

Canceling Planned Action: An fMRI Study of Countermanding Saccades

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We investigated the voluntary control of motor behavior by studying the process of deciding whether or not to execute a movement. We imaged the human dorsal cortex while subjects performed a countermanding task that allowed us to manipulate the probability that subjects would be able to cancel a planned saccade in response to an imperative stop signal. We modeled the behavioral data as a race between gaze-shifting mechanisms and gaze-holding mechanisms towards a finish line where a saccade is generated or canceled, and estimated that saccade cancelation took ~160 ms. The frontal eye fields showed greater activation on stop signal trials regardless of successful cancellation, suggesting coactivation of saccade and fixation mechanisms. The supplementary eye fields, however, distinguished between successful and unsuccessful cancelation, suggesting a role in monitoring performance. These oculomotor regions play distinct roles in the decision processes mediating saccadic choice.

Keywords: countermanding, eye fields, fMRI, inhibition, monitoring, oculomotor, saccades

Introduction

When faced with fastballs approaching 100 miles per hour, professional baseball batters have no other choice but to begin their swinging motion as soon as the pitch is released. Between the moments when the ball leaves the pitcher's hand and when it reaches the plate, a batter may decide that the ball is going to curve wide and begins to cancel the planned action. A race then ensues between the processes giving rise to the swing and the processes giving rise to its cancelation. The outcome of this race is heavily biased by when the signal to cancel the action is detected. For example, success in canceling the swing is more likely when the ball curves early than when the ball curves late in the pitch.

This example highlights several issues that are at the heart of voluntary control of behavior. Control is necessary when the best motor response is uncertain or when a competing response must be overcome. Competition between planned action (e.g. the swing) and the cancelation of that action based on the detection of a stop signal (e.g. the pitch curving wide) has been successfully studied using laboratory analogues of the real-life scenario described above (Logan and Cowan, 1984; Logan, 1994; Schall *et al.*, 2002). *Countermanding tasks*, as they are called, require the voluntary control over the production of movements because an imperative stop signal is infrequently presented instructing the subject that the planned movements should be withheld. Withholding a planned action is a critical demonstration of voluntary control.

In the context of a countermanding task, canceling a planned movement following a stop signal can be modeled as a race between independent GO and STOP mechanisms (Logan *et al.*, 1984; Hanes and Carpenter, 1999) (Fig. 1). Which process first reaches a critical threshold, or finish line, determines whether

the planned response is generated or not. By adjusting the time between the presentation of the stimulus that initiates the GO response processes and the presentation of the stop stimulus, an interval known as the stop signal delay, the probability that either one of the two possible responses will win the race, can be adjusted. Canceling is easier when the stop signal delay is short because one has more time to cancel the movement.

Support for the race model of voluntary control over action comes from behavioral (Logan *et al.*, 1984; Osman *et al.*, 1986; Hanes and Schall, 1995; Hanes and Carpenter, 1999; Cabel *et al.*, 2000; Asrress and Carpenter, 2001; Colonius *et al.*, 2001; Ozyurt *et al.*, 2003) and electrophysiological (De Jong *et al.*, 1990, 1995; Osman *et al.*, 1992) studies of humans performing manual countermanding tasks. The primate saccade system is arguably the best understood system for producing movement and thus is an ideal system to test models of voluntary control of behavior (Carpenter, 2000; Schall, 2001; Glimcher, 2003). Electrophysiological recordings from single neurons in superior colliculus (SC) (Paré and Hanes, 2003), frontal eye fields (FEFs) (Hanes *et al.*, 1998), supplementary eye fields (SEFs) (Stuphorn *et al.*, 2000), and dorsal anterior cingulate cortex (ACC) (Ito *et al.*, 2003) of monkeys performing a saccade version of a countermanding task has provided additional and compelling evidence in support of the race model of voluntary motor control. These studies have shown that the balance between gaze-shifting and gaze-holding mechanisms determines whether or not a saccade will be produced. The presaccadic growth of activity in gaze-shifting neurons is correlated with saccade production, while the growth of activity in gaze holding neurons is correlated with saccade withholding during the performance of countermanding tasks (Hanes *et al.*, 1998; Schall *et al.*, 2000, 2002; Paré and Hanes, 2003). Additionally, there appears to be a class of neurons in the SEF and ACC that contribute to voluntary control of saccadic behavior, not by triggering or inhibiting saccades, but by monitoring task performance variables (e.g. response errors, conflict and consequences) (Stuphorn *et al.*, 2000; Ito *et al.*, 2003).

Voluntary control of behavior can be exerted at any point along the series of processes that evolve over time from sensation to action. Our recent imaging studies of voluntary control of the human oculomotor system have investigated how maintaining past information (Curtis *et al.*, 2004) or anticipating future plans (Curtis and D'Esposito, 2003b) bias the later response decision process towards the desired behavior. Here we ask how control is implemented far down-stream in the perception-action cycle, after the motor plan has been generated. We used a saccade version of the countermanding task in which planned saccades are occasionally canceled (Fig. 2). In a rapid event-related functional magnetic resonance imaging (fMRI) study, we imaged the dorsal cortex and recorded eye position while subjects attempted to countermand saccades

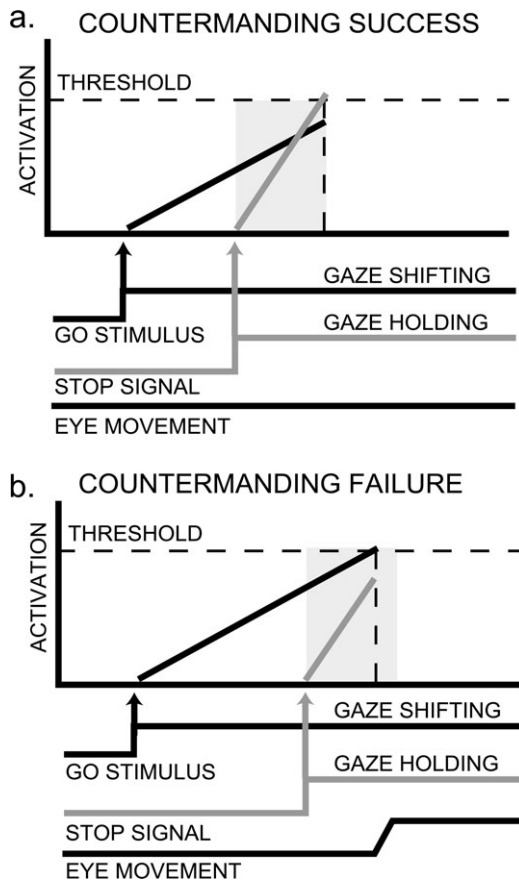


Figure 1. Race model of countermanding task. Performance on the countermanding task has been conceptualized to be a race between GO and STOP processes. The activation of neural GO processes related to shifting gaze (black line) race against the activation of neural STOP processes related to holding gaze (gray line) toward a winner-take-all threshold (dashed horizontal line) that determines whether a saccade is triggered or not. The gray bar represents the time needed to cancel a saccade after a stop signal has been emitted, a time known as the stop signal reaction time (SSRT) a. If the processes leading to holding gaze reach a critical threshold before the processes that lead to shifting gaze, then successful saccade cancellation will occur. b. However, if the gaze shifting processes reach threshold first, then a saccade will be triggered. Notice that in b, the stop signal delay was longer, which resulted in less time for the processes leading to holding gaze to grow to threshold. Manipulating this delay can reliably affect successful saccade countermanding.

during trials in which the stop signal delay was adjusted to psychophysical performance thresholds. We predicted that specific nodes in the cortical oculomotor network would show patterns of activity that can sufficiently account for success and failure of voluntary saccadic control. One of our main goals was to provide a strong translational link from the exquisite electrophysiological data derived from the non-human primates to functional imaging of the human brain.

Materials and Methods

Subjects

Twelve volunteers between the ages of 18 and 33 (five women) were paid to participate. Nine were right-handed, one left-handed, two ambidextrous. All gave informed consent of procedures approved by the University of California, were of good mental and physical health, and denied a history of mental disorders.

Stimuli and Apparatus

Experiments were controlled by a personal computer running E-prime software (Psychology Software Tools, Pittsburgh, PA). Stimuli were

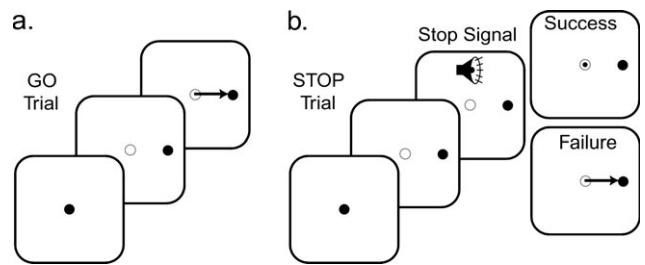


Figure 2. Countermanding task trial schematic. All trials began with central fixation. a. On GO trials, subjects made speeded saccades (depicted by arrow) to the appearance of a peripheral target to the left or right of fixation. This type of trial occurred 60% of the time. b. On STOP trials, an auditory stop signal tone was emitted after a period of time known as the stop signal delay. This signaled the subject to cancel the planned movement. Sometimes the subject was successful and sometimes failed at canceling the planned saccade. Stop trials were relatively rare and occurred on 20% of the trials unpredictably. Twenty percent of the trials were CATCH trials (not depicted) in which no peripheral target appeared and the subject simply remained at fixation.

back-projected onto a tangent screen placed 42 cm away from a small viewing mirror placed right above the subject's eyes. The background was uniform black and the saccade targets were white dots that subtended 0.25° of visual angle and could appear 8° of visual angle either to the right or left of fixation. An auditory 1000 Hz tone was presented to subjects in the scanner via a MR compatible pneumatic tube connected to an audio amplifier. The projector was synchronized to the computer by the vertical refresh. The computer was synchronized to the MRI scanner by a TTL pulse that was delivered at the beginning of every volume acquisition. The computer that recorded eye position (see below) was synchronized to the experimental computer via a serial port connection.

Behavioral Task

Subjects performed eight runs of a saccade countermanding task (Fig. 2). The order of the trials was counterbalanced and yielded a total of 240 GO, 80 CATCH and 80 STOP trials with an equal number of right and left targets. No more than three STOP trials could occur in a row. The intertrial intervals (ITIs) were variable with 50% of the trials being 4, 33% of the trials being 6, and 17% of the trials being 8 s in duration. Trial type, target side and ITI were randomized according to an algorithm designed to optimize statistical power while retaining task unpredictability (Wager and Nichols, 2003). Steps were taken to assure that subjects generated saccades as rapidly as possible. First, STOP trials were relatively rare compared to GO trials. Second, subjects were instructed to make saccades as quickly as possible, and that error on some STOP trials was normal. Third, they were told that the top three fastest subjects would receive an extra \$20 bonus. Catch trials were used for two reasons. First, it served as a non-visual, non-motor control condition. Second, deconvolution in rapid event-related fMRI studies is more robust with increased trial type variability (see *Event-related Data Analysis* below).

During the acquisition of structural images at the beginning of the session, subjects performed ~10 min of practice trials. Using a staircase procedure during this pretesting, we estimated a stop signal delay that resulted in ~50% accuracy. We tried to arrive at psychophysical threshold during pretesting so that during the experiment we would not have to make any changes to the stop signal delay. We did not want to introduce a confound into our comparison of successful and unsuccessful STOP trials. Specifically, we did not want to compare short stop signal delays associated with success to long stop signal delays associated with failure. We wanted to compare success and failure during identical trials, so that brain activation differences cannot be attributed to different sensory events. Nonetheless, during the experiment small changes in the delay were occasionally made for about half of the subjects to maintain approximate threshold. These stop signal delays were adjusted in steps of 16.7 ms (one video refresh at 60 Hz). Six subjects experienced only 1–2 stop signal delays during the scanning because they stabilized near threshold during the pretesting and did not require adjustments to the delay. The rest of the subjects only experienced delays that spanned a short interval (e.g. 100–150 ms). This narrow range of stop signal delays

did not permit the construction of inhibition functions that represent the probability of STOP failure as a function of stop signal delay (Logan, 1994; Hanes and Schall, 1995). Therefore, we calculated stop signal reaction times (SSRT) using the integration method devised by Logan and Cowan (1984) and then applied to saccades by Hanes and Schall (1995). We integrated over the saccadic reaction times (SRTs) for the GO trials starting at the time of target presentation and proceeded until the integral equaled the probability of failing to cancel a saccade at a given stop signal delay. This time represents the theoretical finish of the STOP process, and subtracting the stop signal delay yields the SSRT. The SSRT is an estimate of the amount of time taken to cancel the planned saccade once the stop signal has been given.

Oculomotor Recording and Analysis Methods

Eye position was monitored in the scanner at 60 Hz with an infrared videographic camera equipped with a telephoto lens (Model 504LRO, Applied Sciences Laboratories) that focused on the right eye viewed from a small dielectric flat surface mirror mounted inside the RF coil. Because of difficulties that arise from contact lens, two subjects did not have eye-tracking data; their performance on STOP trials (i.e. correct/error, not SRT) was determined by watching the video images of the eyeball during the task and scoring whether or not a saccade was made towards the target. Nine-point calibrations were performed at the beginning of the session and between runs when necessary. Eye-movement data were scored offline and SRTs were obtained with Grapes, an in-house graphical data display and analysis program. Anticipatory saccades occurring earlier than 160 ms and later than >2 SD were not analyzed.

Image Acquisition

Anatomical and functional images were acquired on a 4 T Varian INOVA MR scanner. Functional volumes sensitive to BOLD contrast were acquired with a TEM send-recvie RF head coil using a two-shot gradient echo-EPI sequence. We scanned eight runs lasting 470 s each, resulting in 3760 volumes total covering the dorsal cortex. Between 18 and 20 axial slices per image were acquired with the following parameters: field of view = 22.4 × 22.4 cm; in-plane resolution (64 × 64) = 3.5 × 3.5 mm; slice thickness = 3.5 mm (no skip); $T_R = 1000$ ms/half k -space; $T_E = 28$ ms; flip angle = 20°.

Regions of Interest

The close proximity of brain regions of interest (ROIs), as well as loss of spatial resolution inherent in spatial normalization (Brett *et al.*, 2002), led to our decision to perform our analysis within ROIs. We derived ROIs using a two-step procedure. First, we drew liberal structural ROIs based on sulcal anatomical landmarks and previous imaging studies. Second, we selected voxels within each ROI that showed a significant main effect of time (i.e. the voxels showed a significant deviation from baseline; see *Event-related Data Analysis* below). The left and right FEFs were defined as the area extending laterally along the precentral sulcus of the dorsolateral frontal cortex beginning at the junction with the superior frontal sulcus (Luna *et al.*, 1998; Kimmig *et al.*, 2001; Curtis and D'Esposito, 2003a,b). The SEFs were defined as the region in and around the paracentral sulcus of the dorsomedial wall, but not extending ventrally into cingulate sulcus (Schlag and Schlag-Rey, 1987; Grosbras *et al.*, 1999; Curtis and D'Esposito, 2003b). The ACC was defined at the dorsomedial wall, in or below the cingulate sulcus, typically quite dorsal (Bush *et al.*, 2000; Paus, 2001; Picard and Strick, 2001). The intraparietal sulcus (IPS) was defined as the lateral sulcus dividing the superior and inferior lobules in the parietal cortices.

Event-related fMRI Data Analysis

fMRI data were motion corrected and smoothed (7 mm FWHM), and voxels outside the brain were masked. Each voxel was mean normalized by run. For each subject, voxel time series for each trial type (CATCH, GO, STOP-success, STOP-fail) was estimated using AFNI's 3D-Deconvolution routine. A series of 16 regressors (delta functions), each corresponding to a single time point, was used to estimate the hemodynamic response time locked to 1 s prior to the onset of the target presentation. The linear combination of these regressors was used to estimate the evoked hemodynamic response for each trial type with

no assumptions about the shape. Time courses were estimated for both rightward and leftward targets (or null targets in the case of CATCH trials). A two-way (trial type by time) ANOVA was performed on the estimated time courses for each voxel, where trial type had four levels (CATCH, GO, STOP-success, STOP-fail) and time had 16 levels (one corresponding to each time point estimated). Within each structurally defined ROI, only the voxels with a significant F -statistic corresponding to the main effect of time were included in further analyses. This procedure effectively selects the voxels that showed some response to the task regardless of trial type. Next, all of the remaining voxels were averaged within the ROI for each time point creating a single spatially averaged time course for each trial. These time courses for each ROI were reanalyzed with a three-way ANOVA (trial type, target side and time) where the trial type by time interaction term was of most interest. This interaction term identified time courses that differed somehow between the trial types. Significant interactions were followed up with two-way ANOVAs that paired each condition against another condition to test for specific differences between trial types or target sides.

Results

Oculomotor Results

Subjects were successful at canceling planned saccades during ~60% of the STOP trials (Fig. 3*a*). Importantly, this level of performance resulted in an average of >30 error trials per subject, a sufficient number of trials to reliably estimate BOLD time courses.

Saccadic reaction times (SRTs; the time between target onset and saccade initiation) were computed for several types of trials in order to compare with other countermanding studies and to evaluate how well the behavioral data are in accord with the race model. First, subjects were slower to initiate saccades on GO trials compared to unsuccessful STOP trials, $t(1798) = 24.78$, $P < 10^{-10}$ (Fig. 3*b*). Second, using the SRT distribution for GO trials and the probability of successful saccade cancellation at a given stop signal delay (see Materials and Methods), we estimated the time needed to cancel a planned saccade once the stop signal had been given; this time is referred to as the *stop signal reaction time* (SSRT). Across our sample the average SSRT was 159 ms; once the stop signal tone was emitted it took ~159 ms to cancel the planned saccade. The average experimentally controlled stop signal delay (i.e. the time between the target presentation and the stop signal) was 157 ms (SD = 31 ms). A discriminant analysis (unweighted by number of observations in each trial type) converged on 316 ms as the best SRT threshold for correctly classifying GO and STOP failure trials, which is also the sum of the mean stop signal delay and the mean SSRT (i.e. 157 + 159 = 316 ms). This time point may be thought of as the finish line of the STOP process. If neural

Table 1
Oculomotor data: individual subjects

Subject	GO	STOP FAIL	SSRT
	Mean SRT ± SD (ms)	Mean SRT ± SD (ms)	Mean (ms)
S01	377 ± 88	338 ± 69	165
S02	403 ± 66	375 ± 70	199
S04	348 ± 77	281 ± 69	144
S05	422 ± 83	390 ± 89	219
S06	257 ± 59	213 ± 60	156
S07	337 ± 83	257 ± 71	150
S08	261 ± 88	239 ± 78	137
S09	317 ± 85	256 ± 72	139
S10	332 ± 91	242 ± 94	112
S11	383 ± 111	342 ± 89	168
Mean	344 ± 88	293 ± 81 ms	159

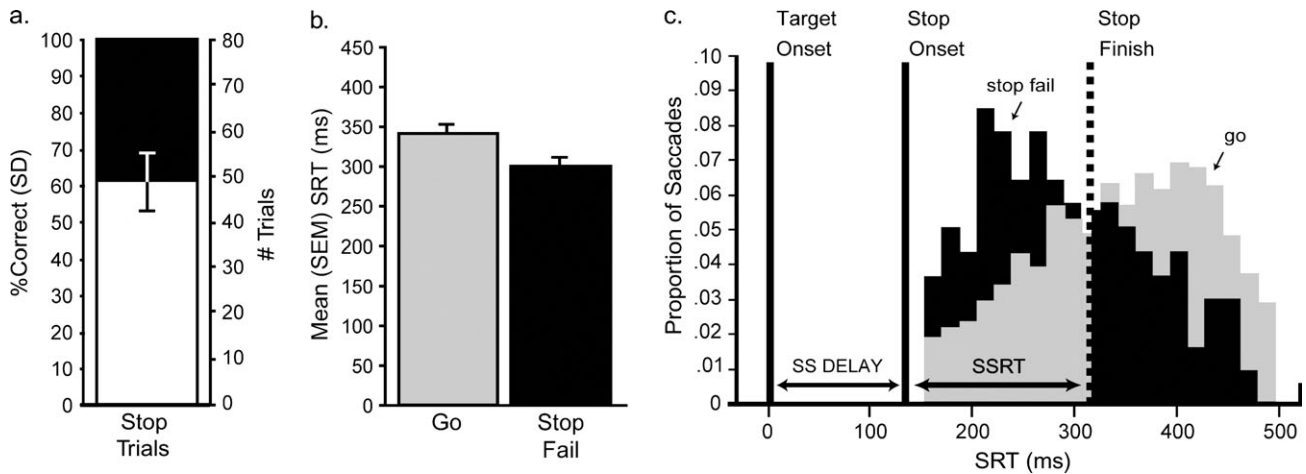


Figure 3. Oculomotor performance on the countermanding task. a. Pretesting and occasionally slight adjustments to the stop signal delay during scanning resulted in a 40% failure rate in canceling the planned saccade after the stop signal was emitted. Black and white areas of the bar denote failed and successful saccade cancellation, respectively, and the error bar represents the SD. The mean stop signal delay used across subjects was 157 ms. b. Saccadic reaction times (SRT) were significantly longer for GO trials (gray) compared to STOP trials in which the subject was unsuccessful at canceling the saccade (black). Bars represent means \pm SEM. c. The relationship between stop signal delay (SS delay), the stop signal reaction time (SSRT), and the distribution of SRTs for GO trials (gray) and STOP failure trials (black). Presenting the stop signal shortly after the saccade target onset, a delay known as the stop signal delay, initiates the STOP process. The STOP process theoretically reaches its finish line or threshold in a period of time referred to as the SSRT, or the mean time needed to cancel a planned action. According to the race model, the GO trials in which the saccade occurred before the estimated SSRT would not have been cancelled if a stop signal had been given, while the trials in which the saccade occurred after the SSRT would have been successfully canceled. Given the estimated SSRT, about 40% of the GO trials would not have been cancelled. The distribution of SRTs on STOP failure trials, in which 60% of the trials fall within the SSRT, further supports the adherence of the saccade data to the assumptions of the race model of voluntary control of action. Note that SRTs on STOP failure trials are occasionally longer than the estimated SSRT because of natural variability in the estimated SSRT and a mixture of SSRTs across subjects.

processes leading to the generation of a saccade did not reach threshold by this time, then it was unlikely that a saccade would be generated. Figure 3c illustrates the relationship between the distribution of GO trial SRTs (gray) and the estimated SSRT. Note that ~60% of the SRTs fall beyond the SSRT cut-off. These are saccades that would have been successfully canceled if a stop signal had been emitted. Also plotted is the distribution of SRTs for the unsuccessfully canceled saccades (black). Note that the majority of these (~60%) fall short of the SSRT cut-off.

Third, we asked if subjects modified their saccadic behavior based on their changing performance and task demands from trial to trial. We compared the SRTs between GO trials that differed only in the trial type that immediately preceded it. Subjects were faster to initiate saccades on GO trials following STOP trials (343 ± 93 ms) than GO trials following other GO trials (390 ± 76 ms), $t(1070) = 16.36$, $P < 10^{-09}$. Subjects were also faster on GO trials that followed successful STOP trials (348 ± 92 ms) compared to GO trials that followed unsuccessful STOP trials (369 ± 92 ms), $t(722) = 4.61$, $P < .003$. The difference in SRT on GO trials as a function of trial type history and performance history strongly implicates an activation of control processes that tracks history and modifies behavior. These oculomotor data together indicate that control processes were indeed being implemented in the service of countermanding planned action.

fMRI Results

We now turn to the fMRI data to examine the neural correlates of these behavioral data during the countermanding task. Two-way ANOVAs with trial type (CATCH, GO, STOP success, STOP failure) and time (16 1 s time points) were performed on the estimated time courses for each subject. All ROIs showed a significant trial type by time interaction. Planned comparison ANOVAs were then conducted to test for differences between paired trial types (e.g. GO versus STOP success).

First, let us consider the midline dorsomedial regions, SEF and ACC. Examining the overall main effect of time (i.e. without regard to trial type) clearly activated segregated foci along the dorsomedial wall in all subjects (Fig. 4). Activation was found in the paracentral sulcus for all subjects corresponding to the SEF and in the dorsal cingulate sulcus corresponding to the ACC. The estimated time courses from these two regions revealed distinct patterns of activation for the different trial types (Fig. 5). The SEF time courses for CATCH and GO trials were not significantly different. However, the time course for STOP success trials was significantly greater than each of these time courses (ANOVA condition by time interaction; all P s < 0.05). Importantly, the time course for STOP fail trials was significantly greater than all other trial types, including the STOP success trials (ANOVA condition by time interaction, $F(1,16) = 2.52$, $P < 0.005$). The SEF was the only ROI that showed a significant difference between successful and unsuccessful saccade cancellation. The difference between STOP success and failure was not statistically significant in the ACC [ANOVA condition by time interaction, $F(1,16) = 1.23$, $P > 0.25$]. Besides this, the pattern of time course differences in the ACC was the same as in the SEF. Both regions seemed to show a particular sensitivity to the trials in which there was conflict between the processes leading to gaze shifting and gaze holding; responses were greater on STOP compared to GO trials.

Next, differences between the trial types were calculated for the dorsolateral ROIs, the FEF and IPS. Although not shown, very robust bilateral activations were found in these regions as might be expected. Instead of considering the left and right hemispheres independently and measuring their responses to left and right visual field targets, our analyses combined the responses from the left and right ROI based on whether the saccade target was contralateral or ipsilateral to the ROI. This method effectively doubles our statistical power and makes sense from a functional neuroanatomical point of view since visual stimuli

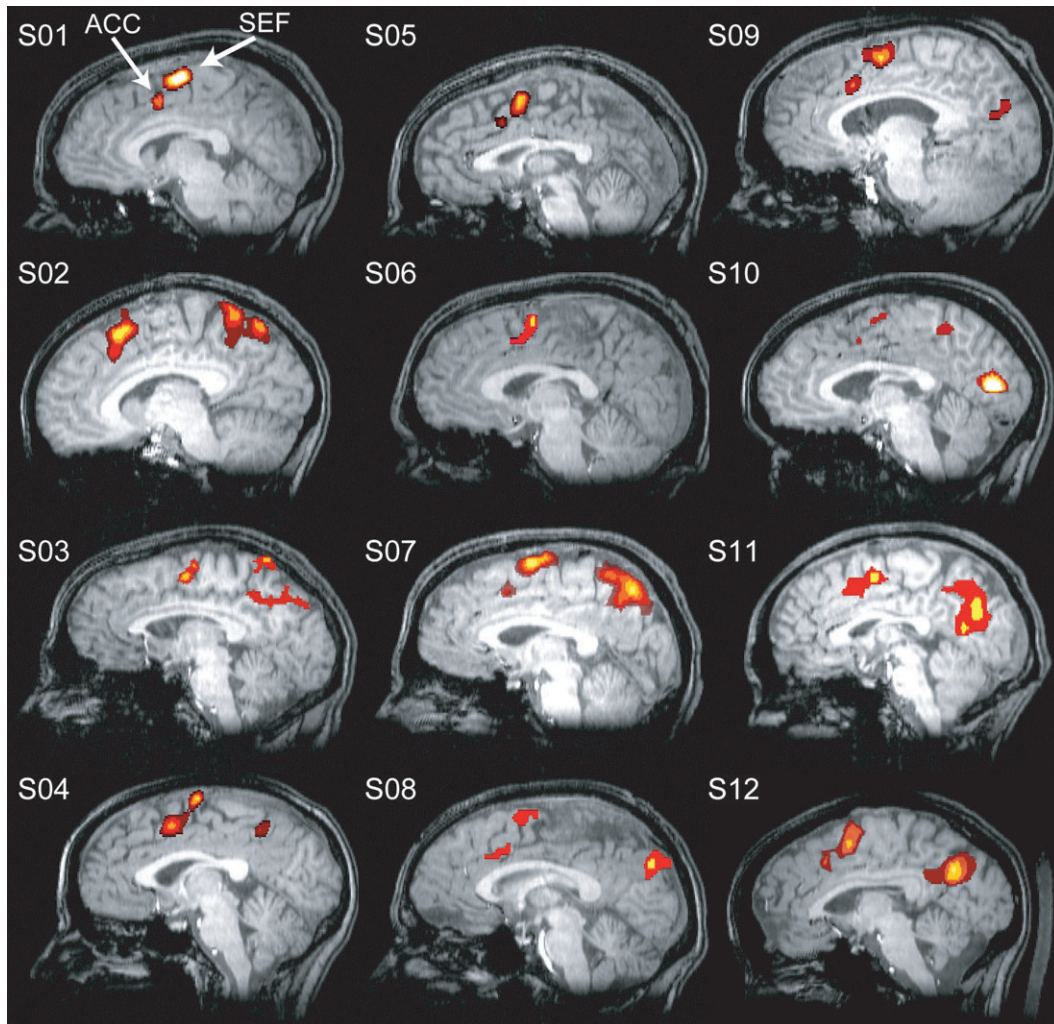


Figure 4. Activations along the dorsomedial wall for each of the 12 subjects. Notice that all subjects showed activity in the paracentral sulcus, corresponding to the supplementary eye fields (SEF), and the cingulate sulcus, corresponding to the dorsal anterior cingulate (ACC). Only one sagittal slice is shown for each subject, but other slices could further illustrate the separation between these two areas. Color overlay represents the main effect of time in a 2-way ANOVA and is thresholded at a minimum of $p < 0.001$. This statistic identifies which voxels showed some response to the task, regardless of the trial type and regardless of the response shape. These voxels made up the SEF and ACC ROIs. The same method was used to identify frontal eye field (FEF) and intraparietal sulcus (IPS) ROIs.

and saccade goals tend to be represented in the contralateral hemisphere. Therefore, we limit the following analyses and plots to contralateral targets, collapsed across hemispheres.

In both FEF and IPS ROIs, time courses for STOP trials were significantly greater than time courses for CATCH and GO trials (Fig. 5) [ANOVA condition by time interaction, $F(1,16) = 3.32$, $P < 0.001$]. No differences were found between successful and unsuccessful saccade cancellation. The FEF but not IPS showed a significant difference between GO and CATCH trials [ANOVA condition by time interaction, $F(1,16) = 2.52$, $P < 0.005$]. In fact, the FEF was the only region that did show a greater response to GO compared to CATCH trials. These time course differences are depicted in Figure 5.

We reasoned that the longer SRT on GO trials following other GO trials compared to GO trials following STOP trials indexed an adjustment of saccadic control. In an attempt to image this process, we estimated the GO trial time courses according to the trial history of whether the GO trial immediately followed a GO trial or a STOP trial. The SEF, but not ACC or any other ROI, was sensitive to this contrast. We found greater SEF activation

on GO trials that followed other GO trials compared to GO trials that followed STOP trials (Fig. 6) [ANOVA condition by time interaction, $F(1,16) = 2.32$, $P < 0.01$].

Discussion

Voluntary control of behavior hinges on the ability to decide between alternative choices, even when the choice is between moving and not moving (Logan and Cowan, 1984; Logan *et al.*, 1984; Schall, 2001). This choice can be modeled as a race between GO and STOP mechanisms (Logan *et al.*, 1984; Hanes and Carpenter, 1999; Schall *et al.*, 2000; Reddi *et al.*, 2003). Following an imperative stop signal, the process that first crosses a critical threshold determines whether a movement will be canceled or not. In the context of the countermanding task, each trial can be broken down into stages of processing in which visual signals are transformed into motor commands whose consequences must be evaluated (Fig. 7). Within the cortical oculomotor network we identified neural activity related to this decision process as well as the monitoring of

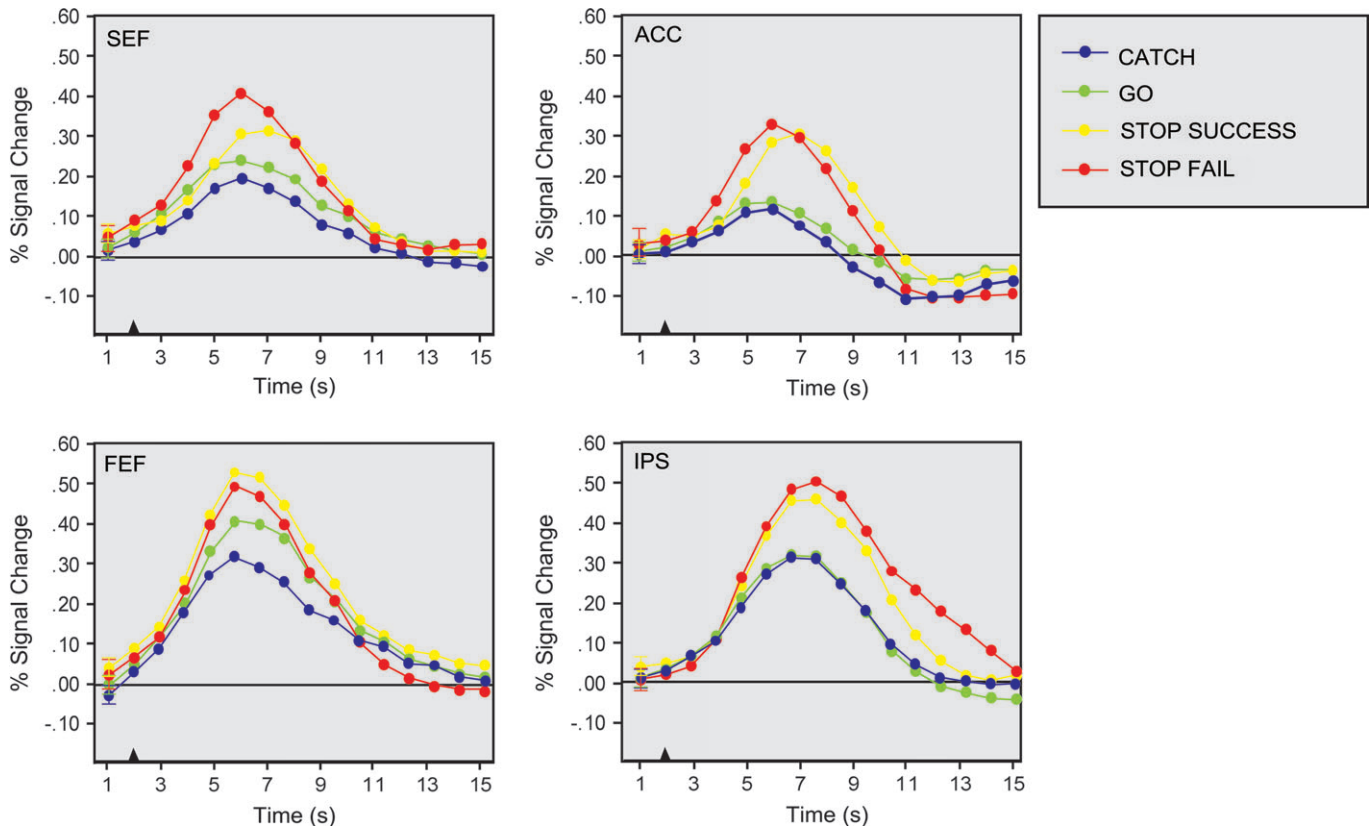


Figure 5. Time courses for each trial type. Each line represents the estimated time course for each trial type, plotted separately for each ROI, in units of percent signal change. The average standard error for the estimated time points are depicted on the first time point for each line. The black triangle at the bottom indicates when the saccade target appeared. See the text for a description of which time courses show a significant trial type by time interaction.

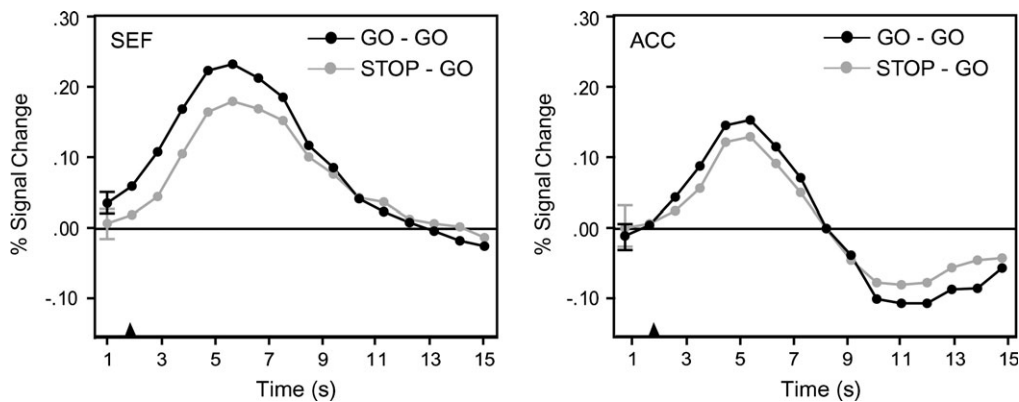


Figure 6. Time courses for GO trials sorted according to trial history. Each line represents the estimated time course for each trial type, plotted separately for the SEF and ACC, in units of percent signal change. The average standard error for the estimated time points are depicted on the first time point for each line. The black triangle at the bottom indicates when the saccade target appeared. In the SEF, but not ACC, responses evoked during GO trials were larger if the preceding trial was a GO trial (GO-GO) compared to if the preceding trial was a STOP trial (STOP-GO). A significantly longer SRT accompanied this increased signal change.

performance variables that can be used to evaluate and adjust behavior accordingly. We find that distinct areas within the cortical oculomotor network were particularly sensitive to the visual, motor and evaluative task requirements.

Overt and Covert Attention

At the beginning of a trial, covert attention was directed to the left and right in anticipation of the target's appearance. Evoked hemodynamic responses to the rare trials in which no target appeared and no saccade was made (i.e. CATCH trials) should be

a good estimate of covert attention since they are largely uncontaminated by additional visual and oculomotor processes. We found large evoked activity in both the FEF and IPS during CATCH trials implicating these regions in the covert direction of attention to the space where the targets were expected to occur. Several studies have reported activation in the FEF and IPS in tasks requiring covert shifts of attention (Gitelman *et al.*, 1999; LaBar *et al.*, 1999; Nobre *et al.*, 2000; Corbetta and Shulman, 2002). On GO trials, in addition to deployment of covert attention, a saccade to acquire the target, an overt shift of

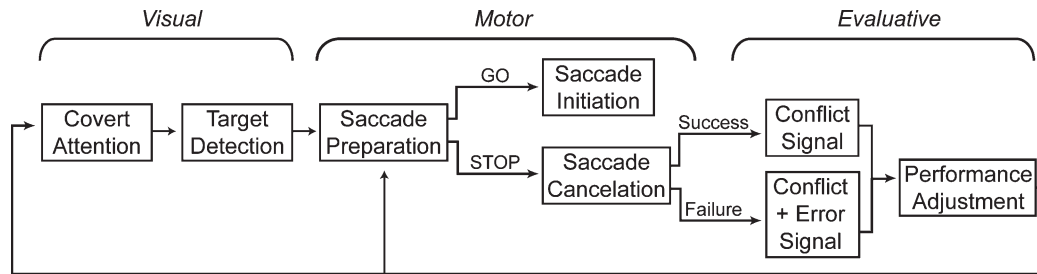


Figure 7. Schematic cycle of processes engaged during the countermanding task. Each trial can be broken down into stages of processing in which visual signals are transformed into motor commands whose consequences must be evaluated.

attention, was computed and triggered. Only the FEF showed greater activity on GO trials compared to CATCH trials and thus was the only region sensitive to the additional oculomotor process. The IPS showed equally large responses to CATCH and GO trials. Although clear evidence exists indicating that the FEF and IPS both produce signals evoked by attentional and motor processes (Sheliga *et al.*, 1995; Colby and Goldberg, 1999; Andersen and Buneo, 2002; Moore *et al.*, 2003; Schall, 2004), these data indicate a relative bias towards motor processes in the FEF and attentional processes in the IPS (Connolly *et al.*, 2002; Curtis *et al.*, 2004).

Control of Saccade Initiation

The reaction times of saccades produced in the countermanding task were consistent with the proposed race model (Logan *et al.*, 1984). First, compared to control trials when subjects made saccades to visual targets and no stop signal was emitted (GO trials), non-canceled saccades made after a stop signals (STOP fail trials) were significantly faster. Second, the majority of these non-canceled saccades were initiated before the SSRT, an estimate of the average minimum amount of time needed to cancel a planned saccade. Therefore, the non-canceled saccades fell disproportionately in the earlier area of the overall SRT distribution. Presumably, the saccades that would have been initiated with long latencies were more likely to be successfully canceled because the processes leading to cancellation had sufficient time to grow to threshold.

As described above, both the FEF and IPS showed large hemodynamic responses on GO trials and only the FEF showed greater responses on GO compared to CATCH trials. We used as a heuristic to evaluate the activation data relating to voluntary control of saccades, a race between GO (i.e. saccade) and STOP (i.e. fixation) processes (Logan *et al.*, 1984). Evoked responses in the FEF were larger on STOP trials compared to GO trials. Most likely this result is due to the coactivation of separate populations of saccade and fixation neurons on STOP trials and activation of only saccade neurons on GO trials (Hanes *et al.*, 1998; Schall *et al.*, 2002). The basis for this interpretation comes squarely from electrophysiological recordings of neurons in the FEF of monkeys performing countermanding tasks (Hanes *et al.*, 1998). The firing rates of FEF saccade neurons begin to grow shortly after the onset of the saccade target and continued growth up to a fixed threshold triggers a saccade. After the stop signal is given, the firing rates of FEF fixation neurons race against the firing rates of saccade neurons toward a finish line that determines whether or not the planned saccade is canceled. As in the monkey FEF, we found evidence for such a race in the pattern of human FEF activity. The mechanisms

involved in this race, saccade and fixation specifically, are clearly key variables that control the voluntary production and withholding of saccades. We also found a similar pattern in the IPS to that in the FEF; evoked responses on STOP trials were greater than on GO trials. Nonetheless, we cannot rule out that the larger evoked responses on STOP trials can be accounted for by an enhancement in non-specific arousal given that these trials were less frequent.

Top-down Control

Most saccade stop signal studies have presented the stop signal stimulus visually at fovea, where the fixation point just extinguished. Reappearance of a stimulus at fixation may invoke bottom-up visual processes that reflexively activate fixation neurons resulting in SSRTs that are typically longer following auditory compared to visual stop signals (Cabel *et al.*, 2000). To avoid this confound, we used an auditory stop signal, which must activate the representation of an arbitrary rule (i.e. *if tone then cancel saccade*). Top-down signals then presumably trigger the activation of fixation neurons and subsequently the neurons that monitor the consequences of behavior. The natural question that then arises is: what is the source of this top-down signal? Although we did not use spatial normalization procedures to pool data across subjects (Brett *et al.*, 2002), we did not see consistent activation across subjects in other frontal and parietal areas that could be the source of these signals. Here, we only present data from the oculomotor ROIs within our prescribed slices through the dorsal part of the cortex. We did not image in other important areas like the inferior frontal gyrus whose damage caused impaired inhibition on stop-signal trials of a countermanding task (Aron *et al.*, 2003, 2004) and also has reciprocal projections in the monkey brain with the SEF and dACC (Huerta and Kaas, 1990; Bates and Goldman-Rakic, 1993). The inferior frontal gyrus, therefore, may be one source of top-down signals on stop trials. However, we do not want to suggest that some area of the prefrontal cortex, like the ventrolateral convexity, could be the substrate for inhibitory control in general, even though this would be one step towards fractionating the *prefrontal homunculus* (for a discussion, see Monsell and Driver, 2000). Instead, we suggest that representations exist solely within the oculomotor network itself that are sufficient to control the required stimulus-response mappings and evaluate and modify performance accordingly (Curtis and D'Esposito, 2003a). Such a suggestion is in opposition to the view that there sits at the top of a hierarchy an executive that controls all non-dominant stimulus-response mappings across all sensory modalities and response domains. More or less parsimonious, depending on how one looks at it, the ability of the oculomotor

system to regulate itself, albeit after learning, is a testable alternative.

Performance Monitoring

We delayed the onset of the stop signal such that subjects were able to cancel planned saccades only ~60% of the time. Several factors determined success in this situation. In the context of a race model, we discussed above how voluntary control over movement production might be mediated by a competition between GO and STOP processes, which in turn would directly and critically determine whether the saccade is successfully canceled. Additionally, the probability of successful behavior increases if one makes strategic modifications based on the evaluation of past performance (Botvinick *et al.*, 2001; Jones *et al.*, 2002). Within the oculomotor network, we found evidence that the SEF and ACC play important roles in performance monitoring.

Both the SEF and ACC showed greater activity on STOP trials compared to GO trials. This difference could be due to performance monitoring, either by monitoring response conflict (Botvinick *et al.*, 2001; Jones *et al.*, 2002) or by the detection of errors (Coles *et al.*, 2001; Holroyd and Coles, 2002). The coactivation of incompatible saccade and fixation mechanisms during STOP trials would result in response conflict. On STOP trials where the saccade was not canceled, in addition to conflict, mechanisms that detect error would be active. The pattern of activity in the SEF was consistent with both of these roles in monitoring performance; activity was greater on canceled STOP trials and even greater on non-canceled STOP trials. Indeed, the firing rates of separate SEF neurons in the monkey increase *after* canceled and non-canceled saccades on STOP trials (Stuphorn *et al.*, 2000). Since the responses did not occur in time to influence the decision process itself, they are related to the evaluation of behavioral choice. Unit recordings from the monkey dorsal ACC during countermanding performance show that the ACC responds exclusively after non-canceled saccades (i.e. errors) and not after successfully canceled saccades (i.e. conflict) (Ito *et al.*, 2003). Our data from the human dorsal ACC, however, show that error-detection processes do not evoke a larger response than that evoked by response conflict alone. A strong interpretation of this result is that conflict monitoring alone (Botvinick *et al.*, 2001) is sufficient to account for the activity in the ACC.

We should note that Schall and colleagues (Stuphorn *et al.*, 2000; Schall *et al.*, 2002; Ito *et al.*, 2003) have argued that there is no conflict in processing during non-canceled saccades because gaze-holding neurons in the FEF are not active on these trials (Hanes *et al.*, 1998). These arguments are based on neural recordings in the FEF at very specific intervals before the saccade is or would have been made. They do not imply that other neurons or other areas of the brain are not sensitive to conflicting gaze-holding and gaze-shifting processes. Two methodological issues regarding the temporal and spatial resolution of fMRI BOLD signals are important here. First, the sluggish nature of BOLD signals do not allow us to distinguish between neural signals emanating from the presaccadic and post-SSRT periods necessary to make these distinctions. Second, the BOLD signals we detect are sensitive to the activity of populations of neurons, in this case both gaze-holding and shifting. Therefore, on erroneous, non-canceled saccade trials we assumed that these trials include an element of error detection as well as an element of conflict between GO and STOP processes.

Performance Adjustment

Monitoring conflict and errors is only useful if this information can be used to adjust future behavior towards better performance (Fecteau and Munoz, 2003). Activity in the SEF tracked adjustments in choice reaction times. Saccade initiation was faster following STOP trials compared to saccade initiation following GO trials. This result is opposite what has been reported previously for behavioral studies of saccade countermanding (Cabel *et al.*, 2000; Kornylow *et al.*, 2003), as well as typical sequential effects of trial type on reaction time (Gratton *et al.*, 1992). These past studies suggest that subjects slow down after they encounter a STOP trial implicating some form of strategic adjustment in performance. We reason that our finding of decreased saccadic reaction times following STOP trials also reflects such an adjustment. Although occasionally occurring, it was statistically unlikely for a STOP trial to follow another STOP trial. The decreased saccadic reaction times indicate that subjects appreciated this probability; subjects may have predicted that another STOP trial was unlikely and thus anticipated less conflict on the upcoming trial. Along with this decreased reaction time, presumably related to less instantiation of control, we found decreased activity in the SEF on trials following STOP compared to GO trials. The activity in the SEF was sensitive to the trial history; when the need for control was not predicted, activity was lower. Therefore, not only does the SEF seem to monitor performance but it also may play a role in the adjustment of future behavior based on past performance.

Conclusion

Voluntary control of behavior can be exerted anywhere along the series of processes that evolve over time from sensation to action. Our recent studies of voluntary control of saccade production have shown how maintaining past information (Curtis *et al.*, 2004) or anticipating future plans (Curtis and D'Esposito, 2003b) can influence the motor decision process towards success. Here we show that control exerted farther down-stream in the perception-action cycle, after the motor plan has been generated, can be seen in the pattern of activity in the human frontal and supplementary eye fields. Moreover, activity related to saccade initiation and performance monitoring in these regions can sufficiently account for success and failure of voluntary saccadic control.

Notes

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