Scaling of the Fore-Aft Vestibulo-Ocular Reflex by Eye Position During Smooth Pursuit

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Semrau, Jennifer A., Min Wei, and Dora Angelaki. Scaling of the fore-aft vestibulo-ocular reflex by eye position during smooth pursuit. J Neurophysiol 96: 936–940, 2006; doi:10.1152/jn.00185.2006. An eye position signal scales the amplitude of compensatory eye velocity in the translational vestibulo-ocular reflex (TVOR). To investigate the origin of such a modulatory signal, we studied the kinetics of the fore-aft TVOR as rhesus monkeys pursued a horizontally moving target at velocities between 0.5 and 30°/s. We found that the “V-shaped” curve of the fore-aft TVOR amplitude as a function of eye position was shifted opposite to the direction of pursuit eye movement. As a result, the tip of the V-shaped curve that occurred close to zero eye position during steady-state fixation was shifted to the right during leftward pursuit and to the left during rightward pursuit eye movements. The faster the pursuit velocity the larger the observed shift. These results suggest that the scaling of the TVOR can precede actual eye position changes by several tens of milliseconds, which averaged 169 ± 87 ms in three rhesus monkeys. Thus, central motor commands, rather than low-level efference copy or proprioceptive information, may be the signals scaling TVOR amplitude.

INTRODUCTION

During forward and backward head and body motion, the amplitude and direction of the evoked compensatory eye movement (translational vestibulo-ocular reflex, TVOR) scales as a function of the spatial location of the foveated target (Angelaki and Hess 2001; McHenry and Angelaki 2000; Hess and Angelaki 2003; Paige and Tomko 1991). For example, when looking straight-ahead and moving forward, only a small eye movement that is opposite for the two eyes should be evoked to keep a near target stable on the fovea. In contrast, while still moving forward but now looking at a target to the right, the eyes need to move rightward, but when looking to the left, the eye movement needs to be leftward. Furthermore, the larger the eccentricity of the target, the larger the evoked eye movement. These kinematic requirements result in a fore-aft TVOR gain (ratio of compensatory eye velocity relative to head velocity) that exhibits a “V-shaped” dependence on eye position (e.g., McHenry and Angelaki 2000; Seidman et al. 1999; Paige and Tomko 1991).

To acquire these kinematic properties, vestibular information about our translation through space must scale with a neural correlate of current eye position, which indicates the location of the target that needs to be foveated. The nature of such a signal remains unknown. Because coding of static eye position is abundant in the neural firing properties of premotor neurons (Chubb et al. 1984; Cullen and McCrea 1993; Fuchs and Kimm 1975; Keller and Daniels 1975; Keller and Kamath 1975; King et al. 1976; McFarland and Fuchs 1992; Scudder and Fuchs 1992; Tomlinson and Robinson 1984), it is commonly thought that it is a premotor or motor corollary discharge of eye position that scales vestibular information for a kinematically appropriate TVOR.

All previous studies, however, used steady-state fixation, conditions that mask the temporal dynamics associated with this on-line modulation of vestibulo-ocular signals. One way to unmask the underlying temporal delays would be to characterize the TVOR under conditions where eye position changes—for example, during tracking of an independently moving target. If indeed a corollary discharge signal of current ocular position directly modulates vestibulo-ocular information processing, the dependence of TVOR gain on instantaneous eye position during smooth pursuit eye movements at different constant speeds should be similar as that during static fixation. Alternatively, it is also possible that the relationship between TVOR gain and instantaneous eye position changes systematically as a function of eye movement speed. In particular, if TVOR amplitude depends on future (rather than current) eye position, the V-shaped fore-aft TVOR dependence on eye position would be expected to shift in the opposite direction of pursuit eye movements (i.e., the minimum amplitude would be observed before the eyes reach the straight-ahead position). Such a result would suggest that the signal responsible for modulating TVOR gain is anticipatory in nature (e.g., motor command). In contrast, if TVOR amplitude depends on past eye position and the V-shaped curve shifts in the same direction of pursuit eye movements (e.g., to the left during leftward pursuit), it would suggest a processing delay that, depending on its size, might suggest a sensory (e.g., proprioceptive; Ashton et al. 1988; Donaldson 2000; Weir et al. 2000) origin.

Here we have investigated these alternatives by characterizing the kinematic properties of the TVOR during high-frequency (5 Hz) fore-aft motion as rhesus monkeys followed horizontally moving targets at different speeds. We found that the V-shaped TVOR curves shifted opposite to pursuit direction by an amount that depended on pursuit speed, which suggests that it is driven by an anticipatory signal regarding future eye position.

METHODS

Three male rhesus monkeys were chronically implanted with a lightweight, circular head-restraint ring anchored to the skull, as well as dual eye coils for recording binocular eye movements within a

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The fast phases of nystagmus were identified and removed on the basis of time and amplitude windows set for higher derivatives of eye velocity. The identified fast phases were visually displayed to interactively correct potential misidentification. In addition to removing the saccadic eye movements, this procedure also automatically eliminated all periods where the animals’ eye movements fell outside the behavioral windows.

Saccade-free data were analyzed on a cycle-by-cycle basis. For each cycle, a mean left and right eye position and velocity were computed by averaging the corresponding data segment. These 200-ms averages provided a reliable measure of the corresponding instantaneous eye position and pursuit velocity for each cycle. Mean eye velocity was then subtracted from the original slow phase velocity signal. The remaining slow-phase eye velocity modulation (after removal of the constant pursuit velocity) was fitted with a sinusoidal function (having two parameters, amplitude and phase) by use of a nonlinear, least-squares algorithm based on the Levenberg-Marquardt method. This allowed us to compute TVOR gain (defined as the ratio of peak eye velocity to peak head velocity), phase (relative to forward head velocity) and the corresponding VAF (variance accounted for), separately for data from each of the left and right eyes. Only complete response cycles (i.e., without any portion that was eliminated due to either a saccade or behavioral window failure) with VAF > 0.75 were included in subsequent analysis.

The dependence of compensatory eye movements on eye position was quantified by examining the dependence of TVOR response gain (computed separately for each cycle) and the respective mean instantaneous eye position, a relationship that was quantified using the equation:

\[ \text{VORgain} = y_o + s \cdot (E - E_o) \]  

where \( E \) is eye position, \( y_o \) is the minimum VOR response gain observed when \( E = E_o \) (typically for static fixation, \( E_o = 0 \)) and \( s \) is the slope with which VOR gain increases with leftward or rightward eye positions (e.g., Fig. 2). To reliably estimate the best-fit parameters without the influence of local minima, we varied each of the three variables through a large range of values and chose as initial conditions those that corresponded to the smallest mean square error and largest VAF. Subsequently, the optimization was repeated an additional 40 times while randomly varying each parameter within 10% of its chosen initial condition value. The final fitted parameters \( (y_o, s, E_o) \) and corresponding 95% confidence intervals, were chosen from the optimization that resulted in the smallest mean square error and largest VAF. Statistical comparisons have been based on linear regression and analysis of covariance (ANCOVA).

**RESULTS**

Three male rhesus monkeys were trained to do a simple saw-tooth pursuit task while experiencing high-frequency (5 Hz) fore-aft motion. The pursuit target moved horizontally from left to right and right to left (as high as ± 30° eccentricity) at constant velocity, as illustrated with two examples, one at low (1°/s) and the other at high (20°/s) velocities, in Fig. 1, A and B, respectively. The lower panels of Fig. 1, A and B show an enlarged scale of a smaller portion of the data in the top panel (vertical dashed lines), with the illustration of the corresponding eye velocity and the simultaneous sinusoidal fore-aft linear acceleration stimulus. For the low-pursuit-velocity example, the sinusoidal eye velocity corresponds to the fore-aft linear acceleration stimulus. For the high-pursuit-velocity example, the sinusoidal TVOR response is superimposed on the approximately 20°/s pursuit-related eye velocity (Fig. 1B, bottom).

**FIG. 1.** Raw data traces taken from pursuit trials at (A) slow (1°/s) and (B) fast (20°/s) target velocities, while the animal was experiencing fore-aft motion (5 Hz). Top traces of A and B show target position (T) and corresponding eye position (Epos). Positive values correspond to leftward eye movements. The large positive spike in A illustrates a saccade that was eliminated from further analysis (see METHODS). The regions within each of the two vertical dashed lines have been expanded to illustrate the corresponding eye velocity (Evel) and linear acceleration (Hacc) (bottom traces). Dotted lines indicate 0° baselines. Data from animal H.

3-magnetic field system (CNC Engineering, Seattle, WA). All surgeries and experimentation were in accordance to institutional and National Institutes of Health guidelines. Details of these procedures can be found in previous publications (Angelaki 1998; Angelaki et al. 2000; Angelaki and Hess 2001).

Animals were seated upright in a primate chair that was secured onto a linear sled (Acutronics, Pittsburgh, PA) and were trained to perform a simple horizontal pursuit task while experiencing fore-aft motion. Specifically, during sinusoidal (5 Hz, ± 0.25°, corresponding to ± 0.25 G) fore-aft motion animals followed a moving laser target that was controlled by a head-fixed x-y mirror galvanometer (General Scanning, Billerica, MA) and was projected onto a vertical screen mounted 18 cm in front of the animal. The target moved horizontally (typically within a ± 30° range) at a constant velocity that was abruptly switched from leftward to rightward (and vice versa) directions (e.g., Fig. 1). In different trials, the velocity of target motion varied as follows: 0.5, 1, 5, 10, 15, 20, 25, or 30°/s.

Behavior was monitored on-line using both version and vergence windows (2° total width) and a juice reward was delivered after each 1.2–2-s interval in which the monkey’s eye movements were within the specified behavioral windows. Stimulus presentation and data acquisition were controlled with custom-written scripts within the Spike2 software environment using the Cambridge Electronics Device (CED, Cambridge, England; model power 1401) data acquisition system. Data were anti-alias filtered (200 Hz, 6-pole Bessel), and digitized by the CED at a rate of 833.33 Hz (16-bit resolution). Positive eye movement directions were leftward and downward, respectively.

All data analyses were performed off-line using custom-written scripts in Matlab (Mathworks, Natick MA). Horizontal and vertical eye movements were calibrated by use of a daily fixation task, then differentiated using a polynomial filter (Savitsky and Golay 1964).
Each cycle of sinusoidal VOR modulation during which the animal's behavior was within the specified windows (see Methods) and did not include a saccadic eye movement was quantified using a sinusoidal fit analysis. Examples of the resulting TVOR gain (in units of °/s per cm/s) and phase from fitted cycles with VAF > 0.75 have been plotted as a function of the respective mean eye position in Fig. 2. As expected from the kinematic requirements of the TVOR and similar to previous studies during static fixation (Angelaki and Hess 2001; Hess and Angelaki 2003; McHenry and Angelaki 2000; Seidman et al. 1999; Paige and Tomko 1991), the fore-aft TVOR gain exhibited a V-shaped dependence on eye position. There was also an abrupt 180° transition in phase, which reflects the reversed direction of the compensatory eye movement. During the low-pursuit velocity example, the tip of the V-shaped curve (where fore-aft TVOR gain is minimum) and the phase reversal occurred at approximately zero eye position and was similar for rightward and leftward pursuit (Fig. 2A); however, when the pursuit velocity was large, in addition to larger variability in the responses, the V-shaped curves shifted in opposite direction for leftward and rightward pursuit directions (Fig. 2B). Whenever the eyes were pursuing a leftward-moving target, the tip of V-shaped curve shifted toward negative (rightward) eye positions. Similarly, when pursuing a rightward-moving target, the V-curve shifted toward positive (leftward) eye positions. In both cases, the shift was in a direction opposite to the direction of pursuit, which suggests that an anticipatory signal related to future eye position could scale fore-aft TVOR gain.

These relationships were quantified by fitting a V-curve (theoretical prediction; e.g., Eq. 1; see Methods) to the plots of TVOR gain as a function of eye position, separately for each pursuit amplitude and direction using the data from either the left or right eye in each of the three animals. Because of large cycle-by-cycle variability, VAF values for these fits ranged from 0.4 ± 0.1 (low pursuit velocities) to 0.1 ± 0.06 (high pursuit velocities). Other than increased variability, the only parameter affected by pursuit was the eye position at which fore-aft TVOR gain reaches a minimum (i.e., the tip of the V-shaped curve; corresponding to parameter \( E_0 \) in Eq. 1) (ANCOVA, \( F[1,89] = 8.6, P < 0.01 \)). In contrast, there was no significant effect of pursuit velocity on the slope of the V-curve (parameter \( s \) in equation [1]; \( P > 0.05 \)).

How \( E_0 \) changed with pursuit velocity is summarized in Fig. 3, separately for data from each of the left and right eyes in each animal. The larger the pursuit velocity the more \( E_0 \) shifted away from zero eye position, with the direction of the shift being always opposite to the direction of pursuit eye movement. These dependences have been further quantified using linear regression (Fig. 3, black and gray lines for right and left eye data, respectively). As summarized in Table 1, all six regressions were significant, with an average slope of 0.169 ± 0.087° per °/s (range, 0.076–0.290). These significant shifts of the V-shaped curve by an amount proportional to eye speed illustrate that a given TVOR gain during a continuous, predictive eye movement was achieved at the time of the corresponding eye position but on average 0.169 s earlier. Equivalently, the scaling of fore-aft TVOR did not use an
instantaneous eye position signal, but rather a signal related to the position of the eyes on average $169 \pm 87$ ms later.

**DISCUSSION**

Using continuous and predictive eye tracking during fore-aft motion, we have shown here that the scaling of fore-aft TVOR gain uses an anticipatory eye position signal. This finding appears at odds with a simple corollary discharge mechanism and raises several questions about the nature of the ocular position-related signal that modulates TVOR gain.

As expected from the geometrical transformation necessary for an eye rotation to compensate for a head and body translation, compensatory eye movements in the TVOR scale with both viewing distance and eye position (Angelaki and McHenry 1999; Angelaki and Hess 2001; Hess and Angelaki 2003; McHenry and Angelaki 2000; Paige and Tomko 1991; Schwarz and Miles 1991; Schwarz et al. 1989; Telford et al. 1997). Despite the behavioral demonstration, however, few studies have explored the origin of the viewing distance/eye position signals that are used to scale TVOR magnitude. The first such study showed in monkeys that the scaling of the rotational VOR by viewing distance could precede the actual change in vergence angle by $>50$ ms, which suggests a cognitive or predictive origin (Snyder et al. 1992). Later monkey studies, however, have failed to show a cognitive or high-level influence. For example, the monkey TVOR does not utilize sensory visual estimates of target distance (Wei et al. 2003), nor does it depend on factors such as spatial attention or an upcoming eye movement (Wei and Angelaki 2006).

The latter behavioral observations have suggested that scaling by viewing distance and eye position might arise from low-level (premotor) efference copies of vergence angle and ocular position. Indeed, premotor cells in the vestibular and prepositus hypoglossi nuclei (including all eye movement-sensitive cell types; i.e., position-vestibular-pause [PVP], eye-head [EH], and burst- tonic [BT] neurons) have been shown to change their firing rates as a function of viewing distance (Chen-Huang and McCrea 1999a, 1999b; McConville et al. 1996; Meng et al. 2005; Meng and Angelaki 2006). Some of these premotor neurons also change their firing rates similarly as eye velocity during the fore-aft TVOR (Meng and Angelaki 2006). Among these premotor groups, those with the largest vergence and eye position dependences were EH and BT cells, which suggest a potentially direct eye position influence on these neuron types (Meng and Angelaki 2006).

If indeed the eye position signal that scales neural firing rates and TVOR amplitude originates from a neural copy of the motor command to move the eyes (corollary discharge), it seems reasonable to expect small, if any, shifts in the V-dependence with pursuit velocity. Thus, the present findings are not easily compatible with a simple, premotor, corollary discharge origin for the eye position-related scaling of these firing rates. The steep dependence of the V-curve’s tip ($E_v$) on pursuit velocity suggests a 76–290-ms anticipation lead in the scaling of the fore-aft TVOR by eye position. These results are in line with those of Snyder et al. (1992) for the scaling of the rotational VOR by vergence angle and imply that central motor commands, rather than low-level efference copy or proprioceptive information, may be what scales TVOR amplitude. Where in the premotor pathway for the VOR this scaling occurs remains unknown, though eye-head cells in the vestibular nuclei and potentially the cerebellar flocculus/ventral paraflocculus might play a major role. The exact nature and origin of such an anticipatory or motor command signal remains to be investigated.

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**REFERENCES**


King WM, Lisberger SG, and Fuchs AF. Responses of fibers in medial longitudinal fasciculus (MLF) of alert monkeys during horizontal and
vertical conjugate eye movements evoked by vestibular or visual stimuli.


