Covert inhibition potentiates online control in a double-step task

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A planned action awaiting execution requires withholding a prepared response. We asked whether such a form of inhibition would interact with online decision processes that require changes in planned responses when new goals are unexpectedly specified. To investigate this issue with respect to oculomotor control, subjects performed, in separate sessions, standard visually-guided (SV) saccades, or memory-guided (MG) and delayed visually-guided (DV) saccades, both of which required withholding a planned saccade. To probe control, a second target (target-step) was presented in some trials after a variable delay that instructed subjects to redirect their gaze to the newly specified target. The time taken to cancel or inhibit the saccade directed at the initial target, the target step reaction time, was calculated using a race model that hypothesizes a covert inhibitory process, and was found to be significantly smaller for memory-guided redirect task (MGR; 94 ms) and delayed visually-guided redirect task (DVR; 96 ms) compared to standard visually-guided redirect task (SVR; 117 ms), suggesting facilitation of online inhibition in MGR and DVR. These results suggest that a tonic level of inhibition interacts with online decision processes to potentiate inhibitory control during double-step tasks.

Keywords: eye movements, stop signal reaction time, saccades, reaction times

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Introduction

Everyday activities such as driving and sports would be impossible without the ability to dynamically adjust one's actions to the changing demands of the environment. A behavioral task used frequently to investigate online control of eye movements is the double-step task (Aslin & Shea, 1987; Becker & Jürgens, 1979; Camalier et al., 2007; Komoda, Festinger, Phillips, Duckman, & Young, 1973; Lisberger, Fuchs, King, & Evinger, 1975; Ray, Schall, & Murthy, 2004; Westheimer, 1954; Wheeless, Boynton, & Cohen, 1966). In this task subjects are typically shown a single target to which a saccade is made. Abruptly changing the location of the target on some random infrequent trials measures the ability of the oculomotor system to compensate or control for the target shift. If the target-step is too late relative to the decision process, subjects shift gaze first to the original target position. If the target-step is early enough, subjects may compensate for the target shift by shifting their gaze to the new location.

Many studies have found that performance during double-step tasks is stochastic and the probability of compensating for the target step by directing gaze to the final target location decreases with the delay of the step, presumably because of the advancing commitment to shift gaze to the initial target location. Performance in the double-step task has been recently modelled as a race between three stochastically independent processes—a process producing the saccade to the initial target location, a process inhibiting or interrupting the preparation of the saccade to the initial target, and an ongoing process producing the saccade to the final target location (Camalier et al., 2007). Alternately, performance can also be modelled as a race between two parallel processes reflecting the preparation of mutually exclusive eye movements, giving rise to saccades directed at the initial target location or to saccades directed at the final target location (Becker & Jürgens, 1979). In contrast to the previous model, control or compensation of the target-step occurs without the explicit necessity of an intervening inhibitory process.

The goal of this study was two fold. First, we wished to test the behavioral predictions arising from alternate race model architectures that explain performance in doublestep tasks. More specifically, we wished to test whether we could find behavioral evidence of the covert inhibitory processes postulated by Camalier et al. (2007). Second, since all previous double-step experiments have utilized visually-guided saccades we wanted to test oculomotor control under conditions when the saccade is generated from a motor plan that is kept in abeyance. Since such saccades awaiting execution require withholding a prepared response, we asked whether such a form of inhibition would interact with online decision processes that require changes in planned responses when new goals are unexpectedly specified, as occurs in target-steps.

To address these issues subjects performed, in separate sessions, standard visually-guided (SV) saccades, or memory-guided (MG) and delayed visually-guided (DV) saccades, both of which required withholding a planned saccade. To probe control, a second target (target-step) was presented in some trials after a variable delay, which instructed subjects to redirect their gaze to the newly specified target. The results obtained from these sets of experiments are interpreted in the context of a race model that can be extended to explain the control of visuallyguided, as well as the control of memory-guided and delayed visually-guided saccades.

Methods

Thirteen naïve subjects with normal or corrected vision performed a saccade task while their eye movements were recorded with their heads stabilized by means of chin, forehead and temple rests. All subjects gave their informed consent in accordance with the institutional human ethics committee of National Brain Research Centre. Experiments were under computer control using TEMPO/VIDEOSYNC software (Reflective Computing, St. Louis, USA) that displayed visual stimuli and sampled and stored eye position and other behavioral parameters. Eye position was sampled at 240 Hz with an infrared pupil tracker (ISCAN, Boston, USA) that interfaced with TEMPO software in real time. All stimuli were presented on a Sony Trinitron 500 GDM monitor (21 inch; 70 Hz refresh rate) placed 57 cm in front of the subject. Stimuli were calibrated with a Minolta CA-96 colorimeter.

Task

The task combines a standard saccadic reaction time task to single targets with a modified version of the double-step task (e.g., Aslin & Shea, 1987; Becker & Jürgens, 1979; Hou & Fender, 1979; Lisberger et al., 1975; Murthy, Thompson, & Schall, 2000) where two targets appear in succession on some trials. The doublestep redirect task was performed under three separate conditions: the standard visually-guided redirect condition (Ray et al., 2004) abbreviated as SVR, a memory-guided redirect (MGR) condition and a delayed visually-guided redirect (DVR) condition (Figure 1).

Each of the conditions or tasks consisted of two different kinds of randomly interleaved trials; no-step trials (60%) and step trials (40%). In SVR, during no-step trials, following fixation for a random duration that ranged from 300-800 ms, subjects were instructed to make a saccade following appearance of the target ($1^{\circ} \times 1^{\circ}$ red;

5.87 cd/m^2). The location of the target was randomized such that it could appear in any one of 6 pre-selected locations at an eccentricity of 18° in either hemifield but not on the vertical meridian. The cue to make a saccade in this task condition was the appearance of the target, which acted as the 'GO' signal. Alternatively in the memoryguided condition, a target $(1^{\circ} \times 1^{\circ} \text{ red}; 5.80 \text{ cd/m}^2)$ appeared for 100 ms. Subjects were instructed to continue fixating till the fixation spot disappeared, which was the 'GO' signal that cued a saccade to the remembered location of the target. The delay in the disappearance of the spot from the appearance of the target, called the hold time, lasted 1000 \pm 300 ms during which subjects had to covertly inhibit the tendency to make a reflexive saccade. Similar to the memory-guided condition, the delayed visually-guided condition required subjects to make a saccadic response after the hold time, but the target was displayed throughout the delay period. For no-step trials, subjects were encouraged to respond quickly by imposing a 400 ms deadline after the 'GO' signal to make the saccade.

On step trials, following the 'GO' signal, a second target $(1^{\circ} \times 1^{\circ} \text{ green}; 5.83 \text{ cd/m}^2)$ would appear unpredictably at another location on the screen (background luminance at 2 cd/m^2) after a certain delay. Those target steps were chosen whose angular separation between the two targets was equal or greater than 90° to discourage the tendency to produce either averaging saccades or curved saccades whose trajectory tracked the target step (Ottes, Van Gisbergen, & Eggermont, 1984). Target step delays or the time of appearance of the second target relative to the first target were chosen such that they occurred within four evenly spaced bins, centered at 57, 100, 157 and 200 ms, with each bin being 28 ms wide. In step trials, subjects were instructed to cancel the planned saccade to the initial target and instead generate a saccade directly to the final target.

Trials were scored as successful if subjects fixated the target within $\pm 2.5^{\circ}$. This was determined online by means of an electronic window centered on the target. Successful trials were accompanied by a sound that provided auditory feedback. Each subject performed the SVR, MGR and DVR tasks on separate days. The temporal sequence of events that occurred in each type of behavioral condition and the resulting behavior is shown in Figure 1.

Prior to each condition, subjects were given written and verbal instructions with some practice trials (\sim 50) before data was collected. On average subjects performed about 400–500 trials for each condition. These trials were run in blocks consisting of approximately 150 trials each, with 10–15 minutes breaks in between blocks.

All offline analysis was performed using Matlab (Mathworks, USA). The analogue eye position data were smoothed from which blinks were removed. A velocity threshold of 30°/sec was used to demarcate the initiation of saccades. The saccade detection algorithm was subsequently verified manually for every saccade. All



Figure 1. Sequence of stimulus presentation and behavioral outcomes in the (A) standard visually-guided redirect task (SVR), (B) memory-guided redirect (MGR) task and (C) delayed visually-guided redirect (DVR) task. In no-step trials subjects were instructed to direct gaze to the target location immediately in SVR; to the target's remembered location after a delay in MGR; or to a visual target after a delay in DVR. In step trials a second target appeared after a random delay instructing subjects to cancel the planned saccade to the initial target and direct their gaze to the final target.

blink-perturbed saccades were eliminated from analysis. All statistical tests were done using SigmaStat or Matlab.

Calculation of target step reaction time (TSRT)

The reaction times of no-step trials along with the compensation function (see Figure 2D), which is a plot of the probability of making an erroneous response in a step trial as a function of the target step delay, provide the necessary data to estimate the time to cancel a planned saccade. This duration is referred to as the target step

reaction time (TSRT) and is analogous to the stop signal reaction time (SSRT) of the countermanding paradigm. Being a covert process, TSRT is not directly available from the behavioral data but an application of a race model provides a means for estimating its duration (Logan, 1994; Logan & Cowan, 1984). To estimate TSRT we used a race model simulated by Camalier et al. (2007) that accounts for performance during a standard visually-guided double-step task (Figures 2A and 2B). According to their model, performance is the outcome of a race between two stochastic, independent processes: a GO₁ process, initiated following presentation of the initial

target; and a STOP process, initiated following presentation of the second or final target. Noncompensated saccades are thought to result when the GO_1 process finishes prior to the STOP process. However the preparation of the noncompensated saccade is terminated if the STOP process finishes first. Another GO_2 process progressing to completion is thought to result in a compensated saccade executed to the new target location.

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TSRT was calculated in three ways using slightly different methods. In the first method, the mean of the compensation function was determined by finding the



target step delay at which the compensation function reached half its maximum value (usually the probability ranges between 0 and 1). The TSRT was calculated by subtracting target step delay from the time at which this probability equals the proportion of saccades made in the no-step distribution. We call this TSRT (inh), that is the TSRT calculated from the mean of the compensation function. To calculate the mean of the compensation function the data were fit by a cumulative Weibull function of the form:

$$W(t) = \gamma - (\gamma - \delta) \cdot \exp(-(t/\alpha)^{\beta}$$
(1)

where t is the target step delay, α is the time at which the function reaches 64% of its full growth; β is the slope; γ is the maximum value of the function and δ is the minimum value of the function (Hanes, Patterson, & Schall, 1998). The Weibull fit, being a monotonic function of t, the target step delay, parameterizes subjects' performance in the REDIRECT task because delaying the onset of the target step signal decreases the probability of successful inhibition/reprogramming. Although there are number of similar functions such as logistic or cumulative Gaussian distributions that can be used to fit such data, we chose the

Figure 2. Method for calculating the target step reaction time (TSRT) based on the race model. A and B. The two possible outcomes of the race model. The race model consists of a GO1 process (red line) and a STOP process (green line) that are racing independently toward their respective thresholds (horizontal grey line). In no-step trials only the GO₁ process is active, and a movement is generated when the GO₁ process finishes. Noncompensated responses to the initial target occur if the GO1 process finishes before the STOP process. If the STOP process finishes before the GO1 process, then the saccade to the initial target is not generated. This allows a subsequent GO₂ process to reach threshold leading to the generation of a compensated response to the second target. C. Illustration of the predictions of the race model. The fraction of the no-step reaction time distribution to the left of the dotted lines should correspond to the proportion of nonconpensated saccades elicited for a particular TSD. The fraction of the distribution to the right of the dotted lines should correspond to the proportion of compensated responses elicited for that TSD. D. The compensation function plots the proportion of target step trials in which a saccade was generated to the initial target as a function of target step delay. Comparison of the plots in D and E (the no-step reaction time distribution) indicates how the probability of making the nonconpensated saccades can be used to measure target step reaction time (TSRT) at a representative target step delay (TSD). The vertical dotted lines indicate the finish time of the STOP process, which is equal to the TSD plus the TSRT. F. The distance between corresponding points on the compensation function (open circles) and the cumulative no-step reaction time distribution (hatched grev line) can also be used to calculate TSRT. (Adapted from Hanes et al., 1998).

Weibull function for three reasons: it provides a good model for psychophysical data (e.g. Nachmias, 1981); it has been used to model performance during similar countermanding tasks (e.g. Hanes et al., 1998); and it provides a good account of observed saccade latency distributions (van Zandt, 2000). Because TSRT calculations are sensitive to the form of the compensation function we analyzed only those cases where this function met pre-specified conditions such that there was at least a difference of 0.5 between the minimum and the maximum value of the Weibull fit to the compensation function (Figure 3). 36/38 sessions obeyed this condition, and their data form the basis of this report.

Because the first method is sensitive to the form of the fit, we also used alternative methods that do not depend on the Weibull fit but rather on the actual data points. The second method estimated the TSRT by measuring the probability of eliciting a noncompensated response from the compensation function for each target step delay. The time at which this probability equals the proportion of saccades made in the no-step distribution when subtracted from the target step delay gives the TSRT at that target step delay. TSRT was estimated by taking an average across the different target step delays and we refer to this as TSRT (int). For the third method, a similar integration of the latency distribution was done for each probability value on the compensation function. Here the compensation function was treated as if it were a cumulative probability density function. TSRT was the difference in time at corresponding points on the no-step cumulative latency distribution and the compensation function (see

Figure 2F). Thus a TSRT was obtained corresponding to every target step delay. Since this method is affected by irregularities on the tail of the no-step reaction time distribution, TSRT was calculated by including only the target step delays for which the probability was between 10% and 90% (Hanes & Schall, 1995). A mean across different target step delays was calculated and referred to as TSRT (cum-int).

Results

Figure 3 shows the performance of subjects during the standard visually-guided redirect task (SVR), the memoryguided redirect task (MGR) and the delayed visuallyguided redirect task (DVR), which were performed in separate sessions by each subject. During step trials, subjects were instructed to cancel the planned saccade to the first target location and generate a saccade to the final target location. Two types of responses were elicited during step trials: either subjects cancelled the planned response to the first target location, producing a compensated saccade to the final target location; or subjects produced a noncompensated saccade, or an erroneous response to the initial target location. An evaluation of a subject's performance was implicit in the compensation function obtained for each subject, which expresses the probability of making a noncompensated saccade as a



Figure 3. A. Compensation function of a representative subject in SVR, MGR and DVR. It depicts the performance of the subject during step trials, plotting the probability of producing an erroneous or a noncompensated response as a function of the target step delay. B. Fitted cumulative Weibull fits to the compensation function for all the subjects in the three different tasks. As expected, compensation for the target step delay increased.

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TSRT	TSRT (cum-int)			TSRT (int)			TSRT (inh)		
Task→Subject↓	SVR	MGR	DVR	SVR	MGR	DVR	SVR	MGR	DVR
SD	140	68	109	126	60	105	109	69	94
AD	119	132	90	111	103	75	110	110	69
DC	125	132	**	111	113	**	108	86	**
GJ	142	125	110	143	103	100	137	95	103
SM	121	109	126	114	106	117	112	102	105
RC	116	89	109	111	96	103	100	84	85
RT	116	112	125	102	89	94	113	91	99
MG	121	104	##	103	82	##	101	102	##
AF	125	126	111	113	93	95	100	85	87
SN	117	85	96	107	68	79	109	69	81
SK	128	93	102	113	93	94	110	77	97
SJ	128	111	86	120	87	78	107	76	70
NJ	##	59	110	##	49	80	##	50	71
Mean (<i>n</i> = 10)	125	105	106	116	90	94	111	86	89

Table 1. TSRT (cum-int), TSRT (int) and TSRT (inh) values for each subject in the three different tasks (SVR, MGR and DVR). Note that the means reflects the data from subjects who performed in all three tasks. *Note:* ** Subject did not perform the task. ## Subject did not fulfill the criterion.

function of target step delay. Figure 3A shows the compensation function of a typical subject in SVR, MGR and DVR. Compensation functions were fit by a cumulative Weibull function (see Methods for further details). The monotonically increasing compensation functions (Figure 3B) show that after short target step delays subjects successfully cancelled a planned saccade to the initial target. However, as expected, the ability to inhibit the planned saccade increasingly diminished at higher target step delays.

Because memory and delayed visually-guided saccades require withholding of a planned response, MGR and DVR probe the control of internally guided responses, as opposed to SVR that accesses control of externally guided saccades. An estimate for the ability to compensate for the target step is the Target Step Reaction Time (TSRT). TSRT is a covert process not directly observable but can be estimated using the subject's compensation function and the no-step reaction time, analogous to the methods employed to access subjects' countermanding abilities (e.g. Camalier et al., 2007; Hanes et al., 1998). TSRT (int), TSRT (inh) and TSRT (cum-int) were calculated for SVR, MGR and DVR for each subject as described in the methods and are shown in Table 1. The TSRT's obtained by these methods were combined to derive a mean TSRT for each subject for each redirect condition and are displayed in Table 2.

Statistical comparisons of TSRT obtained with different methods are summarized in Table 3 for the 10 subjects who performed satisfactorily in all three conditions. The main result of this study was that the TSRT was significantly smaller in MGR (94 ms; t = 4.2, p = <0.001) and DVR (96 ms; t = 4.2, p = <0.001) compared with SVR (117 ms). However, there was no significant difference between TSRT in MGR and the DVR (t = -.5, p = 0.65). These

results are illustrated in Figure 4 and are summarized in Table 3. This result was also robust at the level of individual subjects where 11/12 and 9/10 subjects had a smaller TSRT in MGR and DVR compared with SVR.

Although the race model assumes stochastic independence of the STOP and GO processes (see Figure 2) in the calculation of TSRT, there may be a possibility that these processes are affected by common mechanisms. For example, if attention/motivation or lack of thereof were to slow down the GO process it might also similarly slow down the STOP process. Therefore, shorter TSRT's for

Mean TSRT from the three methods

Task→Subject↓	SVR	MGR	DVR
SD	125	66	103
AD	113	115	78
DC	115	110	**
GJ	141	108	104
SM	116	106	116
RC	109	90	99
RT	110	97	106
MG	108	96	##
AF	113	101	98
SN	111	74	85
SK	117	88	98
SJ	118	91	78
NJ	##	53	87
Mean (<i>n</i> = 10)	117	94	96

Table 2. Mean TSRT corresponding to each subject in the three different tasks (SVR, MGR and DVR). Note that the population mean reflects the data from subjects who performed in all three tasks. *Note:* ** Subject did not perform the task. *##* Subject did not fulfill the criterion.

Statistical analysis for subjects who performed all 3 tasks

	SVR v/s MGR	SVR v/s DVR	MGR v/s DVR
TSRT (cum-int)	<i>t</i> = 2.8, <i>p</i> = 0.012	<i>t</i> = 3.6, <i>p</i> = 0.002	<i>t</i> = −0.2, <i>p</i> = 0.86
TSRT (int)	<i>t</i> = 4.4, <i>p</i> = <0.001	<i>t</i> = 3.9, <i>p</i> = <0.001	<i>t</i> = −0.7, <i>p</i> = 0.52
TSRT (inh)	<i>t</i> = 4.6, <i>p</i> = <0.001	<i>t</i> = 4.2, <i>p</i> = <0.001	t = -0.5, p = 0.60
Mean TSRT	<i>t</i> = 4.2, <i>p</i> = <0.001	<i>t</i> = 4.2, <i>p</i> = <0.001	t = -0.5, p = 0.65

Table 3. Statistical analysis comparing the TSRT calculated through different methods in the different tasks. A statistically significant difference is observed when *t*-tests are done comparing TSRT's obtained in SVR with MGR or DVR for subjects who performed in all three tasks.

MGR and DVR compared with SVR may reflect differences in the no-step reaction times between memory/delayed visually-guided saccades and reflexive saccades. To test this, we calculated the latencies of no-step saccades for the three conditions. The mean no-step reaction time for SVR (247.2 ± 5.9), MGR (242.6 ± 7.3) and DVR (239.9 ± 5.5) were similar and not significantly different from one another (2 tailed *t*-test; MGR vs. SVR, p = 0.86; DVR vs. SVR, p = 0.19; MGR vs. DVR, p = 0.91). For individual subjects that showed a shorter TSRT in MGR and DVR versus SVR, we observed no significant differences or significantly greater no-step reaction times in SVR in 6 out of 11 subjects and in 8 out of 9 subjects, respectively.

Because the estimation of TSRT derives from a race model, we tested its validity for the three conditions. One critical prediction of such a race model is that the latency of noncompensated saccades in all three conditions should progressively approach the no-step saccade latencies with increasing target step delays. This is because the finish times of the STOP process effectively partitions the nostep reaction time distribution such that at a given target step delay, only those saccades from the no-step distribution that have shorter latencies than the target step delay, plus the TSRT, escape reprogramming (see Figure 2). In other words, had a target-step occurred, this subset of no-step saccades would have resulted in noncompensated saccades. Because the finish times of the STOP process is progressively delayed at larger target step delays, the latencies of the predicted noncompensated saccades are also expected to be larger. We tested this prediction by plotting the cumulative reaction time distribution of the observed noncompensated latencies as a function of target step delay (represented by a graded color scheme of red, green and blue for SVR, MGR and DVR tasks, respectively). Figure 5A illustrates the data from a single subject in all three conditions. Consistent with the race model, we find the cumulative distributions are progressively shifted rightward, approaching the nostep distributions as target step delay increases. A further, corollary to this prediction is that all distributions should converge at the shortest latencies, since at these latencies noncompensated saccades would be evoked regardless of the target step delay. Such a pattern produces what is

commonly referred to as the fanning effect and has been shown to exist in behavioral data collected with humans and non-human primates in the SVR task (Camalier et al., 2007). As can be seen in Figure 5A all three task conditions showed clear evidence of the fanning effect.

To quantify the fanning effect, the reaction time corresponding to the 50th percentile of the cumulative noncompensated reaction time distribution was estimated for each target step delay and subtracted from the corresponding value obtained from the cumulative nostep reaction time distribution. Only those target step delays that had a minimum of 5 trials were deemed reliable enough to contribute to this analysis. Because at larger target step delays, the noncompensated reaction time distribution approaches the no-step reaction time distribution, the difference in mean reaction times as a function of target step delay should decrease. The pattern for a representative subject is shown in Figure 5B. The regression slope in SVR, MGR and DVR were -0.38, -0.22, and -0.58, respectively, in accordance with the race model. The fits for all the subjects in the three conditions are shown in the Figure 5C. In accordance with the race model we observed a negative slope for all subjects (except one) and conditions (SVG mean = -0.32 \pm 0.06, min = -0.61, max = 0.01; MG mean = -0.39 \pm



Figure 4. Estimated mean target step reaction time (TSRT) in the three tasks. TSRT was significantly shorter in DVR and MGR relative to SVR, showing that subjects' ability to inhibit was facilitated in DVR and MGR relative to SVR.



Figure 5. Test of the race model. At progressively larger target step delays (TSD; coded in graded colours), the nonconpensated reaction time distribution should approach the no-step reaction time distribution (in black). A. The cumulative reaction time distribution increases as a function of TSD for the representative subject SM. B. The difference of the 50th percentile values from the no-step and the nonconpensated reaction time distributions were plotted as a function of target step delay. The slope of the best-fit regression line to the data was analyzed. Negative slopes indicate that the nonconpensated reaction times progressively increased with target step delay. C. The figure illustrates the results across all subjects in the three tasks. Data showed a negative slope for all subjects (except one), showing that the behavior was in accordance with the race model proposed by Camalier et al. (2007).

0.06, min = -0.74, max = -0.05; DVG mean = -0.41 ± 0.06 , min = -0.65, max = -0.18).

In addition to predicting the general distribution of noncompensated reaction times, we also tested whether the race model could predict the mean noncompensated reaction times. Such a prediction is based on the premise that the finish times of the STOP process at a given target step delay effectively partitions the no-step distributions into two daughter distributions (see Figure 2C). All noncompensated saccades, and hence their central tendencies, should derive from the subset of no-step reaction times that finish the race faster than the STOP process. To test the validity of the race model we selected a central target step delay at the midpoint of the compensation function. Figure 6 is the scatter plot of the observed mean and median reaction time in comparison with the predicted mean and median reaction times, respectively, for all the subjects across the three task conditions. In

accordance with the race model we observed significant correlations in SVR (Mean: r = 0.87, p < 0.01; Median: r = 0.90, p < 0.01), MGR (Mean: r = 0.57, p = 0.05; Median: r = 0.60, p = 0.04), and DVR (Mean: r = 0.88, p < 0.01; Median: r = 0.86, p < 0.01); and linear regressions of the best fit line constrained to pass through the origin had slopes that were statistically indistinguishable from a line of unity slope in SVR (95% confidence intervals for mean: [0.9771, 1.055]; and median: [0.9572, 1.035]); and MGR (95% confidence intervals for mean [0.9838, 1.093]; and median [0.9574, 1.069]), but not in DVR (95% confidence intervals for mean [1.032, 1.095]; and median [1.035, 1.124]).

Because the prediction of the race model was obeyed in all three conditions we tested whether the latency of the noncompensated saccades in MGR and DVR were larger than the corresponding noncompensated saccades elicited from the same target step in SVR. If TSRT's in MGR and



Figure 6. The race model is able to predict central tendencies of nonconpensated reaction times in SVR, MGR and DVR. Scatterplot of observed versus predicted mean (filled magenta) and median (open black) noncompensated reaction time for A) SVR B) MGR and C) DVR.

DVR are shorter than those for SVR, then as predicted by the race model, the shorter the TSRT, the shorter should be the latency of noncompensated saccades that escape control. As predicted by the race model noncompensated saccades were shorter in MGR (201.03 ± 4.1) and DVR (209.6 ± 4) when compared to SVR (215.1 ± 4.6). A twoway ANOVA with respect to task type and target step delay when done for SVR versus MGR showed a significant difference (F = 11.887, p < 0.001), but did not reach significance for SVR versus DVR (F = 3.386, p = 0.07). This result was robust even at the level of individual subjects where 8 out of 12 subjects had mean noncompensated reaction times that were greater in SVR

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than MGR, and 7 out of 10 subjects had mean noncompensated reaction times greater in SVR than DVR. These results are summarized in Figure 7.

In the race model of Camalier et al. (2007) it is assumed that a distinct STOP process races against a GO1 process, encoding the saccade to the initial target. Alternatively, performance may be explained by a race between a GO₁, encoding the noncompensated saccade to the initial target, and a GO₂ process, encoding the compensated saccade to the final target location (GO₁-GO₂ model). If the latter race model was true, the latency of the estimated TSRT (STOP process) should be strongly correlated with the reaction time distribution of compensated saccades (the finish times of the GO₂ process). To test this prediction we performed a correlation analysis (see Figure 8) between TSRT and the reaction time of compensated saccades. Contrary to the expectations of the GO_1 - GO_2 model, we found no significant correlations between the two variables in all task conditions. (SVR - df = 10, slope = 0.13, r =0.37, p = 0.24; MGR - df = 11, slope = 0.35,r = 0.54, p = 0.06; DVR - df = 9, slope = 0.24, r =0.42, p = 0.20). A similar result (discounting the MGR data, where a significant correlation was observed) was also obtained if we used median reaction times, instead (SVR df = 10, r = 0.40, p = 0.20; MGR - df = 11, r = 0.55,p = 0.05; DVR - df = 9, r = 0.41, p = 0.21). We also tested whether the longer TSRTs' associated with SVR were associated with longer compensated reaction times compared with MGR and DVR. Although the mean compensated reaction times were greater in SVR (208.3 \pm 7.4) compared to MGR (197.3 \pm 7.9; p = 0.31, 2-tailed *t*-test) and DVR (190.5 \pm 6.3; p = 0.01, 2-tailed *t*-test), the trend was not particularly robust at the level of the individual



Figure 7. Mean nonconpensated reaction time increase with target step delay and is shorter for MGR and DVR relative to SVR.



Figure 8. Weak correlations between TSRT and mean compensated no-step reaction times suggest that the STOP and GO₂ process producing compensated responses are unlikely to be manifestations of a single underlying process.

subject where only 5/12 and 6/10 subjects showed a significantly larger mean compensated reaction time in SVR compared with MGR or DVR, respectively, as expected from a GO_1 - GO_2 race model architecture. Therefore, although our small sample size precludes a

strong conclusion, taken together our results favor a model that hypothesis an independent covert inhibitory process to better explain performance in double-step tasks.

Since memory and delayed visually-guided saccades were elicited from hold times that were uniformly distributed, the passage of time during the foreperiod may have been used as a signal to warn subjects of the upcoming signal (fixation offset). This is because if the foreperiod (time before a stimulus) is uniformly distributed, the likelihood (conditional probability) that the trigger stimulus (fixation spot offset) will occur in the next instant, given that it has not already occurred, increases with the passage of time within the hold time. Such a warning of an upcoming signal is expected to reduce the time to respond to that signal (Findlay, 1981; Schall & Hanes, 1993). To determine whether our subjects used the uniformly distributed hold times (700–1300 ms) to covertly plan their saccades, we divided the trials into two groups based on the duration of their hold times. Short hold time trials consisted of hold times that ranged from the minimum hold time (700 ms) to the average of the minimum and the maximum hold time that a subject was exposed to. Long hold time trials consisted of hold times that ranged from the maximum hold time (1300 ms) to the average of the minimum and the maximum hold time that a subject was exposed to. Consistent with our hypothesis, we found that in MGR and DVR, mean nostep reaction times across the population decreased with increasing hold times. For MGR the no-step mean reaction time at the longer hold time was 224.2 ms and significantly shorter (p < 0.01, 2-tailed *t*-test) than the no-step mean reaction time at the shorter hold time which was 259.6 ms. For DVR, as well, the no-step mean reaction time at the longer hold time was 223.1 ms and significantly shorter (p < 0.01, 2-tailed *t*-test) than the nostep mean reaction time at the shorter hold time which was 259.7 ms. The effect was robust even at the level of individual subjects where all subjects (n = 13) in MGR and (n = 12) in DVR displayed shorter no-step reaction times at longer hold times (Figure 9A).



Figure 9. A. The no-step reaction times for individual subjects performing MGR and DVR decreases with increasing hold time. B. The TSRT for individual subjects performing MGR and DVR decreases with increasing hold time.

To determine how inhibitory control, as assessed by the TSRT, varied as a function of the degree of planning during the hold time, we measured TSRT as a function of the short and long hold times. Because the number of trials from which compensation functions were derived from was reduced by a factor of two, we restricted our analyses to subjects whose compensation functions were considered satisfactory despite the smaller number of trials. For this we only considered those cases where the difference between the compensation function at the maximum and minimum target step delays were at least greater than 0.5. This ensured that the compensation functions still maintained a monotonic dependence as a function of target step delay despite the smaller number of trials. In 19/25 subjects (for MGR and DVR) good compensation functions were obtained for each hold time. By separating the no-step reaction times into the appropriate hold times as well, the TSRT was calculated by the same methods described earlier, for the short and long hold times. In MGR the mean TSRT across subjects was 95 ± 6 ms in the short hold time while the mean TSRT was reduced to 87 ± 5 ms in the longer hold time (p = 0.06, 2-tailed *t*-test). A similar dependency of TSRT on hold time was obtained in DVR, the mean TSRT in the short hold time being 100 ± 3 ms while the mean TSRT in the long hold time being 95 ± 6 ms (p = 0.32, 2-tailed t-test). Although the effect of hold time on TSRT was not significant, 15/19 sessions showed a decrease in the TSRT value as a function of hold time and is illustrated in Figure 7. In addition, a significant decrease was observed in the TSRT with respect to hold time when the data was collated across the two tasks (p = 0.04, 2-tailed *t*-test). The average TSRT after collation was 97 \pm 3 ms and 91 \pm 4 ms for the shorter and longer hold times, respectively (Figure 9B).

Discussion

In this study we address two important issues concerning the control of saccades as probed by the double-step task. First, we tested the behavioral predictions arising from alternate race model architectures that explain performance in double-step tasks. Second, we have developed a novel oculomotor double-step task to understand how control is implemented under conditions when a saccade is generated from a motor plan that is kept in abeyance. A model of how inhibitory circuits may control such saccades will be presented.

Race models of double-step saccade performance

A major goal of this study was to evaluate different architectures of the race model and, in particular, to gain an insight into the nature of control underlying performance during a double-step task. Where as behavioral results from the stop-signal task (Asrress & Carpenter, 2001; Cabel, Armstrong, Reingold, & Munoz, 2000; DeJong, Coles, Logan, & Gratton, 1995; Hanes & Carpenter, 1999; Hanes & Schall, 1995; Kornylo, Dill, Saenz, & Krauzlis, 2003; Lappin & Ericksen, 1966; Logan & Cowan 1984; Logan & Irwin, 2000; Osman, Kornblum, & Meyer, 1986, 1990; Vince, 1948) have been successfully modeled by assuming a race between two independent processes: a STOP process that cancels movements, and a GO process that prepares movements, the nature of control in a double-step task is not clear. This ambiguity arises because in the context of the redirect task, subjects are required not only to cancel a planned response, but also prepare another response that shifts gaze to a second target. The performance of subjects could be modeled here as a race between two GO processes, namely GO_1 (in response to the initial target) and a GO₂ (in response to the final target), each one of which programs a mutually exclusive movement. These are the compensated and noncompensated responses, respectively. This means that a STOP process is not required. However, a simple analysis of the reaction times of the compensated and noncompensated saccades suggest that in order to simulate the observed compensation functions (Figure 3), the distribution of compensated saccade latencies produced need to be significantly faster than the observed behavioral data. Since compensated saccades are generally observed to be approximately only 7 ms faster than noncompensated saccades (in SVR), this implies that at target step delays of 7 ms the finish times of compensated and noncompensated saccades should be the same, producing compensated and noncompensated saccades with the same probability $(p\{\text{error}\} = p\{\text{cancel}\} = 0.5)$. However, compensation functions from subjects in the SVR reveals that at such target step delays, the probability of making an error was a lot less than 0.5, or conversely the probability of success was much more than 0.5 (Figure 3). Thus one can negate the assumption that a simple direct race between GO₁ and GO₂ can account for the observed data. A similar logic applies to performance in the DVR and MGR tasks based on the general applicability of the same race model architecture for these tasks as well (Figures 5 and 6).

In contrast, an alternate race model that posits a race between the GO_1 process generated as a primary response saccade and a STOP process leading to cancellation of the partially prepared response may better explain the observed performance curves. This model has been tested in formal computer simulations of double-step performance under different stimulus conditions (Camalier et al., 2007), and for every data set examined, the best-fitting model included a STOP process that interrupted the first saccade. The difference in the duration of the STOP processes both within and across task conditions, as accessed by the TSRT, was also used to address the question of whether the STOP and GO₂ processes specify uniquely independent processes or whether they derive in part from the same substrate. If GO₂ (leading up to the compensated saccade) and STOP are part of the same process we expect them to co vary within a task as well as across task conditions. While the lack of correlation in Figure 8 may appear rather weak, some degree of correlation between STOP and GO₂ processes is to be expected even if they are stochastically independent, given that hypothesized STOP and GO₂ reaction time depend on a potentially common process, such as the encoding of the target step. Thus, rather than necessarily confirming the independence of GO_2 and STOP, this analysis, in our mind, refutes the strong hypothesis that these two processes are manifestations of a single underlying process.

That longer TSRTs were not necessarily associated with longer compensated reaction times across task conditions, particularly at the level of individual subjects, also provides complimentary support to the result of the correlational analysis. These evidences, taken together, favor a model that hypothesizes an independent covert inhibitory process to explain performance in double-step tasks. Thus, in the context of redirect task the target step reaction time (TSRT) or the time it takes to cancel a partially planned movement, and hence modify ongoing behavior, is formally equivalent to stop signal reaction time that measures the duration of the STOP process in stop signal tasks (SSRT; Logan, 1994). In fact, our estimate of TSRT in SVR (117 ms) closely matches the SSRT values estimated from other studies (Hanes & Carpenter, 1999; SSRT = 125 ms - 145 ms; Cabel et al., 2000; SSRT = 113 ms; Assress & Carpenter, 2001; SSRT = 128 ms) using versions of the oculomotor visual countermanding (stop signal) paradigms, and forms the basis of the conclusions of this study.

Inhibitory control during delayed saccades

If a covert STOP process is responsible for control in a double-step redirect task then performance may improve when saccades are actively inhibited during their planning. Testing inhibitory control under conditions when a saccade is generated from a motor plan that is kept in abeyance tested this hypothesis in the study; our assumption being that during fixation, potential saccades to other objects in the visual field must be suppressed. Evidence that memory and delayed visually-guided saccades are actively suppressed during fixation derives from different lines of evidences. For example, human patients with frontal lobe lesions have difficulty in suppressing reflexive saccades (Braun, Weber, Mergner, & Schulte-Mönting, 1992; Guitton, Buchtel, & Douglas, 1985; Pierrot-Deseilligny et al., 2003), implicating the dorsolateral prefrontal cortex and the frontal eye fields (FEF) as potential cortical substrates mediating suppression. During the delay of a memory-guided saccade task, there is both spatially selective excitatory and inhibitory neural activity in dorsolateral prefrontal cortex (Funahashi, Bruce, & Goldman-Rakic, 1989, 1993). A central operation attributed to these latter neurons is the suppression of saccadic eye movements during the memory delay (Funahashi et al., 1989, 1993) via prefronto-tectal projections to the superior colliculus (Hikosaka &Wurtz, 1983). Some neurons in the FEF have also shown to be activated selectively in conditions requiring withholding of saccades (Sommer & Wurtz, 2001) in general, as well as to specific locations (Hasegawa, Peterson, & Goldberg, 2004). Indeed, electrical stimulation of selective areas, the so-called "fixation zones" in the FEF (e.g., Burman & Bruce, 1997; Izawa, Suzuki, & Shinoda, 2004) and the superior colliculus (SC; e.g., Munoz & Wurtz, 1993) are known to suppress saccades. That fixation is an active process is also suggested by microstimulation experiments where it is observed that the threshold for evoking saccades by electrical stimulation in the FEF (Goldberg, Bushnell, & Bruce, 1986) and superior colliculus (Schiller & Sandell, 1983) is greater when monkeys fixate compared to when their eyes are freely scanning the environment.

While no direct evidence was obtained for increased inhibition in MGR and DVR relative to SVR in our study, since their no-step reaction times were not significantly different, an indirect measure that suggests covert inhibitory control was being exercised was provided by the socalled foreperiod effect (e.g., Niemi & Naatanen, 1981), in which no-step saccadic reaction times decrease with increasing hold time (Findlay, 1981; Schall & Hanes, 1993). The standard explanation for the foreperiod effect is that subjects use the elapsed time during the foreperiod to get more & more ready to move (e.g., Niemi & Naatanen, 1981). Physiologically, correlates of this covert saccadic planning can be observed in the pattern of activity in movement cells that increase during the hold time (Dorris & Munoz, 1995; Munoz, Dorris, Paré, & Everling, 2000). In order to keep the motor plan from being executed we assume that during the hold timeinhibitory control-presumably through fixation cells of the FEF and/or striatum and/or superior colliculus and/or omnipause neurons of the brain stem, must be exercised failing which subjects are likely to break fixation and direct their saccades to the target. A measure of this inhibitory control or lack there of can be occasionally detected by measuring the frequency of fixation breaks which is expected to increase as a function of hold time in MGR/DVR. In concurrence with this hypothesis we noted that out of a total of 137 fixation breaks observed in MGR across all subjects, 53 occurred at a lower hold time (700-1000 msec) and 84 (1000-1300 msec) at a higher hold time. A similar trend was also observed in DVR, where in the subjects broke fixation 9 times in the shorter hold time and 33 times in longer hold time, out of the 42 fixation breaks observed. This result was also robust at the level of single subjects where 9 out of 13, and 9 out of 12 subjects had a higher propensity of breaking fixation at longer hold times in MGR and DVR respectively. This suggests that during the hold time although saccade to the target was being covertly planned, inhibitory control was being exercised to keep the motor plan from being executed. The relative insensitivity of reaction times with the level of inhibition may be explained within the current framework of oculomotor control where inhibitory control primarily acts as a "gate," preventing the expression of the underlying saccade generating mechanism, the timing of which is the primary determinant of reaction time (Gandhi & Bonadonna, 2005).

Control of memory and delayed visuallyguided saccades

That TSRT values were similar for MGR and DVR suggests a relation between withholding a response (inhibition) and the reduced TSRT obtained in MGR and DVR relative to SVR. Therefore, differences in TSRT across tasks might reflect differential recruitment of the brain's inhibitory system, which is withholding a reflexive response to the flashed target, while subjects perform MGR and DVR saccades. Implementing such a form of inhibitory control would mean that a basal level of inhibition be maintained. Such a tonic inhibition, if it interacts with the STOP process, would mean that the STOP process is potentiated even before it is initiated by the target step. This may contribute to an elevated rise so that it reaches the threshold faster, resulting in a shorter TSRT. Thus the "race" between the GO and the STOP processes would be relatively favored towards the STOP in MGR/DVR in comparison to the SVR task. This effect is modeled in a modified race model depicted in Figure 10, which shows how the STOP signal rises from an already elevated state to reach threshold faster, producing a greater chance for subjects to redirect their gaze to the final target.

This model not only offers the ability to describe and quantitate the ability of the brain to inhibit an action, which is planned and kept in memory for later execution, but has neurophysiological and behavioral predictions that can be experimentally validated. First, if inhibitory control is mediated by fixation neurons in the frontal eye field/ superior colliculus, whose pattern of activity closely matches the timing of the estimated STOP process (Hanes et al., 1998; Paré & Hanes, 2003), then our model predicts that fixation neurons should be active during double-step redirect tasks. Second, our finding that TSRT decreases with hold time predicts that fixation activity should concomitantly increase during the hold time to match the level of movement cells activity that is known to increase similarly during the hold time (Munoz et al., 2000). Such a pattern of increasing inhibition may be a necessary in order to prevent the premature execution of saccades

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Figure 10. Proposed race model for MGR and DVR. A shorter TSRT is observed in case of DVR and MGR relative to SVR. This ability to inhibit faster in case of the former two tasks is explained with the help of a modified race model, where the STOP process is potentiated by a tonic inhibition. The accrual of this inhibition is attributed to the delay period in MGR and DVR when subjects prevent a planned saccade from execution. The new/potentiated STOP process reaches threshold faster resulting in a shorter TSRT. Note that TSRT is the time the STOP process takes to reach threshold.

during the hold time. While a similar pattern of increasing fixation activity has been shown to occur in superior colliculus particularly for longer hold times (>200 ms; see Munoz et al., 2000), this result needs to be validated for conditions in which the fixation spot remains visible throughout the foreperiod. Third, the model predicts enhanced inhibitory control or a shorter TSRT for all voluntary saccade tasks since successful performance in these tasks require inhibition of a prepotent behavioural response. For example, performance in the antisaccade task not only entails making a voluntary saccade to the location opposite to the stimulus (a non-standard stimulus response mapping), but also involves inhibiting the prepotent prosaccade prepared to the location of the stimulus (e.g., Chan, Armstrong, Pari, Riopelle, & Munoz, 2005). Based on data obtained by Pierrot-Deseilligny et al. (2003) who have recently shown that the same group of patients with lesions specific to the dorsolateral prefrontal cortex are not only less efficient at suppressing a saccade

during the memory-guided saccade task but also showed a significantly higher number of errors when asked to perform an antisaccade task, we speculate that TSRT's should be shorter when subjects are required to inhibit planned antisaccade as well. Consistent with this prediction, Geier, Costello, Willford, & Luna (2005) have recently found that systematically increasing the response preparation time before the cue to make an antisaccade improved subjects' performance. As such, our model makes the non-intuitive prediction that inhibitory control should be paradoxically easier for more cognitively demanding tasks. Some support for this prediction derives from some recent results of a study, which (Emeric et al., 2007) which reported that in the countermanding task the probability of non-canceled saccades in a stop trial is often lower when this trial occurs after a 'STOP' trial. This result implies that the corresponding STOP process would also be faster when conflict on the previous trial presumably triggers the 'executive networks' that in turn help recruit a higher degree of inhibitory control (Botvinik, Braver, Barch, Carter, & Cohen, 2001).

Relation to previous studies

Although to the best of our knowledge no previous study has examined inhibitory control under conditions when a saccade is generated from a motor plan that is kept in abeyance, a recent study using manual responses found (Li, Krystal, & Mathalon, 2005) that stopping latencies were longer for larger fore periods, in contrast to what we report here. These authors explained their results on the assumption that a potentiated GO signal might be harder to inhibit, which is reflected in longer stopping latencies. The basis of this discrepancy may lie in the assumption that only the GO signal is potentiated during the foreperiod, unlike in our model where it is assumed that both GO and STOP are potentiated. While the model of Li et al. may be true for manual responses where the level of fixation related activity in oculomotor areas might be independent of the GO signal which is presumably represented in motor cortices there is ample empirical evidence alluded to earlier (Munoz, Dorris, Pare, & Everling, 2000) that fixation activity plays a critical role in the control of gaze. For this reason it is not completely surprising that inhibitory control was not potentiated during the manual task.

That inhibitory control of gaze and manual responses may be different in certain aspects is also raised by the results of other studies which have found that stopping latencies were either not effected, or paradoxically slower under conditions when the STOP process interacted with other forms of inhibition, such as inhibiting prepotent spatially compatible responses while making spatially incompatible responses (Logan & Irwin, 2000); inhibition induced by flanking distractors (Kramer, Humphrey, Larish, Logan, & Strayer, 1994; Ridderinkhof, Band, & Logan, 1999); or inhibition that leads to reduced responsiveness (van den Wildenberg, van der Molen, & Logan, 2002). A possible basis for the paradoxical increase in STOP reaction times was suggested by van den Wildenberg et al. who interpreted their data in the context of the response readiness model (Niemi & Naatanen, 1981). These investigators suggested that certain forms of inhibition that increase reaction times may manifest as an increase in the threshold of responding, which, although expected to produce delayed responding, are also thought to produce responses that are more forceful and hence more difficult to inhibit as well. While differences between task demands and the type of motor responses may preclude a direct comparison between the data sets, an important empirical difference between our results and theirs is that while their manipulations increased reaction times, no difference in reaction times were observed between SVR and MGR or DVR, suggesting that fixation induced inhibition may not operate in the oculomotor system by manipulating the threshold of responding. Based on this observation we suggest that the postulated inhibition induced by active fixation during the hold time may be qualitatively different from the forms of inhibition induced by the other studies.

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