Direct Evidence for a Position Input to the Smooth Pursuit System

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[1]*Centre for Systems Engineering and Applied Mechanics and* [2]*Laboratory of Neurophysiology, Université catholique de Louvain, Brussels, Belgium;* [3]*Centre for Vision Research, York University, Toronto, Ontario, Canada; and* [4]*National Eye Institute, National Institutes of Health, Bethesda, Maryland*

Blohm, Gunnar, Marcus Missal, and Philippe Lefèvre. Direct evidence for a position input to the smooth pursuit system. *J Neurophysiol* 94: 712–721, 2005. First published February 23, 2005; doi:10.1152/jn.00093.2005. When objects move in our environment, the orientation of the visual axis in space requires the coordination of two types of eye movements: saccades and smooth pursuit. The principal input to the saccadic system is position error, whereas it is velocity error for the smooth pursuit system. Recently, it has been shown that catch-up saccades to moving targets are triggered and programmed by using velocity error in addition to position error. Here, we show that, when a visual target is flashed during ongoing smooth pursuit, it evokes a smooth eye movement toward the flash. The velocity of this evoked smooth movement is proportional to the position error of the flash; it is neither influenced by the velocity of the ongoing smooth pursuit eye movement nor by the occurrence of a saccade, but the effect is absent if the flash is ignored by the subject. Furthermore, the response started around 85 ms after the flash presentation and decayed with an average time constant of 276 ms. Thus this is the first direct evidence of a position input to the smooth pursuit system. This study shows further evidence for a coupling between saccadic and smooth pursuit systems. It also suggests that there is an interaction between position and velocity error signals in the control of more complex movements.

INTRODUCTION

Primates use both smooth pursuit and saccadic eye movements to track a visual target. The main goal of saccades is the orientation of the eyes to foveate an object of interest, i.e., to overcome position error, whereas the smooth pursuit system aims to stabilize the image of a moving target on the retina, i.e., to overcome velocity error. In a natural tracking task, both oculomotor systems can work in synergy, and there is a coupling between neural structures involved in the control of saccades and pursuit (Keller and Missal 2003; Krauzlis 2004; Krauzlis and Miles 1998; Krauzlis and Stone 1999; Missal and Keller 2002; Missal et al. 2000). Indeed, behavioral experiments have shown that the saccadic system uses velocity error to predict future target position, program, and trigger catch-up saccades (de Brouwer et al. 2001, 2002a,b). In addition, in the absence of retinal information about motion, the saccadic system has access to extraretinal movement information to compensate for smooth eye displacements (Blohm et al. 2003, 2005). These recent results show the coordination between the saccadic and smooth pursuit systems.

Classically, the smooth pursuit system is regarded as a closed-loop negative feedback system that transforms target motion into an eye movement (Lisberger et al. 1987; Robinson

et al. 1986). However, several behavioral studies indicated that a small target jump during ongoing smooth pursuit could modulate the eye velocity, contrarily to target steps during fixation (Carl and Gellman 1987; Morris and Lisberger 1987). In addition, when a target is stabilized for saccades but not for smooth eye movements, a sudden target jump induces large smooth eye movement responses (Segraves and Goldberg 1994; Wyatt and Pola 1981). Unfortunately, in both experimental conditions, the target carried combined position and velocity information, which introduced the difficulty of isolating effects. Recently, it has been proposed that a neural position error signal in the rostral superior colliculus (SC) might be shared by different oculomotor subsystems, including smooth pursuit (Basso et al. 2000; Krauzlis et al. 1997, 2000). This suggests that the position input to the smooth pursuit system could be at the level of the SC (Krauzlis 2004).

Direct evidence for a position input to the smooth pursuit system is still lacking. This is because of the experimental difficulty of separating a possible position input from the classical velocity input to the system. Here, we used a paradigm where we briefly flashed (position error without velocity information) a salient visual target during two-dimensional (2D) steady-state smooth eye movements. As a result, we found a consistent modulation of the smooth eye velocity that was proportional to position error ($\leq 10°$) and independent of both the initial smooth eye movement and the occurrence of saccades. These data show that there is a position error input to the smooth pursuit system. This position error input evoked a smooth response only if the flash had been selected as a new target.

METHODS

Eight healthy human subjects (age, 23–38 yr; including 3 naïve subjects) without any known oculomotor abnormalities were recruited after informed consent. All procedures were conducted with approval of the Université catholique de Louvain Ethics Committee in compliance with the Helsinki declaration.

Experimental set-up

Subjects sat in a completely dark room with their head restrained by a chin-rest and faced a 1-m distant tangent translucent screen. Two targets were presented. The first target was generated by a Tektronix (Beaverton, OR) 606A oscilloscope with custom optics projecting a 1.5° green pursuit target onto the screen. The second target was a 0.2° red laser spot that was back-projected via M3-Series mirror galvanometers (GSI Lumonics, Billerica, LA). Both targets were controlled

using a dedicated computer running LabViewRT software (National Instruments, Austin, TX). Movements of one eye were recorded with the scleral coil technique (Skalar Medical BV, Delft, The Netherlands) (Collewijn et al. 1975).

Paradigm

All recording sessions were composed of a series of blocks containing 40 trials each. Test trials started with a green target presented for 500 ms at 20° from the center of the screen in a randomly chosen direction (Fig. 1). Afterward, the target performed a step away from the center of the screen and moved at a random velocity (10–40°/s) toward the center of the screen (ramp). The size of the step was calculated in such a way that the target crossed the initial fixation point after 200 ms. At a random time interval of 500–1,500 ms after the ramp onset, a red target was briefly presented (10-ms flash). Its position was offset horizontally and vertically by a random value varying continuously between −10° and 10° from the current position of the ramp target. Thus the red flash could appear ahead of, behind, and perpendicularly offset with respect to the radial trajectory of the green pursuit target. Meanwhile, the green pursuit target continued moving until the end of the trial. We chose the 1,000-ms timing window for the flash presentation to prevent an anticipatory drop of the smooth pursuit eye velocity in expectation of the upcoming flash. All trials lasted for 3 s. Subjects were instructed to follow the green pursuit target and to saccade to the red flash as quickly as possible after its appearance.

In separate recording sessions, we also presented four different types of control trials to seven of the eight subjects. First, a flash was presented during or after fixation (FDF or FAF), and subjects were required to orient their visual axis to the flash as soon as it appeared. Second, a flash was presented during or after visually guided smooth pursuit, and the subjects were instructed to ignore it, i.e., ignore flash during ramp (IFDR) or ignore flash after ramp (IFAR).

FDF. Control trials started with a green central fixation spot. Then, 500–1,500 ms later, a red target was presented (10-ms flash) at a horizontally and vertically randomized position between −10° and 10°. After the flash, the green fixation target remained illuminated for another 1,000 ms. Trials ended with a period of 500 ms in the dark. Subjects were instructed to saccade to the red flash target when it appeared. Thus they had to make a saccade to the memorized position of the flash while the green fixation spot remained visible.

FAF. Control trials also started with a green central fixation spot. However, this fixation target disappeared at a random time between 500 and 1,500 ms after the beginning of the trial. After another 0- to 500-ms period, a red target was presented (10-ms flash) at a horizontally and vertically randomized position between −10° and 10°. Subjects were instructed to saccade to the red flash target when it appeared. Thus the orientation eye movement to the memorized position of the flash was performed in complete darkness.

IFDR. Control trials were exactly the same as test trials, but subjects were instructed to ignore the flashed target and to continue pursuing the green ramp. IFDR control trials were randomly interleaved with IFAR control trials. IFAR controls were similar to test trials, but the green pursuit ramp target was extinguished at a random time between 500 and 1,000 ms after the ramp movement onset and remained extinguished until the end of the trial. At a random time 0–500 ms after the pursuit ramp extinction, a red flash was presented in a ±10° window (horizontally and vertically) around the extrapolated ramp position. Besides this, all stimulus parameters remained the same as for test trials. As for the IFDR controls, subjects were instructed to ignore the red flash during IFAR controls and to continue pursuing the extrapolated ramp trajectory.
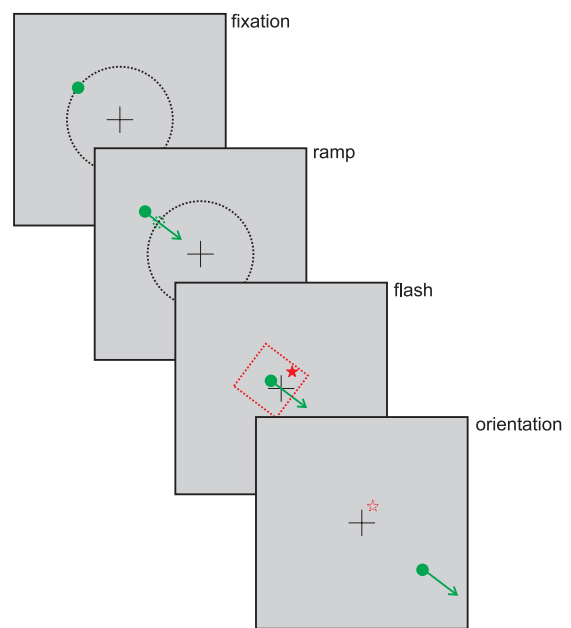

FIG. 1. Protocol. During the 500-ms initial fixation period, the green target (green disk) was presented at 20° eccentricity from the straight-ahead direction (cross). Direction of the initial fixation target was randomly chosen for the target to lie on an invisible 20° circle (dotted). Afterward, the green target (green disk) performed a step away from the center of the screen (green dotted circle indicates initial fixation position) and moved at constant velocity back to the center of the screen (ramp). Between 500 and 1,500 ms after the ramp movement onset, a red target was briefly presented (10-ms flash, red star) at a random position inside a horizontal and vertical 20° window centered on the actual pursuit ramp position (green disk). During the following orientation period, the green ramp target continued moving while subjects were asked to saccade to the memorized position of the flash (red dotted star, invisible).

Data acquisition and analysis

Position signals of one eye and both targets were sampled at 500 Hz using NI-PXI-6025E data acquisition boards (National Instruments). Data were stored on a hard disk for off-line analysis with Matlab scripts (Mathworks, Natick, MA). Position signals were low-pass filtered using a zero-phase digital filter (autoregressive forward-backward filter; cut-off frequency: 50 Hz). Velocity and acceleration were derived from position signals using a central difference algorithm. We normalized our data with respect to the direction of the pursuit ramp. As a result, we obtained two different sets of parameters related to the smooth pursuit, i.e., those parallel to the normalized ramp direction and those perpendicular to the normalized ramp direction. We were particularly interested in the analysis of the perpendicular smooth eye velocity trace. Therefore we removed all saccades from velocity traces. Saccades were detected using a 500°/s^2 acceleration threshold. To remove saccades from velocity traces, we measured the smooth eye velocity 25 ms before and 25 ms after the saccade and interpolated linearly between those values to obtain an estimation of the smooth eye velocity during saccades (de Brouwer et al. 2002a). We chose the 25-ms security margin to be sure that there was no influence of the saccade on the estimated smooth eye velocity. As a result, we obtained the perpendicular smooth eye velocity trace (EV$_s$⊥).

Most of the eye position traces showed one or more orientation saccades toward the memorized position of the flash. However, it has been shown that saccade latency varies across a wide range and is affected by position error and eye velocity in this paradigm (Blohm et al. 2005). In some trials, the orientation could even be made by a purely smooth eye movement. If there was no saccade triggered until 1,000 ms after the appearance of the flash, we called these trials "smooth." This is in contrast with "saccade trials," where orientation

saccades toward the memorized position of the flash were indeed triggered during this 1,000-ms time window. We chose this criterion for the separation between smooth and saccade trials to ensure that the actual orientation movement to the memorized position of the flash was accomplished (Blohm et al. 2003, 2005).

RESULTS

General response properties

We collected a total of 4,675 valid test trials out of which 154 were smooth trials, where no saccade was detected until 1,000 ms after the flash occurrence. Figure 2 shows a typical saccade trial. Figure 2, *A–C*, represents position, velocity, and a spatial representation of eye and targets, respectively. Figure 2*D* shows a detailed representation of the region of interest. The trial represented in Fig. 2 has been rotated to normalize the direction of the initial ramp movement. For the detailed representation of the region of interest in Fig. 2*D* only the perpendicular component of the eye velocity is shown, from the flash onset until 1,000 ms after the flash onset. One can observe that there was a modulation of the $EV_s\perp$ in the direction of the flashed target. Figure 3 shows a typical smooth trial. The detailed representation of the region of interest represented in Fig. 3*D* shows the same modulation of the $EV_s\perp$ in the direction of the flashed target as was the case for the typical saccade trial in Fig. 2*D*. The following analyses were performed on both smooth and saccade trials, and all effects were present in both data sets.

Note that $EV_s\perp$ was relatively small compared with the range of smooth pursuit velocities (10–40°/s), but it was much larger than the mean $EV_s\perp$ noise level during ramp pursuit, i.e., before the flash onset (SD = 0.371°/s). Furthermore, the tracking performance was very good. To test this, we measured the perpendicular eye velocity as well as the perpendicular position error with respect to the pursuit target at the moment of the flash onset. This measure was thus performed before any

influence of the flash on the eye movement. Both measures showed little variability and were constant and close to zero for the whole range of perpendicular flash eccentricities tested below.

Influence of flash position on smooth eye velocity

To describe the global behavior of $EV_s\perp$, all data were aligned on flash onset. Figure 4*A* shows average $EV_s\perp$ traces for different bins of the perpendicular position errors ($PE_{flash}\perp$) at the moment of the flash (all parallel position errors and subjects were pooled). The number of trials in each bin varied from 379 to 482. Positive $PE_{flash}\perp$ values stand for flashes presented in a counterclockwise position relative to the pursuit ramp direction; negative $PE_{flash}\perp$ values were clockwise flashes. We observed a consistent modulation of the mean $EV_s\perp$ by $PE_{flash}\perp$. This effect clearly increased with increasing position error. Furthermore, we found very similar shapes for the mean $EV_s\perp$ for all bins of $PE_{flash}\perp$. It is important to emphasize that the observed $EV_s\perp$ modulation is not caused by the occurrence of a saccade. This is shown in Fig. 4*B* by a comparison of three different data subsets, i.e., trials with a first saccade occurring before 200 ms after the flash onset (solid red line, n = 2,335), trials with first saccade latency >200 ms (solid blue line, n = 2,186), and trials where no saccade at all was triggered (smooth trials, dashed black line, n = 154). Figure 4*B* shows that $EV_s\perp$ modulation is even larger for smooth trials compared with saccade trials. For the data shown here, we interpolated the individual perpendicular eye velocity traces from 25 ms before until 25 ms after the detected saccade and also performed the same analysis with 50 ms. All results were quantitatively the same (data not shown). This shows that the observed phenomena cannot be explained by the removal of saccades. In contrast, we did not observe any $EV_s\perp$ modulation for control trials during fixation (FDF, solid green line, n = 1553) where no pursuit target was presented.
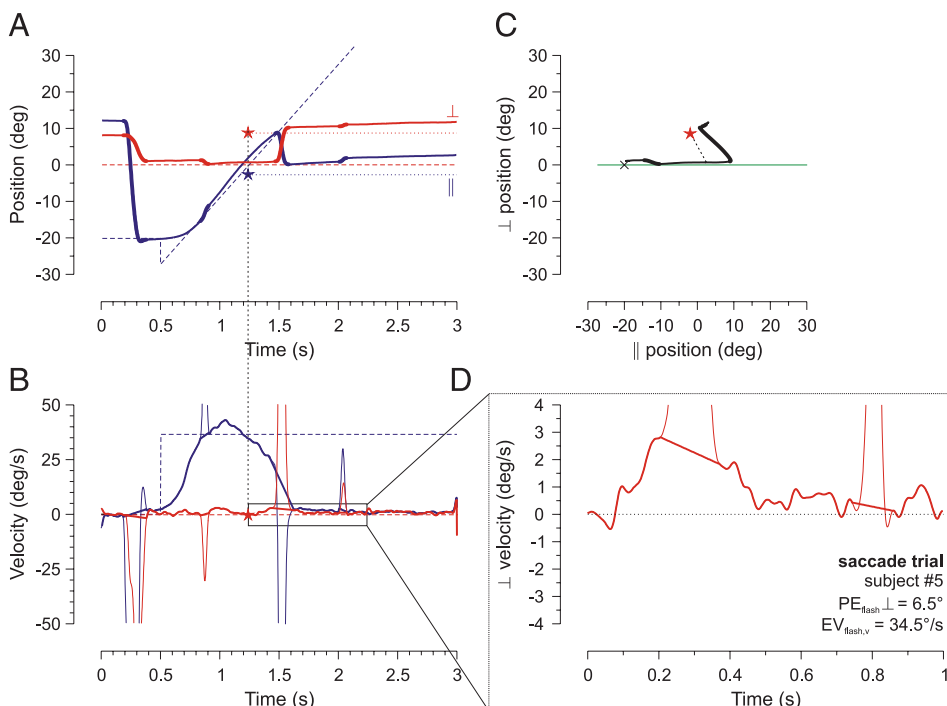

FIG. 2. Typical saccade trial. *A*: eye (solid lines; bold lines: saccades) and target (dotted and dashed lines) positions parallel (blue) and perpendicular (red) to the initial ramp direction. Dashed lines represent the green pursuit target. Star and horizontal dotted lines indicate the memorized flash position. *B*: eye and target velocity. Here, saccades are represented by thin lines. Solid line is the smooth eye velocity. A detailed representation of the perpendicular part of the smooth eye velocity is shown in *D*. *C*: spatial representation of the trial (starting from 500 ms until the end). Dotted line between the star (flash) and eye position trace indicates position error at the moment of flash. *D*: detailed representation of perpendicular eye velocity in the region of interest. Solid lines are without saccades, thin lines represent saccades. *Time 0* corresponds to the onset of flash.

In panel D: **saccade trial** subject #5 $PE_{flash}\perp = 6.5°$ $EV_{flash,v} = 34.5°/s$
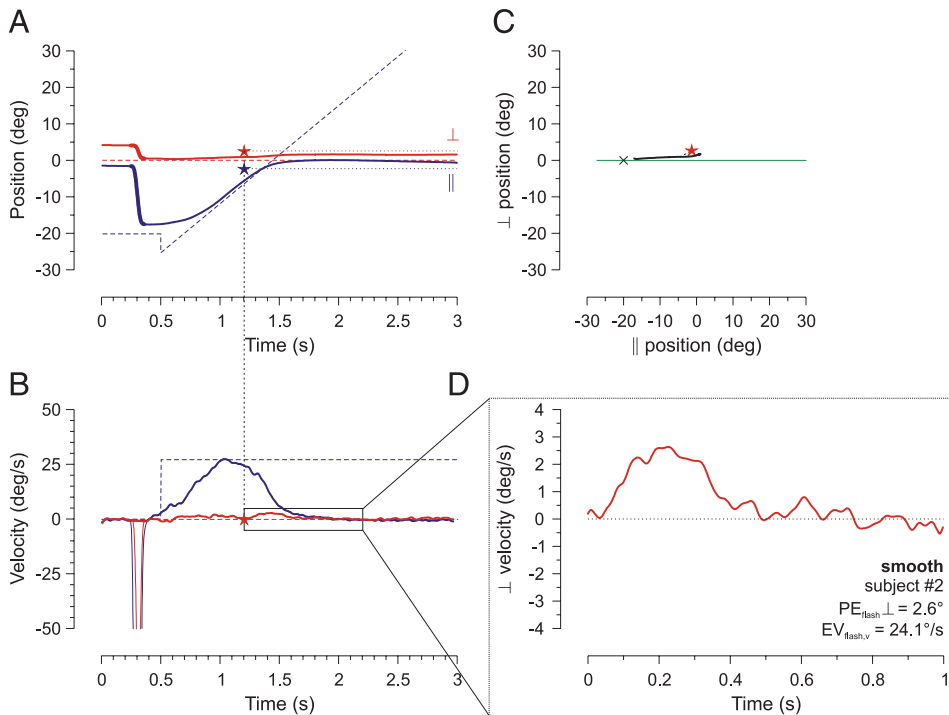
FIG. 3. Typical smooth trial. Same conventions as Fig. 2. *A*: position. *B*: velocity. *C*: spatial representation. *D*: detailed representation of region of interest.

To quantify the $EV_s\perp$ modulation, we measured the total perpendicular smooth eye displacement ($SED_{end}\perp$ = integral of $EV_s\perp$ from the flash onset to 1,000 ms after the flash onset) in Fig. 4*C*. $SED_{end}\perp$ is a good measure of the smooth response to the flash and is less sensitive to noise than the peak $EV_s\perp$. Data were presented separately for saccade and smooth trials. There was a tight dependence of $SED_{end}\perp$ on $PE_{flash}\perp$. The regressions were performed on raw data, and the regression lines had slopes of 0.066 ($P < 0.001$, $n = 4,521$) and 0.115 ($P < 0.001$, $n = 154$) for saccade and smooth trials, respec-

tively. This analysis consolidated the finding that the mean $EV_s\perp$ was strongly modulated by $PE_{flash}\perp$ and showed that $SED_{end}\perp$ increased linearly with $PE_{flash}\perp$. The fact that the regression slope is lower for saccade trials could be due to the linear interpolation of eye velocity that tends to underestimate the smooth eye velocity during the saccade and thus was a conservative measure.

Individual responses to this type of experimental task are variable. Therefore we provide in Fig. 5 data pooled individually for each subject. Note that, for all subjects, the range and
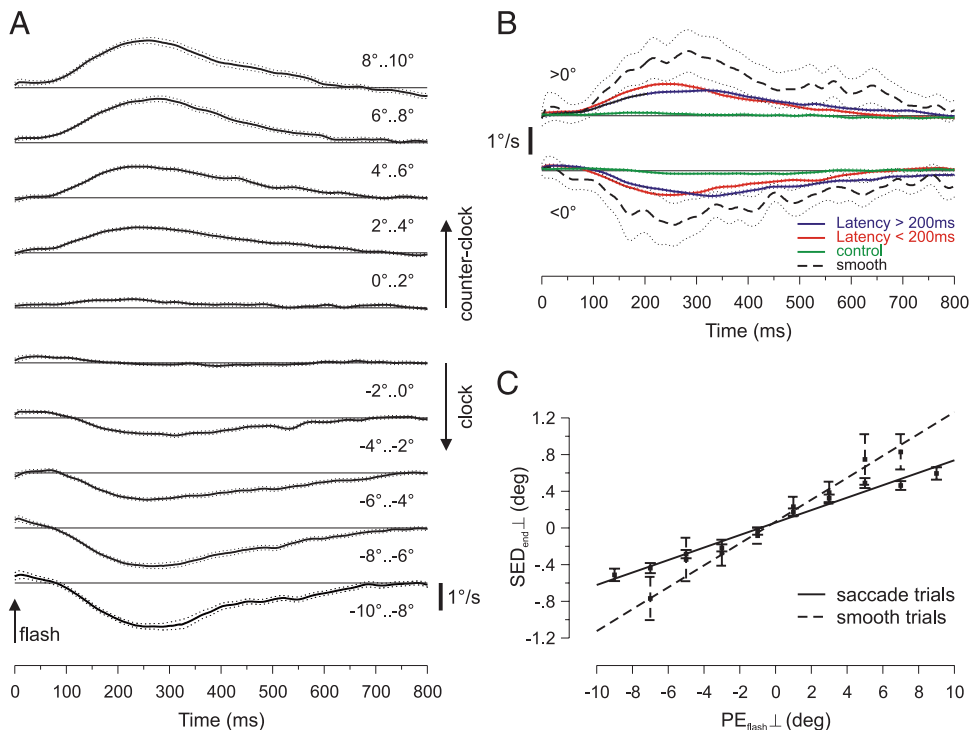

FIG. 4. Average responses for all trials. *A*: mean perpendicular smooth eye velocities (mean $EV_s\perp$) for different bins of perpendicular position error at the moment of flash $PE_{flash}\perp$ aligned on the flash onset (0 ms). Values at the *right* indicate the bin sizes of $PE_{flash}\perp$. *B*: comparison of mean $EV_s\perp$ for trials with early 1st saccades (latency <200 ms, solid red line), trials with later 1st saccades (latency >200 ms, solid blue line), control trials (solid green line), and smooth trials without any saccade after the flash (dashed black line). Data were pooled for all positive and negative $PE_{flash}\perp$ values separately. Dotted lines in *A* and *B* indicate SE (solid/dashed lines). *C*: influence of flash position on evoked smooth eye movements (SEMs). Effect of the perpendicular position error at the moment of the flash $PE_{flash}\perp$ on the magnitude of the perpendicular smooth eye velocity $EV_s\perp$ modulation. Total perpendicular smooth eye displacement ($SED_{end}\perp$) was used as an indicator for the effect. Saccade trials (black) and smooth trials (gray) are shown separately. Solid (saccade trials) and dashed (smooth trials) straight lines are linear regressions on raw data. Squares and error bars indicate mean and SE.
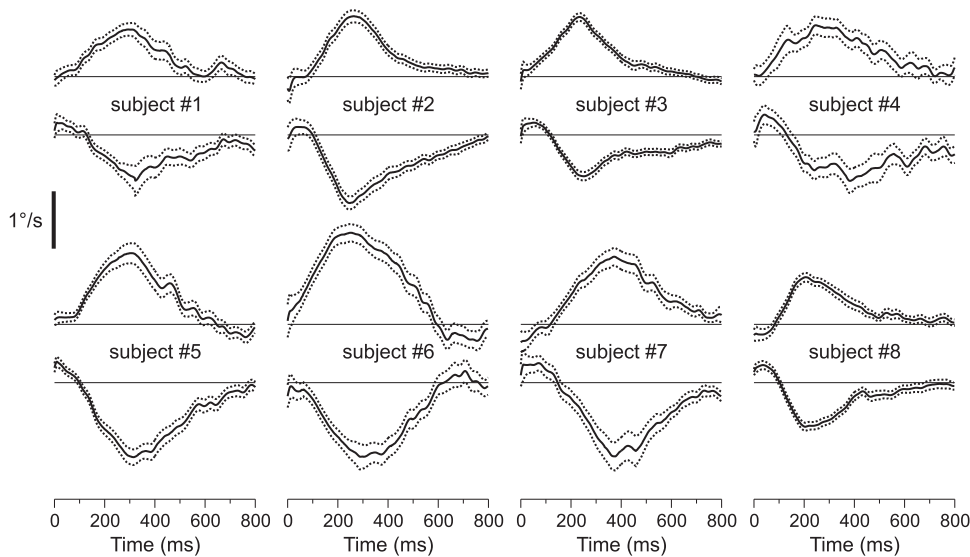
FIG. 5. Individual mean response for each subject. Mean $EV_s\perp$ in test trials are represented for all 8 subjects individually. Data were pooled for all positive and negative $PE_{flash}\perp$ values independently. Solid and dotted lines indicate mean and SE.

distribution of $PE_{flash}\perp$ were approximately the same. Although one can observe some variability between subjects, the basic shape was very similar. However, the amplitude of the response largely varied, i.e., it was double in subject 6 compared with subject 3.

Characterization of movement onset and offset

An interesting aspect of the mean $EV_s\perp$ response is the latency of its onset. Indeed, Figs. 4 and 5 show a consistent, relatively short ($\sim$100 ms) response latency throughout all $PE_{flash}\perp$ values. We computed the mean latency for the smooth $EV_s\perp$ response onset time. Therefore we used an acceleration threshold criterion of $5°/s^2$. This analysis could not be performed directly on each individual $EV_s\perp$ trace, because acceleration signals were too noisy (specifically for small $PE_{flash}\perp$). Thus we used a k-fold subsampling method, also called "bootstrap" (Efron and Tibshirani 1993). This consisted of performing the acceleration threshold analysis $k = 10,000$ times on the mean smooth eye acceleration $EA_s\perp$ trace, computed by taking at each iteration randomly 1/100th of the total data set. Here, the mean $EA_s\perp$ was the first-order derivative (3-point central difference algorithm) of the mean $EV_s\perp$. Once $EA_s\perp$ exceeded $5°/s^2$, we considered this the onset of the velocity response to the flash. Figure 6 describes this procedure and shows the results of this analysis. We found a mean latency of 83 ms (subject variability: 71–104 ms) for the modulation of $EV_s\perp$ by the flash. Our method also provided a SD of 7 ms. However, this was not the SD for individual data, but its size was related to the evaluation method of the latency, i.e., the larger the subset, the smaller the SD. Alternatively, when performing the same analysis but using a velocity threshold [$0.5 \times$ (mean $EV_s\perp$ noise level during pursuit) $= 0.186°/s$] instead of an acceleration threshold, we obtained a mean latency of 86 ± 14 (SD) ms, which was consistent with results presented on Fig. 6.

Another interesting aspect of the description of a transient smooth eye velocity perturbation is the response offset. Again, we performed an analysis similar to the above described k-fold subsampling method ($k = 10,000$) applied on 1/100th of the data set. Therefore we first computed the mean $EV_s\perp$ (by

taking each time randomly 1/100th of the data set) and determined the time of the maximum of the response. Then, we fitted a decaying exponential function on the data, starting 100 ms after the maximum of the response until 1,000 ms after the flash onset. The fit function had the following expression

$$y = a_1 + a_2 \cdot \exp\left(-\frac{x - a_4}{a_3}\right) \qquad (1)$$

To perform this fit, we used standard nonlinear least-squares data fitting by the Gauss-Newton method. We were particularly interested in parameters a_3 (decay time constant) and a_4 (response delay). Note that the offset response delay a_4 was measured relative to the flash onset. Figure 7 shows the results of this analysis. We found a decay time constant $a_3 = 276 \pm 84$ ms (subject variability: 204–330 ms) and a response delay $a_4 = 401 \pm 40$ ms (subject variability: 266–548 ms). However, Fig. 7B shows that the histogram of the decay time constant was not normally distributed. Furthermore, the values of a_3 were quite variable. As in the previous analysis, again the SD was not directly related to the variability of the physical response but to the analysis method.

To compare the parameters of the response offset for the perpendicular and parallel component of the smooth eye velocity, we performed the same analysis on the mean $EV_s\|$. The only difference was that we fitted *Eq. 1* on the data starting at 200 ms after the flash onset (and not 100 ms after the maximum, as this was the case for the mean $EV_s\perp$) until 1,000 ms after the flash onset. The results of this analysis are shown in Fig. 8. Figure 8B shows the histogram of the decay time constant $a_3 = 210 \pm 25$ ms (subject variability: 188–320 ms) and Fig. 8C shows the delay $a_4 = 207 \pm 20$ ms (subject variability: 135–259 ms). Note that the location of the maximum in Fig. 8B was approximately the same as in Fig. 7B, although the shape of the distribution was different.

Origin of pursuit modulation

What is the origin of $EV_s\perp$ modulation? A priori, the $EV_s\perp$ response could be due to a deviation of the ongoing smooth pursuit direction due to the flash. This hypothesis is consistent with a dependence of $SED_{end}\perp$ on $PE_{flash}\perp$. However, this
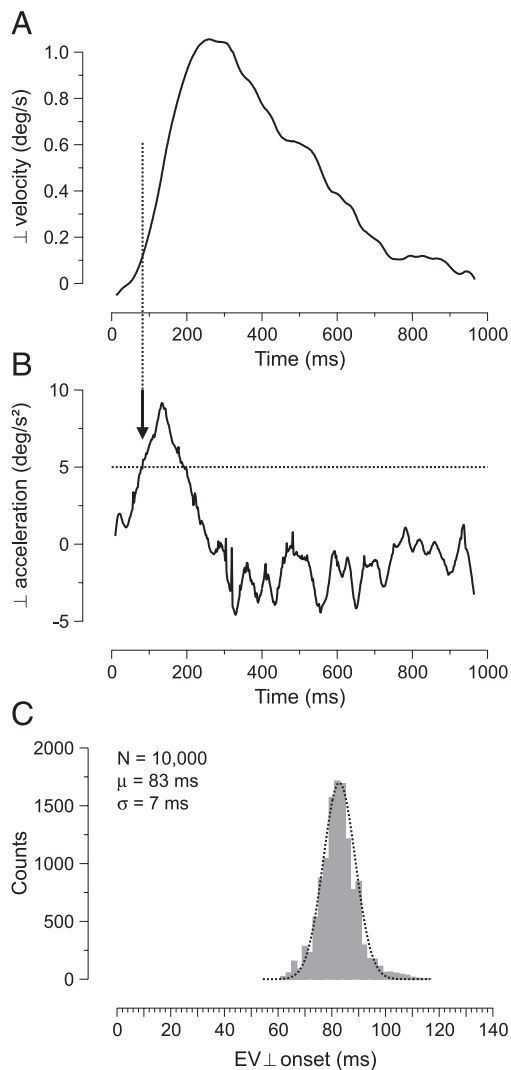
FIG. 6. Mean onset latency of the $EV_s\perp$ modulation. *A*: example of a mean smooth $EV_s\perp$ trace used for the determination of response onset latency. *B*: perpendicular smooth eye acceleration obtained by computing the 1st-order derivative of the mean smooth $EV_s\perp$ in *A*. Horizontal dotted line indicated the threshold used for the onset detection of response. Vertical arrow and dotted line show where the algorithm detected onset for this example. *C*: histogram represents results of the latency evaluation procedure described in *A* and *B*. Dotted curve is a normal distribution fitted on the histogram. Total count (*N*), mean (*μ*), and SD (*σ*) resulting from this method are also indicated.

hypothesis also predicts that the smooth pursuit eye velocity at the moment of the flash $EV_{flash,v}$ should modulate $SED_{end}\perp$. Testing this hypothesis allowed us to study how the visual system handles briefly flashed targets. Into Fig. 9, we plotted $SED_{end}\perp$ as a function of $EV_{flash,v}$. Data were separated in positive versus negative values of $PE_{flash}\perp$ and in saccade versus smooth trials, although the results were not significantly different (*F*-test: $P > 0.05$). As a result, Fig. 9 shows that there was no influence of $EV_{flash,v}$ on $SED_{end}\perp$. Indeed, the slope of all regression lines was not significantly different from zero (*t*-test, $P > 0.05$). Thus the effect of the flash was not simply to alter the heading of the ongoing smooth eye movement. The flash evoked a smooth response that was proportional to position error and independent of the ongoing smooth pursuit eye movement.

Was the modulation of $EV_s\perp$ related to the process of target selection? If the observed effect was due to the selection of the flash as a new target, ignoring the flash should not produce any modulation of the perpendicular eye velocity. To answer that question, we performed an additional control experiment (IFDR, $n = 1260$, see METHODS), which was the same as test trials but subjects ignored the flash. In this situation, we did not observe any consistent modulation of $EV_s\perp$ as shown in Fig. 10 (IFDR, solid blue line). To minimize the influence of the pursuit target on the response, we designed another control situation similar to test trials but in addition to ignoring the flash, the pursuit target was also removed before the flash appeared (IFAR, $n = 1045$, see METHODS). In this condition, the eyes were moving smoothly when the flash was presented in complete darkness. However, we did not observe any consistent $EV_s\perp$ modulation (Fig. 10, solid red line). Thus the flashed target needed to be selected explicitly to evoke a
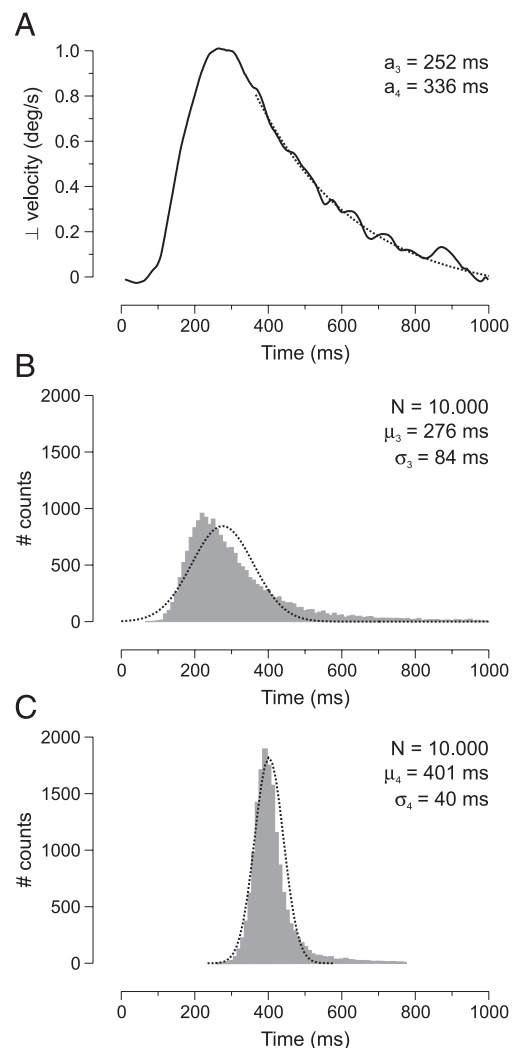

FIG. 7. Response offset for the mean $EV_s\perp$. *A*: example of the exponential fit (dotted line) on the offset of the mean $EV_s\perp$. Values of this particular fit for the decay time constant (a_3) and the delay (a_4) are also indicated. *B*: histogram of the time constant of the smooth response decay (a_3) obtained by the evaluation procedure. Dotted line indicates the fit of a normal distribution on the histogram. Mean (*μ*) and SD (*σ*) of this variable are also given. *C*: histogram of the delay (a_4) obtained by the evaluation procedure. Normal distribution fit (dotted line) and mean (*μ*) and SD (*σ*) of this variable are shown.

A

$a_3 = 217$ ms
$a_4 = 203$ ms

B

$N = 10.000$
$\mu_3 = 210$ ms
$\sigma_3 = 25$ ms
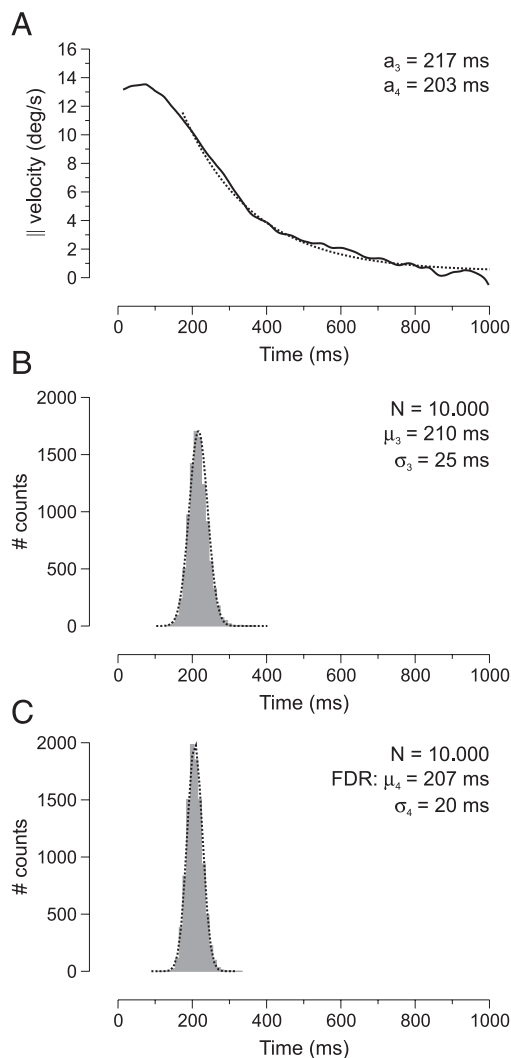
C

$N = 10.000$
FDR: $\mu_4 = 207$ ms
$\sigma_4 = 20$ ms

FIG. 8. Response offset for the mean $EV_s\|$. *A*: example of the exponential fit (dotted line) on the offset of the mean $EV_s\|$ is shown. Values of this particular fit for the decay time constant (a_3) and the delay (a_4) are indicated. *B*: pooled histogram of the time constant of the smooth response decay (a_3). Normal distribution fit (dotted line) and mean (μ) and SD (σ) of this variable are shown. *C*: histogram of the delay (a_4). Normal distribution fits (dotted lines) and means (μ) and SD (σ) of this variable are shown.

smooth response. Finally we confirmed by presenting a flash after the extinction of the fixation target (FAF, see METHODS; $n = 1062$; Fig. 10, solid green line) that there is no response during fixation even if the fixation target is no longer present.

DISCUSSION

General discussion

We used a 2D paradigm (Blohm et al. 2005) that allowed us to present a position error with no velocity (flash) to the oculomotor system and study the smooth eye movement response. Our results show that a target flashed during ongoing smooth pursuit evokes a smooth eye movement toward the flash. In contrast, the same flash stimulus did not evoke any smooth eye movement during fixation, which is consistent with previous findings (Epelboim and Kowler 1993). Furthermore, the velocity of the evoked smooth eye movement was proportional to the position error of the flash (Barnes et al. 1995) and
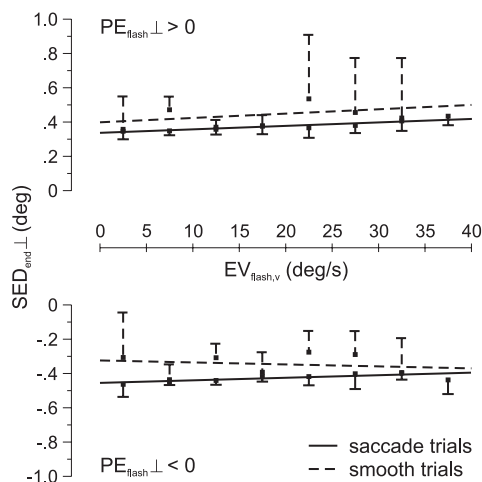

FIG. 9. No effect of ongoing smooth pursuit on evoked SEMs. Influence of smooth pursuit velocity at the moment of the flash $EV_{flash,v}$ on the magnitude of the $EV_s\perp$ modulation. Similarly to Fig. 3C, we used the total perpendicular smooth eye displacement ($SED_{end}\perp$) as an indicator of the potential effect. Saccade trials (black, solid line) and smooth trials (dashed black line) were separated. *Top* and *bottom*: positive and negative $PE_{flash}\perp$, respectively. Regression lines were performed on raw data. They were significantly offset from baseline (*t*-test, $P < 0.001$), but their slopes were not significantly different from 0 (*t*-test, $P > 0.05$). Squares and whiskers indicate mean and SE.

was present for the whole range of tested position errors ($\leq 10°$). The response was independent of the velocity of the ongoing smooth pursuit eye movement and did not depend on the occurrence of saccades. Instead, the two necessary conditions to evoke the smooth eye movement were an ongoing smooth eye movement and the selection of the flash as the new goal. Altogether, this is a striking and direct demonstration of a position input to the smooth pursuit system.

We reported here a short latency (~ 85 ms) modulation of the eye velocity evoked by the presentation of a peripheral flash during ongoing smooth pursuit. Although the response onset latency was very short, this delay was compatible with previously observed data describing the response of the smooth pursuit system to a change in the visual stimulus (Behrens et al. 1985; Ferrera and Lisberger 1995; Knox 1996, 1998; O'Mullane and Knox 1999; Pola and Wyatt 1985; Rashbass 1961; Robinson 1965).

The comparison of the decay time constants for the evoked and ongoing smooth eye movements (276 vs. 210 ms) showed
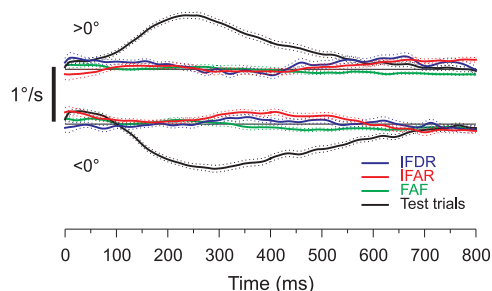

FIG. 10. SEM modulation requires flash target selection. Similarly to Fig. 4B, the mean $EV_s\perp$ was presented over time after flash onset for positive and negative $PE_{flash}\perp$ values independently. Ignore flash during ramp control trials (IFDR, solid blue), ignore flash after ramp control trials (IFAR, solid red), flash after fixation control trials (FAF, solid green), and test trials (solid black) are shown for comparison.

a similar behavior for both components. Clearly, this decay time constant is much longer than the classically reported offset time constant of ~100 ms for the smooth pursuit system (Becker and Fuchs 1985). This could be due to the lack of a visual fixation target in the memory period, which could make it difficult for the system to slow down. In addition, the neural velocity command could still be (at least partially) active, again because of the lack of a sustained stop signal. Indeed, it has been shown that in a similar condition when the target is suddenly stabilized on the retina, the smooth pursuit response decays with time constants up to >500 ms (Pola and Wyatt 1997), depending on the instruction. When passively viewing the stimulus, the same authors still report decay time constants of ~300 ms.

The simplest explanation for the smooth eye movements evoked by the flash was to hypothesize that the flash induced a deviation of the smooth pursuit trajectory. Such deviation might have resulted from a weighted average of the ramp and flash target positions, as this is the case for saccades to extended targets (Vishwanath and Kowler 2003), which are directed to the center of mass. However, our data clearly rule out this deviation from the pursuit trajectory hypothesis because we showed that the evoked smooth eye movements ($SED_{end}\perp$) were independent of the initial smooth pursuit velocity ($EV_{flash,v}$, see Fig. 9). Afterimages have also been reported to influence smooth eye movements (Heywood and Churcher 1971; Yasui and Young 1975). However, in our experiment, a flash-induced afterimage would move parallel to the ongoing smooth pursuit movement, which is inconsistent with the perpendicular smooth eye movement modulation we observed here.

Smooth pursuit gain control

It has been suggested that the modulation of smooth pursuit eye movements due to brief perturbations in target velocity during ongoing smooth pursuit might be due to a gain control element in the smooth pursuit system (Churchland and Lisberger 2002; Schwartz and Lisberger 1994). The same gain control element was proposed to explain recent results concerning a novel form of smooth eye movements evoked by stationary visual stimuli in the monkey (Tanaka and Fukushima 1997; Tanaka and Lisberger 2000). Tanaka and Lisberger (2000) reported that during pursuit preparation, stationary cues evoked smooth eye movements and postulated that this observation was a side effect of the activation of the pursuit gain control element. A priori, a similar mechanism could explain our results. However, the velocity of the evoked movements decreased with cue eccentricity in their study, whereas it increased with position error in our data. More importantly, the smooth movements were always directed away from the cue in their study, whereas here they were directed toward the flash. Thus it is unlikely that our data can be explained only by the same pursuit gain element. The differences between both studies probably result from the different experimental conditions. In the study of Tanaka and Lisberger, the cue was presented during a gap for pursuit preparation, and their monkeys had to suppress saccades. This contrasts with our experiment, where the flash was presented during ongoing smooth pursuit, and orientation saccades were required. Furthermore, when subjects had to ignore the flash

and thus suppress the saccades in our IFDR and IFAR control experiments (similar to the saccadic suppression in the study of Tanaka and Lisberger), no response was observed. This is another argument against a smooth pursuit gain control explanation of our data.

Neural substrate of the position error input to the smooth pursuit system

We reported here that the velocity of smooth eye movements in response to a flash was proportional to position error. The SC encodes a motor map of position error and has been known for a long time to be essential for the control of saccades. Recently, the SC has been proposed to provide the position error input to the smooth pursuit system (Krauzlis 2004). In the cat, sustained electrical stimulation of the SC evokes saccades followed by smooth eye movements (SEMs) (Missal et al. 1996, 2002) that are correlated with the amplitude of evoked saccades (Missal et al. 2002). This suggests that the velocity of SEMs should be proportional to position error. Krauzlis and colleagues showed in the monkey that neurons in the rostral SC encode small position errors (generally <3°) during fixation, saccades, and smooth pursuit (Basso et al. 2000; Krauzlis et al. 1997, 2000). Furthermore, Basso et al. (2000) stimulated electrically as well as inactivated the rostral SC and reported effects on smooth pursuit consistent with the hypothesis that the SC provides a position input to the pursuit system. Position error signals in the SC might not generate smooth eye movements during fixation because the SC output is gated at the brain stem level by omni-directional pause neurons (OPNs). However, Missal and Keller (2002) recently reported that the activity of the OPNs is reduced during smooth pursuit. This could allow the SC output, which encodes position error signals, to influence smooth eye movements only during pursuit and not during fixation (Krauzlis 2004).

This function of the SC in the generation of the observed perpendicular smooth eye velocity modulation due to a position input to the system is also compatible with the role of the SC in target selection (Carello and Krauzlis 2004; Gardner and Lisberger 2002; Horwitz and Newsome 2001a,b; Krauzlis and Dill 2002; Krauzlis et al. 2004; McPeek and Keller 2002a,b, 2004; McPeek et al. 2003). Indeed, in our study, a position stimulus only evoked a robust and consistent smooth pursuit velocity modulation toward the target if the system actively selected this target as its new movement goal. The SC has an important functional role in target selection for both saccades and smooth pursuit; this has been shown in numerous electrophysiological studies (Carello and Krauzlis 2004; Horwitz and Newsome 2001a,b; Krauzlis and Dill 2002; Krauzlis et al. 2004; McPeek and Keller 2002a,b, 2004; McPeek et al. 2003). In addition, it has been shown that microstimulation of the SC biases the target selection process for both saccades and smooth pursuit independently (Carello and Krauzlis 2004) and that the smooth pursuit system automatically selects the same target as the saccadic system (Carello and Krauzlis 2004; Gardner and Lisberger 2002; Krauzlis and Dill 2002). This is fully compatible with our observations and would explain why we did not observe any effect when subjects were asked to ignore the flashed target during ongoing pursuit (IFAR and IFDR controls). We hypothesize that, as a consequence, the

corresponding locus in the SC was not activated when the flash was ignored.

To specifically address the functional role of the SC in the generation of the observed position induced smooth eye movement, we suggest two sets of future electrophysiological experiments. First, recording in the SC during our test trial task, the neural activity should be correlated to the smooth perpendicular eye velocity response. Following our data, this should even be the case if no saccade is triggered. This would be a spectacular result, especially for smooth trials. Second, stimulation of the SC with currents below the threshold to evoke a saccade should deviate the ongoing pursuit trajectory. In this case, the evoked perpendicular smooth eye velocity should be related to the location of the stimulating electrode in SC coding position error.

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