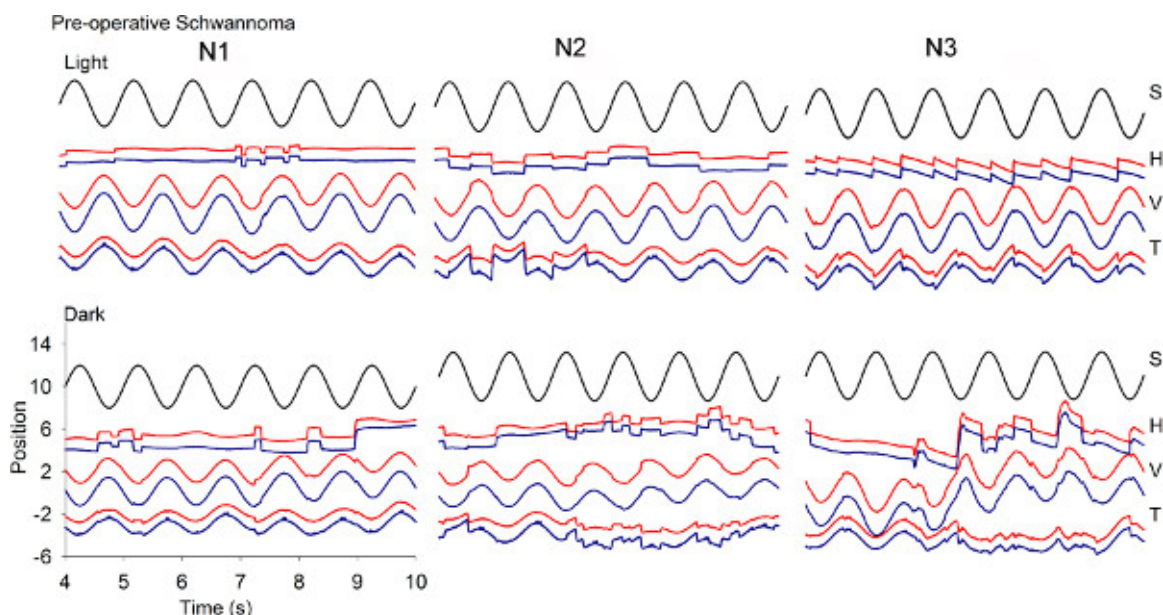
**Figure 11. Mean 3D eye velocity gain for all tested horizontal stimulus axes averaged over all subjects (N = 6) during impulse stimulation.** Dashed line is the vector eye velocity gain response predicted from the vertical and torsion components. Cartoons underneath give a top view of the orientation of the stimulus axis with respect to the head.



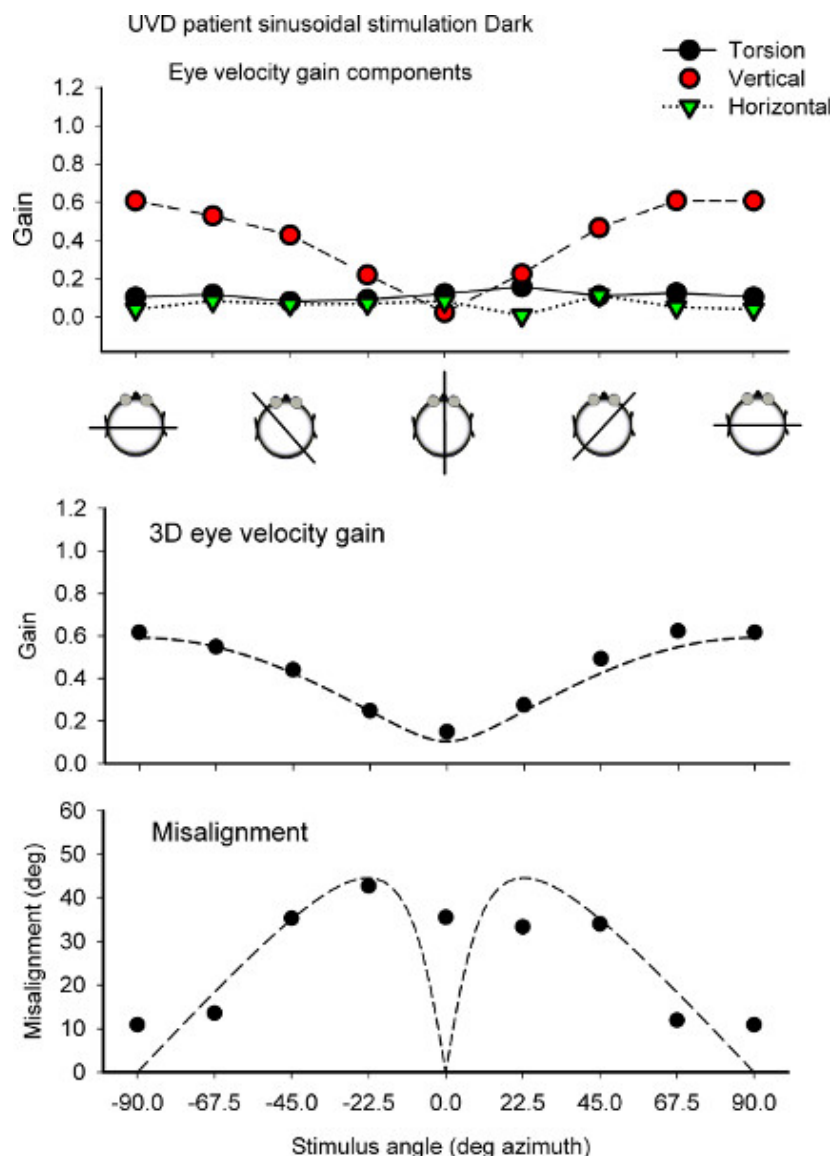
**Figure 12. Misalignment of the response axis with respect to the stimulus axis during impulse stimulation.** The dashed line in the lower panel represents the predicted misalignment calculated from the vector sum of only vertical and torsion eye velocity components in response to pure pitch and pure roll stimulation, respectively. Error bars indicate one standard deviation.



**Figure 13. MRI-scans of three patients with untreated Schwannoma's.** The Schwannoma is indicated in each scan by the circle.



**Figure 14. Examples of time series for the three non-operated subjects in response to sinusoidal stimulation about a horizontal axis 45° azimuth. Upper panel row: Light, Lower panel row: Dark.** In each panel are plotted the right (red) and left (blue) eye horizontal (H), vertical (V) and torsional (T) eye positions. In this and all subsequent figures eye positions and velocities are expressed in a right-handed, head-fixed coordinate system. In this system clockwise (CW), down and counterclockwise (CCW) eye rotations viewed from the perspective of the subject are defined as positive values. Stimulus motion is indicated in each panel by the top black line.



**Figure 15. Gain and misalignment of 3D VOR of UVD subject N2 during horizontal axis sinusoidal stimulation in the dark.** **Top panel:** Gain of the horizontal, vertical and torsional eye velocity components. Cartoons underneath give a top view of the orientation of the stimulus axis with respect to the head. **Center panel:** Mean 3D eye velocity at each tested stimulus axis orientation. The dashed line represents the vector eye velocity gain response predicted from the vertical and torsional components. **Lower panel:** Misalignment of the response axis with respect to the stimulus axis. The dashed line in the lower panel represents the predicted misalignment calculated from the vector sum of vertical and torsional eye velocity components. Notice the low gain for torsion in the top panel and large misalignment in the lower panel. [Click here to view larger figure.](#)

| Subject | Gender | Age (year) | Side of tumor | Tumor size (mm) | Unilateral hearing loss (Fi dB) | Therapy        |
|---------|--------|------------|---------------|-----------------|---------------------------------|----------------|
| N1      | male   | 61         | right         | 4               | 35                              | wait and watch |
| N2      | male   | 64         | right         | 14              | 43                              | wait and watch |
| N3      | male   | 55         | right         | 22              | complete                        | wait and watch |

**Table 1. Relevant clinical findings of the six patients who participated in the experiments.** The unilateral hearing loss described here was before any therapy and expressed in Fi = Flechter index (mean hearing loss of 500, 1,000 and 2,000 Hz).

## Discussion

This paper describes a method to accurately measure 3D angular VOR in response to whole body rotations in humans. The advantage of the method is that it gives quantitative information about gain and misalignment of 3D angular VOR in all three dimensions. The method is useful for fundamental research and has also potential clinical value e.g. for testing patients with vertical canal problems or patients with ill-understood central vestibular problems. Another advantage of the device is the ability to test translational VOR responses<sup>1</sup>. Disadvantages of the system

are 1) the cost aspects in terms of equipment, space and personnel (the current machine was developed for pilot training purposes) and 2) discomfort during the measurements. Accurate eye movement recordings are based on the scleral search coil technique. Due to its superior signal to noise ratio and absence of slip compared to head-mounted infrared camera systems, this is still the only technique to measure VOR responses in humans with high precision. Improvements in slip-free infrared video based eye tracker systems are badly needed.

The data show that in healthy human subjects the quality of the 3D VOR response varies not only in terms of gain, but also in terms of alignment of the eye rotation axis with head rotation axis. As was also found in other studies on 3D VOR dynamics, there is a high gain for horizontal and vertical eye movements compared to torsion. This general property has also been described in lateral eyed animals such as rabbits<sup>13</sup> and frontal eyed animals such as monkeys<sup>14</sup> and humans<sup>4, 9, 15, 16</sup>. The gain of the VOR for stimulation about the cardinal axes is in close agreement with previous studies in humans<sup>8, 17, 18</sup>. There was a small but significant higher gain for pitch head up, compared to pitch head down impulses. This is possibly related to the fact that our impulses were whole body movements in contrast to previous studies that involved stimulation of the neck<sup>19, 20</sup>.

The second main finding is the systematic variation in misalignment between stimulus and response axis. In the light misalignment has minima at roll and pitch, and its maxima at plus and minus 45° azimuth. Quantitatively, the misalignment angles in our study are similar to those reported in monkeys<sup>21, 22</sup>.

In the dark and during impulse stimulation there is a twofold increase in misalignment compared to sinusoidal stimulation in the light over the whole range of tested axes. Under dark and impulse stimulus conditions stimulation about the roll axis results in the largest misalignment. The relatively large misalignment during roll axis stimulation in the dark has its origin in a small but consistent horizontal eye movement component that has in combination with low gain for torsion a relatively large contribution to the vector gain<sup>3</sup>.

Although subjects viewed a fixation target during impulse stimulation, misalignments were not significantly different (t-test  $P > 0.05$ ) from the sinusoidal stimulation in darkness condition. This means that the relatively mild impulse that we used, briefly interferes with visual fixation. As a result of this the response is similar to sinusoidal stimulation in darkness.

The sensitivity of the method is demonstrated in a small group of patients with unilateral Schwannoma's. In this non-operated group that was on a wait and watch policy, subjective problems were variable and relatively mild in the light. Nevertheless, with this method we were able to show that in the dark the proper 3D gain and alignment of the 3D VOR is impaired. Although the group is very small, our data suggest a correlation between tumor size and severity of 3D VOR abnormalities.

## Disclosures

We have nothing to disclose.

## Acknowledgements

Funded by Dutch NWO/ZonMW grants 912-03-037 and 911-02-004.

## References

- Houben, M.M.J., Goumans, J., Dejongste, A.H., & Van der Steen, J. Angular and linear vestibulo-ocular responses in humans. *Ann. N.Y. Acad. Sci.* **1039**, 68-80 (2005).
- Collewijn, H., Van der Steen, J., Ferman, L., & Jansen, T.C. Human ocular counterroll: assessment of static and dynamic properties from electromagnetic scleral coil recordings. *Exp. Brain Res.* **59**, 185-196 (1985).
- Goumans, J., Houben, M.M., Dits, J., & van der Steen, J. Peaks and troughs of three-dimensional vestibulo-ocular reflex in humans. *J. Assoc. Res. Otolaryngol.* **11**, 383-393, doi:10.1007/s10162-010-0210-y (2010).
- Ferman, L., Collewijn, H., Jansen, T.C., & Van den Berg, A.V. Human gaze stability in the horizontal, vertical and torsional direction during voluntary head movements, evaluated with a three-dimensional scleral induction coil technique. *Vision Res.* **27**, 811-828 (1987).
- Robinson, D.A. A Method of Measuring Eye Movement Using a Scleral Search Coil in a Magnetic Field. *IEEE Trans. Biomed. Eng.* **10**, 137-145 (1963).
- Haustein, W. Considerations on Listing's Law and the primary position by means of a matrix description of eye position control. *Biol. Cybern.* **60**, 411-420 (1989).
- Haslwanter, T. & Moore, S.T. A theoretical analysis of three-dimensional eye position measurement using polar cross-correlation. *IEEE Trans. Biomed. Eng.* **42**, 1053-1061 (1995).
- Aw, S.T., et al. Three-dimensional vector analysis of the human vestibuloocular reflex in response to high-acceleration head rotations. II. responses in subjects with unilateral vestibular loss and selective semicircular canal occlusion. *J. Neurophysiol.* **76**, 4021-4030 (1996).
- Aw, S.T., et al. Three-dimensional vector analysis of the human vestibuloocular reflex in response to high-acceleration head rotations. I. Responses in normal subjects. *J. Neurophysiol.* **76**, 4009-4020 (1996).
- Crawford, J.D. & Vilis, T. Axes of eye rotation and Listing's law during rotations of the head. *J. Neurophysiol.* **65**, 407-423 (1991).
- Tabak, S., Collewijn, H., & Boumans, L.J. Deviation of the subjective vertical in long-standing unilateral vestibular loss. *Acta. Otolaryngol.* **117**, 1-6 (1997).
- Tabak, S., Collewijn, H., Boumans, L.J., & van der Steen, J. Gain and delay of human vestibulo-ocular reflexes to oscillation and steps of the head by a reactive torque helmet. II. Vestibular-deficient subjects. *Acta. Otolaryngol.* **117**, 796-809 (1997).
- Van der Steen, J. & Collewijn, H. Ocular stability in the horizontal, frontal and sagittal planes in the rabbit. *Exp. Brain Res.* **56**, 263-274 (1984).
- Seidman, S.H., Leigh, R.J., Tomsak, R.L., Grant, M.P., & Dell'Osso, L.F. Dynamic properties of the human vestibulo-ocular reflex during head rotations in roll. *Vision Res.* **35**, 679-689 (1995).

15. Seidman, S.H. & Leigh, R.J. The human torsional vestibulo-ocular reflex during rotation about an earth-vertical axis. *Brain Res.* **504**, 264-268 (1989).
16. Tweed, D., *et al.* Rotational kinematics of the human vestibuloocular reflex. I. Gain matrices. *J. Neurophysiol.* **72**, 2467-2479 (1994).
17. Tabak, S. & Collewijn, H. Human vestibulo-ocular responses to rapid, helmet-driven head movements. *Exp. Brain Res.* **102**, 367-378 (1994).
18. Paige, G.D. Linear vestibulo-ocular reflex (LVOR) and modulation by vergence. *Acta. Otolaryngol. Suppl.* **481**, 282-286 (1991).
19. Halmagyi, G.M., Aw, S.T., Cremer, P.D., Curthoys, I.S., & Todd, M.J. Impulsive testing of individual semicircular canal function. *Ann. N.Y. Acad. Sci.* **942**, 192-200 (2001).
20. Tabak, S. & Collewijn, H. Evaluation of the human vestibulo-ocular reflex at high frequencies with a helmet, driven by reactive torque. *Acta. Otolaryngol. Suppl.* **520 Pt. 1**, 4-8 (1995).
21. Crawford, J.D. & Vilis, T. Axes of eye rotation and Listing's law during rotations of the head. *J. Neurophysiol.* **65**, 407-423 (1991).
22. Migliaccio, A.A., *et al.* The three-dimensional vestibulo-ocular reflex evoked by high-acceleration rotations in the squirrel monkey. *Exp. Brain Res.* **159**, 433-446 (2004).