Responding with Restraint: What Are the Neurocognitive Mechanisms?

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Abstract

■ An important aspect of cognitive control is the ability to respond with restraint. Here, we modeled this experimentally by measuring the degree of response slowing that occurs when people respond to an imperative stimulus in a context where they might suddenly need to stop the initiated response compared with a context in which they do not need to stop. We refer to the RT slowing that occurs as the "response delay effect." We conjectured that this response delay effect could relate to one or more neurocognitive mechanism(s): partial response suppression (i.e., "active braking"), prolonged decision time, and slower response facilitation. These accounts make different predictions about motor system excitability and brain activation. To test which neurocognitive mechanisms underlie the response delay effect, we performed two studies with TMS and we reanalyzed fMRI data. The results suggest that the response delay effect is at least partly explained by active braking, possibly involving a mechanism that is similar to that used to stop responses completely. These results further our understanding of how people respond with restraint by pointing to proactive recruitment of a neurocognitive mechanism heretofore associated with outright stopping. ■

INTRODUCTION

Many situations in life call for us to respond with restraint. Even as we satisfy an urge by making a movement, we can make the movement in a controlled fashion. For example, one eats one's food carefully rather than wolfing it down to avoid indigestion. To take another example, one can speak slowly and deliberately when diplomacy is needed, although the ideas may be fast and furious. Experimentally, this form of control may be examined by measuring the degree of response slowing that occurs when people respond to an imperative (go) stimulus in a context where they might suddenly need to stop the initiated response compared with a context in which they do not need to stop. Several behavioral paradigms have been used to examine this question (Verbruggen & Logan, 2009b; Zandbelt et al., 2008; Vink et al., 2005; De Jong, Coles, & Logan, 1995). Here, we used the "conditional stop signal task" (De Jong et al., 1995; Figure 1A). In this paradigm, participants initiate a choice response on each trial and prepare to stop themselves when a stop signal occurs. One responding finger is designated as "critical" and another as "noncritical." When the stop signal occurs, participants must try to stop when the initiated response is critical, but they can ignore the stop signal when the response is noncritical. This manipulation leads to significantly slower responses on critical compared with noncritical go trials (Aron, Behrens, Smith, Frank, & Poldrack, 2007; De Jong et al., 1995), which we refer to here as the "response delay effect."

We tested three hypotheses about the neurocognitive mechanisms underlying the response delay effect (Table 1). The first hypothesis is that the response slowing is explained by an active braking mechanism that can proactively suppress the initiated response without canceling it completely. Such proactive response suppression (i.e., active braking) should be reflected in reduced excitability of motor representations that might have to be stopped. Specifically, the braking hypothesis predicts that if the stopping rule says "stop only if an index finger response has been initiated," then the index finger motor representation will show reduced excitability compared with when the rule says "stop only if a little finger response has been initiated." Furthermore, the braking hypothesis predicts that an excitability reduction of the (critical) response that may need to be stopped may even be observed before the go stimulus occurs and not just afterward. This is because the stopping rules are known at the beginning of the experiment, and thus participants may maintain "suppression" of the critical response throughout the whole experiment or at least in anticipation of having to respond.

The second hypothesis for the response delay effect is that the duration of stimulus categorization and response selection stages is prolonged (we refer to this as the "prolonged decision stage" account). One source of this prolongation could relate to the increased cognitive load

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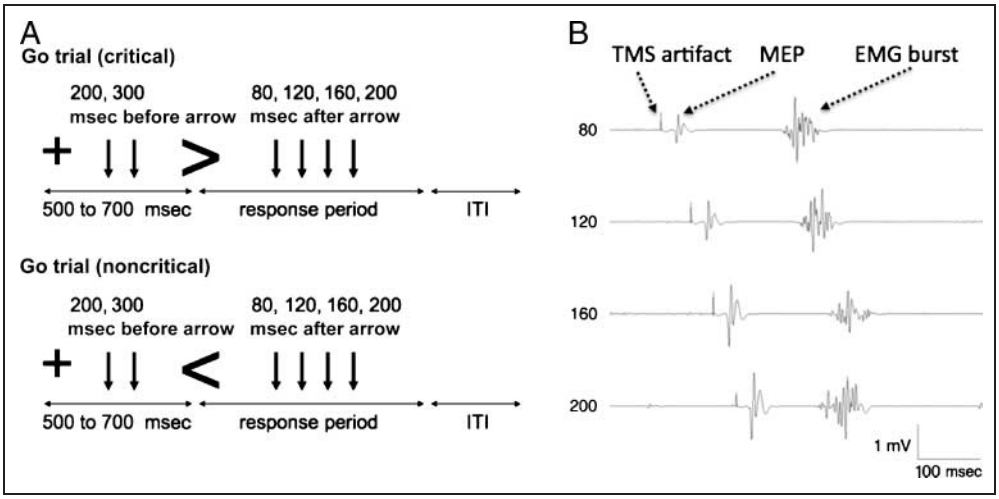

Figure 1. Task and example motor evoked potential (MEP) Traces. (A) Schematic design of go trials (when no stop signal is given) in the conditional stop task. In this example, participants must stop if a stop signal follows a rightward arrow ("critical" direction). The horizontal lines represent time. The cross indicates the beginning of each trial. It is followed by an arrow stimulus indicating that a response should be made with the right button (little finger) or left button (index finger). The vertical arrows indicate the times of TMS delivery—those delivered before the go stimulus are the baseline condition. A TMS stimulus was delivered only once per trial and on some trials not at all. (B) Representative EMG traces from one subject. On each trial, a brief TMS artifact is visible as well as an MEP and an EMG burst (muscle activity). Note that the electromechanical delay is the interval between the onset of EMG burst and the subsequent button press. Note that the MEP increases with time of stimulation, also see Figure 3.

that participants maintain when they expect a stop signal to occur on critical trials. This may influence the efficiency of information processing and could slow down responses on go-critical compared with noncritical trials (see Verbruggen & Logan, 2009b). Another source of the prolongation of the decision stage could relate to an increased response threshold for critical trials. The response threshold determines the amount of information that is required to select a response; if it is increased on critical trials, RTs will increase compared with noncritical trials (Verbruggen & Logan, 2009b).

The third hypothesis is that the execution of the motor response is prolonged because of a slower build up of facilitation in the corticomotor system rather than an active inhibitory process. This slowing (perhaps better described as "hesitancy" or "caution") could be reflected in an increased delay between the initiation of the response and the actual button press. The major difference with the braking hypothesis is that the facilitation hypothesis assumes that no inhibition of motor output is involved.

The second and the third hypotheses (i.e., prolonged decision stage and slower response facilitation) differ from the braking hypothesis in predicting that the difference between critical and noncritical trials will be reflected in differences in motor excitability during the later stages of stimulus categorization and response selection only—whereas the braking hypothesis predicts that an excitability reduction of the response that may need to be stopped may be observed even before the go stimulus occurs (Table 1).

Evaluating the predictions of these three hypotheses requires a technique that can measure the state of specific motor representations with high temporal resolution. Here, we used TMS of the primary motor cortex, using surface electromyography to record evoked potentials from intrinsic muscles of the hand. In Experiment 1, we delivered TMS to the left primary motor cortex at specific time points while participants performed the conditional stop signal task using index and little fingers of the right hand (Figure 1A). We delivered TMS either 200 or 300 msec before the go choice stimulus (baseline), 80 and 120 msec after the go stimulus ("early"), and 160 and 200 msec after the go stimulus ("late"). We expected that the early time points would correspond to a pre-response initiation period because 80 msec and possibly

Table 1. Possible Neurocognitive Mechanisms Underlying the Response Delay Effect

Mechanism	*Motor Evoked Potential*	*Electromechanical Delay*	*Activation of "Stopping" Regions*
Active braking	Go critical < go noncritical (before/after go stimulus)	Go critical > go noncritical	Go critical > go noncritical
Prolonged decision stage	Go critical < go noncritical (after go stimulus)	No difference	No difference[a]
Slower response facilitation	Go critical < go noncritical (after go stimulus)	Go critical > go noncritical	No difference

Different mechanisms make different predictions for MEP, electromechanical delay, and functional MRI data.

[a]Depending which regions are activated, this could be compatible with more than one mechanism.

even 120 msec is too early for visual information to be categorized to determine response selection in a choice RT task, and we expected that the later time points would correspond with the response initiation period.

We measured motor-evoked potentials (MEPs) from the first dorsal interosseous (FDI) muscle of the right hand—an index of corticomotor excitability for the index finger response representation. For each participant, the index finger was critical for one half of the experiment and noncritical for the other half (with the little finger in the opposite pattern). This let us always record electromyography from the index finger while comparing the effects on this finger of the conditional rule (index finger is critical, index finger is noncritical).

We predicted that participants would respond more slowly on go-critical than go-noncritical trials—the response delay effect. The braking hypothesis predicts that the response delay effect would have its counterpart in reduced MEPs at both the early preinitiation time points (80 or 120 msec) and late time points (160 or 200 msec). Showing that MEPs are reduced, relative to baseline, at early time points would provide support for the hypothesis that participants can proactively brake a response tendency even before they know which response they might actually have to make and even before a stop signal occurs. An alternative outcome is that there is no difference in MEPs for critical and noncritical conditions before response initiation (i.e., at 80 or 120 msec), but instead there is a difference at the late time points only (i.e., 160 or 200 msec). This would be consistent with the prolonged decision stage and slower motor facilitation hypotheses as well as with a modified version of the active braking hypothesis. This modified version predicts that an active braking mechanism operates only when the critical response is being initiated to restrain it in anticipation of a possible stop. This would be like starting to stop an incipient motor tendency only when that tendency has been triggered.

Another way to distinguish between the three hypotheses is to examine the electromechanical delay. This refers to the interval between the onset of the EMG burst and the button press on a particular trial. Prior research showed an elongation of the electromechanical delay when suppression of motor output occurred (Coxon, Stinear, & Byblow, 2007). The braking hypothesis and the slower motor facilitation hypothesis predict that the response delay effect would have its counterpart in a prolonged electromechanical delay for critical responses compared with noncritical responses. By contrast, the prolonged decision stage hypothesis predicts similar electromechanical delays for critical and noncritical responses because, by definition, the electromechanical delay is postdecision. Thus, the electromechanical delay is associated with different predictions for the three candidate mechanisms underlying the response delay effect (Table 1).

As the reader will discover below, the results for Experiment 1 are most compatible with a modified version of the braking hypothesis rather than with a purely prolonged decision stage and/or slower motor facilitation accounts. An additional feature of this experiment was a general "MEP suppression" (i.e., MEPs were at below baseline levels for responding and nonresponding fingers at the early time points). To help interpret this finding better, we performed Experiment 2, in which TMS was delivered at the same time points during a choice RT task as for Experiment 1, but without the presence of stop signals. This allowed us to examine if MEP suppression effects found in Experiment 1 might relate to the exigencies of response selection itself rather than to the possibility that a stop is required.

In Experiment 3, we used neuroimaging to further distinguish the hypotheses. If active braking uses a response suppression mechanism that has something in common with outright stopping, then brain regions that are critical for stopping, such as the right inferior frontal gyrus, the pre-SMA, and the subthalamic nucleus region (reviewed in Chambers, Garavan, & Bellgrove, 2009; Aron, Durston, et al., 2007), should also be active during braking (Table 1). We examined this prediction by performing a reanalysis of previously published fMRI data acquired with the conditional stop signal task (Aron, Behrens, et al., 2007). We examined whether brain regions important for stopping are activated more for go-critical than go-noncritical trials.

EXPERIMENT 1: TMS STUDY WITH THE CONDITIONAL STOP SIGNAL TASK

Methods

Participants

Thirteen young adults participated (five males and three left-handed; age, M = 20 years, range = 18–24 years). All participants provided written consent in accordance with internal review board guidelines of the University of California at San Diego, completed a TMS safety screen questionnaire, and had no contraindications to TMS. One participant did not have reliable MEPs and was excluded from further analysis.

EMG Recordings

Participants were seated comfortably in front of an iMac desktop computer (Apple Corporation, Cupertino, CA). They responded with index and little fingers of the right hand, which was placed flat on the table, palm down. The index finger movement was a lateral abduction to the left to depress a key whose surface was perpendicular to the table surface. This movement maximally activated the FDI muscle while minimizing activation of other finger muscles. The little finger movement was flexion downward against a key whose surface was horizontal relative to the table surface. This movement maximally activated the abductor digiti minimi (ADM) muscle (of the "little" finger). Surface EMG recordings were made via 10-mm-diameter

Ag–AgCl hydrogel electrodes (Medical Supplies, Inc., Newbury Park, CA) placed over the FDI and abductor digiti minimi (little finger) muscles. A ground electrode was placed over the lateral epicondyle of the right elbow. The EMG signal was amplified using a Grass QP511 Quad AC Amplifier System Grass amplifier (Grass Technologies, West Warwick, RI), with a band-pass filter between 30 Hz and 1 kHz and a notch filter at 60 Hz. Data were sampled at 2 kHz using a CED Micro 1401 mk II acquisition system and displayed and recorded to disk using CED Signal v4 (Cambridge Electronic Design, Cambridge, UK). MEP analysis was performed using custom software in Matlab R2007a (The MathWorks, Natick, MA).

TMS

We used a MagStim 200-2 system (Magstim, Whitland, UK) with a figure-of-eight coil (7-cm diameter) to deliver a single test stimulus during task performance. To locate the representation of the FDI in the left primary motor cortex, the coil was initially located at a point 5 cm lateral and 2 cm anterior of the vertex. The coil was incrementally repositioned while administering single stimuli to locate the position that produced the largest, reliable MEPs in right FDI. This location was marked on a snug-fitting cap worn by the participant to ensure the consistent placement of the coil through the experiment. Resting motor threshold was determined by finding the lowest stimulus intensity that produced MEPs of at least 0.05 mV amplitude on at least 5 of 10 trials (Rossini et al., 1994). Next, the participant's maximum MEP size was determined by increasing stimulus intensity in 5% increments, starting at resting motor threshold, until MEP amplitude no longer increased with increasing stimulus intensity. Test stimulus intensity was set to produce an MEP amplitude that was approximately half of the participant's maximum MEP amplitude. This ensured that the test stimulus intensity was on the ascending limb of the individual's stimulus–response curve, so that both increases and decreases in corticomotor excitability could be detected (Devanne, Lavoie, & Capaday, 1997).

Task and Procedure

Before TMS preparation, participants completed two practice blocks to familiarize them with the task. Participants subsequently performed a total of six blocks, of 96 trials, with each block containing 24 stop and 72 go trials (576 trials total). Before each block, instructions on the computer screen indicated the critical direction for the stop task, which changed after three blocks. For seven participants, the left response (index finger) was the critical response in the first three blocks, and the right response (little finger) was the critical response in the last three blocks. The order of the mapping rules was reversed for the other participants. By reversing the critical rule half way through the experiment, we could compare MEPs from the right index finger for critical and noncritical conditions.

Instructions emphasized that participants should do their best to respond as quickly as possible while also doing their best to stop the response when an auditory stop signal occurred, but only if the initiated response was in the critical response. If the subject initiated a response on a noncritical trial and a stop signal occurred, the subject was to ignore the stop signal. On each trial, a white fixation cross was displayed on a black computer screen followed by a left- or a right-pointing arrow stimulus (Figure 1A). The time between the fixation cross and arrow stimulus ranged from 500 to 700 msec (steps of 100 msec, $M = 600$ msec).

In every four trials, there was one stop trial and three go trials, and the number of leftward- and rightward-pointing arrows was equal. The delay between the go stimulus (the arrow) and the stop signal, that is, the stop signal delay (SSD), was sampled from four different step-up and step-down staircases to ensure convergence to P (inhibit) of 50% by the end of the experiment. If a stop signal from a particular staircase was presented for the critical direction and the subject responded, then the SSD for that staircase was reduced by 50 msec on a subsequent stop trial; if the subject did not respond (i.e., successfully stopped), then the SSD was increased by 50 msec. SSD values for noncritical trials were yoked to the values for critical trials. The four staircases started with SSD values of 100, 150, 200, and 250 msec, respectively.

In each block of 96 trials, TMS was delivered on 66 trials. We included no-TMS trials to estimate go-critical RT, go-noncritical RT, and stop signal RT (SSRT) uncontaminated by possible effects of the TMS on response emission RT and accuracy (Ziemann, Tergau, Netz, & Hömberg, 1997; Pascual-Leone et al., 1992). SSRT is an index of the speed with which someone stops a motor response (see below). Of the 66 trials on which TMS was delivered, 60 were go trials and 6 were stop trials. On stop trials, the magnetic stimulus could only occur in the baseline (prestimulus) period, whereas on go trials it could occur in the baseline or poststimulus period (Figure 1A). For stop trials, TMS was delivered on 3 trials at 200 msec before the arrow presentation (i.e., baseline, b1) and another 3 trials at 300 msec before the arrow presentation (i.e., b2). For go trials, TMS was delivered on 6 trials for b1 and 6 trials for b2. Baseline MEPs were used to normalize the poststimulus MEPs (see analysis below). On go trials, 12 magnetic stimuli were delivered at each of 80, 120, 160, and 200 msec after the go (arrow) stimulus. On all trials on which test stimuli were delivered in the block, we balanced the number of test stimuli for critical and noncritical directions. We note, with respect to the baseline stimulus, that TMS was delivered on 6 stop trials and 12 go trials per block. Therefore, the probability of a stop given a TMS stimulus was 0.33.

Analysis

Behavioral data. As TMS can speed or prolong RT (Ziemann et al., 1997; Pascual-Leone et al., 1992), and because the

probability of stop signal was slightly different for TMS and no-TMS trials, we separately computed key behavioral indices on trials on which TMS was and was not present. We calculated error rates and median RTs on critical and noncritical go trials for the index finger and computed the response delay effect by subtracting go-noncritical RT from go-critical RT. We also computed the speed of stopping for those blocks where the index finger was critical. We estimated SSRT using the so-called "integration method" (Verbruggen & Logan, 2009a; Logan & Cowan, 1984). In addition, based on some preliminary data (Greenhouse, Verbruggen, & Aron, unpublished observations) we examined whether, across subjects, the response delay effect predicted SSRT.

TMS data. All MEPs from all trials were inspected. First, trials were rejected from further analysis if there was an overlap between the MEP and the onset of voluntary EMG activity, or if the MEP amplitude was smaller than 0.05 mV. Second, trials were sorted by arrow stimulus direction (critical, noncritical), whether the MEP was collected from the responding finger (index responding, index not responding) and stimulation time (baseline [b1 + b2] / 2; 80, 120, 160, and 200 msec). Third, the MEPs recorded were trimmed by removing those trials where the MEPs were more than 3 *SD* from the mean under each condition. On average, 5.3% of the trials (*SD* = 3.4%) were rejected for each participant. Finally, MEPs were normalized in each condition by dividing the average MEP amplitude under a given condition by the mean baseline MEP amplitude. The MEP data reported here are only from the FDI muscle. Representative MEPs for this muscle, across the four time points, are show in Figure 1B. Inspection of the little finger (ADM muscle) data showed that MEPs were smaller and less reliable than those from FDI. This was probably due to the stimulation site being optimized for the FDI muscle. The fact that the critical direction was switched after Block 3 meant that we could examine FDI MEPs when the responding finger was the index finger or when the responding finger was the little finger (and within these conditions, when the index finger was critical and when it was not). For the statistical analysis, we examined FDI MEPs for the two early time points, with a repeated measures ANOVA that included test stimulus interval (80, 120), rule (index finger is critical, index finger is noncritical), and responding finger (index responding, index not responding). We also examined FDI MEPs for the two later time points with a repeated measures ANOVA, which included test stimulus interval (160, 200), critical direction (critical, noncritical), and responding finger (index responding, index not responding).

We also computed root mean square EMG activity in the 100 msec preceding the TMS stimuli for each condition to establish if the muscle of interest (FDI) was "quiet" at the time of MEP recording and to establish if there were systematic pre-TMS differences in muscle activity for conditions of interest. Finally, we also computed the electromechanical delay for go-critical and noncritical trials. EMG burst onset was determined as follows. For each trial, the standard deviation of the EMG trace was established for a "quiet" period of the trial. A threshold was computed, which was three times the magnitude of the standard deviation of the quiet period. An algorithm then determined when it was during the 150 msec before the button press that the electromyograph rose above the threshold. A researcher, blind to condition, then reviewed (and adjusted if necessary) the estimated EMG burst onset. The electromechanical delay refers to the interval between the onset of the EMG burst and the button press on a particular trial. A recent study showed that an elongation of electromechanical delay can be produced by a stopping process (Coxon et al., 2007). Specifically, these authors demonstrated a significantly increased electromechanical delay in a responding muscle when an alternative muscle was stopped, relative to when the alternative muscle did not need to be stopped. Elongation of the electromechanical delay for go-critical trials could relate to active braking via suppression of motor output (Coxon et al., 2007).

Results

Behavior

Table 2 shows behavioral data for all trials, in both the TMS and the no-TMS conditions. Although TMS is sometimes shown to influence RT (e.g., Ziemann et al., 1997; Pascual-Leone et al., 1992), here we found minimal differences between TMS and no-TMS trials: critical RT, $t(11) = 0.5$, $p = .6$; noncritical RT, $t(11) = 0.7$, $p = .5$. This was probably because the TMS stimuli were delivered 200 msec or more before the motor response. Therefore, we report statistical results for all trials. Three participants were left-handed, but an analysis of MEP amplitude showed that handedness was not a factor, $F(1, 10) = 0.27$, $p = .61$; therefore, all 12 participants were analyzed together.

There was a reliable response delay effect as participants responded significantly more slowly on critical than noncritical trials, $t(11) = 7.7$, $p < .001$ (Figure 2A). Participants made very few errors of omission or discrimination on go trials (combined errors, $M = 1.1\%$, $SD = 1.2\%$). The number of combined errors was very similar for go-critical and noncritical trials (go-critical trial, $M = 0.7$, $SD = 0.8$; go-noncritical trial, $M = 0.4$, $SD = 0.9$), $t(11) = 0.9$, $p = .4$. The average SSD at which stop signals was delivered was 228.6 msec (*SD* = 78.7 msec). SSRT was estimated at 257.5 msec (*SD* = 86.8 msec). Importantly, we found that across participants, the response delay effect was correlated with SSRT; i.e., participants who showed a larger response delay effect stopped more quickly (faster SSRT), $t(10) = 2.08$, $p < .05$, robust regression (Figure 2B).

Table 2. Behavioral Data for TMS Experiments 1 and 2

	TMS	*No TMS*	*All Trials*
Experiment 1			
Clinical trials			
Median RT (msec)	522.0 (55.9)	531.9 (73.9)	523.7 (53.9)
Errors (%)	1.1 (1.2)	0.8 (1.5)	0.7 (0.8)
SSRT (msec)			257.5 (86.8)
Mean SSD (msec)			228.6 (78.7)
Noncritical trials			
Median RT (msec)	411.8 (29.4)	416.2 (37.7)	412.3 (29.5)
Errors (%)	0.9 (1.9)	0.0 (0.0)	0.4 (0.9)
Overall			
Response delay effect (msec)	110.2 (52.0)	115.6 (66.9)	111.3 (50.3)
Experiment 2			
Median RT (msec)	418.9 (63.5)	428.1 (65.3)	420.2 (63.9)
Errors (%)	0.7 (0.5)	1.4 (1.5)	0.8 (0.5)

Critical and noncritical RTs refer to trials without stop signals. Values in parentheses are *SD*s.

Corticomotor Excitability

Mean resting motor threshold was 42.3% (*SD* = 3.7%), mean test stimulus intensity was 50.4% (*SD* = 4.4%), and mean baseline MEP amplitude in FDI was 1.25 mV (*SD* = 0.35 mV). The main effects of time point (80, 120, 160, or 200 msec) and rule (index finger is critical, index finger is noncritical) and the interaction between the two were significant (all *p*s < .05). However, our starting hypotheses make different predictions for early and late time points. Therefore, in the following analyses, we will analyze the data for early and late time points separately. To test the braking hypothesis, specifically the idea that participants might proactively suppress the "critical" response representation even before the response is initiated, we examined FDI MEPs for the two early time points. We used a repeated measures ANOVA, which included test stimulus interval (80 and 120 msec), rule (index finger is critical, index finger is noncritical), and responding finger (index responding, index not responding). There was a main effect of interval—FDI MEPs decreased significantly from 80 to 120 msec, $F(1, 11) = 6.4$, $p < .05$ (Figure 3A). There were no further main effects or interactions. Inspection of the pattern in Figure 3A shows that FDI MEP amplitude was reduced below baseline at the 80- and 120-msec time points. To formally test this "MEP suppression," we collapsed the normalized MEP data across responding finger and across rule condition and

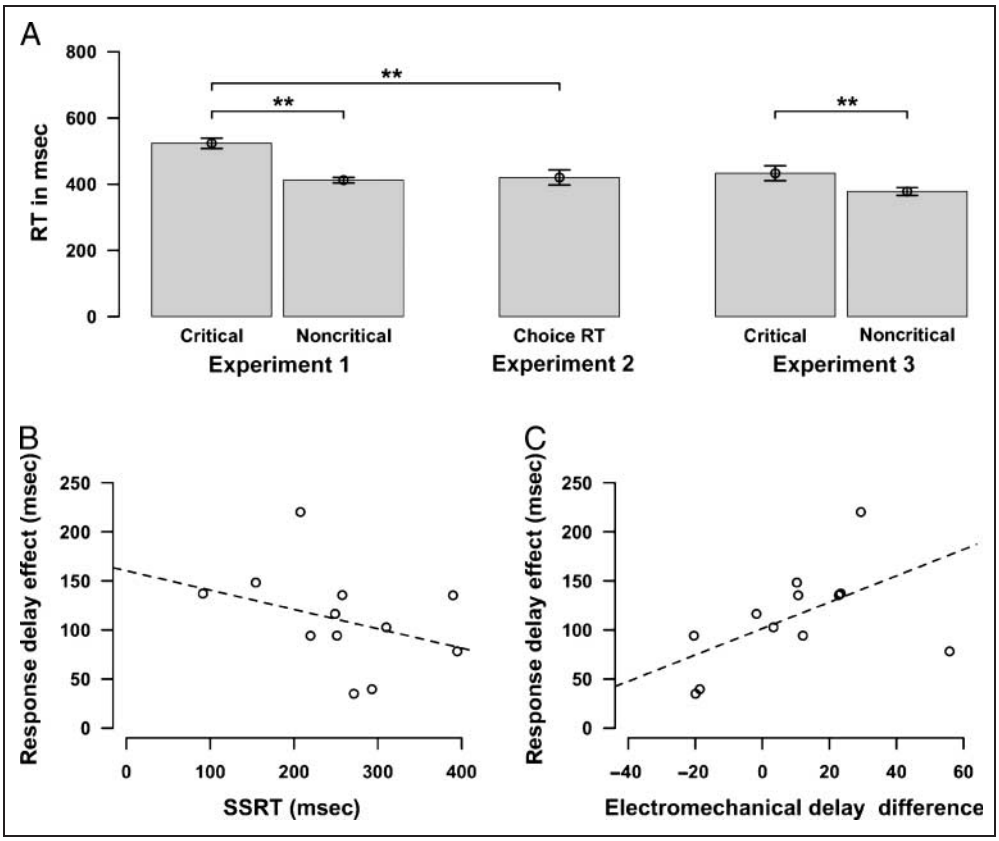

Figure 2. Behavioral and electromechanical delay results. (A) Median RT for the three experiments. In Experiments 1 and 2, the values are for index finger responses. In Experiment 3, critical and noncritical were index or middle fingers for subjects (counterbalanced across subjects). Error bars are *SEM*. These are all trials without stop signals. (B) Negative correlation between the response delay effect (i.e., RT difference between go-critical and noncritical trials) and the SSRT. (C) Positive correlation between the response delay effect and the electromechanical delay difference between go-critical and noncritical trials. Regression lines and *p* values were computed with the use of robust regression by iteratively reweighted least squares to prevent the influence of outliers.

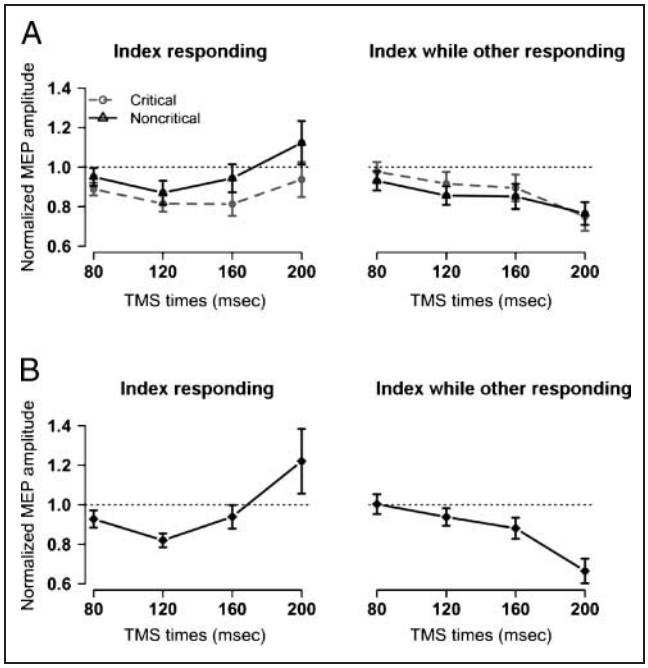

Figure 3. Corticomotor excitability for TMS Experiments 1 and 2. Normalized mean MEP amplitudes are shown for the FDI (index finger) muscle after stimulus presentation. These were computed by dividing the MEPs for each subject in each condition by the baseline MEPs for that subject. The dotted line represents the size of the MEP amplitude at baseline. (A) Experiment 1: conditional stop signal task. (B) Experiment 2: choice RT task (no stop signals). The left side of each panel shows MEPs from the FDI muscle when the stimulus indicates a response with the index finger; the right side shows mean MEP amplitudes, from the FDI muscle, when the stimulus indicates a response with the little finger (ADM).

tested whether the MEP was different from "1." The MEP was significantly suppressed at 80 msec, $t(11) = -1.9, p < .05$, one-tailed, and at 120 msec, $t(11) = -3.0$, $p < .01$, one-tailed.

Second, we analyzed FDI MEPs for the two late time points. As can be seen in Figure 3A, the MEP data show that a response initiation stage is evident at 160 msec and later. We performed a repeated measures ANOVA with test stimulus interval (160 and 200 msec), rule (index finger is critical, index finger is noncritical), and responding finger (index responding, index not responding). There was a main effect of rule—FDI MEP amplitudes were smaller in the critical than noncritical condition, $F(1, 11) = 5.6$, $p < .05$, and an interaction between rule and test stimulus interval, $F(1, 11) = 6.5$, $p < .05$—indicating that the excitability rose more slowly under the critical condition. Moreover, there was a main effect of responding finger—FDI MEP amplitudes were greater when the index was the responding finger than when it was not, $F(1, 11) = 8.0$, $p < .05$, and there was an interaction between responding finger and time, $F(1, 11) = 13.9$, $p < .05$—such that the difference in excitability between responding and nonresponding fingers was larger for the 200-msec time point than for the 160-msec time point.

We performed a pre-TMS EMG validation to make sure that the FDI was equivalently "quiet" across conditions. We analyzed these data with a repeated measures ANOVA, including test stimulus interval (80, 120, 160, and 200 msec), rule (current response is critical, noncritical), and responding finger (index responding, index not responding), with root mean square electromyography as the dependent variable. There were no significant main effects or interactions. Overall, the FDI muscle was "at rest" before magnetic stimulation (root mean square, $M = 0.6$ μV, $SD = 0.1$ μV).

Finally, we found a nonsignificant trend for the electromechanical delay to be longer for go-critical than noncritical trials (critical: $M = 135.5$ msec, $SD = 29.7$ msec; noncritical: $M = 128.6$ msec, $SD = 15.1$ msec; $p = .090$ Wilcoxon test, one-tailed). Interestingly, the electromechanical delay difference between these trials types was strongly correlated with the response delay effect, $t(10) = 8.4$, $p < .001$, robust regression (Figure 2C).

A key result of this TMS experiment was that the difference in the excitability of the FDI representation, between critical and noncritical conditions, only emerges at the 160- and 200-msec time points. This was contrary to the prediction of the braking hypothesis that a difference between these conditions may be observable before the response is initiated by primary motor cortex (Table 1). The finding of a later difference in excitability is consistent with the three possible accounts: a modified active braking account in which the braking mechanism operates when the critical response is initiated as well as the prolonged decision stage and slower motor facilitation accounts. However, other aspects of the data speak against these latter two accounts as explaining all of the response delay effect.

First, there was a significant correlation between the response delay effect and the SSRT—those participants with a longer response delay effect stopped more quickly. This suggests that a process related to the increased slowing could also be related to the faster stopping. It is unlikely that slower motor facilitation would explain this because slower facilitation should not alter the speed of the stopping mechanism, as going and stopping are thought to be independent (Verbruggen & Logan, 2009a). In the current experiment, the SSD was adjusted dynamically—so that if a subject facilitated their motor response more slowly, then the SSD would be adjusted for that and the SSRT estimate would not be influenced. Therefore, the response delay effect/SSRT correlation speaks against the slower motor facilitation account; instead, the correlation between response delay effect and SSRT could be explained by either active braking or prolonged decision stage accounts. If active braking operates via partial response suppression, then starting this process in advance of the stop signal would produce a response delay effect and would also enable faster stopping. Similarly, if a prolonged decision stage relates to increased cognitive load on go-critical trials (i.e., monitoring both a stop goal and a go goal or paying more attention to the occurrence of a stop signal), then this could produce a response delay effect as well as

faster stopping (because the stop goal is already active or because the stop signal is detected more quickly). Thus, the significant correlation between the response delay effect and SSRT is inconsistent with the slower motor facilitation account but is consistent with the prolonged decision stage account and the braking account (Table 1).

Second, there was a significant correlation between the response delay effect and the electromechanical delay difference for go-critical versus noncritical trials. This is compatible with both active braking and slower motor facilitation accounts, but not with a prolonged decision stage account. The electromechanical delay reflects the delay between the EMG burst and the button press and thus corresponds to a stage after a decision about the response has been made, and this could reflect active braking. For example, Coxon et al. (2007) demonstrated a significantly increased electromechanical delay in a responding muscle when an alternative muscle was stopped, relative to when the alternative muscle did not need to be stopped. Thus, elongation of the electromechanical delay for go-critical versus noncritical trials could relate to active braking via suppression of motor output. However, such elongation could also relate to slower motor facilitation. Thus, the significant correlation between the response delay effect and the electromechanical delay difference is inconsistent with the prolonged decision stage account but is consistent with the slower motor facilitation account and the braking account (Table 1).

We note that the idea that subjects slow go-critical responses to increase the probability of successful stopping resembles the idea that subjects slow responses to increase the probability of a correct response in a choice task (i.e., the speed/accuracy trade-off; Rinkenauer, Osman, Ulrich, Muller-Gethmann, & Mattes, 2004; Howell & Kreidler, 1963). In this experiment, we did not observe increased accuracy on go-critical than noncritical trials (but see Verbruggen & Logan, 2009b); however, this may have related to a very slow error rate overall. We assume that the similarity between slowing in anticipation of a stop signal and slowing to prevent an erroneous response exists because in both situations, subjects prolong decision and nondecisional (motor-related) stages to prevent fast responses.

An interesting but unexpected finding from Experiment 1 was a significant suppression of FDI MEPs compared with baseline at the 120-msec time point, both when the index was the responding and the nonresponding finger. Possibly, participants suppress all motor output when a stimulus is detected (or even before it is detected) in the conditional stop task and maintain suppression for critical trials and release suppression for noncritical trials after stimulus categorization and response selection. Alternatively, the general suppression could be due to the exigencies of response selection and thus would be unrelated to the requirement to stop occasionally. To examine this question further, we performed a second experiment in which we again used TMS to probe motor cortex excitability during a choice RT task, but this time without stop signals. These were different participants who knew nothing about the requirement to stop in Experiment 1. Our objective here was to assess whether the general suppression at the early time points was due to the requirement to stop occasionally or whether it was due to response selection itself.

EXPERIMENT 2: TMS STUDY WITH A CHOICE RT TASK

Methods

Participants

Eight young adults participated (four males, all right-handed; age M = 21.8 years, range = 19–34 years). All participants provided written consent in accordance with the internal review board guidelines of the University of California at San Diego, completed a TMS safety screen questionnaire, and had no contraindications to TMS. These were different participants from Experiment 1.

EMG Recordings and TMS

The same methods were used as in Experiment 1 above.

Task and Procedure

Experiment 2 comprised a total of six blocks, with each containing 72 trials. Apart from the number of trials per block and the absence of stop instructions or stop signals, every aspect of task procedure and TMS recording was the same as for Experiment 1 (Figure 1A). Participants were instructed to respond as fast as possible while maintaining accuracy, with a left or a right keypress after the arrow was presented (again using index and little fingers of the right hand). Of the 72 trials in each block, magnetic stimuli were delivered before the arrow on 12 trials (baseline) and after the arrow on 48 trials. There were 12 trials with no magnetic stimuli. As in Experiment 1, 6 magnetic stimuli were given at 200 msec (b1) and 6 at 300 msec (b2) before the arrow presentation to record baseline MEPs. After the go stimulus, 48 magnetic stimuli were given at the same four time intervals as in Experiment 1. These stimuli were equally distributed over the four time points for each arrow direction.

Analysis

Behavioral data. Median RT and percentage omission/discrimination errors were computed for the index finger.

TMS data. Trials were rejected using the same criteria as for Experiment 1. Trials were then sorted by responding finger (index responding, index not responding) and TMS stimulus time (baseline [b1 + b2] / 2; 80, 120, 160, and 200 msec). Data were trimmed and normalized as for

Experiment 1. On average 7.0% of all the trials per subject were rejected (SD = 3.7%). As for Experiment 1, we performed separate ANOVAs for the early and late time points. In addition, we validated our results by computing pre-TMS electromyography in the 100 msec preceding the magnetic stimuli for each condition. The pretrigger electromyography was analyzed as for Experiment 1.

Results

Behavior

A comparison of RT between TMS (M = 418.9, SD = 63.5) and no-TMS trials (M = 428.1, SD = 65.3) revealed no significant differences, $t(7) = -1.8$, $p = .1$; thus, we collapsed RT over all trials. We found that median choice RT in this experiment was significantly faster than critical go RT in Experiment 1 (Experiment 1: M = 523.7, SD = 53.9; Experiment 2: M = 420.2, SD = 63.9), $t(18) = 3.9$, $p < .01$, independent samples t test, but not significantly different from noncritical go RT in Experiment 1 (Experiment 1: M = 412.3, SD = 29.5; Experiment 2: M = 420.2, SD = 63.9), $t(18) = -0.4$, $p = .7$ (Figure 2A). Thus, participants responded to "pure go" trials in this experiment with a similar latency to noncritical go trials in Experiment 1. Again, omission/discrimination errors on go trials were few (M = 0.8%, SD = 0.5%).

Corticomotor Excitability

Mean resting motor threshold was 41.2% (SD = 5.8%), mean test stimulus intensity was 46.9% (SD = 7.5%), and mean baseline FDI MEP amplitude was 1.1 mV (SD = 0.3 mV). Overall, the pattern of results from Experiment 2 closely resembled the findings from Experiment 1 (compare Figure 3A with Figure 3B). For the ANOVA for the early time points (80 and 120 msec), there was a main effect of time, $F(1, 7) = 10.6$, $p < .05$—more MEP suppression at 120 than 80 msec, and a main effect of finger, $F(1, 7) = 17.4$, $p < .01$—excitability was less when the FDI was the responding finger than when it was not.

A key planned analysis was to examine whether significant below-baseline MEP suppression occurred in this experiment. Collapsing across responding finger, we examined whether normalized MEP amplitudes were different from "1." As in Experiment 1, there was a significant "MEP suppression" at 120 msec, $t(7) = -3.55$, $p < .01$, one-tailed. Yet, this effect was not observed at 80 msec, $t(7) = -0.81$, $p = .44$, one-tailed.

For the ANOVA for the late time points (160 and 200 msec), there was a main effect of finger, $F(1, 7) = 7.52$, $p < .05$—where FDI MEP amplitude was greater when it was responding than nonresponding, and an interaction between responding finger and a main effect of time, $F(1, 7) = 7.2$, $p < .05$—the facilitation of FDI MEPs increased from 160 to 200 msec to a greater extent when the finger was responding than when it was not.

For the validation analysis of pre-TMS electromyography, ANOVA was performed with test stimulus interval (80, 120, 160, and 200 msec) and responding finger (index responding, index not responding). There were no significant main effects or interactions. Overall, the FDI muscle was "at rest" before the magnetic stimulation (M = 0.9 μV, SD = 0.4 μV).

The results of Experiment 2 suggest that the general suppression at 120 msec in Experiment 1 was due to the requirement to select responses and not to the requirement to stop occasionally. Based on prior research (Duque & Ivry, 2009; Boulinguez, Jaffard, Granjon, & Benraiss, 2008; Davranche et al., 2007; Hasbroucq et al., 1999; Hasbroucq, Kaneko, Akamatsu, & Possamai, 1997) and as we argue in the General discussion section, it is likely that this MEP suppression is due to the imposition of an inhibitory process when selecting response. This process of inhibiting the corticospinal pathway could begin at the fixation period of the trial or some time before stimulus onset, perhaps to prevent premature responses (as the above authors have argued), or it could be applied around the time of response initiation itself, consistent with neurophysiological models proposing that response initiation is preceded by suppression of competitor motor programs (Mink, 1996). As we only included a baseline at 200 or 300 msec pre-go-stimulus, we cannot judge when the MEP suppression began.

We now return to the question of the neurocognitive mechanisms underlying the response delay effect, observed in Experiment 1. We noted that this behavioral effect could be explained by a prolonged decision stage as well as slower motor facilitation, but it was most compatible with a modified version of active braking. Another way to elucidate between these accounts is to use functional MRI to examine activation for go-critical versus noncritical trials. If active braking occurs via a (partial) stopping mechanism, then brain regions that are key for outright stopping may be activated more for go-critical than noncritical trials (Table 1).

EXPERIMENT 3: REANALYSIS OF fMRI DATA FROM THE CONDITIONAL STOP SIGNAL TASK

Methods

Participants

Fifteen right-handed young adults participated in the fMRI study (10 males; age, M = 28.1 years). All were free of neurological or psychiatric history and gave informed consent according to the institutional review board protocol of the University of California at Los Angeles.

Task and Procedure

The conditional stop signal task was highly similar to the one used in Experiment 1. Full details are provided by Aron, Behrens, et al. (2007). In brief, for the go task, participants

responded as fast as possible with a left or right keypress (using index and middle fingers of the right-hand) to arrows pointing left or right. For the stop task (25% of trials), participants attempted to stop the response when a stop signal was sounded after a particular SSD, but only if the arrow was pointing in the critical direction: for half the participants, this was leftward pointing; for the other half, rightward pointing. There were 32 stop trials and 96 go trials per scan (128 trials total). Each subject performed three scans. In every 4 trials, there was 1 stop trial and 3 go trials, and the number of leftward and rightward pointing arrows was equal. The SSD value for the stop trial was sampled from one of the four staircases in turn. Null events were interposed between every stop or go trial. The duration of null time ranged between 0.5 and 4 sec (M = 1 sec).

Behavioral Data Analysis

This was similar to Experiment 1.

fMRI Acquisition and Processing

Full details are provided by Aron, Behrens, et al. (2007). In brief, images were acquired using a 3-T Siemens Allegra MRI scanner at the Ahmanson-Lovelace Brain Mapping Center at the University of California at Los Angeles. Each scanning run acquired 166 functional T2*-weighted echo-planar images (4 mm slice thickness, 33 slices, repetition time = 2 sec, echo time = 30 msec, flip angle = 90°, matrix 64 × 64, field of view = 200, in-plane resolution = 3.125 mm). The first two volumes in each run were discarded to allow for T1 equilibrium effects. In addition, a high-resolution structural scan (MP-RAGE) was acquired for registration: acquisition parameters, repetition time = 2.3, echo time = 2.1, field of view = 256, matrix = 192 × 192, sagittal plane, slice thickness = 1 mm, 160 slices. Data were preprocessed using the FMRIB software library (www.fmrib.ox.ac.uk/fsl), including realignment, spatial smoothing, temporal filtering, and registration steps.

fMRI Model Fitting

Three different models were fit for the analysis here, with slightly different regressors. These were as follows: (a) the basic model, which included go-critical, go-noncritical, successful stop, and unsuccessful stop trials and a nuisance event consisting of go trials on which participants did not respond or made errors of discrimination (see Aron, Behrens, et al., 2007); (b) the basic model with binned RT, which was the same as the basic model except that separate regressors were created for fast, medium, and slow RT in go-critical and go-noncritical conditions (in each condition, for each scan, the go RTs were split into three roughly equally sized bins); and (c) the parametric model, which was the same as the basic model but with two extra regressors, go-critical parametric and go-noncritical parametric, which added RT as a covariate for each trial type.

fMRI Statistical Analysis

We performed three kinds of analyses. First, an anatomically defined ROI approach to test whether regions of the brain known to be critical for stopping would be activated more for go-critical than noncritical and especially whether this would interact with RT. Our ROIs were the right inferior frontal gyrus, the pre-SMA, and the subthalamic nucleus region based on a prior study (Aron, Behrens, et al., 2007) and on other literature pointing to these as critical "nodes" for behavioral stopping (reviewed in Chambers et al., 2009; Aron, Durston, et al., 2007). Using the results from the basic model with binned RT, we extracted the mean activity for each subject for each level of the rule factor (current response is critical, noncritical) and the RT factor (fast, medium, and slow) and performed ANOVA for each of the three ROIs. Second, we performed whole-brain voxel-based analysis using the basic model. For each subject and for each of three scans, we computed the contrast: go critical–go noncritical. Third, we performed whole-brain voxel-based analysis using the parametric model. For each subject and for each of three scans, we computed the contrast: go-critical parametric–go-noncritical parametric. Analysis was carried out using the fMRI Expert Analysis Tool Version 5.1, part of the FMRIB's Software Library (www.fmrib.ox.ac.uk/fsl). Higher level analysis (one-sample t test) was carried out using ordinary least squares simple mixed effects. For the whole-brain analyses, z statistic images were thresholded using clusters determined by $z > 2.3$ and a (corrected) cluster threshold of $p = .05$ (using Gaussian random field theory).

Results

Behavior

As reported by Aron, Behrens, et al. (2007), participants responded significantly more slowly on go-critical than noncritical trials (median go-critical RT = 433 msec, SD = 85 msec; median go-noncritical RT = 378 msec, SD = 44 msec), $t(14) = 5.7$, $p < .0001$. SSRT was estimated at 266 msec (SD = 53 msec). As for Experiment 1, the SSRT and the response delay effect were negatively correlated ($r = -.26$) so that subjects who responded more slowly on critical than noncritical trials also stopped more quickly, but this was not statistically significant here.

fMRI

Go-critical versus noncritical activation for three ROIs. For the right inferior frontal gyrus, there was a significant main effect of rule (activation was greater when current response was critical than noncritical), $F(1, 14) = 17.5$,

$p < .001$, and a significant interaction between rule and RT (the activation difference between go-critical and noncritical was greatest for the slower RTs), $F(2, 28) = 3.54$, $p < .05$ (Figure 4A). For the pre-SMA, there was a significant main effect of rule (go-critical greater than noncritical), $F(1, 14) = 10.4$, $p < .01$, but no interaction between rule and RT. For the subthalamic nucleus region, there were no significant effects. As an auxiliary analysis, in light of the findings of Experiment 2 that an inhibitory process may be recruited as part of response selection on go trials (even without the potential need to stop), we examined whether go-noncritical activation was above baseline. Significant activation was not present in any of the ROIs (all ps $> .26$), nor was there activation at the voxel level, small volume correction for multiple comparisons in the anatomically defined right inferior frontal gyrus, pre-SMA, and subthalamic nucleus regions.

Whole-brain voxel-based analysis. Go-critical trials activated a large focus of right lateral pFC significantly more than go-noncritical trials ($z > 2.3$, whole-brain cluster corrected). Importantly, this included the right inferior frontal gyrus (max $Z = 4.43$, [52 20 4]; Figure 4B), overlapping with regions of the inferior frontal gyrus that we have previously shown to be activated by outright stopping in these same subjects (Aron, Behrens, et al., 2007). There was also significant activation of the right pre-SMA (max $Z = 3.45$, [10 6 72]), as well as the right superior parietal cortex (max $Z = 4.49$, [42 −44 48]) and the right middle temporal gyrus (max $Z = 4.04$, [58 −26 −2]). At a whole-brain-corrected threshold, no subcortical activation was evident. For the parametric contrast, a significantly stronger relationship between activation and RT was observed for go-critical than for noncritical trials in several right hemisphere regions including the inferior frontal gyrus and the DLPF cortex (max $Z = 3.68$, [50 16 24]), the striatum (max $Z = 3.53$, [14 14 6]), and the parietal cortex (max $Z = 3.4$, [60 −46 30]) (all $z > 2.3$, whole-brain corrected; Figure 4B). There was also activation in the midbrain subthalamic nucleus region; however, without using high-resolution methods, it is difficult to locate this with confidence.

GENERAL DISCUSSION

We examined the neurocognitive mechanisms that underlie the response delay effect that is observed when people anticipate they might need to stop. In a TMS study, we found that corticomotor excitability was lower and increased more slowly for go-critical versus noncritical trials from about 160 msec. We also found that those participants with a larger response delay effect were able to stop their responses more quickly and that those with a larger response delay effect had a bigger difference in electromechanical delay for go-critical than for noncritical trials. In a reanalysis of fMRI data, we found that a prefrontal region (the right inferior frontal gyrus) that is necessary to outright suppress a motor response was more activated for go-critical trial versus noncritical trial, moreover in proportion to the degree of RT slowing.

One explanation for the response delay effect is an active braking mechanism. This could involve partial response suppression, perhaps using the same brain mechanism that is used to stop a response outright. Accordingly, the participant may prepare to partially inhibit a particular effector according to the critical rule, and this could potentially

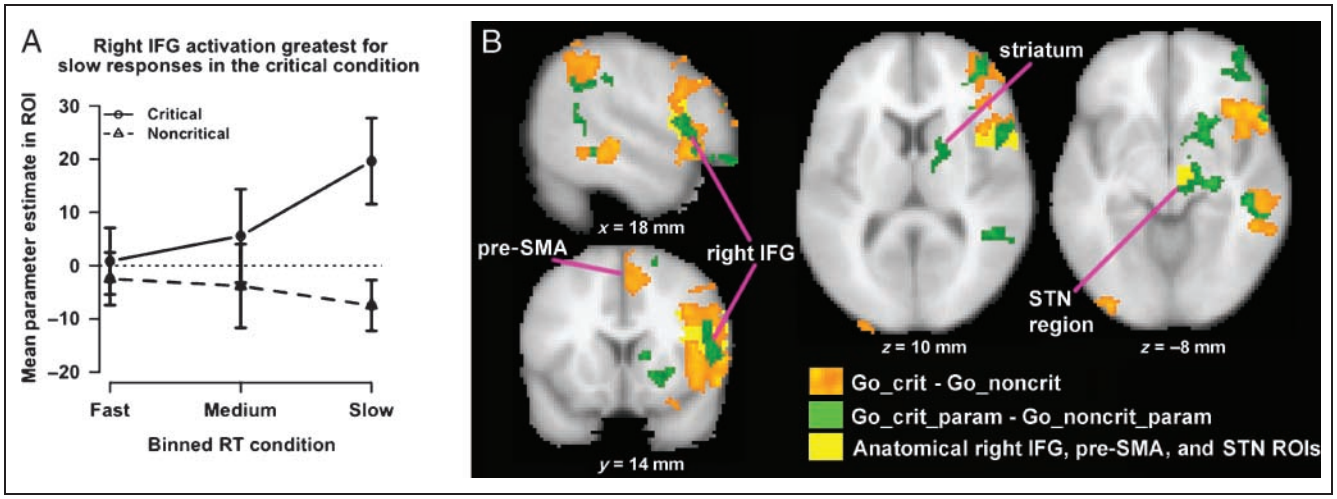

Figure 4. Responding with restraint activates brain regions important for outright stopping. (A) Activation of the right inferior frontal gyrus (IFG), anatomically defined, increases with slower RT in the go-critical but not noncritical condition. Mean activation is extracted from the ROI for each participant for each trial type (in critical and noncritical conditions and at three levels of RT). (B) Whole-brain analyses at the voxel level. Go-critical trials activate several brain regions more than noncritial trials, including the right inferior frontal gyrus (IFG) and the pre-SMA ($n = 15$, voxel threshold $z > 2.3$, whole-brain cluster corrected). Moreover, the correlation between activation and RT is significantly greater for go-critical than noncritical trials in several right hemisphere regions including the right IFG, the striatum, the parietal cortex, and a midbrain region in the vicinity of the subthalamic nucleus ($n = 15$, voxel threshold $z > 2.3$, whole-brain cluster corrected).

occur even before the go stimulus is displayed. However, the results were inconsistent with this prediction: There was no effect of rule (critical versus noncritical) at the early time points of 80 and 120 msec. Instead, we found that the difference between these conditions emerged at the later time points of 160 and 200 msec (i.e., after stimulus categorization and response selection and during response initiation). Although this late effect could be explained by an active braking mechanism that restrains the critical response once it is initiated, it can also be partly explained by a prolonged decision stage account and by slower motor facilitation (Table 1). We argued that the correlation between the response delay effect and the SSRT speaks against the slower motor facilitation account, whereas the correlation between the response delay effect and the electromechanical delay difference speaks against the prolonged decision stage account. Thus, the data from Experiment 1 point most clearly toward a modified version of active braking as a mechanism to explain the response delay effect. Notwithstanding this, it is likely that the different underlying mechanisms are all in play in different participants to differing degrees. In an earlier study that examined a different form of response slowing in the context of stop signals, mathematical modeling showed that the slowing was accounted for by variance in both decision and nondecision (response initiation) stages (Verbruggen & Logan, 2009b).

Active braking could occur through a partially activated stopping mechanism. This predicts that brain regions critical for outright stopping will be activated in relation to the response delay effect. In Experiment 3, we found that this was indeed the case. For the anatomically defined ROI analysis, we observed significantly greater activation for go-critical than noncritical trials in the right inferior frontal gyrus and the pre-SMA (two regions that are critical for outright stopping, see Chambers et al., 2009), and we observed that activation increased with increasing RT more for go-critical than noncritical trials in the right inferior frontal gyrus. The whole-brain voxel-level analysis confirmed these observations with greater spatial resolution. In particular, for the parametric analysis, a significantly stronger relationship between activation and RT was observed for go-critical than for noncritical trials in the right inferior frontal gyrus. However, additional regions of the right hemisphere were also implicated, including the DLPF cortex, the striatum, and the parietal cortex as well as a midbrain region.

This pattern of fMRI data is compatible with both active braking and prolonged decision stage accounts. On go-critical trials, participants have to maintain the goal to stop and the goal to go at the same time, whereas on go-noncritical trials, they only have a goal to go. The increased load, which partly must include the working memory monitoring of the conditional rule, would be expected to activate the DLPF cortex, the head of the caudate, and the parietal cortex, according to a well-established working memory circuitry (Muller & Knight, 2006; Wager & Smith, 2003; Braver et al., 1997; Petrides, 1994), as we observed here. In addition, the added task load could also explain the increased activation of the right inferior frontal gyrus. Activation of this region has been reported for sustained attention, working memory manipulation, and dual task requirements (e.g., McNab et al., 2008; Wager & Smith, 2003; Coull, Frackowiak, & Frith, 1998). Thus, although the right inferior frontal gyrus is critical for behavioral stopping, as shown by lesion studies, activation of this region cannot be taken as definitive evidence that it plays a causal role in active braking. Future research using loss-of-function approaches may be able to elucidate if the right inferior frontal gyrus plays a necessary role in active braking, and imaging with higher temporal and spatial resolution may be able to parse the different functions of the right inferior frontal gyrus with respect to working memory load, sustained attention, and proactive inhibitory control.

This study also provided interesting information about response selection. Experiment 2, which had no stop signals, clarified that the decision phase, which occurs before response initiation, is associated with a reduction of corticomotor excitability (beneath baseline levels). Two aspects of the wider literature suggest that this MEP suppression is related to active inhibition of the corticospinal tract via increased gamma-aminobutyric acid (GABA)-ergic activity in primary motor cortex. First, MEP suppression has been previously reported for a pre-go-stimulus period—in which it may help prevent premature responding (Duque & Ivry, 2009; Boulinguez et al., 2008; Davranche et al., 2007; Hasbroucq et al., 1997, 1999). Such studies have also shown that the corticospinal excitability reduction relates to increases in short interval intracortical inhibition or cortical silent period—both indices of GABA-ergic inhibition in M1. Second, our data from Experiments 1 and 2 indicate that the selection of the responding finger representation within primary motor cortex does not occur until at least 120 msec after the presentation of the go stimulus. After this time point, FDI MEP amplitudes are facilitated when the index finger is about to respond and further suppressed when the little finger is about to respond. The strong suppression of FDI MEP amplitude before activation of the little finger is in line with previous studies of selective finger movement (Beck et al., 2008; Stinear & Byblow, 2003). In particular, it has been shown that intracortical inhibition can be recruited above resting levels, and this contributes to the suppression of MEP amplitude in nonmoving fingers (Stinear & Byblow, 2003; Liepert, Classen, Cohen, & Hallett, 1998). Our findings, in conjunction with the published literature, therefore, suggest that the preinitiation phase in this study was accompanied by active inhibition of all possible response representations. Following this, the initiation phase was accompanied by an even greater inhibition of the nonselected motor representation, possibly by continued/increased GABA-ergic activity in primary motor cortex. It is possible that the putative inhibition in anticipation of response initiation/selection is generated by a premotor cortex circuit rather than the putative prefrontal/basal

ganglia circuit important for outright stopping (or active braking). Consistent with this, we did not observe significant activation above baseline levels for go-noncritical trials for the right inferior frontal gyrus, nor did we observe activation of the subthalamic nucleus region—and yet neurophysiological models propose that response initiation is preceded by suppression of competitor motor programs via the subthalamic nucleus (Mink, 1996). Future research is required to further explore the neural correlates of putative inhibitory processes operating in anticipation of or at the same time as the response initiation.

In summary, we examined the neurocognitive mechanisms underlying the response slowing that is observed in anticipation of a possible stop. We suggest that this is an experimental model for the kind of real-world control that is evident when people respond with restraint. We attained results for two phases: a preresponse initiation phase and a response initiation phase. The preresponse initiation period of the task was associated with a global reduction of corticomotor excitability (beneath baseline levels), and we speculate that this relates to GABA-ergic inhibition of primary motor cortical representations in this early phase. Once the response is selected, the corticomotor excitability of the responding finger's representation increases sharply, whereas that of the nonresponding finger is reduced even further, consistent with continued application of a GABA-ergic inhibitory mechanism. During the response initiation phase, we observed a different pattern, which likely explains the response delay effect. A difference in the rate of corticomotor facilitation for critical and noncritical trials emerged after 160 msec. Corticomotor excitability rose more slowly, under the critical condition. This was compatible with a modified version of the active braking hypothesis as well as with prolonged decision stage and slower motor facilitation accounts. However, other features of the data pointed more clearly to active braking as a mechanism underlying the response delay effect. The difference between go-critical and noncritical trials was also reflected in increased activation of a prefrontal region (the right inferior frontal gyrus) that is required to outright suppress a motor response. Although the imaging results cannot distinguish between active braking and prolonged decision stage (via increased cognitive load) accounts, when taken together with the TMS findings, we suggest that at least part of the response delay effect is explained by active braking and that this is probably reflected in activation of regions of the brain important for outright stopping. Overall, the results further our understanding of cognitive control by suggesting that a neurocognitive system heretofore associated with outright stopping is proactively recruited to enable people to respond with restraint.

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REFERENCES

Aron, A. R., Behrens, T. E., Smith, S., Frank, M. J., & Poldrack, R. A. (2007). Triangulating a cognitive control network using diffusion-weighted magnetic resonance imaging (MRI) and functional MRI. *Journal of Neuroscience, 27,* 3743–3752.

Aron, A. R., Durston, S., Eagle, D. M., Logan, G. D., Stinear, C. M., & Stuphorn, V. (2007). Converging evidence for a fronto-basal-ganglia network for inhibitory control of action and cognition. *Journal of Neuroscience, 27,* 11860–11864.

Beck, S., Richardson, S. P., Shamim, E. A., Dang, N., Schubert, M., & Hallett, M. (2008). Short intracortical and surround inhibition are selectively reduced during movement initiation in focal hand dystonia. *Journal of Neuroscience, 28,* 10363–10369.

Boulinguez, P., Jaffard, M., Granjon, L., & Benraiss, A. (2008). Warning signals induce automatic EMG activations and proactive volitional inhibition: Evidence from analysis of error distribution in simple RT. *Journal of Neurophysiology, 99,* 1572–1578.

Braver, T. S., Cohen, J. D., Nystrom, L. E., Jonides, J., Smith, E. E., & Noll, D. C. (1997). A parametric study of prefrontal cortex involvement in human working memory. *Neuroimage, 5,* 49–62.

Chambers, C. D., Garavan, H., & Bellgrove, M. A. (2009). Insights into the neural basis of response inhibition from cognitive and clinical neuroscience. *Neuroscience and Biobehavioral Reviews, 33,* 631–646.

Coull, J. T., Frackowiak, R. S., & Frith, C. D. (1998). Monitoring for target objects: Activation of right frontal and parietal cortices with increasing time on task. *Neuropsychologia, 36,* 1325–1334.

Coxon, J. P., Stinear, C. M., & Byblow, W. (2007). Selective inhibition of movement. *Journal of Neurophysiology, 97,* 2480–2489.

Davranche, K., Tandonnet, C., Burle, B., Meynier, C., Vidal, F., & Hasbroucq, T. (2007). The dual nature of time preparation: Neural activation and suppression revealed by transcranial magnetic stimulation of the motor cortex. *European Journal of Neuroscience, 25,* 3766–3774.

De Jong, R., Coles, M. G., & Logan, G. D. (1995). Strategies and mechanisms in nonselective and selective inhibitory motor control. *Journal of Experimental Psychology, 21,* 498–511.

Devanne, H., Lavoie, B. A., & Capaday, C. (1997). Input-output properties and gain changes in the human corticospinal pathway. *Experimental Brain Research, 114,* 329–338.

Duque, J., & Ivry, R. B. (2009). Role of corticospinal suppression during motor preparation. *Cerebral Cortex, 19,* 2025–2037.

Hasbroucq, T., Kaneko, H., Akamatsu, M., & Possamai, C. A. (1997). Preparatory inhibition of cortico-spinal excitability: A transcranial magnetic stimulation study in man. *Brain Research, Cognitive Brain Research, 5,* 185–192.

Hasbroucq, T., Osman, A., Possamai, C. A., Burle, B., Carron, S., Depy, D., et al. (1999). Cortico-spinal inhibition reflects

time but not event preparation: Neural mechanisms of preparation dissociated by transcranial magnetic stimulation. *Acta Psychologica (Amsterdam), 101,* 243–266.
Howell, W. C., & Kreidler, D. L. (1963). Information-processing under contradictory instructional sets. *Journal of Experimental Psychology, 65,* 39–46.
Liepert, J., Classen, J., Cohen, L. G., & Hallett, M. (1998). Task-dependent changes of intracortical inhibition. *Experimental Brain Research, 118,* 421–426.
Logan, G. D., & Cowan, W. B. (1984). On the ability to inhibit thought and action: A theory of an act of control. *Psychological Review, 91,* 295–327.
McNab, F., Leroux, G., Strand, F., Thorell, L., Bergman, S., & Klingberg, T. (2008). Common and unique components of inhibition and working memory: An fMRI, within-subjects investigation. *Neuropsychologia, 46,* 2668–2682.
Mink, J. W. (1996). The basal ganglia: Focused selection and inhibition of competing motor programs. *Progress in Neurobiology, 50,* 381–425.
Muller, N. G., & Knight, R. T. (2006). The functional neuroanatomy of working memory: Contributions of human brain lesion studies. *Neuroscience, 139,* 51–58.
Pascual-Leone, A., Valls-Solé, J., Wassermann, E. M., Brasil-Neto, J., Cohen, L. G., & Hallett, M. (1992). Effects of focal transcranial magnetic stimulation on simple reaction time to acoustic, visual and somatosensory stimuli. *Brain, 115,* 1045–1059.
Petrides, M. (1994). Frontal lobes and working memory: Evidence from investigations of the effects of cortical excisions in nonhuman primates. In F. Boller, & J. Grafman (Eds.), *Handbook of neuropsychology* (Vol. 9, pp. 59–84). Amsterdam: Elsevier.
Rinkenauer, G., Osman, A., Ulrich, R., Muller-Gethmann, H., & Mattes, S. (2004). On the locus of speed-accuracy trade-off in reaction time: Inferences from the lateralized readiness potential. *Journal of Experimental Psychology: General, 133,* 261–282.
Rossini, P. M., Barker, A. T., Berardelli, A., Caramia, M. D., Caruso, G., Cracco, R. Q., et al. (1994). Non-invasive electrical and magnetic stimulation of the brain, spinal cord and roots: Basic principles and procedures for routine clinical application. Report of an IFCN committee. *Electroencephalography and Clinical Neurophysiology, 91,* 79–92.
Stinear, C. M., & Byblow, W. D. (2003). Role of intracortical inhibition in selective hand muscle activation. *Journal of Neurophysiology, 89,* 2014–2020.
Verbruggen, F., & Logan, G. D. (2009a). Models of response inhibition in the stop-signal and stop-change paradigms. *Neuroscience and Biobehavioral Reviews, 33,* 647–661.
Verbruggen, F., & Logan, G. D. (2009b). Proactive adjustments of response strategies in the stop-signal paradigm. *Journal of Experimental Psychology: Human Perception and Performance, 35,* 835–854.
Vink, M., Kahn, R. S., Raemaekers, M., van den Heuvel, M., Boersma, M., & Ramsey, N. F. (2005). Function of striatum beyond inhibition and execution of motor responses. *Human Brain Mapping, 25,* 336–344.
Wager, T. D., & Smith, E. E. (2003). Neuroimaging studies of working memory: A meta-analysis. *Cognitive, Affective & Behavioral Neuroscience, 3,* 255–274.
Zandbelt, B., Van Buuren, M., Gladwin, T. E., Hoogendam, R., Kahn, S., & Vink, M. (2008). *Brain regions involved in response inhibition are also activated during anticipation of inhibition*. Paper presented at the Society for Neuroscience.
Ziemann, U., Tergau, F., Netz, J., & Hömberg, V. (1997). Delay in simple reaction time after focal transcranial magnetic stimulation of the human brain. *Brain Research, 744,* 32–40.