Saccade suppression exerts global effects on the motor system

Jan R. Wessel, H. Sequoyah Reynoso, and Adam R. Aron

Psychology Department, University of California San Diego, La Jolla, California; and Neuroscience Graduate Program, University of California San Diego, La Jolla, California

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Wessel JR, Reynoso HS, Aron AR. Saccade suppression exerts global effects on the motor system. J Neurophysiol 110: 883–890, 2013. First published May 22, 2013; doi:10.1152/jn.00229.2013.—Stopping inappropriate eye movements is a cognitive control function that allows humans to perform well in situations that demand attentional focus. The stop-signal task is an experimental model for this behavior. Participants initiate a saccade toward a target and occasionally have to try to stop the impending saccade if a stop signal occurs. Prior research using a version of this paradigm for limb movements (hand, leg) as well as for speech has shown that rapidly stopping action leads to apparently global suppression of the motor system, as indexed by the corticospinal excitability (CSE) of task-unrelated effectors in studies with transcranial magnetic stimulation (TMS) of M1. Here we measured CSE from the hand with high temporal precision while participants made saccades and while they successfully and unsuccessfully stopped these saccades in response to a stop signal. We showed that 50 ms before the estimated time at which a saccade is successfully stopped there was reduced CSE for the hand, which was task irrelevant. This shows that rapidly stopping eye movements also has global motor effects. We speculate that this arises because rapidly stopping eye movements, like skeleto-motor movements, is possibly achieved via input to the subthalamic nucleus of the basal ganglia, with a putatively broad suppressive effect on thalamocortical drive. Since recent studies suggest that this suppressive effect could also impact nonmotor representations, the present finding points to a possible mechanistic basis for some kinds of distractibility: abrupt-onset stimuli will interrupt ongoing processing by generating global motor and nonmotor effects.

inhibitory control; stop-signal task; motor evoked potential; eye movements; saccade countermanding

STOPPING an inappropriate action before execution is an important cognitive control function for limb movements (e.g., stopping one’s step into the street when a car approaches) and eye movements (e.g., avoiding gaze shifts toward irrelevant stimuli in situations demanding sustained attention). A better understanding of how eye movements are stopped is important, as everyday life affords many situations that call for control of eye movements toward distracting stimuli.

Recent evidence shows that rapid stopping of (skeleto-motor) actions is achieved via a nonselective, global signal, leading to reduced excitability across the entire motor system, rather than a specific effector (Badry et al. 2009; Cai et al. 2012; Majid et al. 2012). At the behavioral level, many studies have shown that when one response is stopped the execution of another is delayed (Bissett and Logan 2013; Coxon et al. 2007; MacDonald et al. 2012). At the physiological level, evidence for global stopping comes from transcranial magnetic stimulation (TMS) of primary motor cortex (M1). When a TMS stimulus is delivered over the hand area, corticospinal excitability (CSE) can be indexed via the amplitude of the motor evoked potential (MEP) that is measured by electromyography from the muscles of the hand. In this way, one can index the excitability of the hand representation in the brain with high temporal resolution. Using this method, several studies have now shown that stopping the hand reduces CSE of the leg, when the leg is task irrelevant (Badry et al. 2009; Majid et al. 2012), and stopping speech reduces CSE of the hand, when the hand is also task irrelevant (Cai et al. 2012). Here we test whether stopping eye movements, which are not part of the skeleto-motor system, engages the same global stopping system.

The execution of eye and limb movements involves dramatically different neural circuitry (see, e.g., Wurtz and Hikosaka 1986). In particular, eye movements do not involve M1; they are initiated via circuitry including the frontal eye fields and superior colliculi. Regarding stopping of eye movements, some studies emphasize frontal cortical regions (Boucher et al. 2007; Curtis et al. 2005; Nachev et al. 2005; Schall et al. 2002; Stuphorn and Schall 2006) that differ from those critical for stopping limb movements (Aron et al. 2007; Chambers et al. 2009). However, others do point to overlap, particularly in right inferior frontal cortex and presupplementary motor area (Heinen et al. 2006; Isoda and Hikosaka 2007; Leung and Cai 2007; Michael et al. 2006) and also, notably, in the subthalamic nucleus (STN) of the basal ganglia. For example, a neurophysiological study in monkeys showed increased STN activity for saccade-countermanding and NoGo trials (Isoda and Hikosaka 2008). Hence, a rapid, stopping-generated, cortical input into the oculomotor region of the STN (Matsumura et al. 1992; Nambu et al. 2002) could have broad effects on basal ganglia motor output.

We measured CSE from the hand during an oculomotor stop-signal task (Logan 1983; similar to a saccade-countermanding task, Hanes et al. 1998). On the basis of previous research (Cai et al. 2012; Majid et al. 2012), we predicted that if rapidly stopping eye movements involves a global stop, stopping saccades leads to hand suppression on successful stop trials compared with go trials and failed stop trials.

MATERIALS AND METHODS

Participants

Fourteen (3 women, 11 men) right-handed healthy UCSD undergrads participated in the study (age 18–30 yr, mean 22.7 yr, SE 0.81). Subjects had normal or corrected to normal vision and no history of neurological or psychiatric illness and were not taking any medication at the time of the study. They underwent TMS safety screening, signed written informed consent, and were paid $15/h. The study was...
reviewed and approved by the local ethics committee (UCSD IRB no. 071912).

**Task**

Stimuli were presented on a 21-in. (51-cm horizontal width) CRT monitor with Psychtoolbox-3 (Brainard 1997) and MATLAB 2010a (MathWorks, Natick, MA) running on an IBM-compatible PC. Each trial began with a centrally placed fixation cross and two yellow boxes on either side of the screen (~30° of visual angle from the center) (Fig. 1). After 1 s of fixation, the fixation cross was replaced by a white arrow (go stimulus) pointing to the right or left, with the participants being instructed to direct their gaze into the square on the respective side of the screen as fast and accurately as possible. However, on 33% of trials the arrow turned red shortly after its appearance, requiring the participants to try to stop the impending saccade. The stop-signal delay (SSD) was initially set to 100 ms and was then updated after each stop trial, depending on the participants’ performance on the trial, with an adaptive staircase algorithm: it was prolonged by 50 ms after a successful stop trial and shortened by 50 ms after a failed stop trial, thereby eventually converging on a 50% probability of successful stopping. Participants had 1,000 ms to respond to each arrow. Each trial was 3,200 ms long, with the remaining time after the response window being the intertrial interval.

Participants performed a training phase of 100 trials, during which accuracy and reaction time (RT) feedback were displayed after each response. No TMS was performed during this phase. Then, they performed 600 trials of actual experiment divided into 6 blocks. During this phase, they only received trial-by-trial feedback if they failed to respond on a go trial (reminding them to respond within the response window), and TMS data were collected.

**Eye-Tracking**

Eye movement data were collected with an SMI RED USB (SensoMotoric Instruments, Teltow, Germany) infrared eye-tracking system with a sampling rate of 120 Hz. Participants rested their chin on a table-mounted chin and forehead rest 45 cm away from the screen-mounted eye-tracker. Gaze coordinates were imported into MATLAB in real time. Saccades were detected whenever horizontal gaze shifts occurred with a peak velocity that corresponded to 2° of visual angle in saccadic amplitude (according to the saccadic main sequence; Bahill et al. 1975). This was done by initially displaying 10 stimuli that were offset by 2° of visual angle from the screen center at the beginning of the experiment. Participants were prompted to make saccades toward these stimuli. These gauging trials were then plotted as raw data traces as well as angular velocity (first derivative of the raw data). A velocity detection threshold was then adjusted so that each of these gauging saccades would have been detected. During the experiment, eye-tracking data were read out by MATLAB on each trial and converted to velocity (by calculating the first derivative). The first sample on which the velocity threshold was exceeded (if any) marked the response onset. The system was recalibrated during every break between blocks to ensure steady data fidelity. Trials on which the first saccade was preceded by an eyeblink were discarded. Trials with RT < 80 ms were treated as anticipations (Fischer et al. 1993) and also discarded.

**EMG Recording**

Surface EMG was recorded from the first dorsal interosseous (FDI) muscle of the right hand via Ag-AgCl hydrogel electrodes (Lead-Lok, Sandpoint, ID). A ground electrode was placed over the distal end of the ulna. The signal was amplified with a Grass Q511 Quad AC Amplifier (Grass Products, West Warwick, RI), with a recording band-pass filter between 30 Hz and 1,000 Hz (60-Hz notch). The amplified data were sampled with a CED Micro 1401 MK-II acquisition system (sampling rate: 2,000 Hz) and recorded with CED Signal software (version 4, Cambridge Electronic Design, Cambridge, UK).

**TMS Procedure**

CSE was measured with MEPs elicited by TMS. TMS stimulation was performed with a MagStim 200-2 system (MagStim, Whitland, UK).
UK) with a 70-mm figure-of-eight coil. Hotspotting was performed to identify the hand stimulation locus and correct intensity. The coil was first placed 5 cm lateral and 2 cm anterior to the vertex and repositioned to where the largest MEPs were observed consistently. Resting motor threshold (RMT) was then defined as the minimum intensity required to induce MEPs of amplitudes exceeding 0.1 mV peak to peak in 5 of 10 consecutive probes (Rossini et al. 1994). TMS intensity for the experimental stimulation was then adjusted to 110–120% of RMT (mean intensity = 47.3% of maximum output; min = 36%, max = 60%).

An EMG sweep was started 150 ms before every TMS pulse to obtain an estimate of baseline EMG activity for later artifact correction. TMS stimulation was timed to correspond with the point in time when the stopping-related influence on the motor system should be maximal. To maximize our chances of identifying this timing point, we adopted three different approaches based on earlier studies of stopping-related changes in CSE.

Approach 1. Earlier studies including those of Majid et al. (2012) showed that global stopping effects can be of high temporal specificity: While in their study, stopping the hand led to a significant suppression of leg CSE at 200 and 220 ms after SSD, they found no such effect at SSD + 240 ms [stop-signal reaction time (SSRT)] in their experiment was 246 ms; this means that stimulation in their experiment occurred on average at SSD + SSRT - 46 ms, SSD + SSRT - 26 ms, or SSD + SSRT - 6 ms, with the latter time point showing no global stopping-induced CSE changes]. Hence, we decided to time stimulation to SSD + SSRT - 50 ms, which roughly corresponds to the SSD + 200 ms time point of Majid et al. (2012).

Approach 2. Despite the results presented by Majid and colleagues (2012), other studies do suggest that the motor impact of stopping is indeed to be expected toward the end of estimated SSRT, perhaps even in the last 10 ms (Boucher et al. 2007), which for our approach (2012), other studies do suggest that the motor impact of stopping is independent between the two approaches (and therefore could not be coded as an independent variable in a combined ANOVA). Therefore, we had to make a decision as to which approach to select. We decided to select approach 1, because it approach 1 gave a tighter timing of the stopping process compared with approach 3, which was time-locked to the go process (GoRT - 100 ms), and it was the effect of the stopping process that was of interest in this study; 2) approach 1 produced 200 and 220 ms post hoc differences in stimulation time between trial types (P = 0.7; approach 3: P = 0.25, see above), meaning that comparisons between the trial types would be least affected by differences in stimulation times between trial types; and 3) post hoc, approach 3 produced average stimulation times at around GoRT - 120 ms instead of the intended GoRT - 100 ms (GoRT: 420 ms, compare with the stimulation times above). This was due to the stochastic nature of the RT forecast. Approach 1, on the other hand, (incidentally) turned out to produce values closer to the GoRT - 100 ms time point that was targeted by approach 3. Since global suppression as indexed by CSE of task-irrelevant effectors can be sensitive to very small timing differences, differences in stimulation times of 20 ms can have significant effects [Majid et al. (2012) showed significant differences for 200 and 220 ms after SSD but not for 240 ms]. As we did not have a hypothesis regarding stimulation at GoRT - 120 ms (as approach 3 turned out to produce), we focus on approach 1 in the presentation of results. Regardless of these considerations, however, it should be noted that both approach 1 (SS D + SSRT - 50 ms) and approach 3 (GoRT - 100 ms) produced qualitatively similar MEP results (as did approach 2). See results for further details.

**EMG Analysis**

MEPs were identified from EMG with in-house software developed in MATLAB (MathWorks). Trials were excluded if the root mean square power of the EMG trace 100 ms before the TMS pulse exceeded 0.01 mV (since such prestimulus noise can contaminate the MEP measurement), if the MEP amplitude on a given trial exceeded ±1 mV (which is beyond the resolution of the amplifier and leads to saturation), or if the MEP amplitude did not exceed 0.01 mV (trials in which no MEP was elicited, mostly because of coil misplacement or missing stimulation due to, e.g., coil overheating).

MEP amplitude was quantified with a peak-to-peak rationale, measuring the difference between maximum and minimum amplitude within a time period of 10–50 ms after the pulse. Both automated artifact rejection and MEP quantification were visually checked for accuracy on each individual trial for every data set by a rater who was blind to the respective trial type (go, successful stop, failed stop). MEP amplitudes were then averaged for each condition individually.

**RESULTS**

**Behavioral**

Misses on go trials were rare (probability = 0.02, SE: 0.007). Direction error probabilities were 0.05 (SE: 0.009) and 0.088 (SE: 0.014) for go and stop trials, respectively. The
average number of valid trials per participant was 385 (SE: 9.2) for correct go trials, 76 (3.6) for successful stop trials, and 78.5 (2.6) for failed stop trials. The overall probability of stopping was 0.47 (SE: 0.01; Table 1), meaning that the SSD-staircase procedure was effective at reaching a p(stop) of 0.5 \[a \text{ Wilcoxon signed-rank test revealed no significant group-level differences of p(stop) from 0.5}\]. To ensure that all individual participants met the requirement of p(stop) \text{H_1} \geq 0.5, we also tested the individual stopping success probabilities across the experimental blocks within each data set against a median of 0.5, using the same Wilcoxon test. One participant revealed significant deviations of stopping success rate from 0.5 \[\text{mean p(stop) for this participant: 0.443, } P < 0.03\]. To ensure that this participant’s data did not bias the results in any way, we ran all TMS analyses twice, once on the full sample and once on a limited sample that excluded that participant. TMS results did not differ between both samples in terms of significance but will be reported separately (see next section).

TMS

Full sample. On the basis of previous reports of global stopping (Badry et al. 2009; Cai et al. 2012; Majid et al. 2012), we hypothesized that hand MEP amplitudes would be reduced in the successful stopping trials compared with go and failed stop trials. Descriptively, 12 of the 14 participants showed a reduction of CSE on successful stop trials compared with go trials (Fig. 3A); 11 of 14 showed a reduction of CSE on successful compared with failed stop trials, and 8 of 14 showed the mean RTs instead of the median also yields significant differences: 420 (17) vs. 398 (10) ms, \( P = 0.03, 1\text{-sided}\]. Individual RT distributions can be seen in Fig. 2. As can be seen, data from two participants did not fulfill the requirements of the race model (marked with X in Fig. 2), as their median GoRT were numerically faster than their median failed stop RT. As with the above analysis, in order to ensure that these participants’ data did not bias the results in any way, we ran all TMS analyses twice, once on the full sample and once on a limited sample that excluded those two participants [one of which was the same participant whose p(stop) deviated from 0.5]. As above, TMS results between the samples did not differ but will be reported separately (see next section).

For the assumptions of the race model (and hence, SSRT estimates) to be valid, failed stop RTs need to be faster than correct GoRTs. This was the case in our sample on the group level \[\text{median GoRT} = 412 \text{ ms (SE: 14.4), median failed stop RT: 363 ms (SE: 11.4); } t(13) = 3.0, P = 0.01, d = 0.75; \text{testing}}

Table 1. Behavioral results

<table>
<thead>
<tr>
<th></th>
<th>Correct GoRT, ms</th>
<th>Incorrect GoRT, ms</th>
<th>Failed Stop RT, ms</th>
<th>p(stop), %</th>
<th>SSD, ms</th>
<th>SSRT, ms</th>
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<tr>
<td><strong>Full sample ((n = 14))</strong></td>
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<tr>
<td>Mean</td>
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<td>280</td>
<td>398</td>
<td>47</td>
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<td>236</td>
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<tr>
<td>SE</td>
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<td>17</td>
<td>10</td>
<td>1</td>
<td>25</td>
<td>12</td>
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<tr>
<td><strong>Reduced sample ((n = 12))</strong></td>
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<tr>
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<td>11</td>
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Results are displayed for the full sample as well as the reduced sample of \(n = 12\) participants whose data fulfilled all requirements of the race model. RT, reaction time; SSD, stop-signal delay; SSRT, stop-signal RT; p(stop), probability of successful stopping on stop trials.
a reduction of CSE on failed stop trials compared with go trials (Fig. 3B). On average, MEP amplitude was 0.51 mV (SE: 0.048) for correct go trials, 0.46 mV (SE: 0.046) for successful stop trials, and 0.50 mV (SE: 0.057) for failed stop trials (Fig. 4A). An ANOVA with the factor TRIALTYPE revealed significant differences between the three types of trials \[F(2,27) = 4.67, P = 0.019\]. Importantly, as predicted, MEP amplitude for successful stop trials was significantly reduced compared with go trials \[t(13) = 3.43, P = 0.0045, d = 0.26\] and failed stop trials \[t(13) = 2.5, P = 0.027, d = 0.21\]. Both effects remain significant after Bonferroni correction for multiple comparisons (the comparison between failed and successful stop trials survives this strict correction if it is tested in a 1-sided fashion; this is justified, as this was our exact hypothesis based on prior studies). This pattern very clearly replicates our two earlier studies.

Another way to quantify these results is to normalize the stop trial MEPs by the participants’ go trial MEP amplitudes, resulting in a measure that is equal to 1 in the case in which there are no differences between go trial amplitude and the respective stop trial amplitude. Reduced stop trial MEP amplitudes lead to numbers smaller than 1. Importantly, this measure accounts for differences in overall MEP amplitude and variability between subjects. t-Tests of these values against 1 confirmed the findings from the raw MEP analysis above: Successful stop trials showed ratios significantly smaller than 1 \[\text{mean} = 0.9, \text{SE}: 0.03; t(13) = 3.0, P = 0.01\], whereas failed stop trials showed no such effects \[\text{mean} = 0.97, \text{SE}: 0.04; t(13) = 0.81, P = 0.43; \text{Fig. 4B}\].

Notably, exploratory analyses revealed that the two critical findings of 1) reduced CSE of the hand on successful stopping compared with go trials and 2) absence of such an effect on failed trials compared with go trials could also been observed in both other stimulation time point conditions. This is true for both the raw trial analysis \[\text{approach 2: successful stop vs. go:} t(13) = 2.72, P = 0.017; \text{failed stop vs. go:} t(13) = 0.83, P = 0.42\] and \[\text{approach 3: successful stop vs. go:} t(13) = 1.97, P = 0.07; \text{failed stop vs. go:} t(13) = 0.79, P = 0.44\]. All \[P\] values \[2\text{-sided}\] as well as the normalized MEP analysis \[\text{approach 2: successful stop vs. go:} t(13) = 2.6, P = 0.022; \text{failed stop vs. go:} t(13) = 1.18, P = 0.26\] and \[\text{approach 3: successful stop vs. go:} t(13) = 2.47, P = 0.019\].

Fig. 3. A: scatterplot of go trial amplitudes plotted against successful stop trial amplitudes per subject. Length of the lines represents SE on each measure. Motor evoked potential (MEP) suppression on stop compared with go trials is indicated by values in the lower right half of the plot, below the diagonal line. B: scatterplot of go trial amplitudes plotted against failed stop trial amplitudes per subject.

Fig. 4. A: MEP results in the present study (raw mean amplitude). \[*P < 0.05, \text{**}P < 0.01\]. B: mean normalized MEP amplitudes for both types of stop trials (stop trial MEP amplitudes divided by go trial MEP amplitudes within each subject). \[\text{**}P = 0.01\]. The line at value 1 delineates go trial MEP amplitude. Error bars represent SE.
go: $t(13) = 2, P = 0.065$; failed stop vs. go: $t(13) = 0.87, P = 0.25$; all $P$ values 2-sided).

**Limited sample.** In the subset of 12 participants whose data fulfilled all requirements of the race model (see above), mean MEP amplitude was 0.50 mV (SE: 0.055) for correct go trials, 0.46 mV (SE: 0.054) for successful stop trials, and 0.50 mV (SE: 0.067) for failed stop trials. An ANOVA with the factor TRIALTYPE again revealed significant differences between the three types of trials $[F(2,22) = 3.62, P < 0.05]$. Again, MEP amplitude for successful stop trials was significantly reduced compared with both go trials $[t(11) = 3.11, P < 0.01, d = 0.24]$ and marginally reduced compared with failed stop trials $[t(11) = 2.13, P = 0.057, d = 0.2]$. As in the full sample, $t$-tests of the ratios between both types of stop trials and go trials against 1 confirmed the findings from the raw MEP analysis above: Successful stop trials showed ratios significantly smaller than 1 $[\text{mean} = 0.9, \text{SE}: 0.036; t(11) = 2.7, P = 0.02]$, whereas failed stop trials showed no such effects $[\text{mean} = 0.96, \text{SE}: 0.044; t(11) = 0.84, P = 0.42]$.

**DISCUSSION**

Stopping action has global consequences on the motor system: Stopping the hand reduces CSE in the leg (Badry et al. 2009; Greenhouse et al. 2012; Majid et al. 2012), and stopping speech reduces CSE of the hand (Cai et al. 2012). Here we establish that this effect extends beyond the skeletomotor system. We studied human participants performing an oculomotor stopping task in a head-restrained setup with a TMS coil placed over the hand area of left M1. Using a dynamic estimate of behavior, we delivered TMS stimulation at a point in time that was estimated to correspond to the process of stopping the eyes (i.e., SSRT — 50 ms). We measured CSE for the hand representation, which was task irrelevant, via the amplitude of the MEP recorded from electromyography. We show that when participants successfully stopped eye movements there was reduced CSE from the hand, relative to go trials and relative to failed stop trials, replicating the exact pattern of results of our earlier reports of global stopping using TMS and similar stop-signal designs (Cai et al. 2012; Majid et al. 2012).

This finding is of special importance for several reasons. First, while eye movements are initiated via a dramatically different pathway compared with the hand, leg, and vocal movements of earlier studies, which are all wired via M1, clearly there is some commonality in how eye and noneye movements are stopped (cf. Curtis and D’Esposito 2009). In particular, we suppose that the rapid stopping of eye movements is achieved by fast input from potentially specialized areas within the frontal cortex to the STN, and we suppose that neurons in that territory have a very broad (massive) effect on the motor pallidum (GPi), including on the hand area, and perhaps on all skeletomotor representations. The STN is implicated in stopping (Alegre et al. 2013; Aron and Poldrack 2006; Isoda and Hikosaka 2008; Künn et al. 2004; Mirabella et al. 2012; Ray et al. 2012; van den Wildenberg et al. 2006) and potentially exerts a broad influence on basal ganglia output (Hazrati and Parent 1992; see also Gillies and Willshaw 1998; Mink 1996; Nambu et al. 2002). The STN has been found to be active during successful manual stopping in both LFP and fMRI studies (e.g., Aron and Poldrack 2006; Künn et al. 2004; Ray et al. 2012), and at least one other study also implicates the STN in oculomotor countermanding, apparently via a hyperdirect input from the presupplementary motor area (Isoda and Hikosaka 2007, 2008). We hypothesize that successful rapid stopping via the broad STN-GPi projection temporarily disrupts broad thalamocortical drive, thereby nonselectively suppressing all motor activity.

Second, of high relevance to this study is the fact that motor stopping appears to also affect nonmotor representations. In a recent study, we demonstrated that rapid stopping disrupts ongoing working memory maintenance (Wessel et al. 2012). One explanation for this is that the STN has a very broad effect (Hazrati and Parent 1992), even on nonmotor parts of pallidum; another explanation is that activation of one part of STN spreads to other parts of STN, thus affecting on-motor basal ganglia circuitry (Haber 2003; Temel et al. 2005). Taking together our present result (rapidly stopping eye movements has a global motor effect) with the finding that rapid stopping affects working memory (Wessel et al. 2012) raises an intriguing possibility, namely, that the basis for one kind of distractibility (loss of working memory contents) is a globally induced effect of a canceled (eye) movement. Future research will need to fully explore this possibility, and especially to establish the boundary conditions of which kinds of abrupt-onset distractors (Yantis 1993) and which kinds of saccade cancelation (e.g., stop signal, antisaccade, and other kinds of countermanding tasks; Hasegawa et al. 2004) could generate the effect.

One mentionable difference between our present study and numerous previous reports of saccade countermanding in humans is the comparatively slow SSRT (236 ms) in the present study. Most studies using the saccade-coutermanding task (Hanes et al. 1998) report much faster SSRTs (e.g., Cabel et al. 2000; Cornel and Elyse 2005; Curtis et al. 2005; Hanes and Carpenter 1999). However, a decisive difference between those tasks and our present study is that in those studies prosaccades toward extrafoveally presented target stimuli had to be inhibited when a stop signal occurred. In contrast, here we presented go stimuli that were centrally presented arrows pointing either to the left- or right-hand side of the screen, meaning that an additional perceptual decision process had to be made before emitting a response (as opposed to the unambiguous stimuli in the saccade-coutermanding paradigm), which significantly prolongs GoRT (and, very possibly, SSRT estimates). Indeed, a study contrasting both versions of the oculomotor stop-signal task (Logan and Irwin 2000) did report both prolonged GoRT and SSRT measurements for the version of the task that we used compared with the prosaccade countermanding version. The SSRT estimate for the type of task similar to ours was 195 ms, which was closer to our estimate.

An alternative interpretation of CSE reduction on stop trials is that it relates to a brain arousal signal [e.g., a fast dopamine signal (Redgrave et al. 1999), which would have effects on M1 (Awenowicz and Porter 2002; Huda et al. 2001)] rather than being the sign of motor suppression per se. As we argued previously (Cai et al. 2012), this interpretation is highly unlikely to explain our results, since one would also predict brain arousal on failed stop trials just as there is on successful stop trials. Yet in all three studies the MEP for failed stop trials was not different from go trials, and in both Cai et al. (2012) and Majid et al. (2012) the MEP on go trials was no different from the MEP in the intertrial interval. Moreover, evidence from error processing studies would predict even higher arousal for
failed stop trials compared with successful stop trials (O’Connell et al. 2007; Wessel et al. 2011), yet again all studies unanimously report motor suppression specifically for successful stop trials, whereas failed stopping did not show an effect on CSE. This speaks against a mere arousal explanation.

To our knowledge, obtaining MEPs of task-unrelated effectors is the most effective noninvasive method to quantify global stopping in healthy volunteers. However, other approaches are possible. For example, successfully stopping actions leads to decreases in heart rate (Jennings et al. 1992), i.e., to “cardio-muscular suppression,” which could be a marker of the global nature of motor stopping, even in a non-voluntarily controlled muscle. However, heart rate activity is influenced by a multitude of factors, many of which are not (directly) related to motor processing, e.g., increased effort (Lehle et al. 2009) or infrequent stimuli (Rockstroh et al. 1987). Accordingly, if successfully stopping an impending action is an effortful process or an orienting-like situation, changes in heart rate could merely be a by-product of these processes rather than a direct manifestation of a global motor stopping process affecting the heart muscle. Also, it is of note that failed prosaccade inhibitions in antisaccade experiments have also been shown to induce heart rate deceleration (Wessel et al. 2011), whereas such effects have yet to be reported for CSE on failed stop trials. While slowing of heart rate as a potential indicator of the global nature of motor stopping processes is thus an interesting avenue for future study, TMS-measured CSE is a cleaner operationalization, which shows specific effects for successful motor stops and is directly related to motor activity.

In conclusion, we show that eye movements, despite not being part of the skeleto-motor system, are stopped in a global manner, reducing the excitability of an unrelated effector when stopping is fast and reactive. This finding sheds light on the mechanism underlying global stopping (showing that it is not constrained to the stopping of the skeleto-motor system or of movements that are controlled via M1). It also has potentially important implications for better understanding the relation between stopping of eye movements and the distractibility that is putatively generated by global effects on nonmotor representations.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS


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