Original Research

Stimulation of the Pre-SMA Influences Cerebral Blood Flow in Frontal Areas Involved with Inhibitory Control of Action

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Selection of the most appropriate response necessitates inhibition of competing or prepotent responses. It is important to characterize which cortical areas are relevant to achieve response inhibition. Using the stop signal task, previous imaging studies revealed consistent activation in the right pre-supplementary motor area (pre-SMA). However, imaging alone suffers from the limitation that it can only provide neuronal correlates and cannot establish causality between brain activation and behavior. Repetitive transcranial magnetic stimulation (rTMS) can be used to temporarily interfere with the function of a cortical area considered to play a specific role in the behavior. Thus, we combined rTMS with H215O positron emission tomography (PET) scans during the stop signal task, to test whether rTMS-induced changes in excitability of the right pre-SMA influenced response inhibition. We found that rTMS over the pre-SMA increased the efficiency of the inhibitory control over prepotent ongoing responses. A significant interaction was present in the left inferior frontal gyrus (IFG) along with an increase in regional cerebral blood flow (rCBF) in the left pre-SMA, left IFG, right premotor and right inferior parietal cortex. These areas best fitted the path analysis model in the effective connectivity model. The results of this study suggest that stimulation of the right pre-SMA, by interfering with its activity, may have a significant impact on response inhibition.

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Introduction

Reactive inhibition, i.e., stopping an ongoing movement upon presentation of an external and sudden stimulus, relies on a rapidly acting circuit based on interactions between cortical and subcortical regions. The stop signal paradigm [1], which measures how accurately and rapidly a participant can inhibit an ongoing movement, shows altered performance in patients with focal lesions over the inferior frontal gyrus (IFG) [2] and the pre-supplementary motor area (pre-SMA) [3]. Functional magnetic resonance imaging (fMRI) studies depict these two areas as key players in response inhibition within a ‘stopping’ network that also involves the primary motor cortex (M1), inferior parietal cortex, subthalamic nucleus (STN), and striatum [4–10]. During successful and unsuccessful inhibition, the inhibitory network within the right hemisphere becomes active with the engagement of the pre-SMA and IFG [4] contributing to the magnitude of response inhibition. However, the extent of contribution of each area to inhibition in the stop signal is unknown. One study showed that participants with more efficient response inhibition had greater pre-SMA activation [11], suggesting that perhaps the pre-SMA is critically needed during successful inhibition. Another study, while emphasizing the importance of the pre-SMA and M1 connectivity (closely functionally related) in inhibiting a movement, also suggested that the IFG plays an important role in orienting participant’s attention to adequately inhibit their response [10]. This was also supported by other experiments that showed the role played by the IFG in attention during inhibition and cue detection [12–14]. A recent meta-analysis performed on 21 studies investigating movement inhibition pointed to the functional relevance of the pre-SMA as a controlling area for adaptive behavior [15]. Thus, in the...
current study, we aim to test our hypothesis that the right pre-SMA is important for action inhibition by combining H\textsubscript{2}\textsuperscript{15}O positron emission tomography (PET) with continuous theta burst stimulation (cTBS).

Although neuroimaging studies can provide valuable information about the involvement of specific brain areas in response inhibition, it suffers from the limitation that it cannot determine a causal relation between observed brain activity and behavioral performance [16]. Thus, the specific functional relevance (active role vs. simple epiphenomenon) of those structures during response inhibition remains to be established.

Repetitive transcranial magnetic stimulation (rTMS) attempts to address this issue by temporarily modulating those cortical areas that are considered to play a specific role in the behavior [17]. rTMS is a non-invasive stimulation technique that exerts a temporary and reversible effect in the underlying cortex and distally interconnected brain areas [18,19]. Previous reports suggest that rTMS applied over the IFG or pre-SMA enhances or impairs response inhibition in healthy participants [20–24].

We set up three different experimental analyses. First, the behavioral effect of rTMS during the stop signal task was assessed, predicting that cTBS over the right pre-SMA would influence the efficiency of inhibitory control. Second, we combined cTBS with H\textsubscript{2}\textsuperscript{15}O PET during performance of the stop signal task, predicting that cTBS would affect regional cerebral blood flow (rCBF) in the neural network underlying response inhibition. Finally, we used a connectivity model approach to identify the critical neural interactions modulated by rTMS delivery relative to a sham condition.

Materials and methods

Participants

In the first experiment (i.e., TMS and behavior), we studied 16 right-handed healthy participants (8 men, mean age 26.5 ± 4.1; Edinburgh handedness inventory score 91%). Participants underwent TMS and stop signal task on two separate days. On one day, they performed the task with the right hand and the other day with the left hand. The latter was performed to rule out a potential TBS effect on the contralateral pre-SMA. Participants were excluded on the basis of history of psychiatric and/or neurological disorder, drug or alcohol abuse, pregnancy and migraine. Individual T1-weighted high-resolution MRI images were obtained to screen for structural lesions and TMS target localization. In the second experiment, 8 out of those 16 participants entered into an imaging session where rTMS was combined with PET (Fig. 1). This study was performed at least one week apart from the first behavioral experiment and completed during the same time of the day. The study protocol was approved by the Ethics Committee of the Center for Addiction and Mental Health Research, University of Toronto. Written informed consent was obtained from each participant before taking part in the study.

TMS procedure

A Magstim Rapid\textsuperscript{2} Magnetic Stimulator (Magstim, UK; biphasic) was employed to apply TMS using a figure-of-eight coil (70 mm diameter). Stimulus intensities, expressed as a percentage of the maximum stimulator output, were set at 80% of the active motor threshold (AMT). AMT was defined as the lowest stimulus intensity able to elicit 5 motor evoked potentials (MEPs) of at least 50 \mu V of the contralateral first dorsal interosseous (FDI) muscle, averaged over 10 consecutive stimuli delivered over the right hand motor cortex (M1) at intervals longer than 5 s. During the determination of the AMT, participants were instructed to maintain a steady muscle contraction of 20% of maximum voluntary contraction. Right M1 was marked on the subjects’ scalps to later apply sham TBS.

We used a protocol with three blocks (20 s each) of cTBS (see Fig. 1B); [25–27]. Blocks were separated by 1-min intervals. Each 20 s block consisted of 3 pulses at a rate of 50 Hz repeated every 200 ms (Fig. 1B); [28]. Overall, 300 trains with a total of 900 pulses were applied in each stimulation session. This off-line cTBS protocol produces a long-lasting (up to 60 min) influence limited to the underlying cortex [29,30] and is ideal for our TMS/PET experimental design. The right pre-SMA stimulation was applied with the coil handle placed tangentially to the midline and oriented in a lateral direction inducing the electrical current along the lateral-to-medial axis. The sham condition was delivered over the right hand M1 with the coil tilted 90° ensuring no active stimulation while using the same protocol of cTBS. cTBS was applied following safety guidelines [31,32].

In order to target the right pre-SMA, we used a procedure that takes advantage of the standardized stereotaxic space of Talairach and Tournoux [33] and frameless stereotaxy [34]. A high-resolution MRI (GE Sigma 1.5 T, T1-weighted images, FSPGR with repetition time = 11.9 ms, echo time = 5 ms, flip angle = 40 mm, slice thickness = 1 mm, NEX = 1, matrix size = 256 × 192) of every

Figure 1. Experimental procedure combining cTBS with H\textsubscript{2}\textsuperscript{15}O PET. (A) Timeline of the TMS and H\textsubscript{2}\textsuperscript{15}O PET session. (B) Three cTBS blocks (20 s each) with one-minute break were applied prior the task.
participants' brain was acquired and transformed into standardized stereotaxic space using the algorithm of Collins et al. [35]. The coordinates selected for the right pre-SMA \( (x = 6, y = 20, z = 50) \) were similar to those reported in a previous study [6]. The Talairach coordinates were converted into each participant's native MRI space using the reverse native-to-Talairach transformation. The positioning of the TMS coil over these locations, marked on the native MRI, was performed with the aid of a frameless stereotaxic system (Rogue Research, Montreal, Canada).

### Stop signal task

The stop signal task [1] measures how accurately and rapidly a participant can inhibit an ongoing movement. During the 1st experiment, the task was presented on a computer screen and during the 2nd experiment, inside the PET camera, through video eyewear (DV920; Icuiti Corporation, New York, USA) placed on top of the plastic thermal mask.

The stop signal task consists of a combination of Go and Stop trials (Fig. 2A). On Go trials, a go signal is presented (left or right pointing arrow) and participants are asked to respond as accurately and as fast as possible using their index and middle fingers. On Stop trials, participants were instructed to stop their response when a stop signal (cross) appeared. The stop signal was presented after a go signal with variable stop signal delay (SSD). A total of three blocks of 32 Stop and 96 Go trials each were performed (total of 384 trials).

A typical trial started with a white circular fixation point appearing in the center of the black background of the screen. The fixation point was replaced after 500 ms by a white arrow in the center of the screen, which remained for a maximum of 2 s (Fig. 2). If a participant responded during those 2 s, the arrow disappeared, leaving a black screen until the beginning of the subsequent trial.

For the stop trials, the arrows were replaced with a cross, after a variable SSD. When a participant correctly inhibited a response, the cross stayed on the screen. However, if a participant could not inhibit and responded, the cross disappeared leaving a black screen, ready for the subsequent trial. The SSD value was taken from four staircases that changed throughout the task, based on the participant's response. After a successfully inhibited stop trial, the next stop trial was made more difficult by increasing the SSD by 50 ms. However, if the response was not inhibited, the next stop trial was made easier by decreasing the SSD by 50 ms. The staircase procedure ensured convergence of 50% inhibition across the task. The four SSD staircases started at 100, 150, 200, and 250 ms. The stop signal reaction time (SSRT) was calculated using the tracking procedure by subtracting the average SSD from go RTs. The tracking procedure assumes that a participant inhibits 50% of stop trials across the task and uses the average SSD of the inhibited trials. The faster the SSRT, the better the response inhibition skills from the participant.

A go task was designed as a control condition to contrast with the stop signal task during the scanning sessions (Fig. 2B). This was performed three times for each cTBS condition. The go task consisted of the presentation of right and left pointing arrows that asked participants to respond with their right hand index or middle fingers respectively as fast as possible. A total of 384 Go trials were performed. The go and stop tasks were counterbalanced and intermixed, starting with the stop task followed by the go task.

The instructions given to participants in the stop signal task were to respond to the arrows as fast and as accurately as possible but to also try to inhibit their response when a cross was presented. Twenty practice trials were completed before each experimental session in order to familiarize the participant with the task and to remove practice effects.

For the statistical analysis, we performed a repeated measures ANOVA between conditions. Post-hoc analysis using paired t-tests within subjects' performance was done to compare active vs. sham TBS conditions.

### PET scanning procedure

High-resolution PET/CT scans were obtained with a Siemens-Biograph HiRez XVI (Siemens Molecular Imaging, Knoxville, TN, USA) functioning in 3-dimensional mode with an inplane resolution of around 4.6 mm full width at half-maximum, using oxygen 15-labeled water (H215O) as a radioactive tracer to measure changes in rCBF. After completion of the cTBS (Fig. 1B), 10 mCi H215O was injected into the antecubital vein over 50 s and scanning was performed for 90 s starting 10 s after the injection. The interval between successive H215O administrations was 11 min to allow for adequate decay of radioactivity to background levels. Before the first emission scan, a scout view was obtained to determine accurate positioning of the participant, and a low dose (0.2 mSv) CT scan was acquired for attenuation purpose. Images were reconstructed with a two-dimensional filtered back-projection, resulting in 81 slices with a 256 × 256 pixel-matrix (pixel size, 2 mm).

To minimize head movements during the scanning sessions, participants were restrained using a thermoformed custom head mask and positioned in the scanner using identical laser markers.

The stop signal task was started 2 min prior to each emission scan. In total, twelve emission scans were obtained for each subject. Participants completed four different conditions (cTBS-Stop and go, cTBS-Go alone, sham cTBS-Stop and go, sham cTBS-Go alone) with three acquisition scans per condition (Fig. 1A).

### PET analysis

Image processing and statistical analysis were performed in MATLAB version 7.4 (Mathworks Inc., Natick, MA) using statistical parametric mapping (SPM2; Wellcome Department of Imaging Neuroscience; London, UK) [36].

PET images were (i) realigned to the mean image to correct for inter-scan head movements, (ii) normalized to the standard MNI space template, (iii) the resulting normalized parameter set was used to spatially normalize the individual images and (iv) a final smoothing using an isotropic, Gaussian kernel of 6 mm reduced individual anatomical variability.

To identify rCBF changes associated with the effects of cTBS on stop and go tasks, a multi-subjects \( × \) TBS conditions and covariates model was employed. The following SPM analyses were performed:

1. Main effect of TBS. The contrast between [stop task + go task cTBS] – [stop task + go task sham cTBS] measured the increase in rCBF due to cTBS. The reversed contrast [stop task + go task sham cTBS] – [stop task + go task cTBS] measured the rCBF decrease.
2. Main effect of Task. The contrast between [stop task cTBS + stop task-sham cTBS] – [go task cTBS + go task sham cTBS] measured
the increase in rCBF during the stop task compared to the go task. The reversed contrast [go task cTBS + go task sham cTBS]–[stop task cTBS + stop task sham cTBS] measured the rCBF decrease during the stop task compared to the go task.

3. Interaction analyses. The contrast [stop task cTBS–go task cTBS]–[stop task sham cTBS–go task sham cTBS] measured changes in rCBF during the stop task compared to the go task after cTBS was applied. The reversed contrast [stop task sham cTBS–go task sham cTBS]–[stop task task cTBS–go task task cTBS] measured the rCBF changes during the stop task compared to the go task after sham cTBS was applied.

In all imaging analyses, statistical maps were thresholded at a level of $P < 0.001$ uncorrected with an extent threshold of 20 contiguous voxels. Regions were considered significant at the threshold of $P < 0.05$ corrected at the cluster level using the false discovery rate (FDR).

A restricted volume analysis was used to test specific a priori hypotheses [37,38]. This volume analysis considered voxels within a mask image created anatomically using WFU-PickAtlas tool (http://www.fmri.wfubmc.edu) [39] and based on the automated anatomical labeling (AAL) atlas [40]. Following previous response inhibition evidence [4,6], the areas included were: (i) mPFC (BA6, BA32), (ii) pre-SMA (BA6), (iii) the inferior frontal cortex (BA44), (iv) the motor cortex (BA4), (v) the inferior parietal regions (BA40), and (vi) the basal ganglia, including the STN region, from the AAL template. Clusters in a priori regions were considered significant at threshold of $P < 0.001$, uncorrected for multiple comparisons.

Path analysis (effective connectivity)

Structural Equation Modeling (SEM) was used for the path analysis [41,42]. We tested the goodness-of-fit to assess the stability of the constructed model to identify which of the potential models fit the data best [41]. This was selected according to the goodness-of-fit and the Akaike information criterion, with values of 0.90 or greater indicating a good model fit [43]. The model included mainly areas that were active in the PET contrasts but also regions of interest described in the literature (i.e., right IFG). The regions included in this model are part of a behavioral network defined by anatomical and functional connectivity data [4]. We included error terms that could account for extraneous sources of variance [44] set to 0.50 for all brain regions. Since these paths represented the influence of one region on another region, negative paths were interpreted to represent ensemble inhibition and positive paths net excitation of metabolic brain activity [45]. Once the model was validated, we evaluated the differences in the path model between the two cTBS conditions using a ‘stacked-model method’ [42]. In the null model, the path coefficients were equal across conditions, whereas in the alternative model, path coefficients were allowed to vary between conditions. An omnibus test (null vs. alternative) was performed and statistical significance was determined by differences in the goodness-of-fit ($X^2_{diff}$) at a given degree of freedom. The model construction and path analysis were done with AMOS 20.0 (Small-Walters Co.).

**Results**

**Experiment I – behavioral results**

The right hand performance of the stop signal task achieved an approximate 50% probability of inhibition (pre-SMA 51%, sham 53%; $P = 0.66$). Similar values for probability of inhibition were observed for the left hand performance in both cTBS conditions (pre-SMA 48%, sham 48%; $P = 0.72$).

![Table 1](image)

| Reaction times for the stop signal task for right hand performance. |
|--------------------------|--------------------------|--------------------------|
|                          | cTBS pre-SMA            | cTBS sham M1            | $P$ value |
| Go RTs                   | 378.50 (21.5)           | 397.27 (27.9)           | 0.60      |
| SSD                      | 192.76 (15.3)           | 167.90 (18.0)           | 0.16      |
| SSRT                     | 185.74 (62.1)           | 229.37 (9.9)            | 0.001     |
| Errors                   | 1.46 (0.7)              | 3.08 (2.4)              | 0.78*     |

Values show means and standard errors (in brackets).

**Experiment II – TMS and H215O PET**

The behavioral cTBS effects during the stop signal task in the PET scanner replicated the observations associated with the right hand performance described in Experiment I (SSRT, $P = 0.02$; Go RT, $P = 0.50$) with probabilities of inhibition of 50% (pre-SMA 50%, sham 50%; $P = 0.67$) and significant speeding of SSRTs but no effect on Go RTs (Table 3). To ensure that there was no practice effect for the task performance, subjects performed the stop signal task twice prior to the scan session. Paired t-tests revealed no significant difference in performance in SSRT ($P = 0.19$) nor go RTs ($P = 0.20$). Similarly, go task performance during scanning was not different among sessions suggesting a lack of practice effect.

The imaging analysis showed a significant Task × Stimulation interaction in the left IFG encompassing the medial frontal gyrus (MFG) (BA44–46) (Table 4) (Fig. 3). The main effect of Task revealed a significant rCBF increase in the right premotor cortex (PMC) (BA6). The main effect of stimulation demonstrated a significant rCBF increase on the right frontopolar gyrus (BA10), right subgenual ACC (BA25), right OFC (BA11) and right cerebellum.

![Table 2](image)

| Reaction times for the stop signal task for left hand performance. |
|--------------------------|--------------------------|--------------------------|
|                          | cTBS pre-SMA            | cTBS sham M1            | $P$ value |
| Go RTs                   | 381.12 (13.8)           | 380.59 (14.2)           | 0.97      |
| SSD                      | 155.41 (17.5)           | 160.95 (18.6)           | 0.40      |
| SSRT                     | 225.70 (7.7)            | 219.63 (7.9)            | 0.58      |
| Errors                   | 0.30 (0.1)              | 0.92 (0.4)              | 0.09*     |

Values show means and standard errors (in brackets).

cTBS = continuous theta burst stimulation; RTs = reaction times; SSD = stop signal delay; SSRT = stop signal reaction time; R = right; L = left; pre-SMA = pre-supplementary motor area; M1 = primary motor cortex.

* Wilcoxon test used.
In the post-hoc analysis, voxel-based analysis showed that during sham cTBS, the Stop-Go contrast showed an increase in rCBF over the left IFG (BA46, x = −46, y = 34, z = 12, z-score = 3.87, \( P = 0.004 \) corrected). Interestingly, active stimulation of the right pre-SMA modified the pattern of activation (Fig. 3) with rCBF increase in the left pre-SMA (BA6), left IFG (BA44), right premotor cortex (PMC; BA6) and the right inferior parietal cortex (BA40). No significant rCBF decrease was found during either stimulation paradigms.

Effective connectivity analysis

The areas that best fitted the path analysis model were the right and left IFG, right and left pre-SMA and the right premotor cortex (Fig. 4A). These areas taken from the stop vs. go contrast after sham and active TBS over pre-SMA and from the literature (i.e., right IFG) were used as seeds for voxel-wise covariance analysis. Fig. 4B and C shows the significant interaction among the areas in the model for both TBS conditions. The functional network represented in Fig. 4A was valid to provide sufficient explanation of the data (\( \chi^2(4) = 1.715, P = 0.788 \)) with good model of fit parameters: goodness-of-fit index = 0.91, Akaike information criterion = 54.072. Comparing the models in a between-group analysis (Fig. 4B and C), a significant difference was obtained (\( \chi^2(17) = 28.475, P = 0.04 \)). We further evaluated the differences amongst cTBS conditions relative to the defined model using a ‘stacked-model method’ and found a statistical difference in the pattern of path weight and intensities when comparing sham and cTBS conditions. Fig. 4D shows the path weights with the significant differences between sham and cTBS models. The connectivity results support the cTBS-induced effect over the right pre-SMA with strength of the path weight to the left pre-SMA being reduced in the TBS model. In addition, while certain pathways linking left and right IFG to right pre-SMA were weakened following cTBS, others bypassing the right pre-SMA were strengthened, possibly suggesting a dynamic compensatory response to the TBS-induced disruptive effect.

Discussion

In the current study, cTBS over the right pre-SMA (as compared to sham cTBS) increased the efficiency (i.e., faster SSRTs) of the inhibitory control over prepotent ongoing responses which were paralleled by an increase in rCBF in the left pre-SMA, left IFG, right premotor and right inferior parietal cortex. The SEM connectivity analysis confirmed this cTBS effect over the right pre-SMA by expressing a different pattern of path-weight among those cortical regions when comparing sham with cTBS conditions.

Subthreshold cTBS over frontoparietal regions affects cortical excitability and produces a long-lasting inhibitory effect [27–29]. This prolonged effect may have a major impact not only locally in the underlying cortex but also distally in interconnected areas [18]. Consistent with these observations, in the current study, cTBS of the right pre-SMA modulated task-related rCBF changes in remote regions. In the behavioral study, particularly intriguing was the asymmetrical effect of cTBS on the manual responses. Indeed, the performance of the stop signal task with the left hand was quite different from the right hand since it was not affected significantly. While this observation rules out a possible cTBS effect on the contralateral (left) pre-SMA, one explanation for this different behavior could be attributed to the inter-hemispheric inhibition reported in several TMS studies [46] and that takes place when activity in one hemisphere tends to inhibit the activity in the other hemisphere during movement. In fact, it has been shown that cTBS applied over the right motor region may have a carry-over effect on the contralateral hemisphere (non-stimulated) with increased excitability [47]. This may well explain the increased activation over the left pre-SMA following the cTBS-induced disruption over the right pre-SMA. In other words, the disinhibitory effect triggered by cTBS led to an increased activation in the contralateral (i.e., left) hemisphere during the right hand task performance with faster SSRT. The path modeling analysis confirmed the rCBF changes during the enhanced SSRTs in interconnected cortical regions with particular relevance in the left pre-SMA connection with right premotor area.

Although the right hemisphere is considered to contribute significantly to the response inhibition network, our results showed that homologous areas (i.e., left IFG/MFG; left pre-SMA) in the contralateral hemisphere can be engaged as well in this inhibitory network to compensate for the acute TBS-induced “disruptive” effect of the right pre-SMA functions. Indeed, the role of the left IFG and left pre-SMA in inhibition of actions has been proposed in previous reports [7,48–52]. We found a significant task × stimulation interaction in the left IFG region encompassing the MFG. Patients with a focal lesion over the left IFG presented a worsening of their inhibitory control during the go no-go task with a larger number of commission errors [51], while TMS pulses applied over the left pre-SMA during the stop signal task have shown to affect response inhibition and action errors [7]. Thus, based on current evidence, the IFG is generally believed to be relevant in initiating or ‘calling out’ regions (i.e., pre-SMA) that execute the final inhibitory outcome, thus exerting a “top-down” type inhibitory control of ongoing actions [10,12,13].

From a functional point of view, our results may also be supported by the fact that the pre-SMA is heavily interconnected with IFG, lateral PMC, M1, striatum and STN [4–7,10,53–55]. Interestingly, our PET and SEM data could not detect significant rCBF changes in the STN or striatum as reported in previous fMRI studies [4,5,10]. The absence of changes in these key regions is very likely the result of the block-design paradigm of the PET imaging which...
may represent a methodological limitation and less sensitive approach as compared to event-related fMRI protocols.

While it is clear that IFG and pre-SMA both play a significant role in action inhibition\(^{[4\text{--}7,10,54\text{--}56]}\), there is still a significant debate about their specific contribution. In the current study, we show that both areas are important for action inhibition but the insights obtained from the SEM analysis suggest the significant relevance of the pre-SMA.

The rCBF increase observed in the right premotor cortex following cTBS was in the context of this “compensatory” response which likely played an important role in the preparation and initiation process involved in go trials, where a certain degree of initiation and preparation is embedded within successful and unsuccessful inhibition trials\(^{[57]}\). In fact, it is well known that the premotor cortex is generally involved in executing a response rather than in suppressing it\(^{[23]}\), thus playing a key role in action preparation\(^{[58,59]}\) exerted by increasing its excitability when an upcoming response needs to be generated\(^{[60,61]}\). Thus, in our case, the premotor cortex may have played a role in the selection of appropriate response (go trials) or by executing an overt movement.

**Limitations**

Our study is not exempt from potential limitations; first, the possible order confound. The reason why we adopted the approach described above was motivated by the fact that by applying active cTBS before sham would have produced the risk of the active stimulation effect spilling over into the sham condition, thus compromising the control condition. Bearing this in mind, as discussed above, we tried to overcome this limitation by training the subjects with a practice session before the experiments. Probably by separating the sham and real cTBS into separate sessions, we could have increased the strength of our results. However, other
This dynamic mechanism may be important for understanding the role of the left hemisphere and underlying neural circuits engaged in response inhibition both in healthy participants and patients with neurological disorders.

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