

Supporting Information

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SI Results

Behavior. Overall accuracy for both the original and controlled versions of the SST was very close to 50% for all runs. As is normal in experiments employing the stop signal task, there was a spread of performance across individuals. For the controlled SST, all subjects had accuracies for the first and second runs of between 44% and 56%, except for one subject who, in the first run, scored 42%, and another subject who, in the second run, scored 61%. The same distribution of accuracies was observed for the original version of the task, with the exception of one subject who scored 42% on one run. No subjects had SSD staircases that continued to increase or decrease over the whole duration of the run.

Neuroimaging Results. The pre-SMA also supports inhibitory processes that lead to response slowing as well as stopping. For the low slowing groups, RT difference was 14 ± 13 ms on the first controlled SST run and 8 ± 17 ms on the second run, and the respective values were 65 ± 28 ms and 60 ± 25 ms for the group with high slowing. RT for continue trials in the low-slowing group for the second run of the SST was not significantly different from go trials, whereas, for the other three groups, responses on the continue trials were slower (i.e., run 2 high slowing and both high and low slowing from run 1).

There was no evidence of a major strategic change in the way that individuals were performing the task when continue trials showed either high or low slowing. For both runs of the controlled SST there were no group differences in the number of negative feedback trials, the accuracy of stop trials, the median go RT, the SD of the go RT, the accuracy of go trials, the accuracy of continue trials, or the SSRT.

SI Materials and Methods

Background. The Stop signal paradigm is based on the horse-race model of response inhibition (1). This model proposes that response inhibition is a race between an excitatory and an inhibitory process. The speed of the excitatory process corresponds to the reaction time following the go signal. If the excitatory process is faster than the inhibitory, the response is executed. If the inhibitory process (i.e., the process responding to the stop signal) surpasses the excitatory, the response is interrupted and successfully inhibited. Consequently, the inhibition of a response depends on the relative finishing times of the two processes responding to the stop signal and the primary go signal.

The speed of the inhibitory process (i.e., SSRT) is most often used as a behavioral measure of stop signal response inhibition (1, 2). SSRT is thought to represent the latency between the occurrence of the stop signal and the beginning of the stop process. Because successful response inhibition does not result in an observable response, it must be estimated (1). A slow SSRT decreases the probability that the response is successfully inhibited, which is often found in conditions such as attention deficit/hyperactivity disorder (2).

The horse-race model of SST task performance assumes that RT for the go stimulus is uninfluenced by the presentation of a stop signal in previous trials or by anticipation of it in future trials (2). Nevertheless, presentation of stop stimuli can affect processing of go stimuli, which is a violation of the assumption (3). In addition, presenting the stop signal less frequently leads to a higher probability of commission errors and to faster responses to go stimuli (4). Moreover, SSRT is found to correlate with the mean RT of go trials (5). These findings imply that the use of different strategies may influence the SSRT, challenging the independence assumption of the horse-race model.

SST Design. The interstimulus intervals for trials were fixed (1.75 s) and the trials were randomly ordered, with a fixed proportion of each trial type in each run. Stimulus presentation and scan acquisition was offset with an interstimulus interval of 1.75 s and a TR (repetition time) of 2 s.

Staircase Adaptation Procedure. To reflect individual differences in information processing speed, mean RT for the simple CRT task performed before the SST was used to define the starting point for the SSD adaptation algorithm. In the first run of the SST, the SSD started at the mean go RT of the CRT minus 200 ms. Subsequently, the SSD was adaptively varied every two stop trials. If cumulative accuracy was greater than 50%, the SSD was increased by 50 ms, if less than 50%, the SSD was decreased by 50 ms. A lower limit for SSD was set to 50 ms. With this staircase procedure, a “critical” SSD can be computed for each subject per run, by averaging all trials in which the probability to respond is equal to the probability to inhibit. This critical SSD represents the time delay required for the subject to succeed in withholding a response in the Stop trials for half of the time. SSRT was then calculated by subtracting the critical SSD from the median go trial RT for each run.

Feedback for Slowing on the Task. To attempt to counteract strategic changes in task performance, we introduced a further modification of the SST to limit slowing of RTs that may occur during task performance. We limited the ability of individuals to slow down on go trials. This was achieved by providing feedback in both the original and the controlled versions of the task when subjects slowed their response times and passed a threshold for the speed of their go response. Negative feedback in the form of the words “Speed up!” was presented on the screen in place of the subsequent trial each time a response was made with a reaction time above the 95th percentile of the subject’s current reaction time distribution. The starting point for the RT distribution used to determine the 95% cutoff for feedback was taken from the choice RT task that immediately preceded the first run of the SST. This allowed individual variability in information processing speed to be factored into the starting point for the tracking algorithm. Subsequently, the RT distribution was recalculated on each go trial to update the distribution as the subjects performed the SST.

Training. All subjects received the same amount of training on the task. Subjects performed an initial choice reaction time task and then carried out a run of the original SST of the same duration as in the scanner, i.e., 184 trials (70% go, 20% stop, 10% fixation). To familiarize themselves with the addition of the continue cue, subjects then performed a shorter version of the controlled SST performed in the scanner with 92 trials (50% go, 20% stop, 20% continue, 10% fixation).

MRI Scanning. MRI data were obtained using a Philips Intera 3.0-T MRI scanner using Nova Dual gradients, a phased-array head coil, and sensitivity encoding with an undersampling factor of 2. Functional MRI images were obtained using a T2*-weighted gradient-echo echoplanar imaging sequence with whole-brain coverage (repetition time/echo time, 2,000/30 ms; 31 ascending slices with thickness 3.25 mm, gap 0.75 mm, voxel size $2.5 \times 2.5 \times 5$ mm, flip angle 90° , field of view $280 \times 220 \times 123$ mm, matrix 112×87). Quadratic shim gradients were used to correct for magnetic field inhomogeneities within the brain. T1-weighted whole-brain structural images were also obtained in all subjects.

Paradigms were programmed using Matlab Psychophysics toolbox (Psychtoolbox-3) and stimuli presented through an IFIS-SA system (In Vivo). Responses were recorded through a fiberoptic response box (Nordicneurolab), interfaced with the stimulus presentation PC running Matlab.

Functional MRI Analysis. The first four volumes acquired were discarded to allow for T1 equilibrium effects. Functional MRI data were analyzed using voxel-wise time series analysis within the framework of the general linear model. A design matrix was generated with a synthetic hemodynamic response function and its first temporal derivative. Several types of events were distinguished: go correct (Go), stop correct (StC), stop incorrect (StI), and continue correct (Co). There were, in general, no or very few incorrect responses to go or continue trials (Table 1 in the main text). Feedback trials were included as a separate regressor in the model. To account for variation in the SSD across

runs, we modeled events by using the timing of the SSD as the regressor for each trial. The following individual and run specific contrast images were generated: Co versus Go; StC versus Go; StC versus Co; StC versus StI; StI versus Go; and StI versus Co.

ROI Analysis. To investigate further the effects of attention and response inhibition within the pre-SMA and IFG, an ROI analysis was performed using Featquery within FSL. The pre-SMA ROI we used was based on the coordinates of the peak of activation from the stopping contrast StC versus Co ($x = 20$, $y = 6$, and $z = 62$). We also investigated the pattern of activation in the right IFG. As the contrast of StC versus Co did not activate this region, we used the coordinates of the peak of activation from the contrast of StC versus Go ($x = 44$, $y = 18$, and $z = 16$). ROIs with 10 mm diameter around the peak coordinate were used. The mean percentage signal change associated with each contrast of interest was calculated for all voxels within an ROI.

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Table S1. Local maxima for the contrast of stop correct against go

Region	Z-value	MNI coordinates		
		x	y	z
Right superior frontal gyrus (medial pre-SMA)	4.71	12	12	58
Right superior frontal gyrus (lateral pre-SMA)	4.31	28	8	60
Right middle frontal gyrus	4.39	30	0	44
rIFG	4.18	44	18	16
Right anterior Insular cortex	5.08	36	22	–4
Left intraparietal sulcus	5.17	–32	–46	40
Right supramarginal gyrus	5.45	68	–42	22
Left lateral occipital cortex (superior)	5.6	–26	–82	18
Right lateral occipital cortex (superior)	5.09	30	–72	34
Right lateral occipital cortex (inferior)	4.98	46	–68	4

Local maxima of brain activations for individual clusters from the controlled version of the SST for the contrast of correct stop trials (StC) versus correct go trials (GoC), with associated Z-values. Activation within a cluster may extend into other cortical and subcortical areas. MNI, Montreal Neurological Institute.

Table S2. Local maxima for the contrast continue correct against go

Region	Z-value	MNI coordinates		
		x	y	z
rIFG/middle frontal gyrus	5.22	48	34	20
rIFG (pars opercularis)	4.95	56	20	28
Right frontal pole	5.20	46	38	10
rIFG (posterior)	5.10	46	10	28
Right middle frontal gyrus	4.7	54	22	32
Left IFG/middle frontal gyrus	5.12	-42	10	28
Left IFG (pars triangularis)	4.30	-46	24	20
Left frontal pole	3.60	-42	36	10
Left middle frontal gyrus (posterior)	2.34	-42	2	50
Left IFG (posterior)	4.95	-46	8	30
Right lateral occipital cortex (inferior)	6.16	42	-78	6
Right lateral occipital cortex (superior)	5.74	30	-60	48
Left lateral occipital cortex (inferior)	5.64	-44	78	4
Left lateral occipital cortex (superior)	6.13	-32	-86	18

Local maxima of brain activations for individual clusters of activation from the controlled version of the SST for the contrast of correct continue trials (CoC) versus correct go trials (GoC), with associated Z-values. Activation within a cluster may extend into other cortical and subcortical areas. MNI, Montreal Neurological Institute.

Table S3. Local maxima for the contrast stop correct against continue

Region	Z-value	MNI coordinates		
		x	y	z
Right superior frontal gyrus (medial pre-SMA)	3.22	12	12	58
Right superior frontal gyrus (lateral pre-SMA)	3	20	6	62
Right superior frontal gyrus (lateral SMA)	3.07	18	-4	58
Left paracingulate cortex	3.04	-6	8	46
Right ACC	3.43	6	14	38
Right middle frontal gyrus/superior frontal gyrus	3.13	30	2	48

Local maxima of brain activations for individual clusters of activation from the controlled version of the SST for the contrast of correct stop trials (StC) versus correct continue trials (CoC), with associated Z-values. MNI, Montreal Neurological Institute.

Table S4. Local maxima for the contrast stop incorrect against continue

Region	Z-value	MNI coordinates		
		x	y	z
ACC	4.3	2	24	24
Left rostral ACC	3.47	-12	26	24
Left paracingulate gyrus/ACC	3.06	-6	14	44
Right superior frontal gyrus (medial pre-SMA)	3.81	10	20	52
Paracingulate cortex/pre-SMA (medial)	3.4	2	16	50

Local maxima of brain activations for individual clusters of activation from the controlled version of the SST for the contrast of incorrect stop trials (StI) versus correct continue trials (CoC), with associated Z-values. Abbreviations as in Table S1. MNI, Montreal Neurological Institute.