

Pursuit Responses to Target Steps During Ongoing Tracking

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Submitted 6 August 2006; accepted in final form 30 November 2006

Tarnutzer AA, Ramat S, Straumann D, Zee DS. Pursuit responses to target steps during ongoing tracking. *J Neurophysiol* 97: 1266–1279, 2007. First published December 6, 2006; doi:10.1152/jn.00819.2006. Brief smooth eye-velocity responses to target position steps have been reported during smooth pursuit. We investigated position-error responses in eight healthy human subjects, comparing the effects of a step–ramp change in target position when imposed on steady-state smooth pursuit, vestibuloocular reflex (VOR) slow phases, or fixation. During steady-state pursuit or VOR, the target performed a step–ramp movement in the same or in the opposite direction relative to ongoing eye movements. When the step was directed *backward* relative to steady-state smooth pursuit, eye velocity transiently decreased ($1.3 \pm 0.4\%$; average peak change in amplitude \pm SD), beginning about 100 ms after the step. The amplitude of position-error responses varied inversely with the step size. In contrast, there was little or no response in trials with *forward* steps during steady-state smooth pursuit, when step–ramps were imposed on VOR or when smooth pursuit began from fixation. We hypothesize that during ongoing smooth tracking when a sudden shift in target position is detected the pursuit system compares the direction of ongoing eye velocity with the relative positional error on the retina. In the case of different relative directions between ongoing tracking and a new target eccentricity, a position-error response toward the new target is initiated. Such a mechanism might help the smooth pursuit system to respond better to *changes* in target direction. These experimental findings were simulated by a mathematical model of smooth pursuit by implementing direction-dependent behavior with a position-error gating mechanism.

INTRODUCTION

Smooth pursuit eye movements ensure that images of moving objects of interest are stabilized on the fovea, where visual acuity is best. The neurophysiological and anatomical substrate of smooth pursuit has been extensively investigated in recent years and involves multiple areas within the brain stem, cerebellum, and cerebral hemispheres (Fukushima 2003; Ilg 2002; Krauzlis 2004, 2005; Thier and Ilg 2005). The main stimulus to smooth pursuit is motion of images on the retina (retinal-velocity errors or retinal-slip velocity) (Dodge 1919; Rashbass 1961), but retinal-position errors also can elicit and modify smooth pursuit both in humans (Carl and Gellman 1987; Pola and Wyatt 1980; Wyatt and Pola 1981) and in monkeys (Krauzlis and Miles 1996; Morris and Lisberger 1987). Rashbass (1961) showed that the saccade system can take into account the speed as well as the eccentric position of the target and thus calculate whether a saccade is actually going to be needed based on the original position error. Among other stimuli, Rashbass used a step–ramp paradigm, in which a target

jumped away from the fovea (step) and then moved back toward the fovea at a constant velocity (ramp), so that the target passed through its original starting position around the pursuit reaction time, in the range of 150–200 ms. In this way, the catch-up saccade that is usually required when a target begins moving away from the fovea can be cancelled. As a result, an uncontaminated “pure” smooth pursuit response can be analyzed. Nevertheless, in some experimental conditions subjects occasionally show an initial brief smooth change of eye velocity in the direction of the step (opposite the direction of the ramp) before eye velocity shifts toward matching the ramp velocity and direction. This initial smooth response to the target step has been called a “twitch” (Wyatt and Pola 1987) and is evidence that the smooth pursuit system responds to position as well as to velocity errors (Carl and Gellman 1987; Krauzlis and Miles 1996; Morris and Lisberger 1987; Wyatt and Pola 1987; Wyatt et al. 1989).

It was previously shown in monkeys (Schwartz and Lisberger 1994) and also in humans (Churchland and Lisberger 2002) that responses to brief sinusoidal perturbations in target velocity are enhanced during steady-state pursuit compared with fixation. Similar observations were made for brief background perturbations during pursuit tracking (Schwarz and Ilg 1999; Suehiro et al. 1999). On-line gain modulation of visual-motor transmission for smooth pursuit was proposed as a mechanism of enhanced responses to target velocity perturbations during pursuit (Schwartz and Lisberger 1994). Also, response amplitudes were found to be correlated to the amplitude of the perturbation and were largest when along the same axis as ongoing target tracking, suggesting a continuously modulated gain rather than a binary switch. The location of smooth pursuit on-line gain modulation was postulated to be located downstream of the frontal pursuit area, possibly within the cerebellum (Chou and Lisberger 2004).

It was shown, however, that responses not only to perturbations of target velocity but also to target position errors depend on the current state of the ocular motor system, i.e., whether the step–ramp begins from steady fixation or is imposed on steady-state smooth tracking. If step–ramps are initiated from fixation, position-error responses are relatively small and scarcely influenced by the size of the step, a consistent observation in several studies (Carl and Gellman 1987; Wyatt and Pola 1987; Wyatt et al. 1989). Results from human subjects (Carl and Gellman 1987) and one nonhuman primate study (Morris and Lisberger 1987) indicate that position-error responses are larger and depend on the size of the step whenever step–ramps are imposed on steady-state smooth pursuit. Morris and Lis-

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berger (1987) reported asymmetries of eye acceleration in response to retinal position errors during steady-state pursuit in monkeys; Krauzlis and Miles (1996) described a decrease in eye velocity only when imposing backward perturbations during the onset of pursuit in three rhesus monkeys. An onward-backward asymmetry in favor of backward steps was also reported by Carl and Gellman (1987) in human subjects. Taken together, there is experimental evidence from both human and monkey studies that the response to target steps depends on the state of the pursuit system and on the relative directions of the step and the steady-state smooth tracking; position-error responses appear to be larger for steps directed opposite to the steady-state target ramp.

The mechanisms underlying the position-error response are still unsettled (Carl and Gellman 1987; Morris and Lisberger 1987; Wyatt and Pola 1987). Carl and Gellman (1987) proposed a predefined two-component response of the smooth pursuit system to a position error. They suggested that the pursuit system differentiates the position error over time and therefore responds to a derived retinal-velocity error rather than to a retinal-position error. The proposed mechanism includes a deceleration of smooth tracking resulting from the disappearance of the target from the fovea during steady-state tracking and an acceleration of smooth tracking toward the new target position. Krauzlis and Miles (1996) hypothesized that the effect of perturbations during the onset, maintenance, and offset of pursuit depends on a variable gain in the main forward path of the model within the positive feedback loop of the efferent copy of eye velocity. The variable gain input was modulated during the response as a function of context, so that the responses overshoot for higher gain values. These authors, however, did not simulate responses to position perturbations during ongoing pursuit or the directional asymmetry of the responses. Alternatively, Wyatt and Pola (1987) suggested that the position-error response reflects an early mechanism for detecting target motion. The purpose of the position-error response would be one of preparation for the subsequent main smooth tracking response.

These various hypothesized mechanisms for the position-error response of the smooth pursuit system differ in their functional implications. It is uncertain whether the position-error response is a reflexive response to a given position error [as suggested by Carl and Gellman (1987)] or a manifestation of a target direction detecting algorithm [as suggested by Wyatt and Pola (1987)]. Likewise, it is uncertain whether the response to a position error is generated by a brief velocity signal derived from the change in target position or by a true position input. Recently Blohm and colleagues (2005) presented additional evidence for a position input to the smooth pursuit system.

Attempts to simulate position-error responses during steady-state pursuit in a mathematical model have been limited. Wyatt and Pola (1987) presented a smooth pursuit model simulating eye movements to step-ramp stimuli. Their model used a velocity impulse derived from the position error and restricted analysis to step-ramp stimuli beginning from fixation. Krauzlis and Miles (1996) described a model of smooth pursuit with a variable gain to describe transitions between fixation and smooth pursuit. Although they also reported responses to small position perturbations, they did not simulate these findings.

Here we reinvestigated the effects of position errors on the smooth pursuit system in a relatively large group of healthy human subjects using step-ramp stimuli with an emphasis on how the prior ongoing eye movements affect the step-ramp response. We compared the position-error response between a step-ramp stimulus initiated when the eyes were already moving, either from steady-state pursuit or from a slow phase generated by the vestibuloocular reflex (VOR), and a step-ramp stimulus initiated from fixation. The impact of different types of ongoing eye movements (smooth pursuit and VOR slow phases) on the step-ramp response have not been reported in humans, although qualitative responses to these types of stimuli have been described in monkeys (Morris and Lisberger 1987).

These three stimulus conditions derive from the need to investigate three distinct ocular motor mechanisms. Visual fixation as an independent ocular motor subsystem has been postulated, based on both electrophysiological studies in monkeys and behavioral studies in humans (Leigh and Zee 2006). However, whether residual retinal image motion is reduced by a separate fixation system when the target is stationary and by smooth pursuit when the target is moving is still unsettled. When the head rotates, the VOR produces compensatory, oppositely directed smooth eye movements. The smooth pursuit system is believed to be important in the cancellation of the VOR, i.e., when a target is rotating synchronously in space with the observer.

Although results from the experimental paradigms used in the present study were reported previously, in no prior study were all the paradigms combined in a single group of human subjects under similar stimulus and recording conditions. Because of these limitations, we sought to compare position-error responses under a number of different circumstances in a relatively large group of human subjects. Thus far models of smooth pursuit have simulated responses only to step or step-ramp stimuli beginning from fixation (Wyatt and Pola 1987). It was previously shown, however, that position-error responses during fixation and steady-state pursuit are profoundly different, i.e., they produce smooth changes in eye speed during steady-state pursuit but elicit saccades during fixation (Morris and Lisberger 1987). Previous mathematical models of smooth pursuit (Krauzlis and Miles 1996; Wyatt and Pola 1987) did not simulate the response pattern to step-ramps during steady-state pursuit. In this study, we collected data from a group of subjects in various paradigms and then developed a new mathematical model. Our model accounts for our experimental findings and suggests how position errors are processed during steady-state pursuit. We will conclude with the hypothesis that the position-error response acts as an early response to a change in target direction and in natural circumstances helps the smooth pursuit system to turn around and begin tracking in another direction.

METHODS

Eight healthy human subjects (seven men and one woman; 24–60 yr old) were studied. Informed consent was obtained from all participants according to a protocol approved by the local institutional review board for human subject protection. Data were obtained in two experimental sessions, one in which step-ramps were imposed on ongoing vestibular stimulation and the other in which step-ramps were imposed on steady-state smooth pursuit stimulation. In both

sessions control trials in which smooth pursuit began from steady fixation were also obtained.

Experimental settings

Subjects were seated on a vestibular chair that could be rotated about the earth-vertical axis. The head was restrained in the upright position using a horizontal bite bar made of dental impression material. The target was a red laser dot back-projected onto a tangent screen (eye-screen distance: 1 m) and was displaced horizontally by computer-controlled mirror galvanometers. Approximately 2.5 ms were needed to generate target steps of $\leq 5^\circ$ with the mirror galvanometers. We used a standard laser diode module with a laser power of 0.004 W and a wavelength ranging between 630 and 680 nm. Eye movements were recorded with a single-coil scleral annulus (Skalar, Delft, The Netherlands) mounted on one eye (right eye: six subjects; left eye: two subjects at 1000 Hz). Using a chair-fixed coil frame (side length: 1.02 m), three fields were produced that oscillated at different frequencies (55.5, 83.3, and 42.6 kHz) with intensities of 0.088 Gauss. The search coil was calibrated behaviorally, asking subjects to fix on light-emitting-diode (LED) targets at defined eccentricities (straight ahead and 5 to 30° in 5° steps to the left and right) in the horizontal plane. Further details of the calibration and eye movement recording procedures were reported previously (Bergamin et al. 2001; Ramat and Zee 2003).

Condition A: step-ramps imposed on steady-state pursuit

In this paradigm, subjects sat in a stationary chair facing the tangent screen. Subjects first had to track a visual stimulus (red laser dot, size about 0.2°) that began from an eccentric position and then moved centripetally with constant velocities of ± 4.7 or $\pm 9.4^\circ/\text{s}$. These values were derived from the peak chair velocity achieved by the chair oscillations in condition B, using a frequency of 0.25 Hz and amplitudes of 3° ($\pm 4.7^\circ/\text{s}$ peak chair velocity) and 6° ($\pm 9.4^\circ/\text{s}$ peak chair velocity). By using an ongoing stimulus velocity of $\pm 4.7^\circ/\text{s}$, we were able to compare step-ramp responses imposed on steady-state pursuit (condition A) or on VOR slow phases (condition B) with those starting from fixation (condition C) over a range of ongoing stimulus velocities (steady-state pursuit in condition A, ongoing VOR slow phases in condition B), which can be regarded as being close to fixation velocity.

The initial eccentric position of the target depended on the ramp direction and velocity and was chosen so that the target crossed the midline after 1 s, giving the subject enough time to be able to follow the target smoothly when it reached the straight-ahead position. At this time a step-ramp stimulus was applied. The interval between the initiation of the step and the ramp crossing the initial target position was initially set to 170 ms and changed by ± 10 ms, if the subject was making too many corrective saccades (forward or backward) that would obscure the initial pursuit response. Then a step-ramp stimulus was added to the steady-state pursuit target, resulting in a change in ramp velocity of ± 5 , ± 10 , or $\pm 20^\circ/\text{s}$. The direction of the step depended on the relative direction of the additional ramp stimulus to the previous ramp target. When both ramps had the same direction, a backward step was applied. If, however, the two ramp stimuli had opposite directions, a forward step was used. The size of the step was proportional (using a factor of -0.17) to the velocity of the added ramp to minimize saccadic tracking (Rashbass 1961). Accordingly, to characterize the response to steps of different sizes different ramp velocities had to be used. Because we did not blank the target during the step change in its position, the target was visible during the entire ramp-step-ramp stimulus.

As schematically depicted in Fig. 1, A and B, the step-ramp stimulus was added to the pursuit target, resulting in an overall target velocity after the step that will be called "net ramp velocity." As in backward step trials the two ramp stimuli had the same sign and the

net ramp velocity after the step would always be increased (and unchanged in direction) relative to the previous ramp (Fig. 1A). For forward step trials (Fig. 1B), the net ramp velocity following the step could be 1) in the same direction as the first ramp, but with reduced velocity (i.e., $9.4^\circ/\text{s}$ minus $5^\circ/\text{s}$), 2) approximately zero (i.e., $9.4^\circ/\text{s}$ minus $10^\circ/\text{s}$), or 3) in the opposite direction (i.e., $9.4^\circ/\text{s}$ minus $20^\circ/\text{s}$) as the previous ramp. For each trial type, 15 trials were recorded, resulting in a total of 360 trials for each subject.

Condition B: step ramps imposed on VOR-slow phases

Subjects were oscillated sinusoidally in a rotating chair about an earth-vertical axis at 0.25 Hz using two different amplitudes (3° , 6°), resulting in peak chair velocities of ± 4.7 and $\pm 9.4^\circ/\text{s}$. Subjects were instructed to fixate a flashing (for 10 ms every second) earth-stationary target located in the straight-ahead position, which was where the chair was pointing when it was at its peak velocity in the middle portion of each half-cycle. A flashing target has the advantage that it gives little retinal slip but allows the subject to better attempt to keep gaze stable in space. In this way the gain of the VOR is increased toward 1.0 and the eye is kept in the same relative position in space. At peak chair velocity, when the chair and subject were facing the tangent screen, a step-ramp stimulus was imposed on the ongoing vestibular stimulus.

Figure 1, C–F schematically illustrates condition B. In Fig. 1, C and D, different chair and target motion stimuli relative to space are shown separately. The eventual pursuit target, being earth stationary and flashing during the first 2 s (chair rotation only), became constantly illuminated and started to move in a step-ramp fashion. Figure 1, E and F illustrates the desired eye position relative to the head, which is a combination of both the vestibular and the visual stimulus (eye-in-head = eye-in-space minus head-in-space). Chair and target either were moving in opposite directions (Fig. 1C), i.e., the VOR slow phase and smooth pursuit were driving the eyes in the same direction or chair and target were moving in the same direction (Fig. 1D), i.e., VOR slow phases and smooth pursuit were driving the eyes in opposite directions. Depending on the direction of the pursuit stimulus relative to the VOR slow phase, a backward step (Fig. 1E) or a forward step (Fig. 1F) was applied. Note that, as in condition A, the desired eye position in head is determined by the sum of the two superimposed stimuli. When the stimulus resulted in backward steps (Fig. 1E), the desired eye velocity was increased relative to the VOR slow phase. When forward steps were applied (Fig. 1F), the desired eye velocity could be 1) decreased, but still in the same direction as the VOR slow phase, 2) approximately zero, or 3) in the opposite direction as the VOR slow phase. The timing of the target crossing straight ahead after the step was modified during practice trials (range 160 to 180 ms) to minimize contaminating saccades during the early portion of smooth tracking. Fifteen trials per trial type were recorded, resulting in a total of 360 trials for each subject.

Condition C: step-ramps imposed on steady fixation

Control trials with a single step-ramp starting from fixation were also applied. Step sizes and ramp velocities in condition C were identical to the step-ramp stimuli in conditions A and B. Fifteen trials per trial type were recorded, resulting in a total of 90 trials for each subject.

Data analysis

Recorded raw eye, chair, and laser position signals were processed and analyzed using MATLAB 7.0.4 (The MathWorks, Natick, MA). Zero-phase forward and reverse digital filtering (filtfilt.m, built-in Matlab function, Matlab 7.0.4) was performed on the calibrated eye position traces using a Gaussian filter with a width of 21 samples (from center to 2% of height, single-sided). Eye velocity was obtained

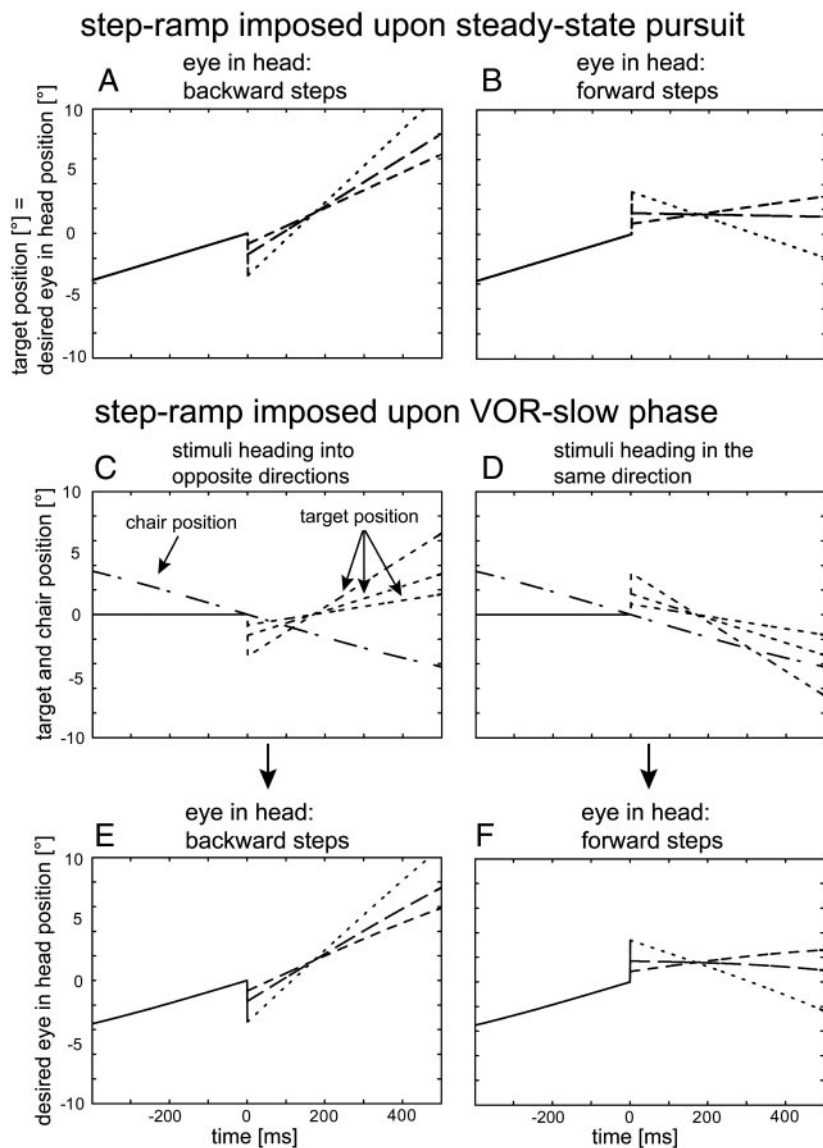


FIG. 1. Schematic illustration of condition A (step-ramps imposed on steady-state pursuit) and condition B [step-ramps imposed on vestibuloocular reflex (VOR) slow phase]. Condition A is shown in A and B: first ramp stimulus (± 4.7 and $\pm 9.4^\circ/\text{s}$ constant velocity during entire trial); step-ramp (± 5 , ± 10 , and $\pm 20^\circ/\text{s}$) imposed. A: forward step trials (ramp and step-ramp into opposite directions). B: backward step trials (ramp and step-ramp into the same direction). Solid lines: target position during first ramp (only $+9.4^\circ/\text{s}$ shown). Short-dashed lines ($\pm 5^\circ/\text{s}$), long-dashed lines ($\pm 10^\circ/\text{s}$) and dotted lines ($\pm 20^\circ/\text{s}$): net target position (ramp + step-ramp) after adding the step-ramp (step-ramp velocity in brackets). Condition B is shown in C–F. C and D: target and chair position. C: chair and target into opposite directions (traces labeled by arrows). D: chair and target into same direction. Dashed-dotted lines: vestibular stimuli (± 4.7 and $\pm 9.4^\circ/\text{s}$ peak chair velocity; only $-9.4^\circ/\text{s}$ shown); dashed lines: visual stimuli (ramp velocity: ± 5 , ± 10 , or $\pm 20^\circ/\text{s}$, consequent step size: ± 0.85 , ± 1.7 , or $\pm 3.4^\circ$). E and F: desired eye in head (VOR slow phase: only $+9.4^\circ/\text{s}$ shown). E: backward step trials. F: forward step trials. Solid lines: desired eye in head during chair rotation only; short-dashed, long-dashed, and dotted lines: desired eye in head during combined chair rotation and moving step-ramp of $\pm 5^\circ/\text{s}$ (short-dashed), $\pm 10^\circ/\text{s}$ (long-dashed), and $\pm 20^\circ/\text{s}$ (dotted), respectively.

by differentiating the calibrated and filtered eye position signal. Eye movement responses to the step-ramp stimulus were preprocessed by subtracting the velocity of the steady-state response to the previous stimulus from the actual eye velocity. In the following we will refer to such adjusted eye velocity as “ Δ eye velocity,” which is the response to the step-ramp only. Traces were aligned with respect to the time at the onset of the step-ramp stimulus and then offset to zero.

About 300 ms after the step-ramp was started, the frequency of saccades increased considerably so we restricted the analysis to the interval from 100 ms before to 300 ms after the onset of the step-ramp. Even by adjusting the interval between the initiation of the step and the ramp crossing the prestep position, many saccades still occurred. Accordingly, a linear interpolation between before and after the saccade was used to estimate the slow-phase velocity during saccades. The beginning and end of saccades were marked manually on the eye-velocity traces; saccades were defined as sudden and transient changes of eye velocity, having peak accelerations of $\approx 200^\circ \cdot \text{s}^{-1} \cdot \text{s}^{-1}$. Individual trials were then inspected and discarded if interpolation was not reliable either because there was a sequence of saccades, leaving no smooth pursuit segments in between, or because the saccades overlapped the beginning or the end of the interval selected. For the data analysis, all remaining trials deviating >2.5 SDs from the average over >25 ms over the selected trial period of 400 ms

were discarded to improve the reliability of the latency detection algorithm by reducing the variability within the data. The median exclusion rate arising from blinks, multiple saccades, or saccades that extended beyond the end of the trial preventing interpolation was still small: 7.4% in condition A and 7.8% in condition B, respectively. In both conditions A and B a median of only 4.8% of all trials was rejected because of a deviation of >2.5 SD from the individual average.

Retinal-error velocity was calculated by subtracting eye velocity from target velocity over the entire 400-ms period analyzed (from 100 ms before to 300 ms after the step-ramp started). Eye acceleration was computed by differentiating eye velocity traces without any additional filtering. The latency of the response was determined using a 3 SD technique with backtracking (Bush and Miles 1996; Carl and Gellman 1987; Johnston and Sharpe 1994): the average and the SD of the data were measured over a period of time before the onset of the stimulus and the time when the data deviate from the average by >3 SD was identified. Then, the tangent to the data, where it crossed the 3 SD threshold was computed, using a linear regression over a 20-ms interval around the crossing point. The interception of the tangent with the previously determined average value was then chosen as the onset of the response. If not stated otherwise, the statistical analysis methods were paired *t*-test ($\alpha = 5\%$), with Holm’s correction whenever

multiple *t*-tests (number of tests = *m*) were performed (Aickin and Gensler 1996; Holm 1979). This method uses an adapted level of significance after performing the null hypothesis on the smallest *P* value ($\alpha = \alpha_0/m$) with Bonferroni correction. For the second smallest *P* value the level of significance therefore is $\alpha = \alpha_0/(m - 1)$ and so on. *P* values were multiplied according to the denominator defined by Holm's correction keeping the level of significance unchanged for all statistical tests, i.e., $P = 0.05$.

RESULTS

Ocular responses to step-ramps

All subjects showed a response to position errors when backward steps were imposed on steady-state pursuit. This was not the case in response to forward steps or in trials starting from fixation.

Figure 2 shows representative calibrated, but otherwise unedited (no saccades removed or offsets imposed), eye-velocity responses from a single trial type (subject 1) to condition A when a step-ramp (ramp speed: $10^\circ/\text{s}$) was added (Fig. 2*B*, backward step) or subtracted (Fig. 2*C*, forward step) to steady-state smooth pursuit of $-9.4^\circ/\text{s}$. Note in Fig. 2*B* the transient decrease in eye velocity (i.e., less negative) in the direction of the backward step before eye velocity increased (i.e., more negative) again to match the new ramp velocity. When forward steps were applied there

was no response in the direction of the step (Fig. 2*C*) for the subject shown here. Figure 2, *D* and *E* shows the eye-velocity responses, similar to Fig. 2, *B* and *C*, but evoked during ongoing vestibular stimulation (with a peak chair angular velocity of $+9.4^\circ/\text{s}$ in this example). With ongoing vestibular slow phases there was neither an ocular response to backward (Fig. 2*D*) nor to forward steps (Fig. 2*E*). Control trials with the subject fixing on a stationary target when a step-ramp was applied (ramp speed: $10^\circ/\text{s}$) are shown in Fig. 2*A*. Again, no ocular motor response to the step can be seen.

In Fig. 3, *A–H* (subpanels 2 and 3; step-ramps imposed on steady-state pursuit), individual average traces of Δ eye velocity are shown for all subjects. For easier comparison, we changed the sign of traces when the sign of the ramp was negative, so that the ramp always had a positive sign and therefore sloped upward. Note that in Fig. 3 the interval shown was restricted to optimize the depiction of the position-error responses; therefore the first 50 ms after the onset of the step-ramp are not illustrated.

Control trials recorded on the same day as condition B were identical to the control trials recorded in the same session as condition A and are therefore not shown in Fig. 3. Position-error responses when the step-ramp started from fixation (Fig. 3, subpanel 1) were found in only two of eight subjects (subjects 3 and 7). For simplification absolute values are used

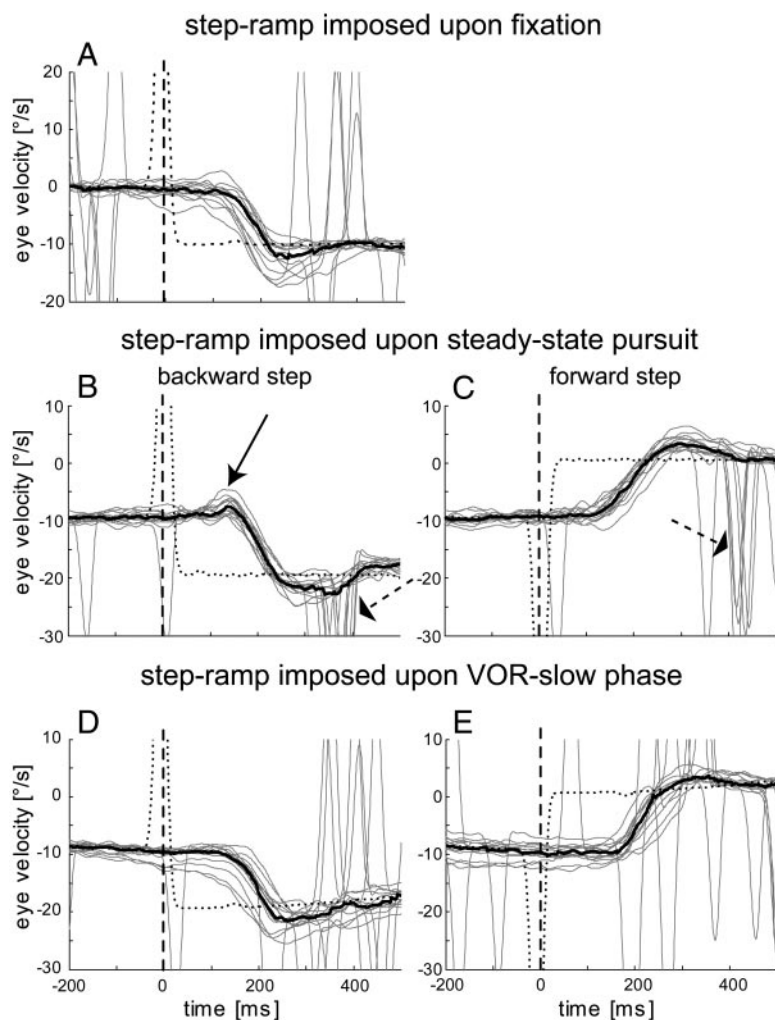


FIG. 2. Examples of eye velocity traces (subject 1) plotted against time, step-ramps imposed on fixation (condition C, *A*), step-ramps imposed on steady-state pursuit (condition A, *B* and *C*) and step-ramps imposed on VOR (condition B, *D* and *E*). 700-ms interval shown; dashed vertical line: onset of step-ramp stimulus (at 0-ms mark). Gray lines: individual eye velocity traces. Black lines: median eye velocity traces. Dotted lines: median target velocity traces. Solid arrow: position-error response. Dashed arrows: catch-up saccades.

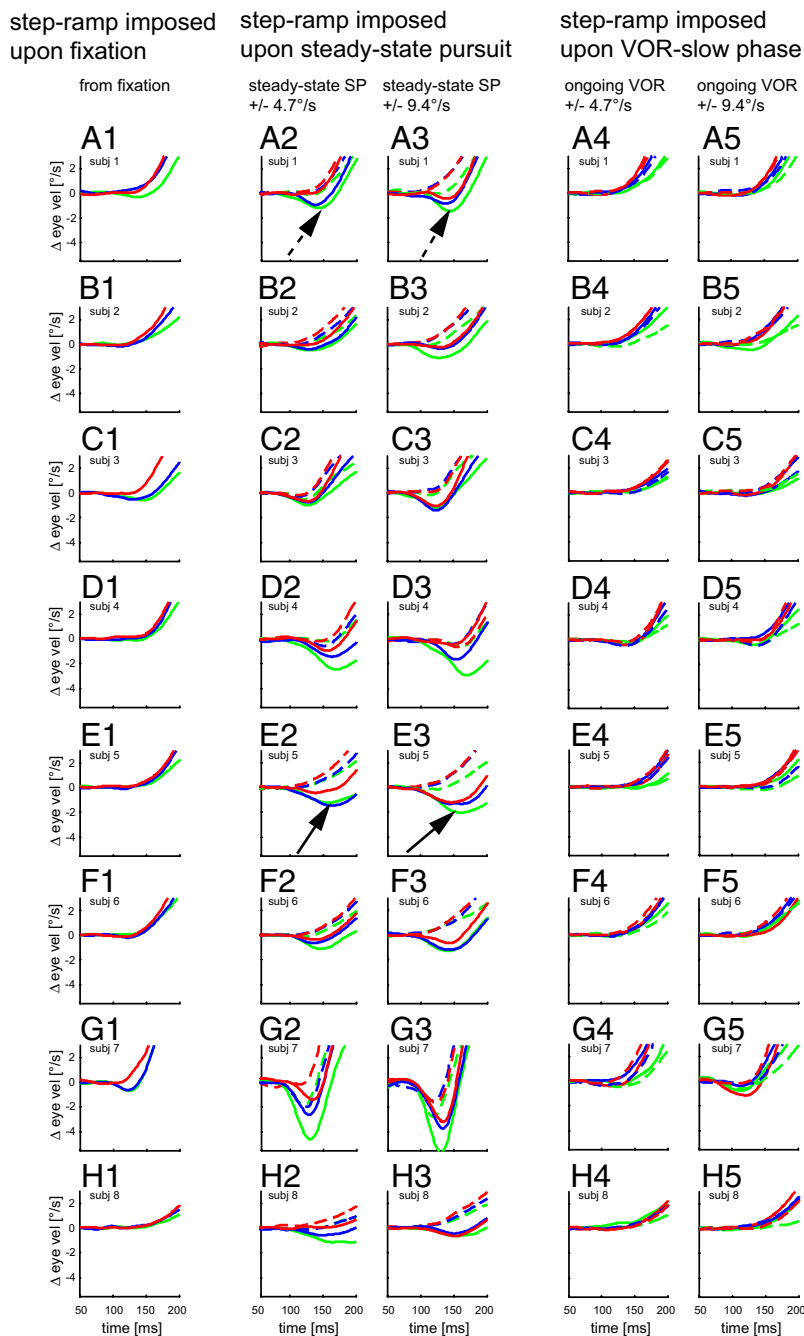


FIG. 3. Individual average traces in condition A (A–H, subpanels 2 and 3 each), condition B (A–H, subpanels 4 and 5 each), and condition C (A–H, subpanel 1 each) for all 8 subjects. Traces represent changes in Δ eye velocity elicited by the step-ramp stimulus. Time is plotted relative to target onset. Ongoing stimulus (steady-state ramp or chair motion): $\pm 4.7^\circ/\text{s}$ or $\pm 9.4^\circ/\text{s}$. Solid lines: backward step trials. Dashed lines: forward step trials. Step-ramp velocities: $\pm 5^\circ/\text{s}$ (green), $\pm 10^\circ/\text{s}$ (blue), $\pm 20^\circ/\text{s}$ (red). Dashed arrows: position-error response in subject 1; solid arrows: position-error response in subject 5.

in the text whenever we refer to the amplitudes of position-error response. During steady-state pursuit all subjects had position-error responses to backward steps (Fig. 3, subpanels 2 and 3), although amplitudes varied considerably among subjects, with extremes in subject 8 (minimal amplitudes) and subject 7 (maximal amplitudes). When analyzing the range of patterns of ocular motor response, typical results are shown by subjects 1 and 5. The position-error responses of these two subjects had different durations (subject 1: 53 ± 32 ms; subject 5: 108 ± 23 ms, mean \pm SD). Unlike subject 1, subject 5 showed little variation in the amplitude of the position-error response as a function of the step size; thus the solid traces for the larger step sizes were closer [compare Fig. 3, A2 and A3

(subject 1) and Fig. 3, E2 and E3 (subject 5)]. Subject 7 (Fig. 3, G2 and G3) showed clear responses to both backward steps and forward steps, although Δ eye velocity was larger for backward steps, which is in accord with findings from the other subjects. An increased gain of response to position errors— independent of the ongoing type of eye movements— could be an explanation for the findings in this subject.

Average Δ eye velocity (“position-error response amplitude”) based on individual mean Δ eye velocity from all eight subjects was calculated for all different trial conditions. In the control trials beginning from fixation, there was no statistically significant change in average Δ eye velocity toward the step ($0.0 \pm 0.3^\circ/\text{s}$). In contrast to the response to step-ramps during

TABLE 1. Peak position-error response amplitudes and latency

	Peak Δ Eye Velocity, $^{\circ}/s$	<i>P</i> -Value	Tracking Onset Latency, ms	<i>P</i> -Value
<i>Controls (from fixation)</i>				
step 0.85 $^{\circ}$, ramp 5 $^{\circ}/s$	0.1 \pm 0.3		120.1 \pm 26.8	
step 1.7 $^{\circ}$, ramp 10 $^{\circ}/s$	0.1 \pm 0.3		119.0 \pm 19.9	
step 3.4 $^{\circ}$, ramp 20 $^{\circ}/s$	-0.1 \pm 0.1		132.0 \pm 7.6	
<i>Steady-state SP: \pm4.7$^{\circ}/s$</i>				
step 0.85 $^{\circ}$, ramp 5 $^{\circ}/s$	1.6 \pm 1.3 vs. 0.3 \pm 0.7	0.008	88.5 \pm 7.9 vs. 123.7 \pm 28.3	0.057
step 1.7 $^{\circ}$, ramp 10 $^{\circ}/s$	1.1 \pm 0.7 vs. 0.3 \pm 0.7	0.002	96.2 \pm 10.9 vs. 114.7 \pm 19.6	0.087
step 3.4 $^{\circ}$, ramp 20 $^{\circ}/s$	0.4 \pm 0.6 vs. -0.2 \pm 0.2	0.041	118.4 \pm 28.4 vs. 121.7 \pm 19.2	0.817
<i>Steady-state SP: \pm9.4$^{\circ}/s$</i>				
step 0.85 $^{\circ}$, ramp 5 $^{\circ}/s$	2.0 \pm 1.6 vs. 0.3 \pm 1.0	0.001	92.2 \pm 8.6 vs. 121.0 \pm 19.3	0.021
step 1.7 $^{\circ}$, ramp 10 $^{\circ}/s$	1.4 \pm 1.0 vs. 0.0 \pm 0.6	0.002	97.4 \pm 12.6 vs. 111.5 \pm 23.0	0.070
step 3.4 $^{\circ}$, ramp 20 $^{\circ}/s$	1.0 \pm 0.9 vs. 0.2 \pm 0.7	0.009	89.4 \pm 22.0 vs. 103.6 \pm 16.8	0.276

Values are means \pm SD. For steady-state SP: backward step trials vs. forward step trials.

steady-state smooth pursuit, an initial change in Δ eye velocity toward the direction of the step was almost always (45 of 48 individual average traces) observed when a backward step was applied. On the other hand only 12 individual mean traces showed a response to forward steps. In general, average peak position-error response for backward step trials decreased with increasing step sizes, as detailed in Table 1.

There was an inverse correlation (first-order linear regression) between the size of the backward step and the peak position-error response amplitude for both the lower ($R = 0.49$, $P = 0.026$) and the higher ($R = 0.46$, $P = 0.034$) steady-state ramp velocity. For all step sizes and both steady-state smooth pursuit velocities, the peak amplitude of the position-error response was significantly larger for backward steps than for forward steps (paired t -test, $P < 0.05$, Holm's correction). The overall duration of the position-error response (defined as the interval between the onset of the position-error response and when the preonset eye velocity was reached again) varied among subjects (see Fig. 3) and was longer with smaller step sizes. The average time to peak amplitude of the position-error response (relative to target onset) was similar for the different sizes of the backward steps. Details about the duration and the time to peak amplitude of the position-error responses are listed in Table 2.

We compared the position-error responses in condition A and condition B, asking whether the response to a step-ramp stimulus depended on the class of ongoing eye movements. Although we used a sinusoidal vestibular stimulus in condition B, which led to a sinusoidal VOR slow-phase response, the

TABLE 2. Average time to peak position-error response amplitude and duration

Trial Condition	Time to Peak, ms	Duration, ms
<i>Steady-state SP: \pm4.7$^{\circ}/s$</i>		
bws 0.85 $^{\circ}$, ramp 5 $^{\circ}/s$	149.6 \pm 22.9	104.6 \pm 34.2
bws 1.7 $^{\circ}$, ramp 10 $^{\circ}/s$	141.5 \pm 14.6	78.6 \pm 22.4
bws 3.4 $^{\circ}$, ramp 20 $^{\circ}/s$	143.6 \pm 13.0	40.4 \pm 31.5
<i>Steady-state SP: \pm9.4$^{\circ}/s$</i>		
bws 0.85 $^{\circ}$, ramp 5 $^{\circ}/s$	144.1 \pm 16.1	91.9 \pm 28.7
bws 1.7 $^{\circ}$, ramp 10 $^{\circ}/s$	142.0 \pm 13.0	73.0 \pm 19.9
bws 3.4 $^{\circ}$, ramp 20 $^{\circ}/s$	139.9 \pm 9.7	73.4 \pm 26.0

Values are means \pm SD; only trial conditions with a backward step (bws) are shown.

change in chair velocity was approximately linear around the time when chair velocity peaked, i.e., when the step-ramp stimulus was applied. Therefore on individual traces, we fit a linear regression to chair velocity during the 100-ms period centered on the time when the target appeared. The slopes were then subtracted from the entire set of traces to compute the response to the step-ramp target only.

In Fig. 3, A to H (subpanels 4 and 5), individual average traces of all subjects for condition B are depicted. For both backward and forward steps averages of peak Δ eye velocity in the direction of the step were $<0.28^{\circ}/s$ and not significantly different ($P > 0.05$, Holm's correction) from zero or the control condition. Thus for condition B subjects showed similar ramp responses to step-ramp targets as those for condition A, but without a position-error response.

Latency to the step-ramp

In condition C (control trials) latency to the step-ramp stimuli ranged from 119 to 132 ms for the different ramp speeds. With step ramps imposed on steady-state pursuit, backward step trials had lower latencies (88–118 ms) than forward step trials (104–124 ms), although these differences were not significant (see Table 1). With step-ramps imposed on ongoing VOR, the ranges of latencies for backward (127–144 ms) and forward step trials (125–144 ms) were similar, with no significant differences ($P > 0.05$, Holm's correction).

Step-induced lag of steady-state pursuit

Retinal-error velocity was increased in all subjects in the case of backward step trials compared with forward step trials. Because the target velocity of the step-ramp stimulus was identical in both forward step and backward step trials, Δ eye velocity traces can be compared directly to illustrate differences in retinal-error velocity as shown in Fig. 4. In all conditions, the maximal difference in Δ eye velocity was reached about 150 to 200 ms after target onset. For steady-state pursuit of $\pm 4.7^{\circ}/s$ (Fig. 4, A–C), the difference in Δ eye velocity decreased slowly after peaking. For steady-state pursuit of $\pm 9.4^{\circ}/s$ (Fig. 4, D–F), the difference in Δ eye velocity diminished faster after peaking, resulting in a shorter plateau.

To further quantify the differences in Δ eye velocity as a function of the direction of the step, we calculated the time (relative to the step) for the eye to reach 25 and 50% of the

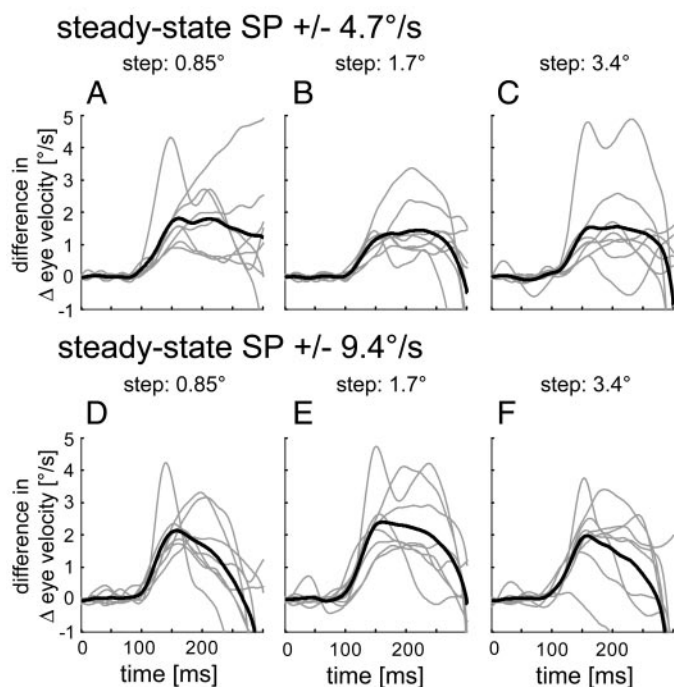


FIG. 4. Individual (gray) and grand average (black) difference (forward minus backward step trials) in Δ eye velocity (i.e., difference in retinal-velocity errors) during the step-ramp stimulus in condition A. x-axis: time relative to step-ramp onset. Steady-state ramp velocity: $\pm 4.7^\circ/\text{s}$ (A–C) or $\pm 9.4^\circ/\text{s}$ (D–F). Step-ramp velocity: $\pm 5^\circ/\text{s}$ (A and D), $\pm 10^\circ/\text{s}$ (B and E), or $\pm 20^\circ/\text{s}$ (C and F).

target velocity, and compared forward step and backward step trials. Note that subject 8 was excluded from this aspect of the data analysis because the 50% level of desired eye velocity was not reached before the 300-ms cutoff time for data analysis. In condition A there was a delay in reaching the 25 and 50% levels (so-called lag) for the backward compared with forward step trials. This delay ranged from 5 ± 10 to 34 ± 19 ms (mean \pm SD) and was significant (paired *t*-test, $P < 0.05$, Holm's correction) in all conditions tested at the 25% level. At the 50% level, the time lag was significant ($P < 0.05$, Holm's correction) in four of six conditions. Linear regression analysis revealed an inverse correlation (first-order linear regression) between the step size and the time lag for both the 25% level (steady-state ramp $\pm 4.7^\circ/\text{s}$: $R = 0.54$, $P = 0.011$; steady-state ramp $\pm 9.4^\circ/\text{s}$: $R = 0.62$, $P = 0.003$) and the 50% level (steady-state ramp $\pm 4.7^\circ/\text{s}$: $R = 0.57$, $P = 0.007$; steady-state ramp $\pm 9.4^\circ/\text{s}$: $R = 0.62$, $P = 0.003$).

Because both the amplitude of the position-error response and the time lag were inversely correlated with the size of the step, we hypothesized that the time lag also would correlate with the amplitude of the position-error response. In Fig. 5, the difference in peak amplitude of the position-error response (backward step trials minus forward step trials) is plotted against the difference in time to reach 25% (Fig. 5, A and B) and 50% (Fig. 5, C and D) of the target velocity, respectively. For a steady-state ramp velocity of $\pm 4.7^\circ/\text{s}$, a clear correlation was found (Fig. 5, A and C), whereas *R*-values tended to be lower with a steady-state ramp velocity of $\pm 9.4^\circ/\text{s}$ (Fig. 5, B and D).

Eye acceleration during the ramp in condition A

The difference in Δ eye velocity—the velocity lag—between forward step and backward step trials (as seen in Fig. 4) decreased over time during the individual trial and crossed zero baseline between 250 and 300 ms after target onset. We therefore analyzed the slope of Δ eye velocity (i.e., acceleration) for both forward and backward step trials by fitting a first-order linear regression over an interval of 20 ms around the times that 25 and 50% of desired eye velocity were reached. Eye accelerations during the ramp after backward steps tended to be higher than those after forward steps for all conditions measured. These differences reached the level of significance ($P < 0.05$, paired *t*-test, Holm's correction) in five of six conditions at the 25% level. However, at the 50% level, no significant differences in their slopes could be found ($P > 0.05$).

DISCUSSION

Here we used a relatively large group of human subjects to quantify position-error responses of the pursuit system under a variety of initial tracking conditions. We confirmed previous observations in humans and monkeys that the response to position errors during smooth pursuit depends on the preceding type of eye movement (smooth pursuit, vestibuloocular reflex, or fixation). Position-error responses to step-ramp stimuli were

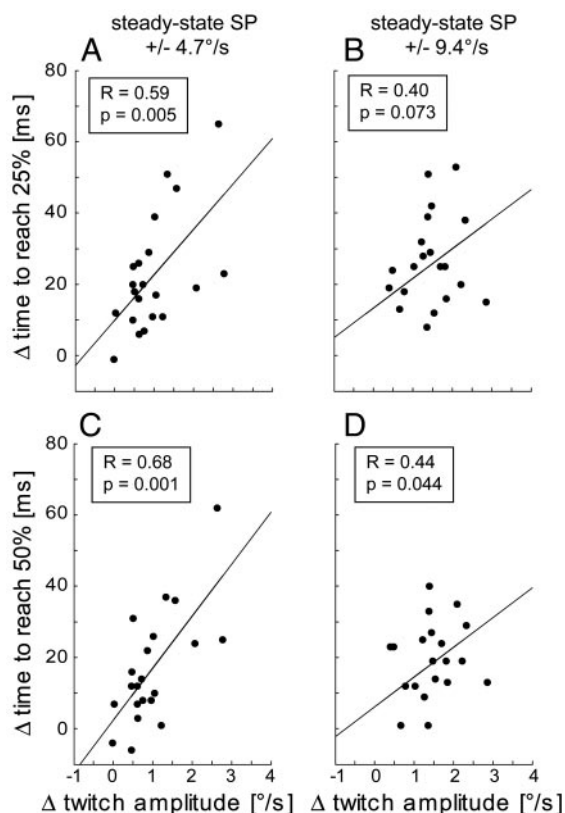


FIG. 5. Correlation between time lag and position-error response amplitude in condition A. Filled circles: individual average differences in time to reach 25% level (A and B) and 50% level (C and D) of desired eye velocity are plotted against consequent position-error response amplitudes. Solid traces: first-order linear regression lines. Steady-state ramp velocity: $\pm 4.7^\circ/\text{s}$ (left column) or $\pm 9.4^\circ/\text{s}$ (right column).

most robust during steady-state smooth pursuit, with significantly larger amplitudes to backward step stimuli. With ongoing VOR or starting from fixation, position-error responses were infrequent and, when they occurred, small. We also showed that the gain of the position-error response varied considerably among our subjects, yet we were able to develop a mathematical model to simulate the findings.

Position-error responses depend on the state of the ocular motor system

The amplitude of the backward step affected the position-error response in trials with smooth pursuit imposed on steady-state pursuit tracking. A decreased sensitivity of the smooth pursuit system to targets further away from the fovea could possibly explain the decreasing position-error response amplitude with increasing step size (Lisberger and Westbrook 1985; Tychsen and Lisberger 1986). Saccades, which are much faster than position-error responses of the smooth-pursuit system, could be used to easily correct large position errors. It might be disadvantageous, however, to use saccades to correct for smaller position errors during tracking because vision would be more impaired during saccades than during the slower pursuit-related position-error responses. The lack of a position-error response during ongoing VOR suggested that there was no significant engagement of the smooth pursuit system during vestibular stimulation. Morris and Lisberger (1987) found little position-error response during VOR paradigms in rhesus monkeys, which is in agreement with our results in humans.

In trials beginning from steady fixation, we found only small and not significant position-error responses with amplitudes $<0.2^\circ/\text{s}$. These position-error responses were smaller and occurred less frequently than those reported by Wyatt et al. (1989). These authors reported average position-error response amplitudes of $0.7 \pm 0.4^\circ/\text{s}$ for backward steps of 2° starting from fixation, in addition, response amplitude was fairly constant over a range ($0.125\text{--}4^\circ$) of backward steps. The discrepancies between our results and those of Wyatt et al. (1989) may relate to differences in the characteristics of the stimulus, such as stimulus size, brightness, and background. Wyatt and colleagues used stimuli with a diameter of 1.5° , whereas our stimulus was about ten times smaller, about 0.2° in diameter. Several studies reported reductions in eye acceleration during the onset of pursuit and in eye velocity during steady-state pursuit when the pursuit targets were projected onto a textured background (Keller and Khan 1986; Kimmig et al. 1992; Mohrmann and Thier 1995). However, this is likely not a cause for the differences between our results and others because the red laser dot was rear-projected onto a translucent screen that provided an untextured background.

Recently, Blohm et al. (2005) reported that during steady-state smooth pursuit, in response to briefly flashed targets, one can elicit smooth eye movements that are proportional to the position error of the flash. This suggests that increasing the distance of the new target relative to the actual tracking position leads to a stronger response to the new stimulus. We found an inverse correlation between the step size and the position-error response amplitude as did Carl and Gellman (1987). How can these seemingly contradictory findings be explained? Blohm and colleagues (2005) restricted their analysis of responses to position errors using eye velocity re-

sponses orthogonal to the ongoing target-tracking trajectory. The fact that a smooth eye-velocity response proportional to the position error is made perpendicular to the ongoing smooth tracking does not exclude a decreasing response to increasing position errors along the axis of the ongoing tracking. As mentioned earlier, position-error responses are likely to depend on the particular context in which they are elicited such as the type of stimuli, background illumination and texture, and range of stimulus parameters. Therefore the type of position-error responses found in our study need not be the same as those elicited in a different setting (e.g., Blohm and colleagues 2005).

When probing the state of the ocular motor system by applying brief target velocity perturbations instead of target steps, significantly larger eye movement responses were evoked if the perturbation was applied during tracking of a moving target than during fixation of a stationary target (Churchland and Lisberger 2002; Schwartz and Lisberger 1994). Depending on the state of the ocular motor system, on-line gain control was previously suggested to be a possible mechanism (Schwartz and Lisberger 1994). There are, however, several important differences between the target velocity perturbations used by Schwartz and Lisberger (1994) and Churchland and Lisberger (2002) and the stimuli used in our study. In our setting a very brief change in target position (step) was followed by a sustained change in target velocity (ramp), therefore suggesting that the perturbation was probing position-sensitive structures rather than velocity-sensitive structures. Also the following change in target velocity did not affect the response to the preceding step, as will be discussed below. Perturbations of target velocity were found to increase on-line gain when target velocity was increased and to decrease on-line gain when target velocity decreased (Churchland and Lisberger 2002). The position-error response evoked by the step-ramp stimuli used in our study correlated inversely with the step size for backward steps, which can be regarded as an inverted gain for position perturbations during steady-state pursuit. A switch, however, as implemented in our model, was necessary to simulate the differences in position-error response comparing forward and backward steps during steady-state pursuit. A continuous gain element taking into account the actual state of the ocular motor system was not sufficient. Taken together there is evidence for both on-line gain control for brief target velocity perturbations and target position perturbations, although the patterns of ocular motor response are different. These differences are probably a consequence of the brain considering other strategies appropriate to respond to target position and target velocity perturbations.

An increased sensitivity to sudden background motion during pursuit tracking was previously reported. By injecting brief full-field motion during the initiation of smooth pursuit, Schwarz and Ilg (1999) and Suehiro et al. (1999) found an asymmetry in the visual processing of global image motion. Whenever the brief background motion was along the direction of the pursuit target, the ongoing smooth pursuit response was temporarily perturbed, which was not the case for background motion opposite to the pursuit target. This direction-dependent gating of perceived global motion to the local motion processing shows features similar to the direction-dependent response to the position-error responses in the absence of background reafferent motion observed in the study presented here.

Whether and how these two direction-dependent asymmetries are functionally related, however, is beyond the scope of this study. Analogous to the ocular motor responses to full-field velocity perturbations, asymmetrical responses to full-field position perturbations with larger eye velocity changes for perturbations along with the target direction might be expected.

Are position-error responses related to the slip velocity?

In our paradigm, the step size and the ramp velocity were always linked; the step size was -0.17 times the ramp velocity (so that the target would go through the fovea 170 ms after the step occurred). Therefore one could argue that the position-error response is not engaged by the retinal-position error, but by the velocity error that is related to the speed of the ramp. In our data, however, the net direction of the target ramp (by adding the velocity of the step-ramp to the ongoing ramp) did not affect the response to the step (see Fig. 1B for details of forward step trials during steady-state smooth pursuit). In other words, whether the net velocity of the ramp changed direction relative to the ongoing ramp target did not alter the response to the position error induced by the step. This finding suggests that the step, and not the net velocity and direction of the ramp (relative to the ongoing ramp), stimulates a position-error response.

By uncoupling the step size and ramp velocity, Carl and Gellman (1987) separated the slip velocity (ramp) and the position-error (step) responses. They used ramp-step-ramp stimuli with equal net ramp velocities before and after the step, showing that position-error responses were still present whenever backward steps were applied. By temporally separating the step and the ramp responses, they were able to observe a delay in the position-error response by postponing the backward step relative to the ramp. Findings from these two experiments strongly suggest that the position-error response is the result of a position and not a velocity error. Assuming this, one would expect no position-error responses in a paradigm using changing ramp velocities only, but no steps. This is what Carl and Gellman (1987) found.

Pola and Wyatt (1994, 2001) studied smooth eye movements during the offset of smooth pursuit. They applied step-ramp stimuli in such a way that the net ramp velocity was zero. For the forward step trials, the eye velocity decreased exponentially reaching zero. For backward step trials, however, initial eye velocity decreased more rapidly and overshoot zero by nearly 3 to 6°/s, returning to zero after about 200 ms. In our study, net ramp velocity was close to zero in some conditions. Nevertheless, the way that the position-error response depended on the relative step direction in our experiments was similar to that reported by Pola and Wyatt (1994), which further supports the hypothesis that the net ramp velocity after the step does not determine the response to the step.

Could the position-error response arise from the pulse of motion of the target?

In our experimental setting mirror galvanometers were used to produce the visual stimulus. This raises the question: is the eye movement response to the change in target position truly driven by a position error? Whenever mirror galvanometers are used, a brief time for the step to be generated is needed (about

2.5 ms in our experimental setting), providing a brief pulse of motion. Thereby the change in eye velocity toward the step could be the response to a velocity rather than to a position error. Several authors used blanking experiments with a high-speed shutter that hid the visual stimulus during the generation of the step, eliminating the perception of a streak (Wyatt and Pola 1987). They found no differences in the position-error response when comparing the ocular motor responses to blanked and nonblanked changes in target position. Carl and Gellman (1987) reported identical accelerations and latencies both under blanked and nonblanked conditions for steps of $\leq 4^\circ$. These two experiments provide strong evidence that in the range of step sizes used in our experimental setting, streaks of the target during the step did not alter the ocular motor response.

This observation, however, does not rule out the possibility that the brain could extract a velocity signal from a change in position signal; that is, the brain does the equivalent of a differentiation between the two positions (before and after the step) over time, even if there is no retinal streak. The observed inverse correlation between the step size and the smooth eye movement response could possibly be velocity based and reflect spatiotemporal tuning of motion detectors, with the larger steps used in our paradigm generating apparent speeds mostly beyond the speed tuning of the visual system. Blohm and colleagues (2005) recently used an experimental paradigm with a position error and no velocity (i.e., a flash), which enabled them to provoke smooth eye movements toward the flash. Position errors $\leq 10^\circ$ were used in their paradigm. The velocity of the evoked smooth eye movement was proportional to the position error of the flash. This finding suggests that in the range of steps tested in our study ($0.85\text{--}3.4^\circ$) velocity saturation does not play a crucial role; therefore it seems less likely that the inverse correlation between the step size and the position-error response is explained by a velocity saturation mechanism. Furthermore, Segraves and Goldberg (1994) studied the independent contributions of position errors and slip velocity to the maintenance of smooth pursuit velocity in the monkey. They concluded that both position errors and slip velocity can drive smooth pursuit eye movements. Also, smooth pursuit eye movements can be modulated in the absence of any retinal velocity error by using retinal afterimages, both foveal (Heywood and Churcher 1971; Yasui and Young 1975) or extrafoveal (Heywood and Churcher 1972; Kommerell and Klein 1971). These observations strongly suggest that retinal position errors can initiate and modify ongoing smooth pursuit.

Implementation of the position-error response into a smooth pursuit model

What might be the mechanism for the striking asymmetry between the position-error response to forward and to backward steps during steady-state pursuit? We hypothesize that the position-error response of the smooth pursuit system is gated by a mechanism that compares the *direction* of ongoing eye velocity with the location of the newly detected target. Depending on their relative directions the gating mechanism would allow a position-related contribution to reach the smooth pursuit system. Consequently, if the direction of tracking were to change, the position-error response would produce an added

change in eye velocity toward the new target. In natural circumstances, this response usually would be associated with a change in direction of the smoothly moving target and so could assist smooth tracking. Such a mechanism would allow the smooth pursuit system to react to directional changes using both position and velocity errors and to avoid any visual “blackouts” associated with small position-correcting saccades.

To quantitatively test our hypothesis of the mechanism generating the position-error response we implemented a mathematical model of the smooth pursuit system including a gating mechanism with a variable gain that depends on the size of the position error. Most of the recent models for smooth pursuit eye movements (Goldreich et al. 1992; Krauzlis and Lisberger 1994; Krauzlis and Miles 1996; Pola and Wyatt 2001; Robinson et al. 1986) did not simulate the position-error response. An early smooth pursuit model reported by Wyatt and Pola (1987) did generate position-error responses, but only when step-ramps were initiated from steady fixation. Krauzlis and Miles (1996) suggested a model of smooth pursuit with a separate input representing a variable gain to account for the responses evoked by small position perturbations timed around the transitions between fixation and smooth pursuit. Although their experimental findings include position-error responses to perturbations during ongoing pursuit, they did not simulate the ocular motor responses to those perturbations. In fact, only a large and transient change of their variable gain input might account for the position-error response, although the mechanism producing such a change and the mechanism responsible for the directional asymmetry would still have to be imposed externally.

Therefore to account for the characteristics of the position-error responses in our experimental data, we developed a model of smooth pursuit with some new features, using Simulink (The MathWorks). The basic model (Fig. 6) is a simplified version of the Robinson et al. (1986) model and similar to the one used by Huebner and colleagues (1990). Our emphasis was not on simulating every aspect of smooth pursuit eye movements but primarily the response to step-ramp stimuli during steady-state pursuit, with emphasis on the position-error response. The model consists of a velocity negative feedback loop computing the error between target velocity and eye

velocity, which the system attempts to drive to zero. The forward path includes a smooth saturation element implemented using a Michaelis–Menten function (Buizza and Ramat 2005) that limits the acceleration of the eyes, followed by a low-pass first-order filter with a time constant ≈ 0.5 s. The feedback path includes a delay of 40 ms and a gain slightly < 1.0 . The gain of the closed-loop mechanism depends on the slope of the saturation nonlinearity at the working point (i.e., given a specific retinal-slip velocity) and, with our parameters, it was slightly > 1.0 for small retinal-slip velocities.

Parallel paths implement a position-error gating mechanism that receives retinal-position error and an efference copy of eye velocity. When the position-error gate is on and this pathway is activated, a signal proportional to the estimate of retinal error, based on target position provided by visual pathways and an efference copy of eye position, is summed with the velocity error at the input of the saturation nonlinearity.

The gating mechanism is illustrated in Fig. 7. The gate compares the direction of the position error with that of the ongoing eye velocity and allows the position-error signal to reach the pursuit mechanism when the two have opposite directions. That is, the gate accepts the position-error input to the pursuit mechanism only if the step causes a position error of the opposite direction. The output of the gating mechanism goes through a nonlinear *foveal* gain element that decreases with increasing eccentricity from the fovea and is zero when the error is null. The foveal gain is similar to that proposed by Pola and Wyatt (2001) in their parallel pathways model as it decreases with increasing target eccentricity from the center of the fovea. Its output is considered as a velocity-error signal and is therefore added to the velocity error along the forward path. This mechanism allows one to reproduce the experimental finding of a decrease in the amplitude of the position-error response with increasing size of the step.

When a step in target position occurs, the velocity feedback loop responds with a small position-error response ($< 0.1^\circ$ amplitude and 10-ms duration) to the spike in velocity caused by differentiating the position step. Such a response is symmetric and occurs independently of the direction of the step. On the contrary, when a backward position step occurs, the sign of the position error is opposite the direction of the ongoing eye velocity and thus the error-gating mechanism will

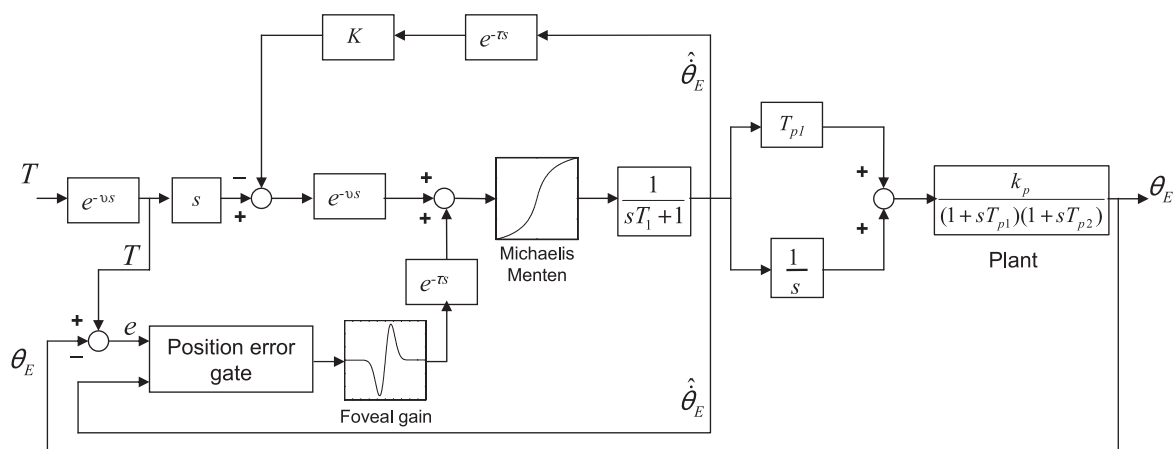


FIG. 6. A model for the position-error contribution to smooth pursuit. Input signal to the model is target position T and the output is eye position θ_E . $\hat{\theta}$ represents the efference copy of eye velocity. Parameters used in the simulations were: $\nu = 0.06$ s, $\tau = 0.04$ s, $T_1 = 0.6$ s, $T_{p1} = 0.2$ s, $T_{p2} = 0.015$ s, $K = -0.85$, $k_p = 1$; Michaelis–Menten nonlinearity $V = 8u/(1 + 0.06|u|)$; foveal gain $V = Aue^{-u^2/(2\sigma^2)}$, where $A = 6.5$ and $\sigma = 1.4$, and u represents the input variable.

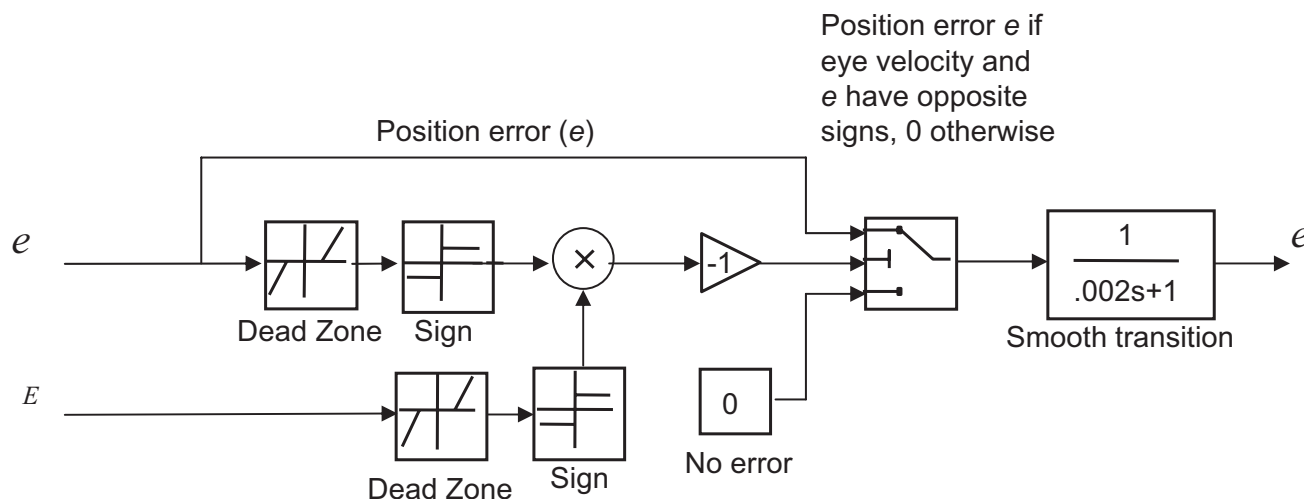


FIG. 7. Position-error gating mechanism. When the sign of the central input is positive (position error and eye velocity have opposite signs) the switch passes the first input (e.g., the position error). When the sign of the central input is negative (position error and eye velocity have the same sign) the switch passes the third input (e.g., 0). Block labeled smooth transition function is used to avoid discontinuities in the first derivative of the output of the gating mechanism.

open and allow the position error, scaled by the foveal gain, to act as a velocity-error signal that is summed to the main smooth pursuit pathway before the saturation element.

To test this model we tried to simulate the mean traces of the recordings on subjects 1 and 5, which we considered representative of the different behaviors shown by normal subjects, as detailed in RESULTS (Fig. 3, A and E, subpanels 2 and 3). The onset, size, and duration of the position-error response in the simulated data (Fig. 8) were comparable to the experimental data from both subjects, suggesting that the nonlinear foveal

gain is a plausible mechanism for scaling the ocular motor response to position errors. Because we were interested in the behavior of the mechanism generating the position-error response, we assumed similar closed-loop gains and delays for both subjects. Therefore the step-ramp stimulus occurred when the model had the same estimate of retinal error (0.3°). To reproduce the behavior of the two subjects we allowed for small changes in the foveal gain nonlinearity of the model. We then ran a nonlinear optimization procedure in Matlab to determine the A and σ parameters of the foveal nonlinearity (see the formula in the legend for Fig. 6) that would best fit the experimental data in a least squares sense. The foveal gain is higher ($A = 6$ vs. 4) and decays more slowly ($\sigma = 1.7$ vs. 1.3) for subject 5 than for subject 1 to account for the larger amplitude position-error responses and the lower range of responses to different step sizes, respectively. In case of forward step trials, only the small position-error response due to the velocity pathway is produced. Results from our simulations support the hypothesis that the position-error gate mechanism accounts for the onward-backward asymmetry that is found experimentally.

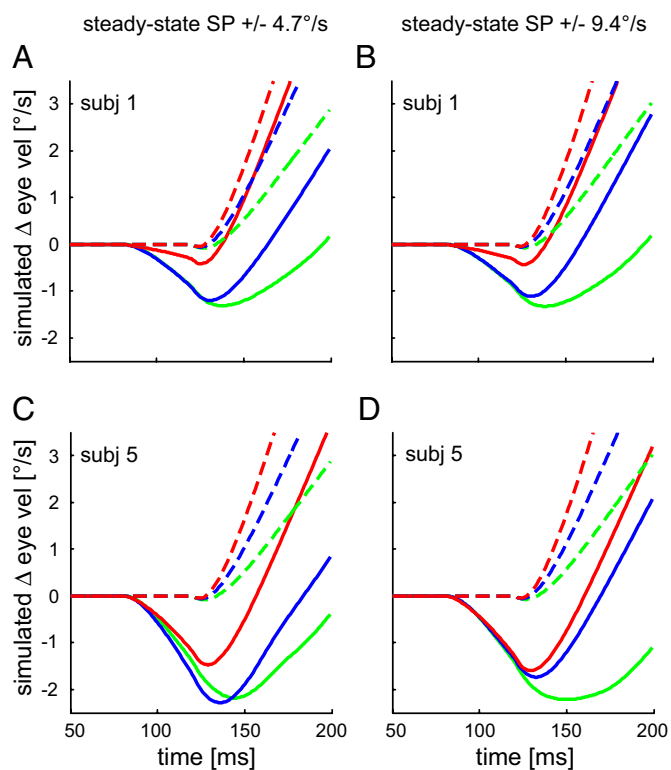


FIG. 8. Simulated data (condition A) for subjects 1 (A and B) and 5 (C and D) with steady-state ramp velocities of $\pm 4.7^\circ/\text{s}$ (A and C) and $\pm 9.4^\circ/\text{s}$ (B and D). Solid lines: backward step trials. Dashed lines: forward step trials. Step-ramp velocities: $\pm 5^\circ/\text{s}$ (green), $\pm 10^\circ/\text{s}$ (blue), $\pm 20^\circ/\text{s}$ (red).

The hemispheric latency hypothesis

Another possible explanation for the different patterns of response to forward and backward steps during steady-state smooth pursuit would be based on the difference in latencies. There could be higher latencies for forward steps, assuming that switching between hemispheres (as is the case for forward steps only under steady-state smooth pursuit) results in a relative delay in the ocular motor response. Such a delayed smooth response to the forward step would be partially obscured by the subsequent ramp response. Because the position-error response is fairly small compared with the increasing velocity-error response, even a linear superposition of the two responses would result in only a minor inflection of Δ eye velocity.

Smooth pursuit eye movements are primarily controlled by ipsilateral cerebral cortical areas, whereas saccades responses to position errors are controlled by the contralateral hemisphere

(Leigh and Zee 2006; Pierrot-Deseilligny et al. 2002). Assuming that the same position-error mechanism is used by the smooth pursuit system, one would expect contralateral hemispheric activation as well, although this remains to be proven. Indeed, Carl and Gellman (1987) discussed such a mechanism, although after taking their and our evidence together, the hemisphere latency difference is an unlikely cause for position-error asymmetry.

The deceleration–acceleration position-error response hypothesis

Carl and Gellman (1987) suggested a preprogrammed, two-component response, resulting in different net eye velocity for forward and backward steps during steady-state smooth pursuit. The first component would lead to a deceleration of target tracking as the target slips off the fovea and the second component would result in an acceleration of tracking into the direction of the step. By summing these two responses, the net response to forward steps should be zero because the two components would have opposite signs. For backward steps, however, a position-error response would be generated because both components would point in the same direction. To cancel any net response to forward steps with the mechanism proposed by Carl and Gellman (1987), the two components would have to be of exactly the same size but with opposite signs. Because of the different mechanisms used to generate these two components, however, responses of equal size over a broad range of step sizes seem improbable.

Position-error–dependent changes in the ramp response

Whenever a position-error response was present, a significant lag in the ramp response was observed. In terms of retinal velocity, the lag induced by the position-error response in target tracking resulted in an increased error relative to trials without a position-error response. Over the first 250 ms after the step–ramp onset, both trials with and without a position-error response show decreasing retinal-velocity errors, although the difference in error remains fairly constant over this time period. This is in agreement with our analysis of the slopes of Δ eye velocity. The similarities between slopes in forward and backward step trials in the later period of the ramp response, together with the significant lag in Δ eye velocity at the 25% level (and partially at the 50% level) for backward step trials, suggest that the position-error response in the case of backward step trials is adding a temporary offset to the ramp response without varying the velocity gain. When smooth pursuit is imposed on steady-state pursuit, there seems to be a trade-off between the response to a perceived position error imposed by the backward step and a quick response to the velocity error imposed by the changing ramp velocity. As discussed earlier, in natural behavior, a backward step would usually be associated with a change in direction of the ramp, so that the position-step response would be in the same direction as the needed ramp velocity.

An anatomical substrate for the position-error response

In our model, we postulate a position-error gate that compares the actual target direction and the direction of a new target and generates different smooth eye movements, depend-

ing on the relative direction of the two targets. We can only speculate about its anatomical location. Potential locations of the position-error response include both the cerebellar flocculus/paraflocculus and the cerebellar vermis (lobule VII) because they are known to be part of the smooth pursuit network (Krauzlis 2004; Thier and Ilg 2005). Areas within the cerebral hemispheres, including the middle temporal area (MT), the medial superior temporal area (MST), the frontal eye fields (FEF), and supplementary eye fields (SEF) also have neurons with activity related to smooth tracking and might be structures where velocity and position information for smooth pursuit are combined. Alternatively, the position-error gate could be implemented in the superior colliculus (SC), another region that was recently found to be involved with the generation of smooth pursuit. Basso and colleagues (2000) used both electrical stimulation and temporary muscimol inhibition in the rostral pole of the SC and hypothesized that the SC provides a position signal that is used by the smooth pursuit eye-movement system. This signal could be the basis for the position-error gate postulated by our model. Further studies are clearly necessary to possibly identify the location of the position-error response.

In summary, we have quantified the position-error response of the smooth pursuit system in a large group of healthy human subjects and have shown that it relies strongly on an already engaged smooth pursuit system. We propose a new model to account for our experimental findings, suggesting that the position-error response reflects an early mechanism of detecting and responding to directional changes in the motion of a target of interest. The location of the position-error response within the smooth pursuit network is unclear and needs further experimentation.

ACKNOWLEDGMENTS

The authors thank D. C. Roberts and A. G. Lasker for technical assistance.

GRANTS

This work was supported by National Eye Institute Grant EY-01849; Swiss National Science Foundation Grant 3200B0-105434; Betty and David Koetser Foundation for Brain Research, Zurich, Switzerland; and the Arnold-Chiari Foundation.

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