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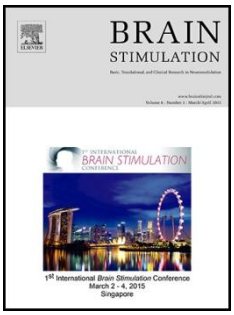

Title: Continuous Theta Burst Stimulation Over the Dorsolateral Prefrontal Cortex and the Pre-SMA Alter Drift Rate and Response Thresholds Respectively during Perceptual Decision-Making

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Continuous theta burst stimulation over the dorsolateral prefrontal cortex and the pre-SMA alter drift rate and response thresholds respectively during perceptual decision-making

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Highlights

- What is the contribution of DLPFC and pre-SMA to perceptual decision-making?
- Two versions of the moving dots task were used
- cTBS over the right DLPFC, pre-SMA and sham stimulation was applied
- Right DLPFC cTBS modulates drift rate as a function of task difficulty
- pre-SMA cTBS modifies boundary separation when accuracy is emphasized

Abstract

Background: The speed-accuracy trade-off (SAT) refers to the balancing of speed versus accuracy during decision-making. SAT is very commonly investigated with perceptual decision-making tasks such as the moving dots task (MDT). The dorsolateral prefrontal cortex (DLPFC) and the pre-supplementary motor area (pre-SMA) are two brain regions considered to be involved in the control of SAT.

Objectives/Hypotheses: The study tested whether the DLPFC and the pre-SMA play an essential role in the control of SAT. We hypothesized that continuous theta burst stimulation (cTBS) over the right DLPFC would primarily alter the rate of accumulation of evidence, whereas stimulation of the pre-SMA would influence the threshold for reaching a decision.

Methods: Fifteen (5 females; mean age=30, *SD*=5.40) healthy volunteers participated in the study. We used two versions of the MDT and cTBS over the right DLPFC, pre-SMA and sham stimulation. The drift diffusion model was fit to the behavioural data (reaction time and error rate) in order to calculate the drift rate, boundary separation (threshold) and non-decision time.

Results: cTBS over the right DLPFC decreased the rate of accumulation of evidence (i.e. the drift rate from the diffusion model) in high (0.35 and 0.5) but not in low coherence trials. cTBS over the pre-SMA changed the boundary separation/threshold required to reach a decision on accuracy, but not on speed trials.

Conclusions: The results suggest for the first time that both the DLPFC and the pre-SMA make essential but distinct contributions to the modulation of SAT.

Keywords: speed-accuracy trade off, perceptual decision-making, continuous theta burst stimulation, DLPFC, pre-SMA.

Abbreviations: DLPFC=dorsolateral prefrontal cortex, pre-SMA=pre-supplementary motor area, cTBS=continuous theta burst stimulation

Introduction

Perceptual decision-making is widely held to involve the process of making a choice from a set of alternative options based on accumulation of information from the sensory systems [1]. It is proposed that sensory information accumulates from a starting point until a threshold is reached favouring one option over another [2]. Making an accurate decision requires spending a longer time to collect the relevant information, making the decision processes slow; whereas making a fast decision entails spending less time in accumulating evidence, with the potential cost of lower accuracy. This so-called speed-accuracy trade off (SAT) [3] has been most commonly investigated in perceptual decision-making tasks, such as the 'moving dots' task (MDT) [4].

One outstanding question is in relation to the brain areas involved in the modulation of SAT [3, 5]. In imaging studies a number of prefrontal areas including the DLPFC [6-11] and the pre-SMA [12, 13], as well as the striatum and the subthalamic nucleus (STN), have been reported to be engaged during performance of tasks that involve modulation of SAT [14]. While evidence from theoretical and imaging studies suggest that the DLPFC and pre-SMA are involved in the modulation of SAT, because of the correlational nature of imaging data, the specific contributions of these regions to SAT regulation is not clear and differs between studies. For example, while both Ivanoff et al. (2008)[6], and Vallesi et al. (2012)[11] found that the right and left DLPFC are respectively involved in the regulation of the amount of information necessary to reach a decision, the results from other studies suggest involvement of the DLPFC in regulation of the speed/rate of data collection [7-9].

Thus, the primary aim of our study was to use the MDT and continuous theta burst stimulation (cTBS) (that has inhibitory effects [15]) over the DLPFC and the pre-SMA to *first* establish whether these brain areas make an essential contribution to modulation of SAT and *second* to identify the nature of their respective contributions to the modulation of SAT. Based on theoretical models [3, 5] and imaging data [7-10] we predicted that cTBS over the right DLPFC would primarily change the rate of accumulation of evidence (i.e. the drift rate), whereas stimulation of pre-SMA would influence the amount of information needed in order to make a decision (i.e. the boundary separation/threshold) during MDT performance [5, 12]. Furthermore, based on the findings from recent studies [11, 16] as a part of the post-hoc analysis, we also analysed the role of the right DLPFC and pre-SMA in the regulation of switching between speed and accuracy strategies.

Materials and Methods

Participants

Fifteen (5 females; 13 right handed, 2 ambidextrous; mean age =30, *SD*=5.40) healthy volunteers participated in the study. All participants had normal or corrected-to-normal vision. None of the participants had a history of neurological, psychiatric or physical illness, head injury or drug or alcohol abuse. Handedness was assessed by the Briggs and Nebbs handedness inventory [17].

Design and procedure

A repeated measures design was used. Continuous theta-burst stimulation (cTBS) over the right DLPFC, pre-SMA and left S1 leg area (sham stimulation) was administered in three different sessions in a randomized fashion. During each session all participants performed two versions of the moving dots task (see bellow). The minimal interval between two consecutive sessions was 5 days (range: 5-16 days).

The joint ethics committee of the UCL Institute of Neurology and the National Hospital for Neurology and Neurosurgery approved the study. Informed consent was obtained from all participants.

The moving dots task

The speed-accuracy version of the MDT manipulated the speed-accuracy instructions (Figure 1A). Participants were required to decide whether a cloud of dots, with a fixed coherence level of 0.5 across trials, moved to the left or the right of the screen. Each dot consisted of three pixels; the diameter of the entire cloud of dots was 250 pixels. At the beginning of each trial, a written cue, either FAST or ACCURATE, was presented pseudorandomly, instructing participants to adopt different levels of cautiousness. The participants decided on the direction of the moving dots by pressing one of two buttons with either their left (for dots moving left) or right (for dots moving right) index finger. Two blocks (100 trials each), with a short break between blocks, were completed by every participant. At the end of each trial, participants received feedback: on speed trials, whenever participants exceeded the reaction time criterion of 400 ms, a TOO SLOW feedback was presented, otherwise they received an IN TIME message. The criterion of 400 ms for the TOO SLOW feedback was adopted from previous studies

[12]. In the accuracy trials, participants were presented with an INCORRECT or CORRECT feedback. If participants exceeded a time criterion of 1500 ms, a NO RESPONSE feedback was presented on the screen. The negative feedbacks were presented in red, while the positive feedbacks appeared in green.

In the coherence version of the task (Figure 1B) the participants were instructed to perform the task as fast and as accurately as possible; no cues for speed or accuracy were used in this task. However, the coherence ('difficulty') level of the moving dots changed between trials. Six levels of coherence were set at 0.05, 0.10, 0.15 0.25, 0.35 and 0.50 with 20 trials per coherence level resulting in a block of 120 trials. Participants performed two blocks of the task. The coherence level was manipulated to make it harder (0.05) or easier (0.5) to decide the direction of the moving dots. At the end of each trial, participants received INCORRECT, CORRECT or NO RESPONSE (if criterion of '1500 ms' was exceeded) feedback depending on their response.

The tasks were programmed and presented using PsychoPy software [18] on a 27 inch wide LG monitor (Flatron W2753VC) with a resolution of 1920 × 1080 and a refresh rate of 60 Hz. Participants sat in a comfortable chair at a distance 100 cm from the monitor. Before each task participants completed practice trials. The order of the tasks performed in a single session was randomized. Completion of both tasks required about 35 minutes.

– insert Figure 1 approximately here –

Continuous Theta Burst Stimulation (cTBS)

Magstim (Magstim Company Ltd, Wales, UK) stimulators (Magstim 200 for single pulse TMS, and Magstim Rapid^2 stimulator for cTBS) were used for stimulation. Active motor threshold (AMT) for the first dorsal interosseus muscle (FDI) was obtained by applying monophasic pulses with a 7 cm figure-of-eight-coil placed tangentially over the participants' right M1 with the handle kept 45˚backwards and laterally over the hotspot for the left FDI. AMT for the tibialis anterior (TA) was obtained by using a double-cone coil (P/N 9902-00; Magstim Co. Ltd) to stimulate M1 for the left leg. AMT was defined as the stimulator output at which a motor evoked potential (MEP) higher than 200 μV was elicited on five out of ten trials while participants maintained an FDI or TA contraction of approximately 20% of their maximal force measured by surface EMG [19].

The cTBS protocol, consisting of a series of bursts of three pulses 20 ms apart repeated every 200 ms for 40 s (600 pulses) [15] was used to stimulate the right DLPFC, pre-SMA and for sham stimulation. The right DLPFC was stimulated with a power of 80% of the ATM for the left FDI by placing the figure-of-eight-coil at a position F4 according to the 10-20 system as described in Beam et al. [20]. We opted to stimulate the right DLPFC rather than the left because there is evidence that in addition to the left DLPFC, already probed in a repetitive TMS study [10], the right DLPFC is also involved in SAT regulation [6, 7]. The pre-SMA was stimulated with 80% of the AMT for the left TA at a point located 5 cm anterior to the hotspot for TA over Cz according to the 10-20 system [21, 22] by using a double-cone coil. The 7 cm-figure-of-eight coil tilted 90° to the surface of the head at 20% of the AMT for FDI was used for sham stimulation over

the S1 area for the left leg, defined as 2 cm posterior to the FDI hot spot in the central midline area [23].

Diffusion model analysis

Diffusion model analysis was performed by the use of *fast-dm* [24]. This program estimates the parameters of Ratcliff's [2] drift diffusion model (DDM). The model can be applied in cognitive tasks with binary decisons, such as the MDT [25]. The basic assumption of this model is that during a binary decisions information accumulates continusously from a certain predifined starting point until it reaches a threshold, when a decision is made. One of the advantages of the DDM model is that the parameters allow for a high degree of information utilisation [26]. Thus, instead of relying solely on the behavioural measures of performance – the mean reaction time (RT) and mean error rate (ER) – the so called problem of common metrics –, performance can be presented by DDM parameters that take into account the distribution of both correct and incorrect RTs [25], which avoids the reliance on different measures. Indeed, by analysing the RT and ER separately the probability of Type I error increases [25]. In addition, whenever differences in performance spread over the two metrics, a reduction of statistical power might occur possibly producing non-significant effects for both RT and ER [25]. Thus, DDM provides a powerful tool for a more detailed analysis of the processes underlying the behavioural measures [26].

Several parameters are calculated from applying the diffusion model [27]. The boundary separation (*a*) represents the difference between baseline activity and the response threshold to reach a decision - the larger the distance between the starting point

and decision threshold, the longer it takes to make a decision, hence the longer the RT and the less likely errors are. Drift rate (v) refers to the speed with which evidence for the correct response accumulates; a high drift rate results in more accurate and faster responses. The non-decision time (t_0) captures the time needed for other processes such as stimulus encoding and motor execution. The starting point (z) reflects possible *a priori* biases in the decision threshold.

One of the important steps when applying DDMs is to decide which of the above mentioned parameters (a, v, t_0, z) are to be fixed and which are to be allowed to vary across conditions. In general, models should be defined as parsimoniously as possibly, as numerous free parameters might lead to overfitting and make the results unreliable especially in cases of low trial numbers [28], which calls for a careful selection of free parameters for the models depending on the task [25]. For example, because changing the characteristics of the sensory information changes the speed of information accumulation, the drift rate should be left to vary freely in tasks with trials with variable sensory content [27]. Therefore, in the coherence task separate drift rates were calculated for each coherence level for the three brain regions – right DLPFC, pre-SMA and sham; the values for the boundary separation and the non-decision time were allowed to vary relative to brain region only.

In contrast, based on the classical proposal that under speed instructions there is a reduction of the distance between the baseline and the threshold, in the speed-accuracy version of the task both, the boundary separation and the non-decision times were calculated separately for ‘speed’ and ‘accuracy’ trials relative to the region of stimulation; whereas the drift rate was allowed to vary freely only for the brain region,

but not for the type of instructions (FAST vs. ACCURATE). Indeed, the results from a recent study have shown that while the effect of the speed-accuracy instructions on boundary separation is present during multiple sessions of the MDT, a presumed effect of speed-accuracy instructions on the drift rate could only be traced at the beginning of training; after training the speed accuracy instructions change solely the boundary separation [29].

The starting point in both tasks was fixed to zero. Optimization criterion based on the Kolmogorov-Smirnov (KS) statistics was used in both tasks. The KS approach yields robust results in the presence of relatively smaller number of trials [25]. The assessment of model fit was performed based on the values of the KS statistics.

The DDM and behavioural parameters were subjected to statistical analysis using SPSS. The Shapiro-Wilk test was used to test for normality. A two-way repeated measure ANOVA with factors brain region (right DLPFC, pre-SMA and sham) and task difficulty/coherence level (0.05, 0.10, 0.15 0.25, 0.35 and 0.50) for the coherence task and brain region (right DLPFC, pre-SMA and sham) and instructions (Speed vs. Accuracy) for the speed-accuracy task, as well as *t*-tests where appropriate, were used to analyze the data. As part of the post-hoc analysis, we also tested the effect of the right DLPFC and pre-SMA on switching between speed and accuracy strategies on the behavioural and DDM parameters. For this analysis, the RTs and ERs in speed and accuracy trials were first separated into "switch" and "no-switch" trials, and then the DDM parameters calculated as explained above. A three-way repeated ANOVA with factors instructions (Speed vs. Accuracy), brain region (right DLPFC, pre-SMA and sham) and switching (Switch vs. No-switch Trial) was then used to analyse both the

behavioural and DDM parameters. If the assumption of sphericity was violated (Mauchly's test), a Greenhouse-Geisser correction was used. Probability value of p=0.05 was used as a criterion for statistical significance. A Bonferroni correction was used to control for multiple comparisons.

Results

Behavioural Measures

Speed-accuracy task - behavioural measures

Mean RT in speed-accuracy task. As expected, the RTs for the speed trials were shorter than for the accuracy trials (F(1,14)=19.34, p=0.001) (Figure 2 A). Although the mean RT after right pre-SMA stimulation was shorter than the RT after right DLPFC or sham stimulation, the main effect of brain region (p=0.254) and the brain region × instructions interaction (p=0.689) were not significant.

– insert Figure 2 approximately here –

Mean ER in speed-accuracy task. Participants made more errors after speed than after accuracy instruction ($F_(1,14)$=17.88, p=0.001) (Figure 2 B). The main effect of brain region (p=0.883) and the brain region × instruction interaction (p=0.571) were not significant.

Post-hoc analysis of the switch vs. non-switch trials. There was no main effect of switching or brain region or any significant interactions on mean RTs or ER (all *ps>0.252*) on both speed and accuracy trials.

296

297 **Coherence task - behavioural measures**

298 *Mean RT in coherence task.* As expected, the main effect of coherence was
299 significant ($F(5,70)=34.48$, $p<0.0001$) (Figure 3A) indicating shorter RTs in higher than
300 in the lower coherence trials. Neither the main effect of brain region ($p=0.494$) nor the
301 brain region × coherence interaction ($p=0.440$) were significant.

302

303 – insert Figure 3 approximately here –

304

305 *Mean ER in coherence version of the task.* The main effect of coherence was
306 significant ($F(5,70)=88.07$, $p=0.001$) with higher ER in low coherence trials (Figure 3B).
307 The main effect of stimulation target ($p=0.922$) and brain region × coherence interaction
308 ($p=0.530$) were not significant.

309

310 **Drift Diffusion Model (DDM) analysis**

311 The Kolmogorov-Smirnov tests revealed no significant results at the alpha level
312 of 0.05 for the model fits in both tasks, indicating that the individual models described
313 the RT distribution well.

314

315 **Speed-accuracy task – DDM results**

316 *Boundary separation in the speed-accuracy task.* As expected, the boundary
317 separation for the speed trials was lower compared to accuracy trials ($F(1,14)=11.41$,
318 $p=0.005$) (Figure 4A). The main effect of brain region was significant ($F(2,28)=4.46$,

319 p=0.021) indicating a significant decrease of the boundary separation after stimulation of
320 the pre-SMA compared to the right DLPFC and sham stimulation. The significant brain
321 region × instructions interaction (F(2,28)=4.26, p=0.024) indicated a differential effect of
322 the stimulation over the pre-SMA depending on instructions. Namely, the decrease of the
323 boundary separation after stimulation of pre-SMA in accuracy trials was significant
324 compared to both right DLPFC (t(14)=2.46, p=0.027) and sham stimulation (t(14)=2.33,
325 p=0.035). By contrast, with speed instructions, the decrease of the boundary separation
326 after pre-SMA stimulation was not significant relative to either the right DLPFC
327 (p=0.067), or sham stimulation (p=0.205). There was no significant difference in
328 boundary separation in either accuracy (p=0.382), or speed trials (p=0.946) when
329 stimulation of the right DLPFC was compared to sham stimulation.
330
331 – insert Figure 4 approximately here –
332
333 *Non—decision time in the speed-accuracy task.* The non-decision time was
334 shorter for speed as compared to accuracy trials (F(1,14)=16.40, p=0.001) (Figure 4B).
335 There was no effect of brain region on the non-decision time (p=0.534). The brain region
336 × instructions interaction was also not significant (p=0.195).
337 *Drift rate in the speed-accuracy task.* As mentioned above, the drift rate was
338 calculated for the brain region regardless of instruction. There was no effect of brain
339 region on the drift rate (p=0.442) in the speed-accuracy task.
340 *Post-hoc analysis of the switch vs. non-switch trials.* There was no significant
341 main effect of switching or brain regions or any significant interactions on the boundary

separation or non-decision time parameters (all *ps>0.156*) on both the speed and accuracy trials.

Coherence task - DDM results

Drift rate in the coherence task. As expected, the main effect of coherence level was significant and the drift rate was lower on trials with lower coherence than higher coherence ($F(5,70)=84.86$, $p<0.0001$) (Figure 5). The main effect of brain region was not significant ($p=0.141$). However, the brain region × coherence level interaction was significant ($F(10,140)=2.03$, $p=0.025$), which indicated a differential effect of stimulation of different cortical regions depending on the coherence level. Namely, there was a decrease of drift rate at high coherence levels (0.35 and 0.5) after stimulation of the right DLPFC compared to the stimulation of the right pre-SMA (coherence level 0.35: $t(14)=-2.69$, $p=0.018$, coherence level 0.5: $t(14)=-2.07$, $p=0.047$) and the sham stimulation (coherence level 0.35: $t_{(14)}=-2.77$, $p=0.015$, coherence level 0.5: $t(14)=-2.53$, $p=0.024$), but not at coherence levels below 0.25 ($p=0.485$). The drift rates were not significantly different for stimulation of the right DLPFC and for sham stimulation ($p=0.230$).

– insert Figure 5 approximately here –

Boundary separation and non-decision time in the coherence task. The boundary separation and the non-decision time were calculated for stimulation of the right DLPFC, right pre-SMA and after sham stimulation regardless of the level of coherence. The effect of stimulated brain region on boundary separation ($p=0.260$) and non-decision time ($p=0.453$) was not significant (see Table 1).

– insert Table 1 approximately here –

Discussion

There are three main findings from the study. First, disruption of the activity of both the right DLPFC and the pre-SMA with cTBS significantly altered the parameters derived from the drift diffusion model compared to sham stimulation. Second, cTBS over the pre-SMA selectively decreased the boundary separation on accuracy trials. Third, cTBS over the right DLPFC decreased the drift rate on high coherence trials (0.35 and 0.5) but not in low coherence trials (lower than 0.25). The latter two findings will be discussed below.

Stimulation of the pre-SMA decreases the boundary separation on accuracy trials

Although imaging studies [6, 12-14, 30] clearly showed engagement of the pre-SMA in SAT control, the functional significance of activation of the pre-SMA in relation to SAT control remained unclear. Our results provide the first evidence that inhibition of the pre-SMA with cTBS induces a decrease in the boundary separation when accuracy is emphasized over speed, suggesting a decrease of the amount of information needed to reach threshold before a decision was made under accuracy instructions.

At first glance this finding may seem to be in contradiction to the imaging literature showing greater activation of the pre-SMA under speed instructions [6, 11, 12, 14], because this would lead to the assumption that since there is a greater activation of the pre-SMA when speed is emphasized over accuracy, stimulation of the pre-SMA

would affect primarily the responses under speed rather than under accuracy instructions. However, activation of the pre-SMA by speed instructions is related to the decrease of the boundary separation [13]; whereas the opposite holds true when accuracy is emphasized - accuracy instructions increase boundary separation; the latter was also shown in our study. Boundary separation represents the level of cautiousness, such that higher boundary separation indicates higher levels of cautiousness as in the case of accuracy trials [27]. Therefore, because the level of cautiousness and boundary separation were higher under accuracy than under speed trials, cTBS was able to selectively alter (decrease) the boundary separation on accuracy trials, and failed to modulate it on speed trials for which the boundary separation was low even before cTBS was applied over the pre-SMA.

Stimulation of the right DLPFC decreases the drift rate in high coherence ('easy') trials

The second key finding of the present study is that stimulation over the right DLPFC selectively decreased the drift rate in high coherence ('easy') as compared to low coherence ('difficult') trials.

Our finding that cTBS over the right DLPFC differentially decreased the rate of accumulation of information as a function of task difficulty is consistent with the fMRI results of Heekeren and coauthors [8, 9], who found that the DLPFC is more active during easy decisions than during harder decisions, which is in turn in line with the theoretical assumptions that areas representing decision variables at a more abstract level show greater activation on trials when the available sensory evidence required to make a

411 decision is greater, such as on the easier trials. In a recent fMRI study, however, by using
412 a visual searching task Vallesi et al [31] found higher activation of the right DLPFC on
413 target-absent and salient trials, when the stimuli should be evaluated to prevent false
414 alarms; and target-absent and non-salient trials, when the cognitive system should be
415 engaged more extensively in visual search to check for the absence of the target stimulus,
416 i.e. on harder trials. Similarly, Fleck et al. [32] reported a greater activation of the right
417 DLPFC for low (harder to decide) than for high confidence (easier to decide) trials during
418 episodic retrieval/visual perception tasks. The difference in the results from these studies
419 and the results from our study and the studies mentioned before [8, 9] might be due to the
420 difference in tasks used: while Fleck et al. [32] and Vallesi [31] (but see also [33, 34])
421 used more complex tasks that engage frontal cognitive abilities more extensively, in our
422 study as well as in the study of Heekeren et al. [9] a MDT task was used to assess
423 perceptual decision-making, which does not depend as extensively on frontal control
424 mechanisms. Similar results have also been reported with a facial recognition as a
425 measure of perceptual decision-making [8, 10].

426 Philiastides et al. [10] applied 1 Hz rTMS over the left DLPFC for 12 minutes and
427 examined two levels of difficulty on the facial recognition test. 1 Hz rTMS over the left
428 DLPFC reduced the drift rate, providing evidence for left DLPFC involvement in the
429 process of evidence accumulation. Our study extends the findings of Philiastides et al.
430 [10] in two important ways. First, we showed that stimulation of the right DLPFC could
431 also decrease the drift rate, hence suggesting that there is no specific hemispheric
432 specialization for the involvement of the DLPFC in relation to accumulation of sensory
433 information. Second, with our six levels of task difficulty we have shown that that the

decrease of drift rate by right DLPFC stimulation is a function of the level of task difficulty, i.e. the rate of accumulation of sensory evidence was distorted by cTBS on high coherence (easy) trials (0.35 and 0.5) and was not changed by stimulation on low coherence (difficult) trials (0.05, 0.1, 0.15 and 0.25). Furthermore, the use of cTBS, which has longer lasting effects of about 45-60 minutes [15] covered the whole period of task performance in our study, rather than the first half of the trials only, as in the Philiastides et al. [10] study. Therefore, our data and the data from Philiastides et al. [10] provide further evidence that the DLPFC is important in linking sensation to action, as previously shown in animal studies [35, 36].

The effect of switching between speed and accuracy strategies has been recently addressed in a few studies from the Valessi group [11, 16]. In a fMRI study with healthy participants, they first showed that switching from a quick to an accurate strategy was associated with activation of the left middle frontal gyrus [11]. In a later study employing patients with brain tumors (and after their subsequent surgical removal) located in the left or right prefrontal cortex, they found that flexibility of selecting an accurate strategy after adoption of a fast strategy is impaired in patients with left prefrontal tumors [16]. We, however, failed to find any effect of stimulation of the right DLPFC or pre-SMA on switching strategies. Campanella et al. [16] compared the effect of brain tumors in patients with left and right prefrontal lesions and found a failure to flexibly switch from speed to accuracy instructions in patients with left prefrontal lesion only, but not in patients with right prefrontal brain tumors, suggesting that the switching between speed-accuracy strategies might be functionally segregated in the left prefrontal cortex. In addition, while we used the MDT in our study, they used a color discrimination task,

457 which might also explain the differences in the results obtained in this study and their
458 studies. However, the effect of stimulation on switching between strategies was not a
459 primary aim of our study and it was examined as a post-hoc analysis.

460 There are a few limitations of the study. Even though the RT and ER in general
461 showed similar trends as the parameters derived from the DDM, the differences between
462 stimulated brain areas failed to reach significance for these measures. However, there
463 were significant effects when comparing the DDM parameters. As noted in the methods
464 section, one of the advantages of the DDM model is that the DDM parameters allow for a
465 high degree of information utilisation relative to the behavioural measures [26], since the
466 DDM parameters take into account the distribution of both correct and incorrect RT
467 simultaneously. Thus, instead of solely relying on behavioural measures, the performance
468 as presented by the DDM parameters allows for more subtle inferences about the
469 mediating processes [25]. Furthermore, in the speed-accuracy task we used a fixed
470 criterion of 400 ms such that whenever the reaction time of the participant exceeded the
471 value of 400 ms a "TOO SLOW" feedback appeared on the screen. However, this
472 criterion might have been too strict for some and too lenient for other participants.
473 Adjustment of the feedback criterion more flexibly according to each individual's average
474 speed may have been more appropriate. We, however, decided to use a fixed criterion of
475 400 ms based on the previous studies [12], which also makes the results of this study
476 more directly comparable to the results of these previous studies. We used a double cone
477 coil for cTBS, which is considered suitable for stimulating deeper brain structures such as
478 the pre-SMA [37]. However, taking into account the size of the coil and the overall low
479 spatial resolution of TMS [38], an effect due to stimulation of other more superficial

prefrontal areas cannot be completely ruled out. Nevertheless, the difference in the effects of stimulation of the pre-SMA versus DLPFC on the DDM parameters in both tasks argues against this possibility. Another factor, which might have limited stimulation accuracy, is our reliance on craniometric measures to localize target areas instead of a neuronavigation system. However, the craniometric measurement have been used successfully many times in TMS research so far [20-22] and have been shown to be able to reach desired cortex regions reliably [39]. Furthermore, there is a high inter-participant variability of TBS protocols on neurophysiological outcome measures [40]. Indeed, some participants respond to the cTBS "as expected" (i.e. inhibition of the cortical activity), others do not show any response to the protocol, while for other participants cTBS may produce the opposite effect – a facilitation rather than inhibition of cortical activity [41]. This variability might be due to inter-individual differences in the recruitment of interneuron networks [41], but can also be accounted for by the different level of contraction/relaxation of the recording muscle, i.e. it can be abolished by tonic contraction while cTBS is applied [42], or it can even be reversed to facilitation by phasic contraction of the muscles [43]. Nevertheless, we were very persistent in our demands to the participants to relax the muscles as much as possible. In addition, it is known that the effect of cTBS depends on the stimulation intensity [40]. However, we were very cautious to apply cTBS at the level 80% of the AMT at FDI for each participant. There is still a need for more meticulous recruitment of participants in future studies based on their individual response to cTBS.

Conclusions

In conclusion, the selective decrease of boundary separation on accuracy trials with stimulation over the pre-SMA, and the decrease of the drift rate on high but not low coherence trials with stimulation over the right-DLPFC, provide evidence that causally relates pre-SMA and the right-DLPFC to the regulation of SAT. The 'selective influence' assumption of the DDM refers to the idea that changes in specific cognitive processes such as urgency or increased caution selectively influence one parameter of the model [44], which has been supported by simulated data (e.g. Ratcliff and Frank, 2012 [45]). Our data provide support for the 'selective influence' assumption by showing that cTBS-induced disruption of the pre-SMA and DLPFC selectively alter boundary separation and drift rate respectively.

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Figure 1. The Moving dots task used in the study; A) Speed-accuracy version of the task; B) Coherence version of the task, in which the coherence (difficulty) level of the moving dots was manipulated.

Figure 2. Mean Reaction Time in milliseconds (*ms*) (A) and Mean Error Rate in the speed and accuracy trials after stimulation of the right dorsolateral prefrontal cortex (right DLPFC), right pre-supplementary motor area (pre-SMA) and after sham stimulation.

Figure 3. Mean Reaction Time in milliseconds (*ms*) (A) and Mean Error Rate for 6 different coherence levels after stimulation of the right dorsolateral prefrontal cortex (right DLPFC), right pre-supplementary motor area (pre-SMA) and after sham stimulation.

Figure 4. Effect of stimulation (right dorsolateral prefrontal cortex – right DLPFC, pre-supplementary area – pre-SMA and sham) on boundary separation (A) and non-decision time (B) in speed-accuracy task as a function of instructions (Speed vs. Accuracy). The significant effects of stimulation are marked with *.

Figure 5. Effect of stimulation (right dorsolateral prefrontal cortex – right DLPFC, pre-supplementary area – pre-SMA and sham) on the drift rate as a function of the coherence level of the task. The significant effects of stimulation are marked with *.

681 Table 1. Mean boundary separation (a) and mean non-decision time (t_0) before and after
682 continuous theta burst stimulation over the right dorsolateral prefrontal cortex (r-
683 DLPFC), pre-supplementary area (pre-SMA) and during sham stimulation in the
684 coherence version of the moving dots task.

	a before	SD	a after	SD	t_o before	SD	t_o after	SD
r-DLPFC	0.903	0.275	0.914	0.248	0.373	0.076	0.345	0.059
pre-SMA	0.831	0.220	0.811	0.136	0.378	0.058	0.367	0.056
sham	0.952	0.272	0.894	0.237	0.388	0.065	0.364	0.052

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