Voluntary Control of Multisaccade Gaze Shifts During Movement Preparation and Execution

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INTRODUCTION

All voluntary acts entail a decision process, whether implicit or explicit. Since a fundamental goal of the oculomotor system is to choose objects of interest in the visual scene to which gaze is directed, saccadic eye movements provide a logical paradigm to study the decision process that precedes movement execution. A task particularly well suited to study oculomotor decisions is the double-step task (Aslin and Shea 1987; Becker 1972; Becker and Fuchs 1969; Henson 1978; Logrand Cowan 1984) to estimate the time it takes to inhibit a planned saccade (Camalier et al. 2007; Kapoor and Murthy 2008; Lisberger et al. 1975; Murthy et al. 2009). Using this race model, the duration required to cancel the planned saccade can be estimated and has been called the target step/switch reaction time (TSRT), which is analogous to the stop signal reaction time used in the countermanding task (Hanes et al. 1998; Logan and Cowan 1984) to estimate the time it takes to inhibit a planned saccade (Camalier et al. 2007; Joti et al. 2007; Murthy et al. 2001) Therefore in addition to studying how decisions are made, the double-step task can be used to study how control is implemented by the oculomotor system, using a similar race model framework that has been successful in modeling performance in countermanding tasks.

The goal of this study was to extend behavioral predictions arising from the race model framework that have been proposed to underlie the control of single saccades to instances involving multisaccade gaze shifts, which often occur when subjects make saccades to highly eccentric targets (eccentricity >15°; Becker 1972; Becker and Fuchs 1969; Henson 1978; Prablanc and Jeanmerod 1975; Prablanc et al. 1978; Weber and Daroff 1972). In such instances the target is foereated by an initial hypometric saccade that undershoots the target and is then followed with a secondary saccade. Therefore on double-step trials if subjects fail to inhibit the initial hypometric response to the initial target, they have the opportunity to inhibit the secondary response and direct gaze to the newly specified target. Since control can manifest at multiple levels—either before the gaze shift begins or during the intersaccadic interval separating intervening saccades—we asked whether a unitary mechanism would suffice to explain oculomotor control.

In addition to understanding how our brains control multi-gaze shifts, we also used this paradigm to assess whether the programming of multisaccade gaze shift might also involve a ballistic stage of processing that is refractory to voluntary control. Although previous behavioral (e.g., Logan 1994) and...
neurophysiological studies (Hanes and Schall 1995; Hanes et al. 1998; Paré and Hanes 2003) support the notion of a race to a single threshold, the location of the threshold in relation to movement execution is unclear. One possibility is that the threshold occurs before saccade execution, providing a distinct point of no return in saccadic decision making (e.g., Osman et al. 1986). Modeling countermanding behavior supports this model and has estimated the point of no return at 28–60 ms before saccade execution (Kornyo et al. 2003). Alternatively, it is possible that saccade programming has no ballistic stage and can be controlled even during the execution of saccades. Evidence in support of this derives from countermanding studies in which hypometric saccades are generated, presumably from an interaction of the STOP process during the execution of the noncanceled saccade (Camalier et al. 2007; Colonius et al. 2001; Ozyurt et al. 2003; Walton and Gandhi 2006). In addition, many double-step studies have provided evidence of gaze errors being corrected very rapidly, sometimes resulting in trajectories that are curved toward the target following initial errors (Becker and Jurgens 1979; Findlay and Harris 1984; McPeek et al. 2003; Minken et al. 1993; Port and Wurtz 2003; Van Gisbergen et al. 1987). In this study we examine which of these two alternatives explains performance during multisaccade gaze shifts.

METHODS

Subjects

Fifteen naive subjects (ages between 18 and 32 yr), with normal or corrected vision, performed the redirect task (see Task for details). Their eye movements were recorded with their heads stabilized by means of a chin and forehead rest. All subjects gave their informed consent in accordance with the institutional human ethics committee of the National Brain Research Centre. Subjects were monetarily rewarded after every session to keep them motivated.

Task

The redirect task (Murthy et al. 2001; Ray et al. 2004) is a modified version of the classic double-step task (Aslin and Shea 1987; Becker and Jurgens 1979; Komoda et al. 1973; Lisberger et al. 1975; Ray et al. 2004; Westheimer 1954; Wheelless et al. 1966). The task consists of two kinds of trials: no-step trials in which a single target is presented (i.e., target is “not stepped” to another location) and step trials in which two targets are presented in succession. On 50% of the trials, referred to as no-step trials, following fixation for a random duration that ranged from 300 to 800 ms, a single green target (1° × 1°), with the International Commission on Illumination (CIE) chromaticity coordinates [273 615 7.1], appeared on the screen on a background, with CIE chromaticity coordinates of [220 300 0.06] (see Fig. 1A, top left). The location of the target was randomized such that it could appear in any one of eight locations centered on an imaginary circle with a radius of 30°. Subjects were instructed to quickly make a saccade to the target. They were given verbal instructions to increase the speed if their saccade latencies exceeded 400 ms.

In step trials, after the presentation of the first target, a second (1° × 1°) red target, with CIE chromaticity coordinates of [632 330 7.8], appeared randomly at another location on the screen (see Fig. 1B, top right) at an angular separation equal to or >90° to avoid averaging of the saccades to the two target locations (Ottes et al. 1984). The time of appearance of the final target relative to the initial target, called target step delay (TSD), was varied randomly from about 20 to 230 ms. The appearance of the second target served as a “redirect” signal instructing subjects to inhibit the partially planned saccade to the initial target and direct gaze to the final target. Random interleaving of the two trial types prevented the subjects from delaying the initial saccade, in anticipation of the second target. Step trials in our task differed from the earlier double-step studies in two main respects: the initial and final targets were of different colors, to ease distinction between the targets, especially at shorter TSDs; further, the initial target did not disappear with the appearance of the final target.

Trials were scored as successful, and conveyed to subjects by auditory feedback, if subjects made the saccade to the green target in a no-step trial and to the red target in a step trial, fixating the respective targets within an electronic window of ±5° centered on the target.

Data collection and analysis

Experiments were under computer control using TEMPO/VIDEO_SYNC software (Reflective Computing, St. Louis, MO) that displayed visual stimuli and stored sampled eye position. Eye position was sampled at 240 Hz with an infrared pupil tracker (ISCAN, Boston, MA) that interfaced with the TEMPO software in real time. All stimuli were presented on a Sony Tritonix 500 GDM monitor (21 in.; 70 Hz refresh rate) placed 34 cm in front of the subject. Stimuli were calibrated with a Minolta CA-96 colorimeter.

To calibrate our eye tracker (see also Kornyo et al. 2007) subjects made saccades with increased fixation times (mean = 500 ms ± 30%) and postaccadic times (mean = 500 ms ± 30%). For these trials we measured the SD of the eye tracker positions during a 100 ms fixation period. The estimate of the inherent noise of the tracker was 0.01°. The spatial accuracy of the tracker was estimated by measuring the mean saccade endpoint location during 100 ms of postaccadic fixation time. The median of these endpoints on three different trials to the same target was about 0.9°, which was an estimate of saccadic accuracy.

At the beginning of each session, subjects were given written and verbal instructions followed by some practice trials (~50). On average, subjects performed about 500 trials per session, with breaks every 200 trials. A typical session lasted about 1 h, with each subject performing four to six such sessions.

All analysis and statistical tests were performed off-line using MATLAB (The MathWorks, Natick, MA). Blinks were removed from the eye position data and a velocity threshold of 30°/s was used to demarcate the beginning and end of saccades. The accuracy of saccade detection was subsequently verified manually.

Classification of hypometric trials

Any trial in which the amplitude of the primary saccade fell short of the target by ≥6° was considered a hypometric response. We have used a fairly large amplitude cutoff to include only those trials that involved large corrections. Previous work has shown that when the error is large, the secondary saccade is executed much faster than when the error is small (<20° of the target eccentricity, which in our case is 6°; Becker 1972; Becker and Fuchs 1969; Becker and Jurgens 1979; Henson 1978; Prablanc and Jeannerod 1975; Prablanc et al. 1978; Weber and Daroff 1972). These differences in reaction times have been suggested to arise as a consequence of the oculomotor system using two different algorithms for error correction. In the case of large errors, fast correction can occur without waiting for the retinal reafferent signal. On the other hand, when the error is small the retinal information is awaited because the predictive correction is likely to be too noisy to prepare precise small corrections. Since our study focused on comparing hypometric errors with hypometric corrections (see Fig. 1, B3 and B4), which entailed fairly large corrections, we sought to ensure the same for the former so that we could contrast the effect of control, independent of potential differences in the algorithms that might be used to prepare the corrections.
Race model and estimation of target step reaction time

Performance in the double-step redirect task has been recently modeled as a race between three stochastically independent processes: 1) a GO process (GO1), producing the saccade to the initial target location; 2) a process inhibiting or interrupting the preparation of this saccade to the initial target (STOP); and 3) another GO process (GO2), producing the saccade to the final target location (Camalier et al. 2007; see Fig. 2). On step trials, the STOP process is assumed to be initiated following the appearance of the final target that attempts to cancel the partially prepared response to the initial target (GO1). The two processes, assumed to be independent of each other, race toward the threshold. The winner of the race decides the behavioral outcome. When the STOP process wins the race, the saccade to the initial target is inhibited. This allows the second GO process (GO2) to elicit a saccade to the final target, resulting in a successful response (see Fig. 2A). When the STOP process loses the race, the first saccade is made to the initial target and is referred to as an erroneous response. Subsequently, a corrective saccade redirects gaze to the final target (see Fig. 2B).

The race model provides a measure of the duration of the inhibitory process, which we refer to as the target step reaction time (TSRT). TSRT is analogous to the stop signal reaction time.
three methods of estimating the TSRT were used in the current study. The first method assumes that TSRT is a random variable and is based on the logic described by Logan and Cowan (1984; see also Hanes et al. 1998). Here, the mean TSRT equals the difference between the mean no-step reaction time and the mean of the compensation function. If the compensation function ranges from a probability of 0 to 1, then its mean is the difference between the probability of responding at the $i$th TSD minus the probability of responding at the $(i-1)$th TSD multiplied by the $i$th TSD summed over all TSDs (Logan and Cowan 1984). Since the actual compensation functions often have a minimum $>0$ and/or a maximum of $<1$, the mean of the compensation function was rescaled to reflect the actual range of the response probability. This was done by dividing the mean of the compensation function by the difference between the maximum and the minimum probabilities of responding (also see Idealizing compensation functions in the following text for details). To provide an estimate that was less sensitive to random variability, we fit a Weibull function, $W(t)$ (see RESULTS for details) to the compensation function (Hanes et al. 1998; Kapoor and Murthy 2008). An estimate of the mean of the best-fit compensation function was then given by

\[
\text{Mean of compensation function} = \frac{\sum_{i} [W(t) - W(t-1)] \cdot i}{W(t_{\text{max}}) - W(t_{\text{min}})}
\]

where $t$ ranges from the minimum to the maximum TSD in 1 ms intervals.

The second method, the median method, involves calculating the TSRT by subtracting the median of the compensation function from the median of the no-step reaction time distribution.

The third method, the integration method, provides an estimate of the TSRT at each TSD. Assuming that the duration of the STOP process is constant across TSDs, in this method TSRT was estimated by integrating over the no-step reaction time distribution until the integral equaled the observed proportion of erroneous saccades in the compensation function (see Fig. 2C). The reaction time at the integrated value yielded the finish time of the race—i.e., the longest saccadic reaction time at which the GO process finished before the STOP process could inhibit it. Thus the time between the appearance of the redirect signal and this finish time is the TSRT for this TSD.

The TSRTs obtained from the preceding methods can vary, depending on the distribution of the STOP signal. To obtain a more robust estimate, we thus averaged the three estimates of TSRT to provide a single composite measure, which we refer to from now on as the TSRT obtained using the conventional race model analysis.

**Race model simulations.**

We used the linear accumulation to threshold with ergodic rate (LATER) model (Carpenter and Williams 1995; Hanes and Carpenter 1999; Hanes and Schall 1996; Reddi et al. 2003), which has provided a good description of saccade reaction times, to simulate the GO and the STOP processes. The two processes are stochastic in nature, with their rate of rise varying from trial to trial and can be described by a Gaussian distribution (see Fig. 3). In all our estimations and predictions using the race model, the variance of the GO and STOP processes were included, in addition to the mean, to improve accuracy.

**MONTE CARLO METHOD.** We used MATLAB to perform Monte Carlo simulations to estimate the rates of the GO and STOP processes, as in other studies (Colonius et al. 2001; Hanes and Carpenter 1999; Walton and Gandhi 2006). For each simulated trial, the rate of accumulation of the GO process, denoted by $r_{GO}$ (in Hz), which defines its slope (Fig. 2, A and B), was chosen randomly from a Gaussian distribution with mean $\mu_{r_{GO}}$ and SD $\sigma_{r_{GO}}$. The threshold was
The race model assumes that the GO and STOP processes are stochastically independent (Logan 1994)—i.e., the underlying GO process is not altered by the presence of the STOP process in the step trials. If this assumption holds, then for a given TSD, the finish times of the STOP process partitions the no-step reaction time distribution such that only those saccades that have shorter latencies than the sum of the TSD and the average latency of the STOP process (TSRT), escape inhibition (see Fig. 2C). Testing the validity of the race model has been traditionally performed using the mean latency of the STOP process. However, given that the processes involved are stochastic we therefore included the variances for a stringent and conservative method that was primarily aimed at establishing violations of the race model. For this it was important to show that the timing of erroneous saccades could not be accounted for by the subset of even the slowest STOP processes. In practice this was tested by STOP2σ (see Fig. 3), which is the latency of the STOP process that is slower than the mean STOP rate by 2σ. Since 2σ accounts for 97.5% (leaving the upper tail of 2.5%) of the STOP distribution, we intuitively expected a 2–3% violation by using this criterion. However, it is important to note that because of the statistics of sampling, this percentage violation represents the average expected violation. Since the purpose of the analysis was aimed at testing the limits of the race model, it is important to establish the upper bound of the expected violation. This number is given by Chebyshev’s theorem, which states that at most 1/k² proportion of trials can occur in the range μ ± kσ. Therefore when k = 2 we get 0.25. However, since this includes both tails of the distribution, this has to be halved if just the upper tail is considered. Thus values of violation >12.5% would invalidate the race model. In practice a trial was declared a violation if its latency exceeded the sum of the TSD, the target step reaction time, and the time equivalent to 2SDs of the rate of the STOP process by at least 15 ms, the latter being the resolution of the TSD bin size.

MAXIMUM LIKELIHOOD METHOD. We also performed parameter estimation using a maximum likelihood approach as described by previous studies (Cornel and Elsley 2005; Kornyl et al. 2003; Walton and Gandhi 2006). To estimate the parameters that defined rGO, we initially computed the inverse of the no-step reaction time distribution. The mean and SD of the rates of the GO process were directly obtained running the “fmincon” optimization routine in MATLAB. We repeated this procedure 50–75 times, with different sets of initial parameter values, to ensure convergence to the global minima.
Idealizing compensation functions

In practice, compensation functions seldom spanned the entire psychometric range (from 0 to 1). This means that at shorter TSDs subjects sometimes failed to compensate when they should have and, at longer TSDs, they managed to compensate unexpectedly. Such behavior can systematically affect the compensation function and lead to biased parameter estimates. We therefore corrected for this bias by making certain assumptions about the subject’s strategy. If $\alpha$ (the lower asymptote to the Weibull fit of the compensation function) is the proportion of trials a subject failed to inhibit at the shortest TSD, we considered $\alpha$ to be the proportion of trials when subjects ignored the final target. In simulations, these trials can be incorporated by withholding the STOP process. Similarly, if $\beta$ (the upper asymptote to the Weibull fit of the compensation function) is the maximum value of the compensation function, we considered $(1 - \beta)$ to be the proportion of trials when the subjects ignored the initial target. In simulations, these trials can be incorporated by not initiating the GO process. An equivalent approach that yields the same outcome is to treat the subjects’ performance in the remaining fraction of trials $(\beta - \alpha)$ to be ideal. We rescaled subjects’ compensation functions between 0 and 1 to reflect the ideal compensation function, which was used to obtain bias free parameter estimates. However, we also carried out analyses without rescaling. Although this changed the parameter values of the STOP and the GO processes and the estimated fraction of violations, the percentage of secondary saccades violating the cutoff was nevertheless very high, compared with erroneous first saccades. Thus the basic results did not change due to rescaling.

RESULTS

We used the redirect task to understand how inhibitory control is exerted to achieve goal directed movements. In this task, subjects were instructed to make a saccadic eye movement to the initial target as soon as it appeared (no-step trials). However, if a second target subsequently appeared (step trials), subjects were asked to cancel the partially planned saccade to the first target and direct their gaze to the second target. In step trials, subjects sometimes compensated for the target step—i.e., inhibited the initial saccade and directed gaze toward the final target (see Fig. 1B1: successful response). However, at other times, they failed to inhibit the saccade toward the initial target—i.e., their response was not successfully inhibited (see Fig. 1B2: erroneous response). On reaching the initial target, however, they made a subsequent corrective saccade toward the final target.

The targets appeared at 30° eccentricities. Subjects attempting to foveate often made (on average across subjects 11.5 ± 2SE%) a set of two saccades instead of a single saccade: the primary saccade followed by a secondary saccade (see Fig. 1A2, hypometric response in a no-step trial). We embodied this behavior in the context of the redirect task to assess inhibitory control during multisaccade gaze shifts, where control can manifest at multiple levels: either before the saccades began, during the saccade, or even during the intersaccadic interval.

Performance of subjects

In the redirect task, the TSD was varied across trials. Although subjects typically find it easier to inhibit at shorter TSDs, it is harder to do the same at longer TSDs, presumably because they are more committed to the initial target. We plotted the probability of making a saccade to the initial target in step trials as a function of increasing TSDs. We considered this behavior to be biased parameter estimates. We therefore corrected for this bias by making certain assumptions about the subject’s strategy. If $\alpha$ (the lower asymptote to the Weibull fit of the compensation function) is the proportion of trials a subject failed to inhibit at the shortest TSD, we considered $\alpha$ to be the proportion of trials when subjects ignored the final target. In simulations, these trials can be incorporated by withholding the STOP process. Similarly, if $\beta$ (the upper asymptote to the Weibull fit of the compensation function) is the maximum value of the compensation function, we considered $(1 - \beta)$ to be the proportion of trials when the subjects ignored the initial target. In simulations, these trials can be incorporated by not initiating the GO process. An equivalent approach that yields the same outcome is to treat the subjects’ performance in the remaining fraction of trials $(\beta - \alpha)$ to be ideal. We rescaled subjects’ compensation functions between 0 and 1 to reflect the ideal compensation function, which was used to obtain bias free parameter estimates. However, we also carried out analyses without rescaling. Although this changed the parameter values of the STOP and the GO processes and the estimated fraction of violations, the percentage of secondary saccades violating the cutoff was nevertheless very high, compared with erroneous first saccades. Thus the basic results did not change due to rescaling.

FIG. 4. Compensation functions. Plot showing the probability of making a saccade to the first target as a function of TSDs calculated taking into account the spatial location of the targets and separated into bin sizes of ± the refresh rate of the monitor (14.3 ms). Data for 9 representative subjects, superimposed by a best-fit Weibull function (see RESULTS for details), show that the probability of making the erroneous first saccade increases with increasing TSDs.
where $t$ is the TSD, $\alpha$ is the time at which the function reaches 64% of its full growth, $\beta$ is the slope, $\gamma$ is the maximum value of the function, and $\delta$ is the minimum value of the function. Given the nature of the task, $\gamma - \delta$ can be used as an index to assess how the subjects performed. In all our sessions $(\gamma - \delta)$ was $> 0.5$.

Race model analysis: quantifying the ability to inhibit

We obtained the parameters of the rates of the GO process by simulating the cumulative no-step reaction time distribution using the Monte Carlo method as well as the maximum likelihood based method (see METHODS). The simulated and the observed cumulative no-step reaction times for the nine typical subjects are shown in Fig. 5. The goodness-of-fit was ascertained by computing the correlation coefficient ($r^2$), which was on average 0.98 (max $= 0.99$; min $= 0.95$). The $r^2$ value was used to decide the better of the estimates from the two methods, which was then used for all further analyses. Columns 1 and 2 of Table 1 and Table 2 list the parameters (mean and SD) obtained using the Monte Carlo approach and the maximum likelihood based approach, respectively.

Step trials were simulated on the basis of the race model described in Fig. 2. The parameters of the GO process that were obtained as mentioned earlier were used to estimate the parameters of the STOP process using the Monte Carlo method (see Table 1, column under STOP), which were then used to simulate the compensation functions (see Fig. 6). The goodness-of-fit was ascertained by computing the correlation coefficient ($r^2$), which was on average 0.89 ± 0.02 (max $= 0.95$; min $= 0.65$). We also performed the same procedure using the maximum likelihood based procedure, which also yielded similar results (see Table 2, column under STOP). The goodness-of-fit was on average 0.88 ± 0.02 (max $= 0.95$; min $= 0.64$).

We used the parameters of the rate of STOP process to find an estimate of the latency to STOP or the target step reaction time (TSRT; see METHODS) by computing the time taken by the observed cumulative no-step reaction time distribution (black) and, when compared with the observed distribution (light gray), shows good correlation. Data (binned every 25 ms) are shown for the 9 representative subjects.

TABLE 1. Parameter estimation based on the Monte Carlo method

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<th>Subject</th>
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<th>Nonhypometric GO($\sigma$)</th>
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Values are means (\(\mu\)) and SD (\(\sigma\)) for the nonhypometric GO process, the hypometric GO process, and the STOP process for each subject.

FIG. 5. Comparison of the observed and simulated cumulative no-step reaction time distributions. Parameter estimates (mean and SD) for the GO process were obtained from both the Monte Carlo method and the maximum likelihood based method. The better of the estimates from the 2 methods (see RESULTS for details) was used to simulate the cumulative no-step reaction time distribution (black) and, when compared with the observed distribution (light gray), shows good correlation. Data (binned every 25 ms) are shown for the 9 representative subjects.
reach the threshold (i.e., $1/\mu_{\text{stop}}$ ms after the visual delay). The average TSRT across subjects calculated in this fashion ($101.2 \pm 5.9$ ms) was comparable to the TSRT estimate ($107 \pm 5$ ms) that was derived by conventional methods using the race model (described earlier in Race model and estimation of target step reaction time in METHODS). In addition, the two TSRT estimates were strongly correlated [Pearson’s $r = 0.86$, $P = 0.000036$] with the mean slope of the regression line close to unity (slope = 0.94; intercept = 0.083), indicating that our simulated parameters provided a good description of the behavioral data (see Fig. 7).

We next tested the validity of the race model for all the subjects by checking the percentage of erroneous saccades whose reaction times violated the STOP2 cutoff. The percentage of violation for every subject is tabulated in column 1 of Table 3 and Table 4 for the percentage of violations calculated by the Monte Carlo method and the maximum likelihood based method, respectively. The percentage of trials that violated the cutoff was on average 10.29% (min = 3.1%; max = 17.4%). Eleven of 15 subjects are within the prescribed cutoff demarcated by the STOP2 criterion. However, these percentages are an average across TSDs. To get a better picture we separated these trials that violated the cutoff into three different groups based on the TSDs. On closer inspection, the percentage of

![FIG. 7. Comparison of TSRT obtained by conventional methods vs. TSRT obtained by simulating the race model. Each circle represents datum from one subject. The broken line represents the fit derived from a linear regression of the data. The simulated and the observed TSRTs are strongly correlated, indicating that simulation provides a good description of the behavioral data.](image)

![FIG. 6. Comparison between simulated and observed compensation functions. Observed compensation functions (solid gray circles) are best fit with Weibull functions (adapted from Fig. 4). Simulated compensation functions (solid black triangles) generated for the 9 representative subjects using the parameters obtained based on Monte Carlo simulation (see Monte Carlo method in METHODS) show good correlation with the observed data.](image)

<table>
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<th>Subject</th>
<th>GO ($\mu$)</th>
<th>GO ($\sigma$)</th>
<th>STOP ($\mu$)</th>
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Values are means ($\mu$) and SD ($\sigma$) for the nonhypometric GO process, the hypometric GO process, and the STOP process for each subject.
Inhibitory control during a hypometric response

**PRIMARY SACCADE.** Analogous to the earlier analysis, we tested the validity of the race model for primary saccades of the hypometric response. The percentage of violation for every subject is tabulated in column 2 of Tables 3 and 4. The percentage of trials that violated the cutoff was on average 13.0% (min = 3.4%; max = 23.8%). Eight of 15 subjects are within the prescribed cutoff demarcated by the STOP2 criterion. Thus the race model failed to account for the timing of the secondary saccades of hypometric errors.

**SECONDARY SACCADE.** On step trials, when subjects made an initial hypometric saccade toward the first target, two interesting behavioral patterns resulted. Although on some trials they managed to correct midway following the initial erroneous saccade (referred to as a hypometric correction; see Fig. 1B3), on others, they failed to do so and instead made a secondary saccade to the initial target, foveating the final target only in the subsequent saccade (referred to as hypometric errors; see Fig. 1B4).

We were interested to assess the ability to inhibit the multisaccade gaze shift at the level of the secondary saccade. We reasoned that the secondary saccade, which was erroneous in the given context, should be inhibited by the STOP process and be superseded by a corrective saccade to the final target, resulting in a hypometric correction. Although we do not know when the secondary saccade preparation starts, the extent of its inhibition is still expected to conform to the parameters of the STOP process. Assuming the same parameters of the STOP process, as in the earlier case, we determined the percentage of secondary saccades that occurred beyond the latency predicted by STOP$_{2a}$ and found it to consist of a large proportion (average = 78.29%; min = 31.74%; max = 100%) for every subject examined (see column 3 of Tables 3 and 4 for results using the Monte Carlo method and the maximum likelihood based method, respectively). At all TSDs every subject violated the cutoff at early (20, 50, and 80 ms; min = 87%; max = 100%; mean = 99%; 15/15 subjects violated the cutoff), intermediate (110 and 140 ms; min = 50%; max = 100%; mean = 84%; 15/15 subjects violated the cutoff), and late (>170 ms; min = 0%; max = 100%; mean = 53%; 14/15 subjects violated the cutoff) TSDs. In contrast to the first saccades, a large percentage of secondary saccades (78%) violated the cutoff that could not be accounted for by the upper bound established by the STOP$_{2a}$ criterion. Thus the race model failed to account for the timing of the secondary saccades of hypometric errors.

Next, to understand the magnitude of this violation we quantified the latencies of the saccades that violated the cutoff. The extent of violation of erroneous first saccades that violated the cutoff was 51 ms (min = 20 ms; max = 87 ms). Likewise, the extent of violation of erroneous primary saccades that violated the cutoff was 38 ms (min = 12 ms; max = 52 ms). In contrast, the secondary saccade reaction times occurred well beyond the cutoff time. The extent of violation of the secondary saccades that violated the cutoff was 114 ms (min = 73 ms; max = 157 ms). To compare and contrast the extent of

### Table 3. Percentage of violation from the Monte Carlo method

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<th>Secondary Saccade</th>
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violation we have plotted a typical subject’s data (latencies of erroneous first saccades along with those of secondary saccades) for a particular TSD (see Fig. 8A). In Fig. 8B we pooled the data across TSDs and aligned it with respect to STOP2o (depicted by “0” on the x-axis). In contrast to the erroneous first saccades a significantly greater proportion of secondary saccades occur at latencies greater than STOP2o consistently across subjects (Wilcoxon rank sum between the two distributions, P < 0.001 for all subjects). The extent of violation signifies the inability of the oculomotor system to inhibit the secondary saccade and is indicative of the failure of voluntary control. In other words, these data point to the existence of a ballistic stage of saccade programming during the intersaccadic interval in a multisaccade gaze shift.

If the secondary saccade is not inhibited then what could explain the production of hypometric corrections? We hypothesized that hypometric corrections could be a result of the STOP process interrupting the first saccade during execution, following which a GO2 process redirects gaze to the final target. This hypothesis has three predictions, which we examined in turn. First, a midflight truncation by STOP process implies that the frequency of hypometria must be greater in step trials that engage a STOP process, compared with no-step trials, which do not. To test this prediction, we plotted the percentage of hypometria during step trials and no-step trials for each subject (see Fig. 9A) and found this value to be significantly greater (Wilcoxon rank sum, P = 0.046 for the pooled data) in step trials (mean = 17.36%), compared with no-step trials (mean = 11.47%) for all subjects (15/15), favoring the role of STOP process in midflight truncation.

Second, we examined whether the primary saccades in hypometric corrections are qualitatively different from their no-step counterparts, as a result of being generated as a consequence of STOP mediation. To test this, we plotted their amplitudes (see Fig. 9B) and found the median amplitude of primary saccades in hypometric correction trials to be less than the same in no-step trials for 14/15 subjects; the difference was significant for 11/15 subjects (Mann–Whitney U test, P < 0.05), conforming to the hypothesis that the STOP process interrupts the first saccade during execution, leading to a hypometric correction.

Third, if the primary saccade (the first saccade in the hypometric correction) began as a normal saccade but was truncated midflight by STOP process, it would modify the typical bell-
shaped velocity profile to that of a skewed one. We used the ratio of acceleration duration to deceleration duration to quantify the degree of this skewness in the saccade velocity profile (Van Gisbergen et al. 1987; Van Opstal and Van Gisbergen 1987). We calculated the acceleration duration and the deceleration duration separately for four different amplitude bins (<7, 7–12, 12–18, 18–25°) for primary saccades and their amplitude-matched no-step counterparts, including only horizontal saccades in the analyses, as has been done in past studies (Van Gisbergen et al. 1987; Van Opstal and Van Gisbergen 1987). Figure 10 shows the acceleration durations (top panel), deceleration durations (middle panel), and the ratio of the two (bottom panel) as a function of amplitude for the entire group. Acceleration and deceleration profiles show a monotonically increasing relation as a function of amplitude, in general agreement with past work. We also observed that whereas the acceleration duration across amplitudes is closely matched (one-way ANOVA, \(F = 0.15, P = 0.69\)), the deceleration duration is significantly less for primary saccades, compared with their corresponding no-step counterparts (one-way ANOVA, \(F = 9.24, P = 0.0024\)). The ratio of the acceleration duration to the deceleration duration is also significantly different (one-way ANOVA, \(F = 4.96, P = 0.026\)), suggesting that the primary saccade of a hypometric correction trial, on average, accelerated normally but decelerated more abruptly, compared with the primary saccade of the no-step hypometric trial. Taken together, these results favor the generation of primary saccades in hypometric corrections as a consequence of the STOP process interrupting the GO process during execution, leading to truncation of the erroneous first saccade.

Based on the earlier results, we modified the race model to account for midflight truncation by allowing STOP and GO processes to compete beyond the saccade planning stage into its execution stage (see Fig. 11A). Such a race model should predict a systematic relation between the frequency of hypometric corrections and the reprocessing time: the time from the onset of the second target until the end of the first saccade. At shorter TSDs, corresponding to longer reprocessing times, the STOP process, having an early start, is more likely to inhibit the GO process before saccade execution begins, producing successful responses (see Fig. 1B1) and almost no hypometric corrections. On the other hand, at longer TSDs, corresponding to shorter reprocessing times, the STOP process would be unable to interrupt the GO process during either the planning or the execution stage and would result in nonhypometric erroneous first saccades (see Fig. 1B2), whereas for certain intermediate TSDs the likelihood of the STOP process colliding with the GO process during saccade execution would be greater, increasing the frequency. Thus the frequency of hypometric corrections is expected to peak at intermediate reprocessing times but decrease not only at longer but also at shorter reprocessing times. Figure 11B shows the observed frequency as a function of reprocessing times for the nine typical subjects. The frequency distributions conform to the predictions of the extended race model, which further validates the hypothesis that hypometric corrections are generated as a consequence of

![Graph A](attachment://graph_a.png)

![Graph B](attachment://graph_b.png)

**FIG. 9.** Evidence for the role of STOP in truncation of erroneous first saccades leading to hypometric corrections: I. A: plot shows the percentage of hypometria in step trials (black) vs. no-step trials (orange) for all subjects. Step trials, consisting of hypometric corrections and hypometric errors, were greater in number, compared with no-step hypometric trials. B: box plots compare the primary saccade amplitudes of hypometric correction trials (yellow) with those of no-step hypometric trials (orange) across subjects. The median amplitudes of the primary saccades are shorter for hypometric corrections, compared with those of no-step hypometric saccades in 14/15 subjects. These results favor the role of STOP in truncation of erroneous first saccade during execution.
Table 10. Evidence for role of STOP in truncation of primary saccades leading to hypometric corrections: II. Plots compare velocity skewness of primary saccades of hypometric corrections (in gray) with their amplitude-matched no-step counterparts (in black). The acceleration duration across amplitudes (A) are similar, whereas the deceleration durations (B) are significantly shorter for primary saccades in hypometric corrections, compared with their no-step counterparts. C: the ratio of acceleration duration to deceleration duration is significantly greater for primary saccades of hypometric corrections, compared with no-step primary saccades. Data are pooled across subjects and consist of only horizontal saccades binned into 4 amplitude bins (<7, 7–12, 12–18, and 18–25°). Note that the error bars are smaller than the markers in many cases. Primary saccades of a hypometric correction, on average, accelerated normally but decelerated more abruptly, compared with primary saccades of no-step trial, suggesting a STOP-mediated truncation of the erroneous saccade during execution.

In this study, we addressed for the first time how the brain controls multisaccade gaze shifts by testing the predictions of a race model that has been used to successfully describe performance in double-step tasks. In the process, we have shown that, first, a saccade can be inhibited not only centrally during its programming but also peripherally during its execution, by the operation of unitary inhibitory control that can account for subjects’ performance. Second, the intersaccadic interval in a multisaccade gaze shift is a ballistic stage not subject to voluntary control. To the best of our knowledge, this is the first clear demonstration that the brain implements a point of no return in sensorimotor decision making.

Race model of double-step saccade performance

In earlier studies of the classical double-step task (Becker and Jurgens 1979; Lisberger et al. 1975), the performance of the subjects was accounted for by assuming two underlying processes: a GO1 process activated by the first stimulus and a GO2 process by the second stimulus, with the resulting saccade being the outcome of a race between the two. Recently Ludwig et al. (2007) also attempted to model double-step data using a subtle modification of the GO1–GO2 model. Their model includes broadly tuned activation units whose activity increases if the stimulus is in their response field and they undergo a passive decay if the stimulus moves away (disappears) from the response field. However, it must be emphasized that their simulated double-step paradigm differs from ours in a crucial respect—in their paradigm when the target steps to a new location it disappears from its earlier location. Thus it makes sense and may suffice to account for reduction in activation of the GO1 units by passive decay. However, in our paradigm the first target stays on even after the second target appears (see Fig. 1). This leads to constant activation of the units, thus preventing passive decay. Thus an active inhibitory process is needed to decrease the activity of the GO1 units to allow the GO2 units to rise and reach the threshold. In a similar vein, a mutual inhibitory interaction between the GO1 and GO2 processes (lateral inhibition) is also unlikely to produce the frequency distribution of the hypometric corrections seen in Fig. 11 suggesting as an estimate of the finish time of the STOP process to calculate TSRT. The TSRT calculated in this fashion, which quantified the time taken to inhibit the erroneous saccade during execution, was on average 152 ± 3.9 ms (min = 124 ms; max = 191 ms) and was typically greater than the TSRT for inhibiting the first saccade in the programming stage (calculated using the conventional methods for the non-hypometric first saccade) by 44 ± 9 ms.

A question that arises at this point is whether this TSRT for inhibiting a saccade during execution is different from the TSRT for inhibiting a saccade before it began? In other words, do they represent two distinct sources of inhibitory control or a common inhibitory mechanism acting at central and peripheral levels? We tested this by plotting the two TSRTs against each other for all subjects (see Fig. 12) and found a significant correlation between the two (Pearson’s correlation r = 0.77, P = 0.0008), consistent with the mechanism of unitary inhibitory control manifesting at different levels.

DISCUSSION

In this study, we addressed for the first time how the brain controls multisaccade gaze shifts by testing the predictions of a race model that has been used to successfully describe performance in double-step tasks. In the process, we have shown that, first, a saccade can be inhibited not only centrally during its programming but also peripherally during its execution, by the operation of unitary inhibitory control that can account for subjects’ performance. Second, the intersaccadic interval in a multisaccade gaze shift is a ballistic stage not subject to voluntary control. To the best of our knowledge, this is the first clear demonstration that the brain implements a point of no return in sensorimotor decision making.
behavioral outcome that we observe. In a task like the redirect task, where the GO\textsubscript{1} process is always given a head start, it will always be more activated than the GO\textsubscript{2} process. Thus its inhibitory influence on the GO\textsubscript{2} process will be more than vice versa. As a consequence such an interaction will never allow the expression of the GO\textsubscript{2} process. Therefore, in the absence of an active inhibitory process that interrupts the current motor program (the GO\textsubscript{1} process) it is hard to understand how competing motor programs that begin later can ever get to be expressed at the behavioral level.

In contrast, our model that includes an inhibitory STOP process is congruent with evidence from other studies using more detailed simulations (Camalier et al. 2007; see also Verbruggen and Logan 2008) that point to the existence of a STOP process that starts following the appearance of the second target, which inhibits the GO\textsubscript{1} process to allow the GO\textsubscript{2} process to compensate for the target step. Thus redirecting saccades in double-step tasks is presumed to require an inhibitory process. The duration of this covert inhibitory process, the target step reaction time (Camalier et al. 2007; Murthy et al. 2009), can be quantified by adapting the theoretical framework developed to calculate the stop signal reaction time (Logan 1994). Although our estimates of TSRT (101 ms from simulations; 107 ms from conventional methods) may be a bit lower than the SSRT values estimated from some studies using versions of the stop signal paradigms (SSRT\textsubscript{Hanes} \textsubscript{Carpenter} \textsubscript{1999} = 125–145 ms; SSRT\textsubscript{Assress} \textsubscript{and Carpenter} \textsubscript{2001} = 128 ms; SSRT\textsubscript{Cabel} \textsubscript{et al.} \textsubscript{2000} = 113 ms; SSRT\textsubscript{Kornylo} \textsubscript{et al.} \textsubscript{2003} = 112 ms), they are nevertheless comparable to estimates from other studies. Lower TSRT could be due to a higher than usual proportion of step trials in our task (50%) compared with earlier paradigms (e.g., 35%: Hanes and Carpenter 1999; SSRT\textsubscript{Hanes} \textsubscript{and Carpenter} \textsubscript{1999} = 125–145 ms; SSRT\textsubscript{Assress} \textsubscript{and Carpenter} \textsubscript{2001} = 128 ms; SSRT\textsubscript{Cabel} \textsubscript{et al.} \textsubscript{2000} = 113 ms; SSRT\textsubscript{Kornylo} \textsubscript{et al.} \textsubscript{2003} = 112 ms).
Hierarchical control: unitary control at multiple levels

Consistent with previous work (Camalier et al. 2007), the current study explains behavior in a redirect task as arising from an interaction of GO₁, GO₂, and STOP processes, where the initial target initiates the GO₁ process and the final target initiates the GO₂ and the STOP processes. In this race model framework the STOP process may interrupt the GO process during the planning stage or sometimes, albeit infrequently, during the execution stage, leading to premature truncation of the first saccade. If this were true then the incidence of hypometric correction would be a function of the duration of the first saccade, which in turn is related directly to its amplitude. In fact earlier studies that have used smaller target eccentricities have reported few such hypometric responses (eccentricity = 15°: Colonius et al. 2001; Ozyurt et al. 2003; eccentricity = 16–20°: Walton and Gandhi 2006; eccentricity ≈ 10°: Camalier et al. 2007) or none (e.g., in monkeys, eccentricity = 9°: Hanes and Carpenter 1999; Hanes and Schall 1995; in humans, eccentricity = 3–3.5°: Assress and Carpenter 2001; Kornylo et al. 2003), whereas we have observed relatively higher frequency of hypometric corrections (~15%), despite a very generous amplitude cutoff (6°) that is likely to be due to the larger target eccentricity (~30°) used in this study, which has allowed greater time for the STOP signal to interact with the saccade during its execution, thus lending support to the hypothesis that the STOP process can interrupt the GO process during saccade execution.

Our observation that such an interaction between the GO and STOP processes can also occur at the level of saccade execution implies that inhibitory control manifests at multiple levels in the oculomotor system. Previous studies that have implicated the superior colliculus (SC) fixation neurons during countermanding behavior (Paré and Hanes 2003) have shown the time course of reactivation (~104 ms) of these neurons closely corresponds to and precedes (~25 ms) the behavioral estimates of the cancellation times, the SSRT (analogous to TSRT). The modulation of frontal eye field (FEF) fixation neurons also occurs in the same timescale (Hanes et al. 1998).

In our study the duration of the STOP process required to halt the primary saccade under preparation is more or less similar in duration (107 ms) to the fixation neurons of the SC and FEF. However, the duration of the STOP process required to halt the primary saccade in execution is significantly larger (152 ms). Thus for the latter form of control we speculate the involvement of neurons further downstream to the SC and FEF.

Based on studies showing midflight saccade interruption by the stimulation of the brain stem omnipause neurons (OPNs; Keller 1974, 1977; Keller and Edelman 1994; Keller et al. 1996), we speculate that the reactivation of OPN may lead to inhibition of saccades during their execution. However, because this inference is indirect we cannot rule out the role of upstream neurons such as SC and FEF fixation neurons as well.

A conceptual issue that these data raise is whether inhibitory control occurring at multiple levels is equivalent to the brain implementing multiple independent STOP processes (Coxon et al. 2007; DeJong et al. 1995; van den Wildenberg and van der Molen 2004) or, alternatively, a unitary control mechanism that manifests at multiple levels. One line of evidence that would favor the former hypothesis is the observation that the TSRT to inhibit the saccade during execution is consistently greater (by ~44 ms) than the TSRT to inhibit the saccade before it begins. However, because the two sets of TSRTs were strongly correlated, this suggests a shared basis for control (Morein-Zamir et al. 2004; van Boxtel et al. 2001), which undermines the independent hypothesis. Taken together, these data seem to suggest the contribution of neurons that inhibit saccade production across different brain areas such as the frontal eye fields (Burman and Bruce 1997; Hanes et al. 1998; Izawa et al.
Ballistic stages in saccade programming: is there a point of no return?

Cognitive theorists have long since speculated that information processing stages underlying sensorimotor behaviors may be distinguished into controlled and ballistic stages (Bartlett 1958; Osman et al. 1986). Although controlled stages are thought to be under central control with respect to whether they ultimately lead to overt movement (Logan 1981), ballistic stages are believed to be inextricably linked to overt movement and thus cannot be stopped once they begin. The temporal boundary between controlled and ballistic stage is typically referred to as the point of no return (Bartlett 1958). Although it is intuitive to think that fast voluntary movements are difficult to modify or to cancel, especially prior to overt movement (e.g., Henry and Harrison 1961; Slater-Hammel 1960), experimental evidence for a point of no return has remained inconclusive (Cavina-Pratesi et al. 2004; Dejong et al. 1990; Logan et al. 1984; McGarry and Franks 1997; Osman et al. 1986, 1990; van Boxtel et al. 2001).

Kornylo et al. (2003) used a saccadic countermanding paradigm to look for evidence of the point of no return in the oculomotor system. In this study, the performance in a saccade countermanding task could be simulated only by assuming a ballistic stage of 28–60 ms for humans and 9–25 ms in monkeys for saccadic eye movements. In contrast, other studies (Colonius et al. 2001; Corneil et al. 1999; Walton and Gandhi 2006) have observed hypometric saccades during the execution of an erroneous first saccade, presumably due to midflight control, arguing against the notion of a ballistic stage. Although the above-cited studies have focused on single saccades using a countermanding paradigm, we have probed multisaccade gaze shifts using a redirect task in conjunction with the race model that provides a more rigorous test of the notion of a point of no return. Our finding that the proportion of erroneous first saccades violating the STOP2cutoff could be interpreted as evidence of a possible ballistic stage. However, in contrast to the first saccades (both nonhypometric and hypometric), a vast majority of secondary saccades violated the cutoff defined by STOP2 by a surprisingly large extent (~114 ms in duration and ~78% in frequency). Further, unlike the first saccades, these violations were not restricted to the short TSDs. As a result, we argue that the programming of the secondary saccades reflects a ballistic stage not subject to voluntary control. We consider the following arguments that could be made against this hypothesis. One could argue that the secondary saccades were produced as a result of presenting the final target during the saccadic dead time (Ludwig et al. 2007), which is the point in time during saccadic preparation at which no new visual information can change the upcoming movement. Saccade dead time is typically around 80 ms prior to the movement onset (Findlay and Harris 1984) and is assumed to be caused by the afferent and efferent delays in the transmission of information between the eye and the brain regions responsible for generating the oculomotor commands (Becker 1991; Ludwig et al. 2007; Van Loon et al. 2002). We can rule out this argument since there was more than adequate time (median latency across subjects ~215 ms) for visual information to modify the decision process. Alternatively, one could suppose that inhibiting the secondary saccade could be more difficult and therefore the underlying race model could require a STOP process with a longer duration. In other words, one can assume that hypometric corrections and the hypometric errors are outcomes of a different race model. A number of reasons rule out this possibility. First, if hypometric errors are generated from a race model, they ought to be the shorter-latency secondary saccades than the corrective saccades of hypometric corrections. However, in 14/15 subjects this was not the case ($P < 0.05$, one-tail t-test). Second, even the higher TSRT, indicative of the peripheral STOP process, could not account for roughly 70% of the violations. Last, one could argue that hypometric errors represent instances when the subject did not initiate the STOP process. However, if this were true the proportion of violation should be similar for both the first saccade and the secondary saccade. However, because the proportion and the extent of violation are significantly greater for secondary saccades, despite using the same underlying race model, this possibility can be ruled out. Thus the most parsimonious explanation to account for the long latencies of the secondary saccades is if we assume that the intersaccadic interval in a multisaccade response is a ballistic stage.

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