Exp Brain Res (2007) 181:307–320
DOI 10.1007/s00221-007-0933-0

RESEARCH ARTICLE

Behavioral analysis of predictive saccade tracking as studied by countermanding

Wilsaan M. Joiner · Jung-Eun Lee · Mark Shelhamer

Received: 21 November 2006 / Accepted: 27 February 2007 / Published online: 3 May 2007

Abstract The ability to make predictive saccadic eye movements is dependent on neural signals that anticipate the onset of a visual target. We used a novel paradigm—based on the saccade-countermanding task—as a tool to investigate rhythm saccade pacing and to provide information on the mechanisms of predictive timing. In particular, we examined the ability of normal subjects to stop a sequence of periodically paced eye movements when cued by a stop signal that was presented at different times with respect to the last target of the sequence (stop signal delay, SSD). The timing of the stop signal affected the ability to stop the saccadic sequence (make a saccade to a central target rather than to the peripheral alternating targets) in different ways, depending on the preceding tracking behavior. For the same SSD, subjects cancelled fewer trials during predictive tracking (promoted by tracking targets alternating at a fast pacing rate, 1.0 Hz) than during reactive tracking (tracking alternating targets at a low pacing rate, 0.2 Hz). In addition, on non-canceled trials, there was an increase in the delay of the corrective saccade to the central target with increasing SSD for pacing at 0.2 Hz, but the timing of the corrective saccade remained near constant for 1.0 Hz pacing. In examining the timing between movements, we estimate that the repetitive GO process that drives the saccades during *predictive* tracking begins earlier and has a shorter duration than the repetitive GO process during *reactive* tracking. These behavioral results provide further insight into the initiation process of predictive responses. In particular, the reduced reaction time and the corresponding short duration of the predictive process may result from a faster accumulation of neuronal discharge to a relatively fixed threshold.

Keywords Saccade · Prediction · Countermanding · Stop signal · Motor control

W. M. Joiner (✉) · J.-E. Lee · M. Shelhamer
Department of Biomedical Engineering,
The Johns Hopkins University, School of Medicine,
720 Rutland Avenue/606 Traylor Bldg.,
Baltimore, MD 21205, USA
e-mail: wjoiner@bme.jhu.edu

M. Shelhamer
Department of Otolaryngology, Head & Neck Surgery,
The Johns Hopkins University, School of Medicine,
Baltimore, MD 21287, USA

Introduction

Previous studies of repetitive saccadic eye movements in normal human subjects have demonstrated that either reactive or predictive tracking can be induced, depending on instructions and the frequency of the target pacing (Stark et al. 1962; Ross and Ross 1987; Zambarbieri et al. 1987; Shelhamer and Joiner 2003; Isotalo et al. 2005). Saccadic tracking of targets at a low pacing frequency (0.2 Hz) usually promotes reactive behavior: the eye movement occurs after the target jump with a latency of approximately 150–220 ms. Tracking at a high pacing frequency (1.0 Hz) typically encourages predictive behavior: the saccade usually occurs with a reduced latency (less than what is required for processing visual information, approximately 80 ms), or before the target jump, resulting in a negative latency (<0 ms).

Our earlier work demonstrated a behavioral phase transition between reactive and predictive eye tracking of alternating targets (Shelhamer and Joiner 2003). As noted above, when subjects tracked the targets at a low pacing frequency (0.2 and 0.3 Hz) they made reactive eye

movements. As pacing frequency monotonically increased, subjects made an abrupt transition at a critical frequency (near 0.7 Hz) to a predictive response and continued this behavior at the higher pacing frequencies (0.9 and 1.0 Hz). In addition, we showed that predictive tracking at the higher pacing frequencies is mediated by an internal clock (Joiner and Shelhamer 2006). That is, when subjects track a periodic visual stimulus alternating at a high rate (e.g., 1.0 Hz), they use an internal estimate of stimulus timing to pre-program the eye movement timing. This means that during predictive tracking the process that drives the saccadic response must start before a target appears.

The above results imply that we might be able to determine the timing of this process (the GO process) with the proper paradigm. Countermanding is one such paradigm, as it looks at the ability to stop or *alter* a response based on the relative timing of the prevailing GO process and an unexpected stop signal. We use a paradigm that is based on countermanding to explore the timing of the GO process involved in generating sequences of predictive saccades.

The countermanding task requires subjects to withhold a planned movement in response to a variably delayed stop signal (Logan and Cowan 1984; Logan 1985, 1994). Initial experiments utilizing this paradigm examined responses to single trials. As an example of such a study (Logan et al. 1984), subjects responded to a visual stimulus, presented intermittently, by pressing a key. Occasionally, and randomly, a stop signal was presented (a tone), signaling the subject not to respond on that trial. The tone was given at different times with respect to the onset of the visual stimulus to determine the effect of the timing of the stop signal on the ability to inhibit the response.

Previous countermanding studies have also utilized single saccadic eye movements made in response to peripheral targets (Hanes and Schall 1995; Hanes and Carpenter 1999; Asrress and Carpenter 2001; Kornylo et al. 2003; Paré and Hanes 2003; Curtis et al. 2005). These studies reported that (1) the ability to cancel the eye movement decreased as the delay of the stop signal increased and (2) this decrease typically followed a sigmoid relationship with the delay (represented by the logistic function). These experiments have been modeled as a race between a ''GO'' process (initiated by the appearance of an eccentric target) and a ''STOP'' process (initiated by the stop signal such as an auditory cue), to a pre-specified threshold. A movement is triggered once the ''GO'' process finishes (by reaching threshold). The latency of the eye movement reflects the duration of this GO process. A movement is cancelled if the STOP process finishes before the GO process. (To be true to the original race model formulation, we will refer to the execution of a planned saccade as the completion of the GO process and the canceling of a planned saccade the completion of the STOP process.) The process that initiates a single reactive saccade has also been modeled as a linear accumulation to threshold with a growth rate (the inverse of the saccade latency) that varies from movement to movement (LATER model: Carpenter and Williams 1995; Reddi and Carpenter 2000). This model has been used to interpret data obtained from the countermanding task (Hanes and Carpenter 1999) and predicts the probability of successfully inhibiting a saccadic eye movement as a function of stop signal delay as well as the latency distribution for non-cancelled saccades. In addition, this rise-to-threshold behavior has been identified in single-neuron recordings of the frontal eye fields and superior colliculus (Hanes and Schall 1996; Hanes et al. 1998; Paré and Hanes 2003) and supports the theory of a trigger threshold in movement initiation; saccadic eye movements are initiated when the neural activity reaches a specific fixed threshold level.

The studies cited above examined and modeled the effects of various stop signals in the countermanding of single (non-repetitive) reactive eye movements. Only one prior study has examined the countermanding of anticipatory eye movements, in this case smooth pursuit (Jarrett and Barnes 2003.) In the present report the countermanding paradigm is applied to saccadic tracking at predictive and reactive pacing frequencies, 1.0 and 0.2 Hz, respectively. Our goal is to use countermanding as a tool to investigate the timing of the saccade-initiation process in these two tracking conditions. We discuss how the differences in this initiation process may be reflected in the neural activity of the superior colliculus and frontal eye fields during the two tracking conditions.

Methods

General

The eye movements of four subjects were recorded while they performed a saccade tracking task. Informed consent, according to the local institutional review board, was obtained from each participant. Data were acquired on a PC-compatible Pentium 166-MHz computer running real-time experiment control software developed in-house. Horizontal eye movements were recorded with a Series 1000 Binocular Infrared Recording System (Microguide), at a sampling rate of 1000 Hz. Prior to data acquisition the system was calibrated by having subjects fixate targets at known locations. Subjects were seated in a stationary chair, and head movements were restricted with a chin rest.

Experimental paradigm

A single trial tested one of the pacing frequencies (0.2 or 1.0 Hz) at one of nine stop signal delays (SSD of –300, –150, –100, –50, 0, 50, 100, 150, and 300 ms). Subjects completed 10 trials at each SSD for the two pacing frequencies (180 trials total). The pacing frequency of the target, the number of cycles, and the SSD were chosen randomly from trial to trial; sessions were randomly divided into 10 blocks (approximately 20 minutes each) of 18 trials each. Between each trial subjects were given a one-minute break. Subjects completed two blocks a day over five days. As depicted in Fig. 1A, each trial began with a period of fixation (2 s) at the center target (0°). Next, peripheral targets (±15°) alternated at either 0.2 or 1.0 Hz for 5 to 8 cycles (10–16 eye movements). At the end of the sequence, the stop signal (the center fixation light) was illuminated at one of the SSD times with respect to the last target jump of the pacing sequence. (The center target can be described in many ways: the stop signal, stop target, or countermanding target. The terms are interchangeable but we will generally call it the ''stop signal.'') Figure 1B displays the target trajectory for the example described in Fig. 1A.

As depicted in Fig. 1A and B, if the SSD is 300 ms then the center target comes on 300 ms *after* the last target jump; if the SSD is –300 ms then the center target comes on 300 ms *before* the last target jump. A sequence is canceled if, on the last target jump, the subject makes a saccade to within 5° of the center target (the countermanding target). This is depicted in Fig. 1C; the sequence is cancelled if the subject makes a saccade (beginning at –15°) landing between –5° and 5°. A sequence is not canceled if the subject makes an eye movement past the center stop target (that is, with a magnitude greater than 20°), in the direction of the next target of the pacing sequence. For the example presented in Fig. 1C, a non-cancelled sequence would result from a saccade landing between 5° and 15°. Subjects were instructed to ''look at the targets'' and to ''quickly look at the center target when it comes on.''

Deviation from previous countermanding studies

Unlike previous countermanding studies, our stop signal does not tell the subject to cancel a saccadic eye movement but rather to make a saccade to a different target. In other words, the illumination of the center light is a signal to ''stop pacing'' not to ''stop making all saccades.'' These previous studies estimated the duration of the STOP process (the stop signal reaction time, SSRT) by comparing the *inhibition function* (the probability of the subject canceling a planned movement, as a function of SSD) and the cumulative latency probability distribution from trials at which the stop signal was not given. The relative time shift between the two curves gives an estimate of the time between the onset of the stop signal and the crossing of the threshold. Though we did determine the *inhibition function* for each subject and pacing condition, we did not calculate the stop signal reaction time for several reasons: First, our definition of a cancelled sequence is the occurrence of an

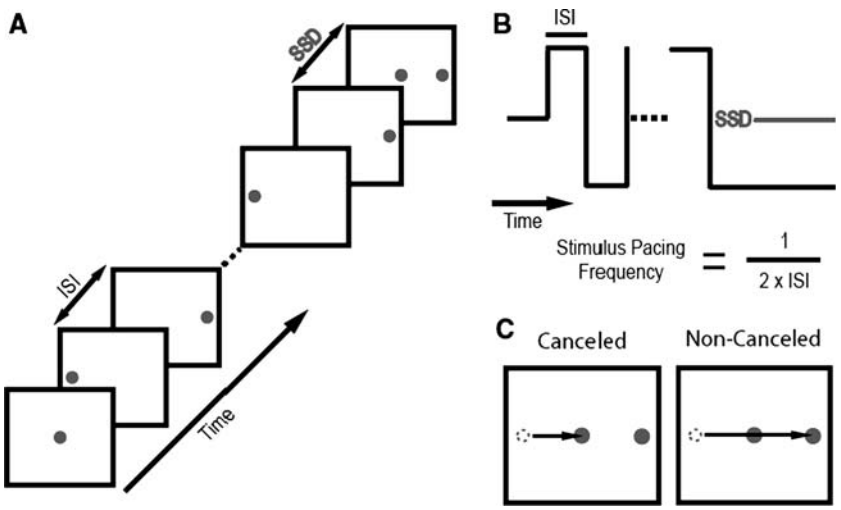

Fig. 1 Sequence of target displays for a single trial. (**A**) Each trial began with a period of fixation at the center target. Following this, the center target was extinguished and the peripheral targets alternated at either 0.2 or 1.0 Hz. After a random number of target jumps the center stop target was again illuminated, after a delay with respect to the last target jump of the sequence (Stop Signal Delay, SSD). (**B**) The target trajectory for the example illustrated in **A**. (**C**) The arrow represents the saccade that occurs after the stop target. On non-cancelled sequences subjects made a saccade to the next peripheral target of the sequence despite the stop signal. On cancelled sequences subjects made a saccade to the center target

eye movement to a *different* target than the ones in the ongoing stimulus sequence, but an eye movement nonetheless. As stated above, prior studies sought to cancel the movement totally and as a result the calculation of a stop signal reaction time *per se* is appropriate. In this report we only wish to show qualitatively that the difference in the cumulative latency probability distributions at the two pacing rates (Fig. 3) supports the difference we see in the inhibition functions for the two tracking behaviors (Fig. 5). Second, the number of trials at each SSD (10 trials) was insufficient to statistically validate an estimate of stop signal reaction time, and obtaining more trials would prove experimentally difficult. (The data presented were gathered from ten 20-minute blocks over 5 days of testing for each subject.) Finally, we do assume that the appearance of the center light (the countermanding cue) initiates an internal STOP process, but the estimation of its duration is not necessary for interpreting the results. That is, we can assume a STOP process as in Fig. 2, but the difference in countermanding behavior between the two tracking modes can be attributed to differences in the rise and timing of the repetitive GO process driving the saccades. It is not necessary to consider the reaction time of the stop signal in our interpretation.

Instead of calculating the SSRT, we were specifically interested in estimating another unobservable parameter of our countermanding task: the duration of the GO process during predictive tracking. The duration of the GO process during reactive tracking can simply be estimated from the latency of the second saccade of the eye movement sequence. (At the beginning of repetitive tracking the subject has no prior information as to the timing of the stimulus and it follows that the first two saccades made are reacting to rather than predicting the alternating stimulus (see Fig. 7).) However, this estimation method cannot be utilized during predictive tracking; when saccades occur with a low or negative latency (saccade occurs before the stimulus) other methods must be utilized to estimate the GO process. The purpose of the inhibition functions in this study was to determine if a given SSD yields different effects depending on whether the subject is making a sequence of reactive saccades or a sequence of predictive saccades. This information can then be used to determine the timing and duration of the repetitive GO process (described below) that drives the saccades to the pacing targets. Additionally, unlike the SSRT estimate, there is enough data (10 trials at the 9 SSDs, 90 trials) to statistically validate these GO process estimates.

In addition to estimating the duration of the GO processes we were also interested in determining how long it took to correct for a saccade to the wrong spatial location and whether that correction time varied according to the relative timing of the stop signal. That is, we wanted to determine the time required to correct for the non-cancelled movement—how long (inter-saccade interval) it took to correct for such a movement by making a saccade to the countermanding center target—during the two tracking conditions.

Data analysis

Analysis of eye-tracking data was done off-line. Eye velocity was calculated using a four-point digital differentiator based upon a least-squares derivative algorithm (Savitzky and Golay 1964). This iterative method fits a third-order polynomial to each data point and the preceding and following two values, and then finds the derivative of the fitted polynomial. This method introduces less noise than conventional differentiators. Saccade onset was estimated as the time point eye velocity exceeded 60 deg/s. Saccade latency was the difference between the onset of the primary eye movement and the onset of the target in

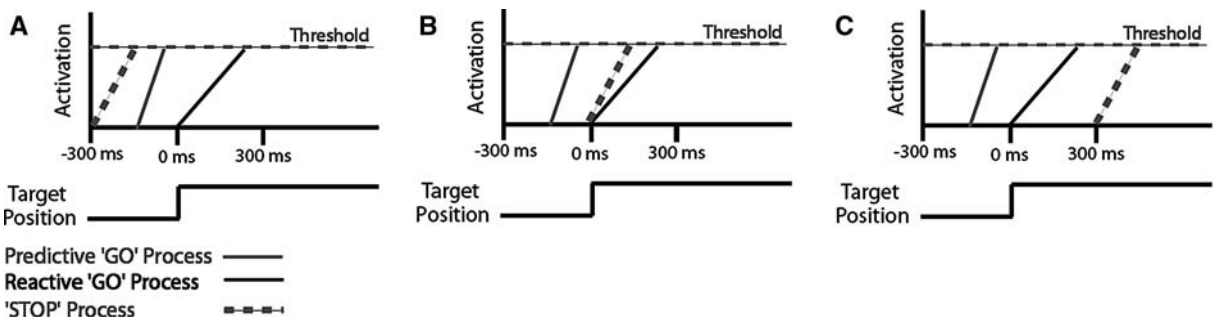

Fig. 2 Race model depiction of the observed behavioral results. The activation of the GO process for predictive saccades (gray solid line) begins before stimulus onset and increases faster than for the reactive case (*black solid line*). As a result, the timing of the STOP process (*thick gray dashed line*) affects the countermanding of predictive and reactive saccades differently (for simplicity, the analysis assumes that the rate of rise to threshold is constant). When the stop signal is given at the time of pacing stimulus onset (SSD of 0 ms), reactive saccades are cancelled whereas predictive saccades are not. **B** When the stop signal is given 300 ms before or after the pacing stimulus (SSD of –300 or 300 ms) both movements are either cancelled (**A**) or executed/non-cancelled (**C**)

each trial. The inter-saccade interval was the time between consecutive primary saccades. Many previous reports (see Goossens and Van Opstal 1997; Honda 1997) defined the inter-saccade interval as the time between the offset of one saccade and the onset of the next saccade. We chose to examine the time between consecutive saccade onsets because this measure allows a direct comparison between stimulus and response timing. Furthermore, it is the *initiation* time of saccades that is of interest to us, and the timing of successive initiations is best represented by comparing successive onset times.

Interpretation in terms of the race model

The behavioral results of the countermanding task have typically been depicted in terms of the race model (Logan et al. 1984). This framework has been successful in examining the decision process guiding different movement types (Corneil and Elsley 2005; Liston and Krauzlis 2005), and the effects of different countermanding cues (Cabel et al. 2000) and stimulus characteristics (Hanes and Carpenter 1999). This is also the framework we will use to interpret our behavioral results. The race model posits a theoretical race, to a constant threshold, between two processes: a GO process initiated by the appearance (or anticipated appearance) of a stimulus, and a STOP process initiated by a cue to stop the movement. If the STOP process finishes first (by reaching threshold first), the movement is cancelled. If the GO process finishes first, a movement is initiated once the threshold is crossed. The race model interpretation of our results is depicted in Fig. 2. As suggested by latency histograms (Fig. 3, see ''Results''), activation of the GO process during predictive tracking (gray solid line) begins before each jump of the target stimulus, while activation of the GO process during reactive tracking (black solid line) begins at the time of the

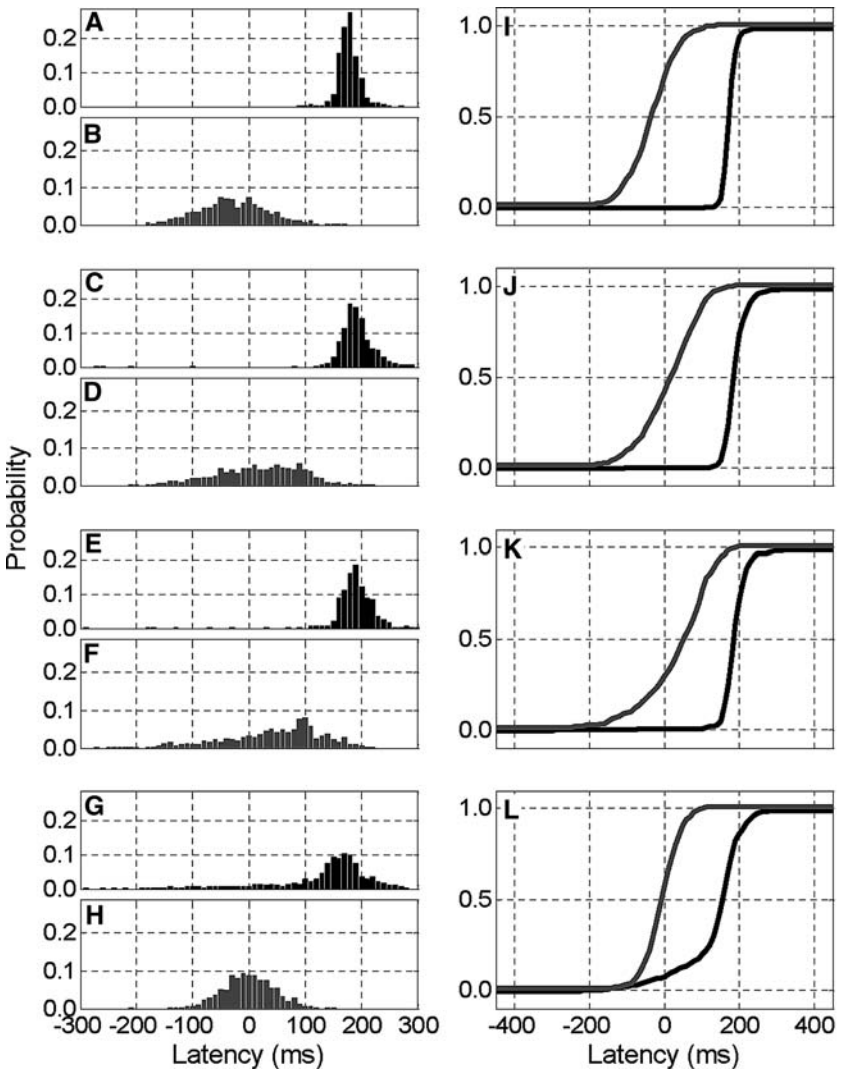

Fig. 3 **A-H** Saccade latency probability distributions for the four subjects (black—0.2 Hz pacing, gray—1.0 Hz pacing). **I–L** The cumulative latency probability plots obtained from the probability distributions presented in the left column. For example, panel **I** represents the data in panels **A** and **B**

stimulus jump (0 ms). In the figure, the stop signal (thick gray dashed line) is given at three different times (SSD of –300, 0, and 300 ms, panels A, B, and C). (In this graphical representation the activation of the STOP process is depicted to (1) increase at a constant rate and (2) be the same for both pacing rates. For reasons discussed above, we did not estimate of the duration of the STOP process, but we depict this behavior in Fig. 2 to be true to the original race model formulation.) If the stop signal is given at the same time as the stimulus jump (panel B) then reactive saccades are cancelled whereas predictive saccades are not. That is, the STOP process finishes before the *reactive* GO process but after the *predictive* GO process. If the stop signal is given 300 ms before (panel A) or after (panel C) the pacing stimulus, the STOP process finishes either before (cancelled) or after (non-cancelled) the GO process, respectively.

Results

Experimental findings

Figure 3 presents data for all subjects at the two pacing frequencies. Histograms of saccade latency are plotted in the left column (black—0.2 Hz, gray—1.0 Hz) in panels A–H. The distributions were formed from the saccade latency during steady-state tracking for all trials (i.e., excluding the first three and last saccades) at each pacing frequency (approximately 700 saccades for each pacing frequency). The corresponding cumulative distributions are plotted in the right column for each subject (panels I–L). The separation between the saccade latency histograms obtained at the two pacing rates results in an obvious gap (between –150 and 100 ms) between the cumulative distributions. One would expect that in comparing the two pacing rates, the biggest difference in the ability to cancel an eye movement would occur within this timing range. As an example, consider panel I. If the stop signal is given at the same time as the next target jump (SSD of 0 ms), then that SSD should theoretically cancel a smaller percentage of trials for 1.0 Hz than for 0.2 Hz pacing, because the cumulative probability of a saccade at 1.0 Hz is greater. However, if the stop signal is given where the two plots are equivalent (such as -300 ms in panel I), then the ability to cancel the next movement should be similar for the two pacing rates.

The results for subject A are shown in Fig. 4 for trials at three different SSDs (–300, 0, and 300 ms, top, middle, and bottom rows, respectively) at the two pacing frequencies (0.2 and 1.0 Hz, left and right columns). LED target position is shown as a thin black line and eye position as a thick gray line in each panel. The black dashed line in each panel marks the onset of the stop signal (the central target) for each trial. At the SSD of –300 ms the subject is able to cancel the next saccade of the ongoing sequence at both pacing frequencies (panels A and D) by making an eye movement to the center target. This can clearly be seen in the smaller panels of Fig. 4 which display, on an expanded time scale, target and eye positions between –0.5 and 1.5 s

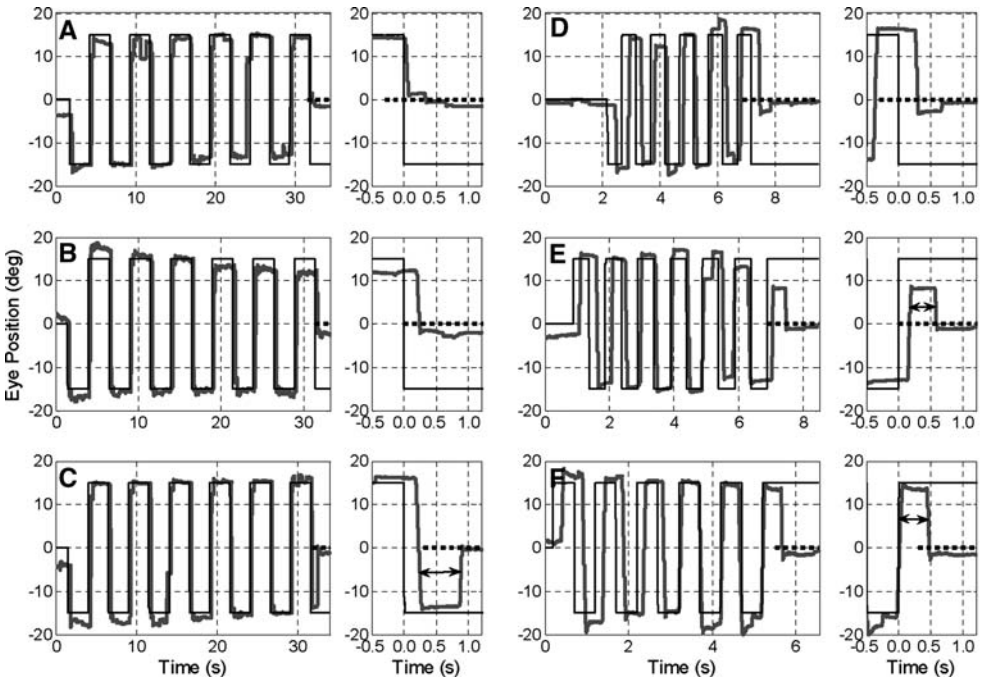

Fig. 4 Eye movement data for subject A at 0.2 Hz (**A-C**) and 1.0 Hz (**D-F**) pacing. Results for trials at three SSD are shown: –300 (**A, D**) 0 (**B, E**) and 300 ms (**C, F**). The smaller panels are detailed plots of target and eye position from –0.5 to 1.5 s with respect to the last target jump of the sequence. Target position is shown as a thin black line and eye position as a thick gray line in each plot. The black dashed line represents the stop signal (appearance of the center target, 0°). The double arrow in panels **C**, **E**, and **F** marks the length of the inter-saccade interval (time required for correction) when the sequence was not cancelled

with respect to the last eccentric target jump of the sequence. At the SSD of 0 ms the subject is able to cancel the movement at 0.2 Hz pacing (saccade is made to the central countermanding target, panel B) but is unable to do so at 1.0 Hz pacing (saccade is made past the countermanding target toward the next expected pacing target, panel E). At the SSD of 300 ms the subject is unable to cancel the movement at either 0.2 or 1.0 Hz pacing (panels C and F). In all non-cancelled trials, however, the subject eventually makes a corrective saccade to the center target, after a delay marked by the double arrows. (The double arrows in panels C, E, and F are discussed below in relation to Fig. 6.)

Derivation of inhibition function from data

Figure 5 displays the cumulative latency distributions and countermanding results for all subjects at 0.2 (top row) and 1.0 Hz (bottom row) pacing. (Each column represents a single subject.) The solid lines in each panel are the cumulative latency distributions displayed in the right column of Fig. 3. The thick **x** marks the proportion of trials (out of 10) that was cancelled for a given SSD. In other words, the **x** at 0 ms and 0.2 probability in panel A signifies that this subject cancelled the final eye movement of the sequence in 2 out of the 10 trials tested at 0.2 Hz pacing with a SSD of 0 ms. As demonstrated in previous countermanding studies, the relationship between the ability to cancel the movement and the SSD can be represented by the logistic function:

$$y = \frac{1}{1 + ae^{-bx}}.$$

The dashed lines presented in Fig. 5 are the logistic function fit to the proportion of trials cancelled at each SSD for each subject and pacing condition. (The r^2 values for all logistic function fits were >0.95.) As described in ''Methods'', these dashed line curves are the *inhibition functions* for each subject. That is, they relate the probability of inhibiting the movement to the stop signal delay. In all cases, these inhibition functions are to the left of the corresponding cumulative latency distributions, indicating the delay between the initiation and completion of the STOP process (the SSRT).

We were interested in how long it took to correct for a non-cancelled movement at the two different pacing rates. Comparison of correction time allows us to further determine the effect of tracking behavior on canceling the sequence of eye movements. On non-cancelled trials subjects corrected for the erroneous movement (made to the next expected pacing target) by then making a saccade to the stop signal (center countermanding target). That is, there was an interval of time between the non-cancelled movement to the peripheral target and the corrective saccade to the center target. Examples of this correction time are marked by the double arrows in Fig. 4D–F. Figure 6 plots the inter-saccade interval for non-cancelled trials at each pacing frequency (black—0.2 Hz, gray—1.0 Hz) separately for each subject (panels A–D). (Only SSDs that resulted in non-cancelled movements at both pacing

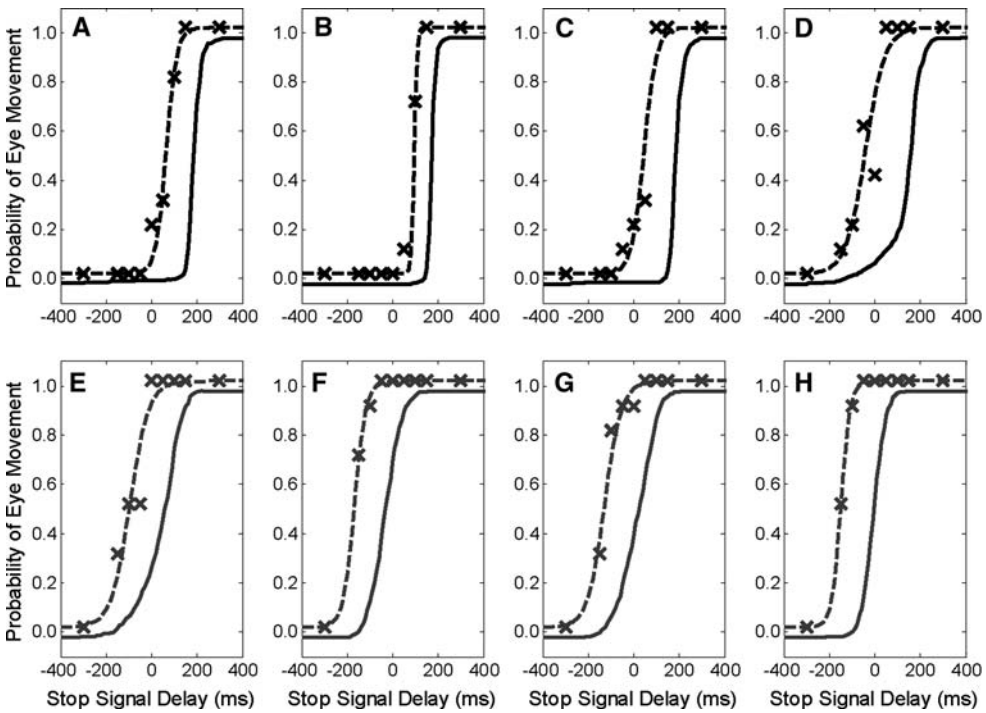

Fig. 5 Behavioral results for all subjects (each column represents one subject) during the countermanding task. **A-D** Cumulative latency probability plots (*solid line*) and inhibition functions (*dashed line*) for the four subjects at 0.2 Hz pacing; **x** represents the proportion of canceled trials at the respective stop signal delay. **E–H** Results for the same subjects at 1.0 Hz pacing. Interpretation is the same as the panels in the top row

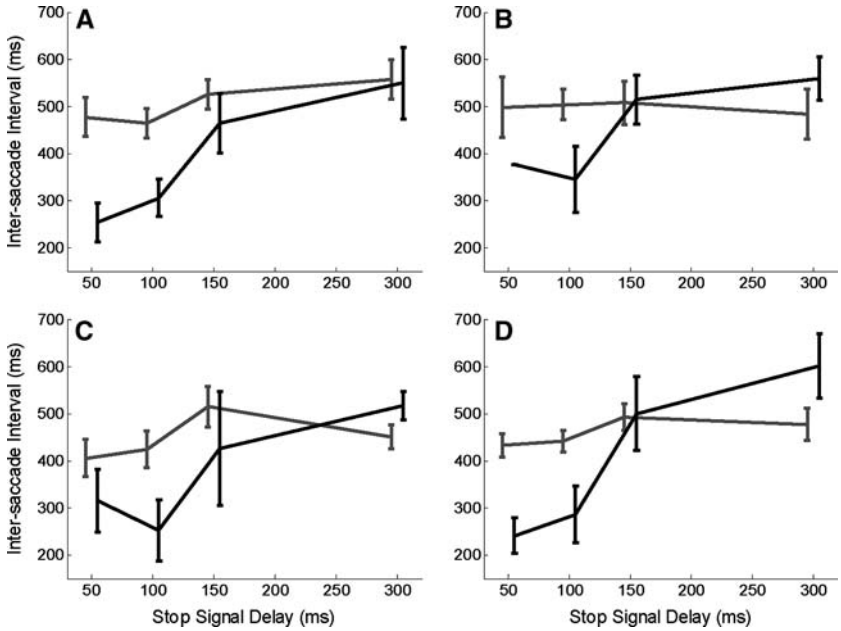

Fig. 6 The inter-saccade interval for the correction on non-canceled trials at SSD of 50, 100, 150, and 300 ms. Each panel displays the results for one subject. The error bars represent one standard deviation from the mean. The subjects in panel B only made one non-canceled movement at the SSD of 50 ms at 0.2 Hz pacing (no error bars for this data point)

frequencies are presented: SSD of 50, 100, 150, and 300 ms.) As shown, during reactive saccades at 0.2 Hz pacing there is a systematic increase in the corrective inter-saccade interval as the SSD increases, for all subjects. However, during predictive saccades at 1.0 Hz pacing the inter-saccade interval is relatively constant at approximately 500 ms. This is a key finding as it demonstrates that the spatial component of the *predictive* movements can be altered by visual information, but this same information cannot change the temporal aspect: subjects delay the corrective movement to the new spatial location (center target) after a preprogrammed interval consistent with the stimulus pacing rate. This is not the case for sequences of reactive movements, where the timing of the corrective movement depends on the time at which the stop signal is presented.

Comparing repetitive GO processes

The results presented above suggest that there is a difference in the timing of the repetitive GO process during reactive and predictive tracking. In addition to their timing, we are also interested in estimating the amount of time required for the process to finish (to reach threshold). We do this by examining the change in the timing between saccades (inter-saccade interval), and saccade latency, during the 1.0 Hz pacing condition.

In Fig. 7 the mean latency of the first five saccades for all trials at (A) 1.0 Hz and (B) 0.2 Hz pacing are plotted for each subject (error bars represent one standard deviation across 90 trials). The black dashed line marks a saccade latency of 80 ms. At 1.0 Hz pacing (Fig. 7A) the initial two movements have a reactive latency (mean latency >180 ms). After the third movement, latency decreases and reaches a predictive value (<80 ms) by the fifth saccade. As expected, at 0.2 Hz pacing (Fig. 7B) saccade latency remains reactive over the first five saccades.

Based on the above results, we see that the first inter-saccade interval at 1.0 Hz pacing is the result of two reactive (high-latency) movements. This reflects the fact that the subject does not know the timing of the stimulus until after at least two saccades (one interval) and so it follows that these first two saccades should be reactive. If over the course of the trial (several target alternations) the timing between saccades did not change then the saccades would continue to be reactive, as in the 0.2 Hz pacing case. However, the saccade latency decreases to a predictive value (Fig. 7A) which indicates a change in the timing between saccades. Thus we examined how this timing between movements—the inter-saccade interval—changed during 1.0 Hz trials. An example for one trial is shown in Fig. 8. Panel A shows the eye and target positions (gray and black traces, respectively) and the first four saccades (black circles) of the trial; panel B shows the corresponding saccade latency (black **x**). In agreement with Fig. 7A, the first two saccades of the trial have reactive latencies (178 and 194 ms) while the fourth movement has reached the predictive state (–56 ms). As noted earlier, the saccade latency reflects the time required for a GO process to finish and trigger the movement. We wished to quantify how the timing between saccades changed, as a reflection of the duration of the GO process that initiates the response. Panels C, D, and E show eye-movement data presented in panel A aligned to the relative time of the saccade. That is,

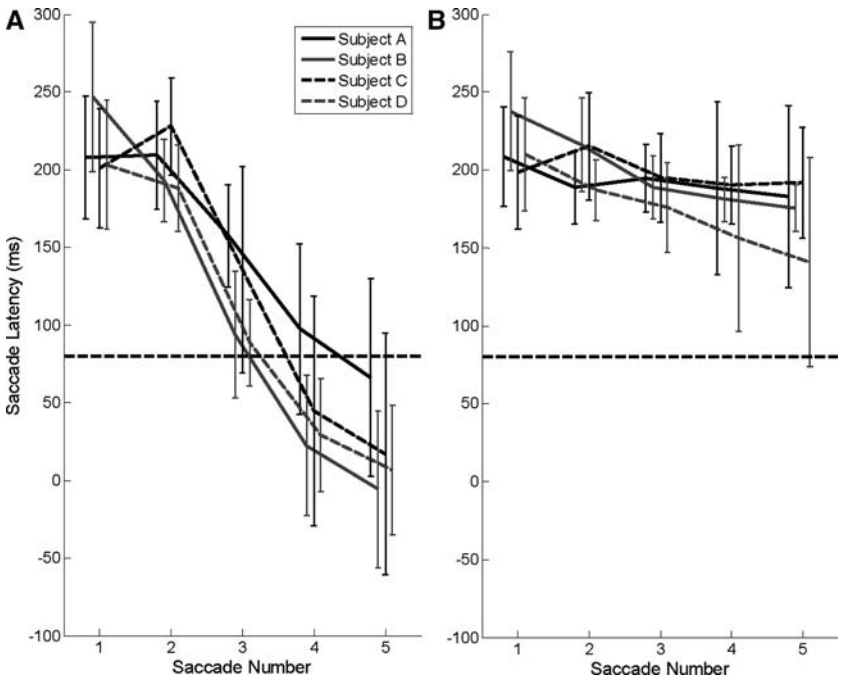

Fig. 7 The saccade latency of the initial five saccades for all trials at 1.0 Hz (**A**) and 0.2 Hz (**B**) pacing. The error bars represent one standard deviation from the mean for 90 trials

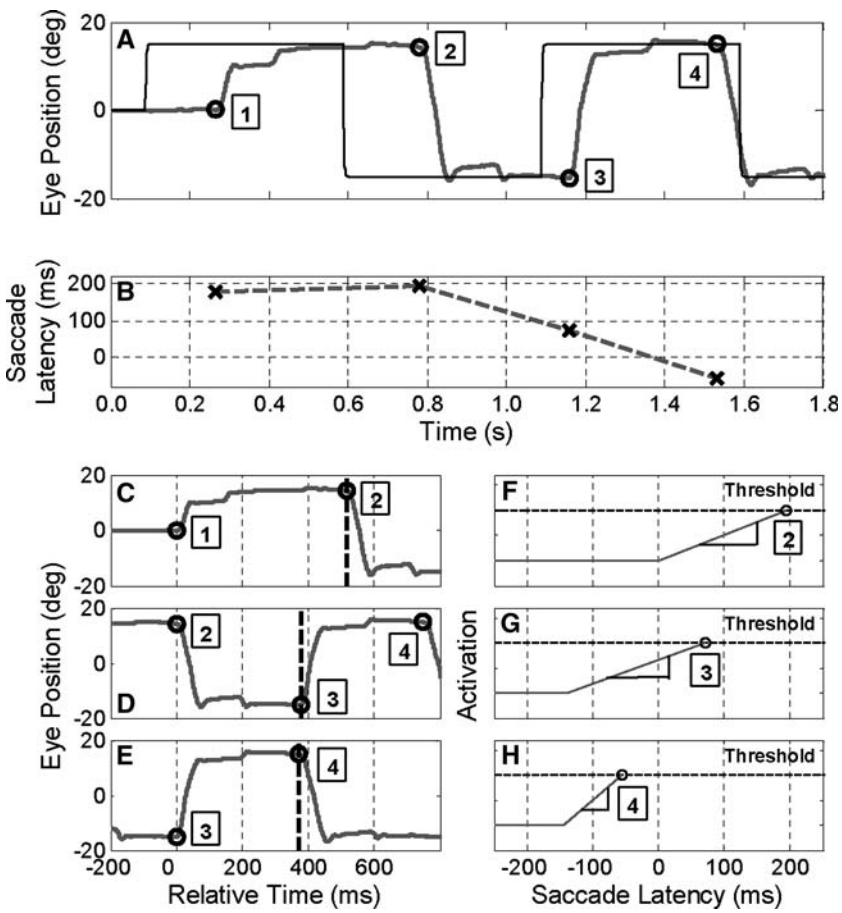

Fig. 8 **A** Eye and target position (*gray and black traces*) for the first four saccades (*black circles*) of a 1.0 Hz pacing trial. **B** The corresponding saccade latency with respect to target onset for each saccade (*black* **x**). **C–E** The eye movement data presented in panel **A** aligned to the relative time of the saccade. For example, in panel **C**, 0 s represents the time of the first saccade, but in panel **D** 0 s marks the time of the second saccade. The *dashed vertical black line* marks the time of the second saccade of the inter-saccade interval in each panel. **F–H** The hypothetical start and finish points of the GO process for the second, third, and fourth saccades of the sequence

in panel C, 0 ms represents the time of the first saccade, but in panel D, 0 ms marks the time of the second saccade. The dashed vertical black line marks the time of the second saccade of the inter-saccade interval in each panel. As shown in panels C, D, and E, over the first four saccades the time between saccades decreases (the black dashed line moves to the left). We infer that after the interval between the two initial reactive eye movements, the change between intervals marks a change in the initiation of the GO process, and the time of the saccade relative to the stimulus jump marks the termination (reaching the threshold). For example, if we assume that the GO process for the second reactive movement begins at the stimulus jump (0 ms in panel F) then the change in the inter-saccade interval represents the GO process being activated earlier relative to the stimulus jump. This is depicted in panels G and H; the initiation point of the GO process begins earlier relative to the stimulus jump based on the cumulative difference between the intervals. The rise of activation of the GO process for the second, third, and fourth saccades is depicted in panels F, G, and H. In these panels 0 ms marks the time of the target jump. In panel F, for the second saccade, the GO process begins at the target jump (0 ms) and ends at the time of the saccade (194 ms). Thus, the duration of the GO process for this saccade is 194 ms. In panel G, the initiation of the GO process is shifted to the left (the second interval is 138 ms shorter than the first so the GO process begins 138 ms earlier than the stimulus jump) and ends at the time of the saccade (72 ms). The estimated duration of the GO process for this saccade is 210 ms (138 + 72). (Though estimated, the GO process duration for this first predictive saccade was not the focus of the analysis for reasons discussed below.) In panel H, the initiation of the GO process is again shifted to the left by 6 ms. (The difference between the third and second intervals added to the difference between the second and first intervals.) The GO process begins 144 ms (138 + 6) before the target jump and ends at the time of the saccade (–56 ms) resulting in a duration of 88 ms. As shown, for the reactive movement (panels F) the duration of the GO process is long. However, by estimating the point of the GO process's initiation using the difference between the inter-saccade intervals, we see that the duration of the GO process for the predictive movement (panel H) is very short.

We compared the estimated duration of the GO process for reactive and for predictive saccades. The first two saccades of each 1.0 Hz pacing trial were reactive, and the third, while occasionally predictive, was not used in further analysis since it occurred at the transition between reactive and predictive behaviors. That is, we only analyzed predictive saccades extracted from a specific sequence: two (or more) reactive saccades (as always the case for the first two movements of the 1.0 Hz trials) followed by two (or more) consecutive predictive saccades. Thus, the analysis estimated the predictive GO-process duration of only those saccades that occurred with latencies of less than 80 ms and were immediately preceded by another predictive saccade. (Any common visual delay time is subtracted out when comparing the initiation of two reactive or two predictive saccades. Therefore, in estimating the predictive GO process durations, we skipped the interval between the second and third saccades since they were triggered by different mechanisms and might have different visual delays.) The probability distributions for the duration of the GO process for the two types of movements are shown in Fig. 9 for all subjects. We performed a Wilcoxon rank sum test (the Mann–Whitney U test) to compare the distributions for reactive movements (Fig. 9, panels A, C, E, and

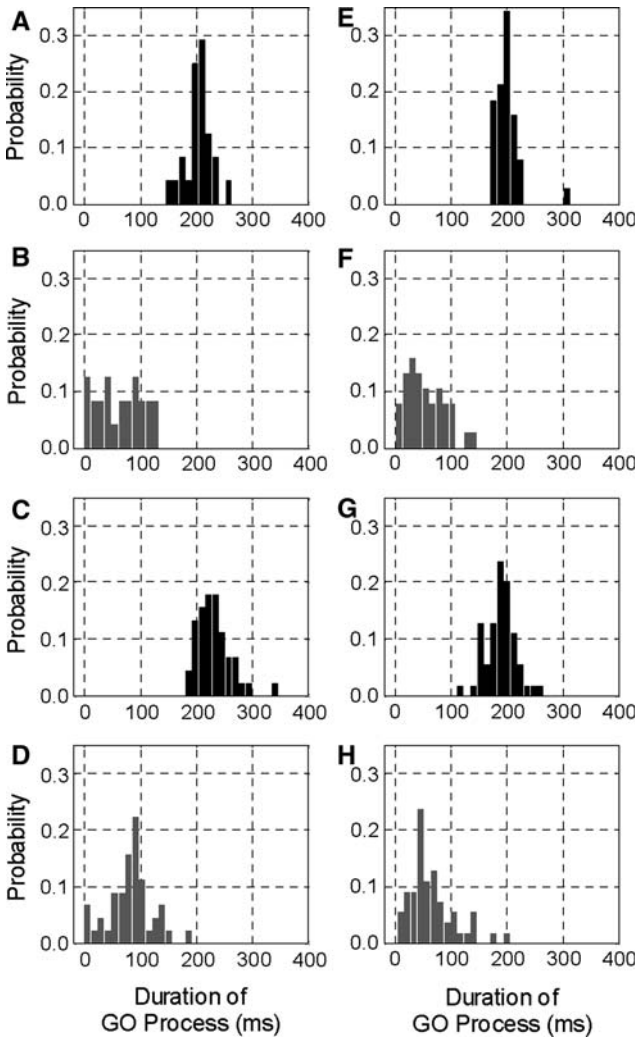

Fig. 9 **A, C, E and G** GO process duration probability distributions for reactive eye movements. **B, D, F and H** GO process duration probability distributions for predictive eye movements. Data is aligned by column and row; for example, the data presented in panels **A** and **B** are for the same subject

G) to those for predictive movements (Fig. 9, panels B, D, F, and H), individually for each subject. The duration of the GO process was significantly shorter for predictive movements than for reactive movements for all subjects (*P* values for subjects A–D: 3×10^{-9}, 6×10^{-14}, 3×10^{-16}, 2×10^{-18}). These results are also summarized in Table 1.

Discussion

In this report we have examined the ability of four normal subjects to modify (by saccading to an unexpected stop target) an ongoing eye movement sequence at two different pacing frequencies, 0.2 and 1.0 Hz. Our goal was to use a modification of the standard saccade-countermanding task to analyze the timing and duration of the repetitive processes that initiate the saccades during reactive and predictive tracking. There were four general findings: (1) The ability to cancel the sequence decreased as the timing of the stop signal relative to the final target in the pacing sequence, the stop signal delay (SSD), increased. (2) For SSDs between –150 and 100 ms, subjects cancelled fewer trials during predictive tracking than during reactive tracking, whereas for SSDs outside of this range the ability to cancel the trial was the same for the two tracking behaviors. (3) On non-canceled trials, the time required for correction (an eye movement back to the center stop target) increased with SSD for pacing at 0.2 Hz, but remained near constant for 1.0 Hz pacing. (4) Steady-state predictive behavior for 1.0 Hz trials was the result of a change in the timing between saccades (the inter-saccade interval). Our analysis of these changes suggests that the GO process during predictive tracking occurs earlier and finishes faster than during reactive tracking.

Relation to previous behavioral studies

The estimated duration of the GO process for repetitive tracking at 0.2 and 1.0 Hz pacing is shown in Table 1. The GO process durations for 1.0 Hz pacing were less than those for 0.2 Hz pacing for all subjects. In addition, both durations are generally less than those reported for single reactive eye movements for human subjects (Hanes and Carpenter 1999; Kornylo et al. 2003). This finding is especially interesting for eye movement tracking at 0.2 Hz pacing. Previous studies (Carpenter and Williams 1995; Dorris and Munoz 1998) have shown that stimulus probability can alter reaction time and neuronal discharge patterns. We hypothesize that the shorter duration of the repetitive reactive GO process could represent the storage of previous timing and spatial information even when making reactive eye movements. This storage of information could therefore be the outcome of some limited dependence on previous trials even when these trials are reactive eye movements.

Table 1 The mean and standard deviation of the GO process duration during 0.2 and 1.0 Hz pacing

Subject	Duration of GO process (ms)	
	0.2 Hz pacing	1.0 Hz pacing
A	203.7 ± 22.1	64.5 ± 38.0
B	200.0 ± 22.5	58.1 ± 34.2
C	231.4 ± 31.8	82.0 ± 38.2
D	189.6 ± 27.1	65.3 ± 40.7

In addition to the difference in GO process duration, the tracking mode also affected the ability to correct for a non-cancelled sequence. When correcting for the non-cancelled movements there was a steady increase in the corrective inter-saccade interval as the SSD increased for 0.2 Hz pacing (Fig. 6, black lines). However, at 1.0 Hz pacing the inter-saccade interval was relatively constant near the inter-stimulus interval of the pacing frequency, 500 ms (Fig. 6, gray lines). This difference was most apparent at the SSD of 50 and 100 ms. For the same SSD, the correction time when making reactive movements was shorter than when making predictive movements; except for subject C, in Fig. 6C (SSD of 50 ms) the black error bars are below the gray error bars for all subjects. Even though the stop signal appeared at the same time relative to the stimulus jump, at 1.0 Hz pacing subjects could not correct for their mistake until after approximately 500 ms. When this result is compared to 0.2 Hz pacing, it is clear that this duration cannot be attributed to long reactive movements back to the center target; the reaction times at 0.2 Hz pacing are faster at the SSD of 50 and 100 ms. These results suggest that at 1.0 Hz pacing the interval between movements is preprogrammed even when a saccade to a new position is required; there may be a dissociation between timing and position when predictably tracking the alternating targets. Therefore, it would be interesting to determine to what extent spatial and temporal prediction are linked in this task.

The positive relationship between the time required for correction (inter-saccade interval) and the appearance of a new stimulus has been shown for reactive eye movements during double-step experiments (Becker and Jurgens 1979). In these experiments, starting from fixation, the target jumps to a new location and then, following a pre-determined delay, steps again (either forward or backward) a pre-determined distance. For example, starting at 0°, the target could jump to 30° and following an inter-step time would jump back to 15°. In the experiment conducted by Becker and Jurgens the inter-step times tested were 50, 100, 150, and 200 ms. They found a negative correlation between inter-saccade interval and *delay* (the difference

between the reaction time of the first saccade and the inter-step time). That is, the time between the initial saccade and the second saccade to the new target position decreased as *delay* increased. (In relation to our study, a large SSD is equivalent to a short *delay* as defined by Becker and Jurgens. For example, the SSD of 300 ms presented in Fig. 4C corresponds to a short *delay* whereas a SSD of 0 ms for the same data is equivalent to a long *delay*.) Though we did not present the inter-saccade interval data in terms of the *delay* defined by Becker and Jurgens, it is clear in Fig. 6 that the largest intervals for correction occurred at the smallest *delays* (i.e., the largest SSDs). Thus, there is a similar effect of inter-step time on the corrective inter-saccade interval for single reactive saccades and reactive saccades made in sequence.

One prior study (Jarrett and Barnes 2003) examined the cancellation of anticipatory movements. Utilizing a paradigm that induces anticipatory smooth pursuit the authors examined the ability of normal subjects to halt these pre-programmed movements at two different target speeds (20 and 40 deg/s). The stop signal was an auditory cue given at four different SSD prior to target onset (–320, –240, –160, and –80 ms). Similar to the results we found for 1.0 Hz pacing, this study found that the ability to inhibit the anticipatory movement decreased as the SSD increased and approached 0 ms. A more recent study (Barnes et al. 2005) found that the duration of the pursuit response to a predictable visual stimulus is pre-programmed. Subjects repeatedly tracked a constant-velocity stimulus presented for a constant duration. After several such trials, during which subjects learned to reduce their pursuit velocity as the stimulus ended, the stimulus duration was unexpectedly increased. On these new trials, eye velocity declined as if the target had actually been extinguished at the previously experienced time, even though the target remained visible; subjects pre-programmed the time of the termination of their responses based on prior experience of their motor action. This result is similar to the finding of a constant time required for correction at 1.0 Hz pacing (Fig. 6): subjects pre-program the timing of the saccadic eye movement response and cannot correct for the error until after this interval.

The findings presented in Fig. 6 are also related to results previously found for manual movements such as typewriting (Logan 1982). In that study experienced typists were presented with a word (three, five or seven letters in length) and instructed to cease typing when a stop signal (a tone) was given. Similar to the difference between inhibition functions for the two pacing rates presented in Fig. 5, the probability of inhibition was higher for keystrokes with longer latencies. (The latency of a keystroke was the time that letter key was pressed with respect to presentation of the word. Thus, the first letter in a word always had shorter latency than the last letter.) For example, it was more difficult to inhibit the first rather than the last letter of a word. In addition, when given the countermanding tone in the middle of typing a word, subjects did not finish typing the word and then stop. Rather, they stopped typing one or two keystrokes after the stop signal. In other words, the units processed in typing were single letters and not words. This is different from our results for 1.0 Hz pacing where subjects were not able to inhibit the last movement when the stop signal was given in the middle of the 500 ms interval; they waited approximately until the 500 ms interval had passed until they made the corrective movement to the center target. This behavioral difference is the result of the timing structure during the repetitive saccade tracking task. The ability to make repetitive predictive saccades to an alternating stimulus is the due to the internalization of the stimulus timing (Joiner and Shelhamer 2006). However, similar to reactive tracking, the single movements made during the typing task are not required to correspond to any specific timing pattern and therefore can be stopped (after a delay) by the stop signal.

Unlike other countermanding studies, in this report we have investigated the ability to stop reactive and predictive eye movements made in sequence. Therefore, some differences from these previous studies are worth mentioning. For example, most previous countermanding experiments (Hanes and Schall 1995; Hanes and Carpenter 1999; Cabel et al. 2000; Asrress and Carpenter 2001; Kornylo et al. 2003; Corneil and Elsley 2005) used an *inhibition function* approach to estimate the stop signal reaction time, the latency of the internal inhibitory signal. (We did not calculate the stop signal reaction time for several reasons as listed in ''Methods''.) In this report we only wished to show qualitatively that the difference in response latency distributions and the resulting cumulative probability distributions (Fig. 3) at the two pacing rates supports the *inhibition function* results we see experimentally (Fig. 5). Second, unlike other countermanding studies, our definition of a cancelled sequence was the occurrence of an eye movement to a different target than the ones in the ongoing stimulus sequence, but an eye movement nonetheless. Prior studies (Hanes and Schall 1995; Hanes and Carpenter 1999; Cabel et al. 2000; Asrress and Carpenter 2001; Kornylo et al. 2003; Corneil and Elsley 2005) sought to cancel the movement totally. However, as noted above, because of this difference we could calculate how long it took to correct for an un-cancelled saccade to the wrong spatial location, and whether that time varied according to the relative timing of the stop signal.

The GO process for predictive movements

The countermanding paradigm has provided insights into the neural basis of the decision process of reactive response

generation (Hanes and Schall 1996; Hanes et al. 1998; Stuphorn et al. 2000; Ito et al. 2003; Paré and Hanes 2003; Curtis et al. 2005; Aron and Poldrack 2006). As described earlier, the decision and response preparation process that leads to the initiation of a motor act has been modeled as a linearly rising decision signal to a pre-specified threshold (Carpenter and Williams 1995; Reddi and Carpenter 2000). The decision signal starts to rise at a constant rate in response to the appearance of a target, and triggers a reactive movement once the threshold is reached. Neural activity in the superior colliculus (SC) and frontal eye fields (FEF) has been shown to demonstrate this rise-to-threshold pattern (Hanes and Schall 1996; Hanes et al. 1998; Paré and Hanes 2003).

As stated in the Introduction, a saccadic eye movement is classified as predictive when it occurs with a latency less than what is required for processing visual information ($\leq$ 80 ms). However, this latency only marks the time of the motor response, not when the decision was made to make the response. Due to neural delays, a subject's decision to make a predictive movement must have occurred before the motor act and prior to the stimulus. Here, by examining the changes in inter-saccade interval, we have estimated that the timing and rise of the GO process for a predictive movement begins prior to the stimulus onset for that saccade, and rises faster than in the reactive case. That is, once the decision to make the movement has been made, we estimate that it takes less time to trigger a predictive movement than a reactive movement. In addition, the finding that SSDs between –150 and 100 ms affect the countermanding of the saccadic sequences differently (Fig. 5) suggests that the difference in activity should be apparent approximately 150 ms prior to the target jump. These results are depicted in terms of the race model in Fig. 2. As suggested by the results presented in Fig. 9, in each panel the repetitive predictive GO process (gray trace) begins earlier and rises faster than the repetitive reactive GO process (black trace). When the stop signal is given at the same time as the stimulus jump (Fig. 2B), reactive saccades are cancelled whereas predictive saccades are not: the STOP process reaches the threshold before the reactive GO process but after the predictive GO process. This theoretical description is supported by the results presented in Figs. 3 and 4; the SSD of 0 ms cancels most eye movement sequences at 0.2 Hz pacing, but not at 1.0 Hz pacing. When the stop signal is given 300 ms before (Fig. 2A) or after (Fig. 2C) the stimulus the STOP process reaches threshold either before (cancelled) or after (non-cancelled) each respective GO process. (There are, however, other scenarios in which the GO process for a predictive movement could have the same duration as that of a reactive movement and still reach threshold in time to yield a reduced latency. For example, in addition to being initiated before the stimulus, the threshold to trigger a movement may be lower for the predictive case. Conversely, the initial baseline activity of the GO process for predictive movements may be higher than in the reactive case. We believe that the neural data are most consistent with our interpretation as discussed below.)

There is indirect data from monkey recordings that the duration of the GO process to trigger a predictive movement may be shorter than for the reactive case, but that the initial baseline activities are the same. Dorris and Munoz (1998) recorded neural activity in the intermediate layers of the SC during both reactive (latency between 130 and 180 ms) and predictive (latency < 70 ms) saccades. The discharge rate of the SC prior to the movement was approximately the same for both movement types, but rose faster and terminated earlier with a saccadic response for the predictive movements (see their Fig. 10). This supports our interpretation that there is a difference in the duration of the GO process between the two movement types (Fig. 9). (It should be noted that in the Dorris and Munoz study the peak activity in the SC at which reactive saccades were made was greater than for predictive saccades suggesting a lower threshold for predictive saccades. Therefore, a variable threshold (or variable baseline) may also account for the difference between repetitive predictive and reactive saccade generation. However, the decrease in latency for the predictive saccades appears to be mostly due to the faster rise in SC activity rather than to a decrease in peak activity. That is, if the activity during the predictive movement was projected to the same peak activity as for the reactive movement (assuming the same threshold) the total duration of the rise in SC activity would remain shorter for the predictive movement and the response would still occur before the reactive saccade. Therefore we believe these data are most consistent with our interpretation: a relatively fixed threshold and a latency difference due to differences in the initiation and duration of the GO process.)

In addition to the SC, neural activity in the FEF demonstrates a rise-to-threshold pattern in triggering reactive movements. This area has also been shown to play a role in predictive eye movements: lesions to the FEF impair the production of predictive saccadic responses (Rivaud et al. 1994), and predictive saccade tracking elicits greater activity in the FEF when compared to fixation (Simó et al. 2005). Unlike reactive movements, in the predictive case there is no need for processing the visual information. This may be reflected in the reduced amount of time to trigger the movement; the shorter duration of the GO process in the predictive case may be due to the internal storage of the required parameters of the movement (timing, amplitude, and direction) in a memorization loop (Gaymard et al. 1998). If correct, it would be interesting to determine when

the neural activity in the FEF and SC begins to rise and to compare the accumulation rate and threshold level between reactive and predictive movements. This data could then be used to distinguish between various models of the predictive GO process (variable versus constant baseline, accumulation rates, and thresholds).

Acknowledgements Supported by NIH T32-MH20069, NSF BCS-0615106, and EY015193. The authors would like to thank Dale Roberts and Adrian Lasker for help with experimental design.

References

Aron AR, Poldrack RA (2006) Cortical and subcortical contributions to Stop signal response inhibition: role of the subthalamic nucleus. J Neurosci 26:2424–2433

Asrress KN, Carpenter RH (2001) Saccadic countermanding: a comparison of central and peripheral stop signals. Vision Res 41:2645–2651

Barnes GR, Collins CJ, Arnold LR (2005) Predicting the duration of ocular pursuit in humans. Exp Brain Res 160:10–21

Becker W, Jurgens R (1979) An analysis of the saccadic system by means of double step stimuli. Vision Res 19:967–983

Cabel DW, Armstrong IT, Reingold E, Munoz DP (2000) Control of saccade initiation in a countermanding task using visual and auditory stop signals. Exp Brain Res 133:431–441

Carpenter RH, Williams ML (1995) Neural computation of log likelihood in control of saccadic eye movements. Nature 377:59–62

Corneil BD, Elsley JK (2005) Countermanding eye-head gaze shifts in humans: marching orders are delivered to the head first. J Neurophysiol 94:883–895

Curtis CE, Cole MW, Rao VY, D'Esposito M (2005) Canceling planned action: an FMRI study of countermanding saccades. Cereb Cortex 15:1281–1289

Dorris MC, Munoz DP (1998) Saccadic probability influences motor preparation signals and time to saccadic initiation. J Neurosci 18:7015–7026

Gaymard B, Ploner CJ, Rivaud S, Vermersch AI, Pierrot-Deseilligny C (1998) Cortical control of saccades. Exp Brain Res 123:159–163

Goossens HH, Van Opstal AJ (1997) Local feedback signals are not distorted by prior eye movements: evidence from visually evoked double saccades. J Neurophysiol 78:533–538

Hanes DP, Carpenter RH (1999) Countermanding saccades in humans. Vision Res 39:2777–2791

Hanes DP, Patterson II WF, Schall JD (1998) Role of frontal eye fields in countermanding saccades: visual, movement and fixation activity. J Neurophysiol 79:817–834

Hanes DP, Schall JD (1995) Countermanding saccades in macaque. Vis Neurosci 12:929–937

Hanes DP, Schall JD (1996) Neural control of voluntary movement initiation. Science 274:427–430

Honda H (1997) Interaction of extraretinal eye position signals in a double-step saccade task: psychophysical estimation. Exp Brain Res 113:327–336

Isotalo E, Lasker AG, Zee DS (2005) Cognitive influences on predictive saccadic tracking. Exp Brain Res 165:461–469

Ito S, Stuphorn V, Brown JW, Schall JD (2003) Performance monitoring by the anterior cingulate cortex during saccade countermanding. Science 302:120–122

Jarrett CB, Barnes GR (2003) The volitional inhibition of anticipatory ocular pursuit using a stop signal. Brain Res Cogn Brain Res 17:759–69

Joiner WJ, Shelhamer M (2006) An internal clock generates repetitive predictive saccades. Exp Brain Res 175:305–320

Kornylo K, Dill N, Saenz M, Krauzlis RJ (2003) Canceling of pursuit and saccadic eye movements in humans and monkeys. J Neurophysiol 89:2984–2999

Liston D, Krauzlis RJ (2005) Shared ''GO'' signal explains performance and timing of pursuit and saccadic eye movements. J Vis 5:678–689

Logan GD (1982) On the ability to inhibit complex actions: a stop-signal study of typewriting. J Exp Psychol Hum Percept Perform 8:778–792

Logan GD (1985) On the ability to inhibit simple thoughts and actions: II stop signal studies of repetition priming. J Exp Psychol Learn Mem Cogn 11:675–691

Logan GD (1994) On the ability to inhibit thought and action: a users' guide to the stop signal paradigm. In: Dagenbach D, Carr TH (eds) Inhibitory processes in attention, memory, and language. Academic Press, San Diego, pp 189–239

Logan GD, Cowan WB (1984) On the ability to inhibit thought and action: a theory of an act of control. Psychol Rev 91:295–327

Logan GD, Cowan WB, Davis KA (1984) On the ability to inhibit simple and choice reaction time responses: a model and a method. J Exp Psychol Hum Percept Perform 10:276–291

Paré M, Hanes DP (2003) Controlled movement processing: superior colliculus activity associated with countermanded saccades. J Neurosci 23:6480–6489

Reddi BA, Carpenter RH (2000) The influence of urgency on decision time. Nat Neurosci 3:827–830

Rivaud S, Muri RM, Gaymard B, Vermersch AI, Pierrot-Deseilligny C (1994) Eye movement disorders after frontal eye field lesions in humans. Exp Brain Res 102:110–120

Ross SM, Ross LE (1987) Children's and adults' predictive saccades to square wave targets. Vision Res 27:2177–2180

Savitzky A, Golay MJE (1964) Smoothing and differentiation of data by simplified least squares procedures. Anal Chem 38:1627–1639

Shelhamer M, Joiner WM (2003) Saccades exhibit abrupt transition between reactive and predictive, predictive saccade sequence have long-term correlations. J Neurophysiol 90:2763–2769

Simó LS, Krisky CM, Sweeney JA (2005) Functional neuroanatomy of anticipatory behavior: dissociation between sensory-driven and memory-driven systems. Cereb Cortex 15:1982–1991

Stark L, Vossius G, Young LR (1962) Predictive control of eye tracking movements. IRE Trans Hum Factors Electron 3:52–57

Stuphorn V, Taylor TL, Schall JD (2000) Performance monitoring by the supplementary eye field. Nature 408:857–860

Zambarbieri D, Schmid R, Ventre J (1987) Saccadic eye movements to predictable visual and auditory targets. In: O'Regan JK, Lévy-Schoen A (eds) Eye movements: from physiology to cognition, Elsevier, New York, pp 131–140