Published in final edited form as:

Neuroscience. 2013 August 29; 0: 73–81. doi:10.1016/j.neuroscience.2013.04.029.

Scaling of compensatory eye movements during translations: virtual versus real depth

J. Dits¹, W.M. King², and J. van der Steen¹

¹Department of Neuroscience, Erasmus University Medical Centre Rotterdam, Dr. Molewaterplein 50, 3000 DR Rotterdam, The Netherlands ²Department of Otolaryngology, University of Michigan Medical Center, Ann Arbor, MI 48109

Abstract

Vestibulo-ocular reflexes are the fastest compensatory reflex systems. One of these is the translational vestibulo-ocular reflex (TVOR) which stabilizes gaze at a given fixation point during whole body translations. For a proper response of the TVOR the eyes have to counter rotate in the head with a velocity that is inversely scaled to viewing distance of the target. It is generally assumed that scaling of the TVOR is automatically coupled to vergence angle at the brainstem level. However, different lines of evidence also argue that in humans scaling of the TVOR also depends on a mechanism that pre-sets gain on a priori knowledge of target distance.

To discriminate between these two possibilities we used a real target paradigm with vergence angle coupled to distance and a virtual target paradigm with vergence angle dissociated from target distance. We compared TVOR responses in six subjects who underwent lateral sinusoidal whole-body translations at 1 and 2 Hz. Real targets varied between distance of 50 and 22.4 cm in front of the subjects, whereas the virtual targets consisting of a green and red LED were physically located at 50 cm from the subject. Red and green LED's were dichoptically viewed. By shifting the red LED relative to the green LED we created a range of virtual viewing distances where vergence angle changed but the ideal kinematic eye velocity was always the same. Eye velocity data recorded with virtual targets were compared to eye velocity data recorded with real targets. We also used flashing targets (flash frequency 1Hz, duration 5 ms). During the real, continuous visible targets condition scaling of compensatory eye velocity with vergence angle was nearly perfect. During viewing of virtual targets, and with flashed targets compensatory eye velocity only weakly correlated to vergence angle, indicating that vergence angle is only partially coupled to compensatory eye velocity during translation. Our data suggest that in humans vergence angle as a measure of target distance estimation has only limited use for automatic TVOR scaling.

Keywords

vestibulo-ocular reflex; binocular eye movements; vergence

© 2013 IBRO. Published by Elsevier Ltd. All rights reserved.

Correspondence to: J. van der Steen, Department of Neuroscience, Room Ee1259, Erasmus MC Rotterdam, P.O. Box 1738, 3000 DR Rotterdam, The Netherlands, j.vandersteen@erasmusmc.nl, Tel: +31-10-704-3572.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Introduction

In primates, gaze stabilization during translational head movements is mediated by vestibular and visual mechanisms, resulting in compensatory eye movements that minimize retinal image motion across the fovea. The translational vestibulo-ocular reflex (TVOR) responds to linear accelerations sensed by the otoliths of the vestibular system: neural signals relayed by the vestibular nuclei and oculomotor nuclei produce compensatory eye movements at very short latency. The relative contribution of vestibular and visual sensory inputs to gaze stabilization depends on the frequency or acceleration of head motion. Visual systems are mainly active at frequencies up to 1 Hz, whereas the contribution of the translational vestibulo-ocular reflex (TVOR) becomes significant at 1 Hz and increases with frequency (Paige et al., 1998).

In contrast to the angular VOR, the TVOR gain in the dark without a target is quite low (Paige, 1991). Presumably, this occurs because the response of the TVOR is viewing distance dependent. Geometry dictates that the amplitude of compensatory eye movements must increase with decreasing viewing distance, which is confirmed by experimental data in humans and non-human primates (Crane and Demer, 1998) (Paige, 1989) (Paige et al., 1998) (Ramat and Zee, 2003) (Schwarz and Miles, 1991) (Snyder and King, 1992) (Telford et al., 1997)

Many studies claim that vergence angle determines the amplitude of the response (Angelaki, 2004) (Crane and Demer, 1998) (Paige, 1989) (Wei and Angelaki, 2004). The notion that vergence angle modulates the gain of the TVOR is an attractive hypothesis because vergence angle is directly encoded by neurons located in the brainstem (Mays, 1984, Gamlin and Clarke, 1995) and indirectly by neurons in the vestibular and perihypoglossal nuclei that encode monocular eye position (McConville et al., 1994) (Zhou and King, 1998). Findings in favour of an important role for encoded vergence angle include: an increase in TVOR gain after use of prism lenses to dissociate vergence angle from actual target distance (Paige, 1989); a decrease in gain with inadequate vergence angles (Ramat and Zee, 2003) scaling of TVOR gain to target distance from the earliest onset of movement during stepwise motion stimuli (Angelaki, 2004); and a minor role for monocular visual cues (Wei et al., 2003).

Although the vergence angle hypothesis is computationally attractive, vergence angle may not directly modulate TVOR gain since other studies in humans describe TVOR gain modulation that cannot be explained solely by vergence angle. Ramat and Zee (Ramat and Zee, 2003) noticed an increase in gain with a decrease in vergence angle in one of their subjects. Viirre and Demer (Viirre and Demer, 1996) found a discrepancy between TVOR gain and vergence angle during eccentric rotation up to 2 Hz. These findings suggest that the “gain” setting of the TVOR depends on other cues. For example, Snyder and King (1992) found that anticipation plays an important role in distance scaling. They found scaling to target distance in advance of vergence eye movements a finding that argues against a causal role for vergence angle. Similarly, Clement and Maciel (Clement and Maciel, 2004) found that target-distance dependent modulation of the angular vestibulo-ocular reflex (AVOR) at 0.8 Hz is more dependent on *perceived* target distance than on the actual target or fixation distance. It has also been shown that a priori knowledge of the direction of head movement and fixation of a target (head-fixed or earthfixed) play important roles in gaze stabilization (Ramat et al., 2005) (Zhou et al., 2002). Furthermore, during predictable motion stimuli, predictive smooth pursuit eye movements could play a role in target distance dependent TVOR scaling (Barnes and Paige, 2004) (Yasui and Young, 1984). The TVOR and smooth pursuit system both have foveal dependent responses with similar kinematics and are likely to partially share the same central neural pathways (Adeyemo and Angelaki, 2005). Other factors that might play a role in scaling TVOR amplitude in relation to target distance are

accommodation, motion parallax and visual cues. However, the contribution of these factors has been found less important in humans than in monkeys (Hine and Thorn, 1987) (Paige, 1991).

Recently, it was proposed that an estimate of spatial orientation or internal representation is necessary for perception as well as for the control of reflexive eye movements and postural responses (MacNeilage et al., 2008). This implies that scaling of TVOR is not merely a brainstem or cerebellar mediated reflex loop dependent on instantaneous vergence angle, but that its state depends on an internal representation of 3D space built from visual, vestibular and possibly eye position cues related to extraocular proprioception (Wang et al., 2007, Xu et al., 2011). Thus, an alternative explanation for TVOR scaling is that there is a central representation of a target's spatial location that determines both the vergence angle and the magnitude of the TVOR. In support of this idea, (Gamlin and Yoon, 2000) described neurons located in the prearcuate cortex immediately rostral to the frontal eye fields that discharged in relation to vergence eye movements and whose discharge preceded those eye movements by 28 msec. Many of these neurons were also responsive to the visual presentation of a near target prior to any motor response; thus, they encoded a representation of the target's location in depth and could provide a signal to modulate the TVOR. In support of this suggestion, Gamlin and colleagues (Gamlin et al., 1996) showed a possible pathway linking the prearcuate cortex to a precerebellar nucleus (nucleus reticularis tegmenti pontis) implicated in the control of voluntary eye movements.

Experimental and theoretical evidence further suggest that different spatial orientation estimates may underlie perception (e.g. target depth) and motor action (e.g., ocular vergence angle) (Merfeld et al., 2005) (Zupan and Merfeld, 2005). Also for the TVOR there may not be a tight link between depth perception and binocular eye position information, as vergence eye movements provoked by visual disparity do not need to be accompanied by depth perception (Collewijn et al., 1991) (Erkelens and Collewijn, 1985).

In the present study we address the mechanisms of gaze stabilization during translations in humans. Our aim was to determine the relative contribution of visual, vestibular and eye position cues on the central target representation and its effect on scaling compensatory eye movements.

Methods

Subjects

Eye movements were recorded from six subjects. Subject 1, male, age 56, is one of the authors (J.S.). The other five subjects (4 males, 1 female, age between 22 and 35 years) were naïve with respect to the goal of the experiment. Written informed consent was obtained from all subjects prior to the experiments. None of the subjects had a history of inner ear pathology or impaired stereoscopic vision (according to the random dot stereo test), and all subjects were able to see the targets clearly. The mean inter-ocular distance of the subjects was 6.5 ± 0.2 cm. Experimental procedures were approved by the Medical Ethical Committee of the Erasmus University Medical Center and adhered to the Declaration of Helsinki for research involving human subjects.

Experimental setup

Visual targets—The experiment was performed in a completely dark room. Visual targets consisted of black-coated 2.3 mm optic fibres, one end of which was connected to a light emitting diode (LED); the other (open) end pointed towards the observer as a visual target. We used two different kinds of targets: real targets and virtual targets

The real targets were positioned at 22, 26, 31, 38 and 50 cm distance from the centre between the observer's eyes, and were located directly in front of the subject (figure 1A).

The virtual target lights were aligned horizontally and perpendicular to straight-ahead gaze at a distance of 50 cm from the observer (figure 1B). These targets consisted of a green light aligned with the left eye and five red lights spaced at 2 cm intervals towards the right of the green target. Virtual targets were shown pairwise (the green light in combination with one of the five red lights). Subjects viewed the paired targets through red-green anaglyphic filters such that each eye saw one of the two lights. The LED targets were arranged in such a way that the vergence angles needed to fuse the virtual targets were identical to the vergence angles needed to fixate the real targets. Thus, when subjects viewed the virtual targets, vergence angles were dissociated from physical target distance allowing us to study the effect of vergence angle independent of target distance. The distance between the observers' eyes and the theoretical interception of the lines of sight of both eyes was defined as virtual fixation distance. The virtual fixation distance thus reflected the vergence angle of the eyes needed to fuse the virtual targets and not the physical location of the targets.

In addition to the continuously illuminated targets, we presented flashing real and virtual targets. These targets had a flash frequency of 1 Hz and a flash duration of 5 ms. These values were chosen based on data from pilot experiments which showed that higher flash frequencies or longer flash durations resulted in higher gains, probably due to an increase in visual feedback. Another advantage of the 1 Hz flash frequency is that during 1 and 2 Hz platform motion the visual target appeared at the same location relative to the platform with each flash. This also minimized the possible predictive effects of storage of planned eye movements in working memory by the subject. To eliminate long-term memory effects we presented the flashing target paradigms prior to the continuous target condition. Target distances were presented in a random order.

Motion stimuli—During the experiment, the subject was seated in a chair on a six degrees of freedom motion platform (FCS-Moog, Nieuw-Vennep, The Netherlands) (Houben et al., 2005). The subject's body was securely fastened with a 5-point harness. In addition, a vacuum cushion and an individually moulded bite board were used to completely immobilize the head relative to the platform (Houben et al., 2005, Goumans et al., 2010).

The platform delivered sinusoidal sideward whole-body translations at 1 and 2 Hz, with a peak-to-peak amplitude of 5 and 2.5 cm, respectively. The duration of each movement was 20 seconds and contained a fade-in and fade-out period of 2 s (a linear increase/decrease in amplitude).

The motion platform was equipped with a laser device at backside of the platform base aimed at a photocell mounted on the wall. This photocell produced a light intensity related voltage. This voltage level was sampled along with the eye movement data (see below) and enabled us to time the actual delivered motion stimuli with the eye movement responses within a millisecond (Houben et al., 2005, Goumans et al., 2010).

Eye movement recordings—Eye movements were recorded with scleral search coils. We used a standard 25-kHz two-field coil system (Model EMP3020; Skalar Medical, Delft, The Netherlands) based on the amplitude detection method by Robinson. The field coils were mounted on the motion platform so the search coils recorded eye position relative to the head. Standard dual coils embedded in a silicone annulus (Skalar Medical, Delft) were inserted in each eye. Before insertion, the eyes were anesthetized with a few drops of oxybuprocain (0.4%) in HCl (pH 4.0). Both coils were pre-calibrated in vitro by mounting them on a gimbal system placed in the center of the magnetic fields. We sampled the coil

data at 1000 Hz on a CED system (Cambridge Electronic Design, Cambridge, UK). Subjects were instructed to fixate a series of five targets (central target and a target at 10 degrees left, right, up and down). Targets were back projected onto a translucent screen at 186 cm distance. The subjects fixated each target for ten seconds. Data were stored to a hard disk for further analysis.

Data analysis

Eye movements made to a 5-point calibration pattern were used to transform voltage into Fick angles. After calibration, we digitally smoothed the data by applying a 2-point moving average. After smoothing, saccades were removed using velocity and acceleration (typically $2000^{\circ} \cdot s^{-2}$) thresholds and a duration criterion (10–185 ms). Eye movement parameters (amplitude and frequency) were obtained by conversion of the data to the frequency domain using a Fast Fourier Transform (FFT). Peak eye velocity was calculated by multiplying the amplitude of the eye movement by the fundamental frequency of the stimulus motion.

To compare data from individual subjects with ideal performance, a computer model was constructed with Matlab's SimuLink to compute the eye velocity needed to accurately compensate for head translation for each of the virtual and real target positions. Next, for each subject, a linear regression of eye velocity as a function of vergence angle was performed for each of the real or virtual experimental conditions (real or virtual targets viewed continuously or strobed $\times 2$ frequencies = 8 conditions). For statistical analysis, data were pooled across all subjects for each condition so as to compare group performance in each paradigm.

Results

Real and virtual target paradigms were tested under two conditions: continuous lighting and flashing of the targets. Examples of raw eye movement recordings under the different conditions are shown in figure 2. For both real and virtual target paradigms there were major differences in response amplitude in the continuous and flashing target conditions. The response amplitude to the flashing targets was always smaller than to the continuously illuminated targets.

The other major difference in eye movement response between the real and virtual targets was their dependency of viewing distance. The real targets had response amplitudes that were directly related to viewing distance. This relation is shown in the top panel of figure 3. In this plot vergence angle is plotted on the y-axis (zero vergence at top), whereas the gaze angles of the left (blue) and right (red) eyes are plotted on the X-axis. The panel shows an increase in gaze amplitude and vergence angle as a function of viewing distance. Gaze trajectories become larger for near viewing distances, consistent with the geometrical requirement for keeping the eyes on target during the linear translations.

The lower panel of figure 3 shows as an example a gaze vergence plot of eye movements in response to the targets at all presented virtual distances. For any virtual distance, the gaze amplitude of the right and left eye remained the same regardless of the vergence angle required to fuse the virtual target by shifting the left eye (blue traces) to the right.

To determine the relationship between peak eye velocity and real and virtual viewing distance, we plotted for each subject's eye velocity as a function of vergence and fitted the data with a linear regression. The slope of this regression line estimates the extent to which eye velocity is related to vergence angle.

Figure 4 shows the peak eye velocity as a function of vergence angle. The solid line in each panel shows the expected eye velocity for the continuously viewed real target condition. The slope of this line, 4.92 °/s per degree of vergence represents the expected ideal relationship between eye velocity and vergence angle. The horizontal dotted line at 35 °/s is the expected eye velocity for the virtual target condition. Since the virtual targets are all located at the same distance from the subject, there is no effect of vergence angle on the expected eye velocity (slope = zero).

As expected, under continuously viewed real target conditions, eye velocity scaled well with vergence angle (square symbols in the upper panels of figure 4). The slope of the pooled regression line was 2.8 °/s per degree of vergence for 1 Hz translations (upper left panel) and was highly significant ($p < 0.001$). For 2 Hz translations, the slope was reduced (1.9 °/s per degree of vergence) but still highly significant ($p < 0.001$). In contrast, despite a similar range of vergence angles, there was a much weaker relationship between eye velocity and vergence for continuously viewed *virtual* targets at either frequency. For 1 and 2 Hz translations, the slopes of the pooled regressions were statistically significant ($p < 0.01$) but significantly smaller (1 Hz: 0.27 °/s per degree of vergence; 2Hz: 0.58 °/s per degree of vergence) than the slopes for real targets (circular symbols).

When the real targets were flashed, the slopes of the regression lines were further reduced (figure 4, lower panels) and were not significantly different from zero ($p < 0.01$, see table 1) for either real or virtual targets at either frequency.

Discussion

Our results show that during translational passive whole body motion the gain of horizontal compensatory eye movements is proportional to target distance. Eye velocity scales with vergence angle for real targets when there is continuous visual feedback, but this relationship is weakened when vergence angle is changed without changing target distance and breaks down completely when targets are flashed so as to eliminate visual feedback.

TVOR scaling and vergence angle

In several studies it was concluded that the amplitude of TVOR compensatory eye movements scale with target distance and that this scaling is mediated by vergence angle. Paige et al. (Paige et al., 1998) tried to isolate the TVOR from visual cues by using imagined targets. Initially, a target was seen during sinusoidal self-motion, then it disappeared and subjects were asked to continue to fixate the target in their imagination. During fixation of these imagined targets, vergence angle as well as the gain of the eye movements decreased considerably. They concluded that the change in eye speed was the result of the decrease in vergence angle. However, it is also plausible that in this study decreases in both vergence and eye speed had the same cause: an inability to fixate the imagined target or to accurately remember its spatial location. In agreement with Paige (Paige, 1989), Wei et al. (Wei and Angelaki, 2004) using high frequency stimulation and Ramat et al. (Ramat and Zee, 2003) concluded that vergence angle was the most important factor contributing to TVOR scaling. However, in the latter study, other possibilities could not be excluded. Indeed, in a later report, Ramat et al. (Ramat et al., 2005) emphasized a possible role of cognitive factors in determining TVOR eye velocity. The new aspect of our study is that we used a virtual target paradigm that dissociated vergence from other target distance cues in order to directly test the hypothesis that vergence angle determines TVOR eye velocity scaling. The virtual target paradigm is different from two other widely used target arrangements, head-fixed (HF) and earth fixed (EF) (Paige, 1989), that either promoted the TVOR (EF) or required its suppression (HF). The virtual target paradigm enables us to dissociate the magnitude of the vergence angle from the kinematical correct TVOR amplitude; TVOR eye speed should not

be scaled in relation to vergence angle, but is also not suppressed. We believe this paradigm is fundamentally different since complete suppression of the TVOR could be due to a mechanism other than modulation of TVOR gain.

The results of our experiment show that there is only a weak correlation of vergence angle to scaling of the TVOR. Furthermore, the data during fixation of flashing virtual targets, suggest that in contrast to monkeys, vergence angle in humans is not nearly as strong a determinant of eye velocity as in monkeys (Angelaki, 2004).

Our data also agree very well with the findings of Ramat and Zee (Ramat and Zee, 2003) who used side-to-side velocity steps (heave). Steps have a broad frequency spectrum, and the fact that Ramat and Zee found only partial compensation is a further argument in favour of a weak vergence angle related TVOR scaling across the whole frequency spectrum.

Paige et al. (Paige et al., 1998) studied visuo-vestibular interactions using two target paradigms: earth-fixed (EF) and head-fixed (HF) targets, and compared compensatory eye movements when real or imagined targets were viewed. Based on their findings, smooth pursuit and/or predictive mechanisms could have contributed to our subject's responses over the frequency range we employed. We believe, however, that this is unlikely. We asked stationary subjects to track moving targets located at distances comparable to those used in the TVOR experiments.

Figure 5 illustrates smooth pursuit gain for a typical subject over a frequency range of 0.25 to 2.0 Hz. The data show (1) that smooth pursuit gain decreases as a function of frequency (gain ~ 0.7 at 1 Hz and ~ 0.25 at 2 Hz) and (2) smooth pursuit gain is essentially unmodulated by target distance or vergence angle. Based on these data, we can estimate the eye velocity needed to track the virtual targets with smooth: at 1 Hz, the expected eye velocity is $0.7 \times 35^\circ/\text{s} = 24.5^\circ/\text{s}$ (Fig. 4, dashed gray line); at 2 Hz, the expected eye velocity is $0.3 \times 35^\circ/\text{s} = 10.5^\circ/\text{s}$, Fig. 4, dashed gray line). Clearly, at 1 Hz actual eye velocity is less than predicted and at 2 Hz, eye velocity is greater than predicted. Furthermore, smooth pursuit of targets (Figure 5) was associated with a frequency dependent phase lag ranging from $14.6 \pm 8.3^\circ$ at 1 Hz to $42.3 \pm 14.2^\circ$ at 2 Hz. In contrast, the phase lag of the TVOR for the virtual targets was independent of frequency ($3.7 \pm 7.0^\circ$ at 1 Hz; $11.8 \pm 10.2^\circ$ at 2 Hz).

We also used flashing target conditions in order to eliminate the influence of smooth pursuit (Figure 4, lower panels). A similar experimental manoeuvre to reduce the influence of smooth pursuit was performed before by Han et al. (Han et al., 2005) who used stroboscopic illumination at 4 Hz, with a flash duration of 30 ms. In their experiments flash frequency was increased with increasing frequency of head movements in order to keep the same number of flashes per cycle of head movement. These higher frequencies and relatively long flash durations could, however, also increase the visual feedback and lead to an overestimate of the vestibular contribution to compensatory eye velocity. To minimize visual feedback, we flashed our targets at 1 Hz, regardless of the frequency of head (and body) movement. Moreover, we used a shorter flash duration of 5 ms, which had an additional advantage: the subject saw an effectively stationary visual target, once per cycle (1 Hz) or once per two cycles (2 Hz head movement). Thus, the stationary target provided no information to the smooth pursuit system about the required velocity of the eye movements, (e.g., zero as in the HF paradigm) but did provide feedback about target distance. In this way, we selectively shut down the smooth pursuit system without suppression of the TVOR.

TVOR and accommodation

Wei et al. (Wei et al., 2003) demonstrated that despite comparable vergence angles TVOR scaling was more accurate when real targets were viewed than when virtual targets were viewed. In agreement with our data, in their “vergence-only” condition, vergence was dissociated from actual target distance and the TVOR still scaled with viewing distance (see their figure 6). Since the scaling was insufficient to match vergence angle, they concluded that a signal related to accommodation must have been used to correct TVOR eye velocity toward a value appropriate for the actual distance of the target. In contrast to the hypothesis of Wei et al, we do not find an important influence of accommodation since eye velocity was much less than expected based on vergence angle when subjects viewed flashed near targets. Unfortunately, we are not able to precisely determine the influence of accommodation for two reasons. First, the cut end fibre optic target presented a poor accommodative point stimulus, whereas Wei et al. (Wei et al., 2003) used a fixation dot as well as an array of dots filling the peripheral retina. Furthermore, during the virtual target condition, accommodation would be compromised because vergence was dissociated from accommodation, which is a non-physiological situation (Hung et al., 1984). We therefore conclude that accommodation does not contribute to TVOR scaling.

TVOR scaling and visual cues

Motor signals related to vergence angle or accommodation, sensory cues such as disparity or motion parallax, or perceptual information might be used to determine target distance and scale the TVOR. Wei et al. (Wei et al., 2003) evaluated the relative importance of all these different factors. In that study, monkeys were translated laterally at 5 Hz while they viewed a variety of visual stimuli that included real targets projected onto a movable screen and an array of visual backgrounds (random dot stereograms) designed to present texture and disparity cues that were consistent or inconsistent with vergence. Their main conclusion was that visual cues that accurately or inaccurately cued target distance were relatively ineffective in scaling TVOR responses. Our study suggests that in humans, however, visual cues are important for TVOR scaling: a single point visual stimulus is sufficient to produce significant TVOR scaling. The key difference with the study of Wei et al. (Wei et al., 2003) is that we presented only a foveal fixation target, whereas visual backgrounds are whole retina stimuli that may contribute to spatial knowledge but would not necessarily determine target depth in a laboratory environment.

Cognitive factors

Ramat et al. (Ramat et al., 2005) found that TVOR gains can be enhanced or suppressed by cognition. In their paradigm, prior knowledge of the direction of head movement and the context of the target (earth-fixed or head-fixed) influenced the TVOR response within 100 ms of the onset of head movement (Snyder and King, 1992). This result suggests an influence of cognition on the TVOR at the earliest stage of the response, either via a direct cortical connection to the vestibular nuclei or indirectly via the cerebellum (e.g., by a pathway similar to that described by Gamlin and colleagues (Gamlin et al., 1996)). Previously, Zhou et al. (Zhou et al., 2002) found rapid contextual TVOR learning in the monkey. Cognition is a factor that is difficult to rule out. On the one hand, all of the subjects knew that they were sinusoidal translated and that the targets were earth fixed. On the other hand, the Angelaki experiments (Angelaki et al., 2003) and Ramat et al. (Ramat et al., 2005) experiments only required discrimination of earth from head fixed targets. As in the study of Paige (Paige, 1989), this task is fundamentally less complex than our task which required recognition of target distance in the absence of any other visual reference and scaling of the TVOR response with target distance.

Acknowledgments

We thank Dr. P. Mulder (Department of Biostatistics, Erasmus MC, Rotterdam) for his help with the statistical analysis.

We thank Prof. dr. G.R. Barnes for his advice and comments on the flashing target conditions.

Grants

This work has been supported by NWO grants B95-417 and ZONMW grant 911-02-004

References

- Adeyemo B, Angelaki DE. Similar kinematic properties for ocular following and smooth pursuit eye movements. *J Neurophysiol.* 2005; 93:1710–1717. [PubMed: 15496490]
- Angelaki DE. Eyes on target: what neurons must do for the vestibuloocular reflex during linear motion. *J Neurophysiol.* 2004; 92:20–35. [PubMed: 15212435]
- Angelaki DE, Zhou HH, Wei M. Foveal versus full-field visual stabilization strategies for translational and rotational head movements. *J Neurosci.* 2003; 23:1104–1108. [PubMed: 12598596]
- Barnes GR, Paige GD. Anticipatory VOR suppression induced by visual and nonvisual stimuli in humans. *J Neurophysiol.* 2004; 92:1501–1511. [PubMed: 15331647]
- Clement G, Maciel F. Adjustment of the vestibulo-ocular reflex gain as a function of perceived target distance in humans. *Neurosci Lett.* 2004; 366:115–119. [PubMed: 15276229]
- Collewijn, H.; van der Steen, J.; van Rijn, LJ. Binocular eye movements and depth perception. Cambridge: Cambridge University Press; 1991.
- Crane BT, Demer JL. Human horizontal vestibulo-ocular reflex initiation: effects of acceleration, target distance, and unilateral deafferentation. *J Neurophysiol.* 1998; 80:1151–1166. [PubMed: 9744929]
- Erkelens CJ, Collewijn H. Motion perception during dichoptic viewing of moving random-dot stereograms. *Vision Res.* 1985; 25:583–588. [PubMed: 4060612]
- Gamlin PD, Clarke RJ. Single-unit activity in the primate nucleus reticularis tegmenti pontis related to vergence and ocular accommodation. *J Neurophysiol.* 1995; 73:2115–2119. [PubMed: 7623103]
- Gamlin PD, Yoon K. An area for vergence eye movement in primate frontal cortex. *Nature.* 2000; 407:1003–1007. [PubMed: 11069179]
- Gamlin PD, Yoon K, Zhang H. The role of cerebro-ponto-cerebellar pathways in the control of vergence eye movements. *Eye.* 1996; 10(Pt 2):167–171. [PubMed: 8776444]
- Goumans J, Houben MM, Dits J, van der Steen J. Peaks and troughs of three-dimensional vestibulo-ocular reflex in humans. *J Assoc Res Otolaryngol.* 2010; 11:383–393. [PubMed: 20177730]
- Han YH, Kumar AN, Reschke MF, Somers JT, Dell'Osso LF, Leigh RJ. Vestibular and non-vestibular contributions to eye movements that compensate for head rotations during viewing of near targets. *Exp Brain Res.* 2005; 165:294–304. [PubMed: 15889244]
- Hine T, Thorn F. Compensatory eye movements during active head rotation for near targets: effects of imagination, rapid head oscillation and vergence. *Vision Res.* 1987; 27:1639–1657. [PubMed: 3445495]
- Houben MMJ, Goumans J, De Jongste AHC, Van der Steen J. Angular and linear vestibulo-ocular responses in humans. *Ann N Y Acad Sci.* 2005; 1039:68–80. [PubMed: 15826962]
- Hung GK, Semmlow JL, Ciuffreda KJ. The near response: modeling, instrumentation, and clinical applications. *IEEE Trans Biomed Eng.* 1984; 31:910–919. [PubMed: 6396218]
- MacNeilage PR, Ganesan N, Angelaki DE. Computational approaches to spatial orientation: from transfer functions to dynamic Bayesian inference. *J Neurophysiol.* 2008; 100:2981–2996. [PubMed: 18842952]
- Mays LE. Neural control of vergence eye movements: convergence and divergence neurons in midbrain. *J Neurophysiol.* 1984; 51:1091–1108. [PubMed: 6726313]

- McConville K, Tomlinson RD, King WM, Paige G, Na EQ. Eye position signals in the vestibular nuclei: consequences for models of integrator function. *Journal of vestibular research : equilibrium & orientation*. 1994; 4:391–400.
- Merfeld DM, Park S, Gianna-Poulin C, Black FO, Wood S. Vestibular perception and action employ qualitatively different mechanisms. II. VOR and perceptual responses during combined Tilt&Translation. *J Neurophysiol*. 2005; 94:199–205. [PubMed: 15730979]
- Paige GD. The influence of target distance on eye movement responses during vertical linear motion. *Exp Brain Res*. 1989; 77:585–593. [PubMed: 2806449]
- Paige GD. Linear vestibulo-ocular reflex (LVOR) and modulation by vergence. *Acta Otolaryngol Suppl*. 1991; 481:282–286. [PubMed: 1927396]
- Paige GD, Telford L, Seidman SH, Barnes GR. Human vestibuloocular reflex and its interactions with vision and fixation distance during linear and angular head movement. *J Neurophysiol*. 1998; 80:2391–2404. [PubMed: 9819251]
- Ramat S, Straumann D, Zee DS. Interaural translational VOR: suppression, enhancement, and cognitive control. *J Neurophysiol*. 2005; 94:2391–2402. [PubMed: 15901755]
- Ramat S, Zee DS. Ocular motor responses to abrupt interaural head translation in normal humans. *J Neurophysiol*. 2003; 90:887–902. [PubMed: 12672783]
- Schwarz U, Miles FA. Ocular responses to translation and their dependence on viewing distance. I. Motion of the observer. *J Neurophysiol*. 1991; 66:851–864. [PubMed: 1753290]
- Snyder LH, King WM. Effect of viewing distance and location of the axis of head rotation on the monkey's vestibuloocular reflex. I. Eye movement responses. *J Neurophysiol*. 1992; 67:861–874. [PubMed: 1588387]
- Telford L, Seidman SH, Paige GD. Dynamics of squirrel monkey linear vestibuloocular reflex and interactions with fixation distance. *J Neurophysiol*. 1997; 78:1775–1790. [PubMed: 9325347]
- Viiire ES, Demer JL. The human vertical vestibulo-ocular reflex during combined linear and angular acceleration with near-target fixation. *Exp Brain Res*. 1996; 112:313–324. [PubMed: 8951399]
- Wang X, Zhang M, Cohen IS, Goldberg ME. The proprioceptive representation of eye position in monkey primary somatosensory cortex. *Nat Neurosci*. 2007; 10:640–646. [PubMed: 17396123]
- Wei M, Angelaki DE. Viewing distance dependence of the vestibulo-ocular reflex during translation: extra-otolith influences. *Vision Res*. 2004; 44:933–942. [PubMed: 14992837]
- Wei M, DeAngelis GC, Angelaki DE. Do visual cues contribute to the neural estimate of viewing distance used by the oculomotor system? *J Neurosci*. 2003; 23:8340–8350. [PubMed: 12967996]
- Xu Y, Wang X, Peck C, Goldberg ME. The time course of the tonic oculomotor proprioceptive signal in area 3a of somatosensory cortex. *J Neurophysiol*. 2011
- Yasui S, Young LR. On the predictive control of foveal eye tracking and slow phases of optokinetic and vestibular nystagmus. *J Physiol*. 1984; 347:17–33. [PubMed: 6707954]
- Zhou HH, Wei M, Angelaki DE. Motor scaling by viewing distance of early visual motion signals during smooth pursuit. *J Neurophysiol*. 2002; 88:2880–2885. [PubMed: 12424322]
- Zhou W, King WM. Premotor commands encode monocular eye movements. *Nature*. 1998; 393:692–695. [PubMed: 9641680]
- Zupan LH, Merfeld DM. Human ocular torsion and perceived roll responses to linear acceleration. *J Vestib Res*. 2005; 15:173–183. [PubMed: 16286699]

Highlights

In humans vergence angle as a measure of target distance estimation has only limited use for automatic TVOR scaling.

Continuous visible targets lead to perfect scaling of compensatory eye velocity with vergence angle.

During viewing of virtual targets, and with flashed targets compensatory eye velocity only weakly correlated to vergence angle

Figure 1.

The two real and virtual target paradigms. Panel A shows the real targets that were located at 5 distances from the subject. Panel B shows the ‘virtual targets’; six optic fibre tips (top circles): one green fibre on the left (filled circle) and five red fibres on the right (open circles). These are seen through red and green filters (bottom bars): the left eye could only see the red fibres; the right eye only the green fibre. Only two fibres were switched on at the same time: the green one and one of the red ones. The distance to the intersections of the lines of sight of both eyes (striped circles) was defined as virtual target distance. The target distances of the virtual targets in B matched those of the real targets in A. Note that for the furthest virtual target, the green and red fibre are located at approximately the same position. This target therefore resembles a real target.

Figure 2.

Example (subject 2) of platform position (upper panel), and eye movements (lower four panels) recorded with the search coil system, under the four different target conditions: real continuous, virtual continuous, real flashed and virtual flashed. Upper traces in each panel represent left eye positions, the lower traces right eye positions. Dashed vertical lines indicate the moments in time at which the flashes occurred. Upward deflections: rightward horizontal eye movements.

Figure 3.

Gaze versus vergence angle during whole-body translations at 2 Hz. In this plot vergence angle is plotted on the y-axis (zero vergence at top), whereas the gaze positions of the left (blue) and right (red) eyes are plotted on the X-axis. The panel shows that for real targets (upper panel) there is an increase in gaze amplitude and vergence angle as a function of vergence. Gaze trajectories become larger for near viewing distances, consistent with the geometrical requirement for keeping the eyes on target during the linear translations.

The lower panel of figure 3 shows as an example a gaze vergence plot of eye movements in response to the targets at all presented virtual distances. For any virtual distance, the gaze

amplitude of the right and left eye remained the same regardless of the vergence angle required to fuse the virtual target by shifting the left eye (blue traces) to the right

Figure 4.

Peak eye velocity as a function of vergence angle during 1 and 2 Hz sinusoidal translations (left and right panels respectively). The solid line in each panel shows the expected eye velocity for the continuously viewed real target condition. The slope of this line, 4.92 °/s per degree of vergence represents the expected ideal relationship between eye velocity and vergence angle. The dashed line is the expected eye velocity for the virtual target condition. Data from individual subjects are indicated with different colours. Squares: real targets, Circles: virtual targets. Upper panels: continuously lit targets, Lower panels: strobed targets.

Figure 5.

Smooth pursuit gain as function of sinusoidal stimulation frequency and viewing distance . Frequency range was between 0.25 and 2.0 Hz. Viewing distance varied between 189 and 26 cm. Smooth pursuit gain decreases as a function of frequency is not modulated by target distance or vergence angle.

Descriptive parameters of the fitted regression lines for eye velocity and vergence for the individual subjects and group means for the different conditions.

Table 1

	1 Hz					2 Hz			
	N	Intercept	Slope	r ²	p	Intercept	Slope	r ²	p
Real Targets									
Continuous	6	0.24	2.8	0.61	0.000	2.3	1.9	0.69	0.000
Strobed	6	3.4	0.38	0.09	0.120	2.6	0.69	0.18	0.020
Virtual Targets									
Continuous	6	12.1	0.28	0.27	0.003	8.7	0.58	0.23	0.008
Strobed	6	4.9	-0.02	0.0	0.924	4.1	0.47	0.16	0.028