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Anodal tDCS over SMA decreases the probability of withholding an anticipated action

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Abstract

Previous research has shown that the supplementary motor area (SMA) is critical in movement inhibition. Recently it was shown that applying transcranial direct current stimulation (tDCS) over SMA affected participants' ability to inhibit their movement in a stop-signal reaction time task (Hsu et al. 2011). Of interest in the current study was whether modulating SMA excitability using tDCS would have similar effects in an anticipation-timing stop-signal task. Participants performed 2 sessions each consisting of a pre- and post-tDCS block of 160 trials in which they were instructed to extend their wrist concurrently with the arrival of a pointer to a target (i.e., a clock hand reaching a set position). In 20% of trials (stop trials) the pointer stopped 80, 110, 140, 170, or 200 ms prior to the target, and on these trials participants were instructed to inhibit their movement if possible. Anodal and cathodal tDCS (separated by at least 48 hours) was applied for each participant between the pre- and post-tDCS blocks. No change in the proportion of successfully inhibited movements on stop trials was found following cathodal tDCS ($p > .05$). However, anodal tDCS resulted in a decreased proportion of successfully inhibited movements on stop trials ($p = .002$), and an earlier movement onset on control trials ($p < .01$). This suggests that the SMA may be more involved in initiation than in inhibition of anticipatory movements. Furthermore these data suggest that differences in initiation and inhibitory processes exist between stop-signal reaction time and anticipation-timing stop-signal tasks.

Keywords: tDCS; Supplementary motor area; Anticipation-timing; Inhibition

Introduction

Anticipation of external events allows people to act concurrently with, instead of in reaction to, environmental stimuli. However, such actions must sometimes be inhibited. For example, a "checked swing" in baseball involves both anticipating the arrival of the ball and later inhibiting the swing. One method that has been used to investigate these types of actions in the laboratory is an anticipation-timing task where a stop-signal is occasionally presented. Slater-Hammel [1] had participants perform a task in which they were instructed to lift their finger from a signal key concurrently with the arrival of a revolving pointer to an indicated position. If the pointer stopped prior to the target position, then participants were told to try to inhibit the finger lift. The probability of successfully inhibiting the movement at various latencies was determined by manipulating the times at which the pointer stopped with respect to the anticipated "go." Participants were able to successfully withhold the action in 50% of trials if the pointer stopped 166 ms prior to the target; after this time the movement was committed to action in a majority of trials – which Slater-Hammel termed the "point of no return" [see also 2]. The processes underlying stop-signal tasks have been represented as a horse race between the processes responsible for initiating the action and processes responsible for inhibiting the action, such that the movement is or is not carried out depending on which of the two processes reaches the response decision threshold first [3].

In anticipation-timing tasks, activation related to motor preparatory processes appears to be delayed until shortly (150 - 300ms) prior to the anticipated time of response [4, 5]. Motor inhibitory activation appears to involve a similarly short time-course when presented in an anticipation-timing paradigm that includes a stop-signal [6]. In these types of tasks, motor inhibition is suggested to occur via a reduction in excitability of the active motor areas specific to the action coupled with increased activity in inhibitory brain areas [6]. One cortical area suggested to mediate the inhibitory processes is the supplementary motor area (SMA) [7, 8]. The SMA can be divided into two motor subsections: the posterior portion (SMA-proper) and the anterior portion (pre-SMA) [9], both of which have been shown to be involved in movement inhibition. For example, functional magnetic resonance imaging (fMRI) was used to show that the SMA was active in inhibiting the

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execution of movements that were primed in advance using motor imagery [10] or passive movement [8]. In addition, fMRI data showed that both the pre-SMA and the SMA-proper showed increased activation during a muscle relaxation task compared to an active contraction task [11]. Notably, other imaging studies found that the pre-SMA was involved in inhibiting movement during a stop-signal reaction time (SSRT) task - where an imperative "go" signal is presented and sometimes followed at short latency by a stop-signal [12, 13]. Specifically, increased activation in pre-SMA correlated positively with successful inhibitory control during the stop-signal task [14]. Together, these data suggest that although the two areas are distinct, they may cooperatively play a role in motor inhibition [11].

Given the evidence for strong involvement of the SMA in motor inhibition, it was of interest whether modulating SMA excitability would affect stopping performance in an anticipation-timing task involving a stop signal [e.g., 1]. Transcranial direct current stimulation (tDCS) is a non-invasive technique used to modulate neural activity in which a weak electrical current is applied over the scalp for short periods of time. Several recent neurophysiological studies have shown that stimulation results in polarity-dependent modulation of the underlying brain tissue. Using TMS to index changes to corticospinal excitability following tDCS over primary motor cortex, it has been shown that cathodal tDCS hyperpolarizes the neurons underlying the site of stimulation, leading to decreased excitability, while anodal stimulation depolarizes and increases the excitability of the tissue [see 15 for a review]. Moreover, recent findings have also shown that changes in excitability can in turn influence functions associated with the modulated cortical areas. As such, tDCS can be used to elucidate the function of specific brain areas in the production of actions. For example, when tDCS was applied over pre-SMA during a SSRT task the probability of a successfully inhibiting action after the presentation of a stop-signal was increased following anodal tDCS and decreased following cathodal stimulation [16].

It has been suggested that the involvement of inhibitory neural circuits may vary depending on task requirements. For example, inhibitory circuits involved in go/no-go tasks overlap with but are distinct from those involved in stop-signal tasks [17]. More relevant to the current experiment, because the involvement of inhibitory neural circuits may differ between stop-signal tasks with different timing parameters (i.e., anticipation-timing with stop-signal vs. SSRT) it was thought that modulating SMA during an anticipation-timing task would elucidate differences between them. Therefore, the current study investigated how applying tDCS over SMA affected performance in an anticipation-timing task involving a stop-signal. Seing as SMA is thought to contribute to action inhibition it was hypothesized that anodal tDCS applied over the SMA would result in a higher proportion of stopped responses at the various tested times; that is, an increase in the ability to inhibit an anticipated action. Conversely, it was thought that cathodal tDCS would result in a decrease in successful inhibitions.

Methods

Participants

Twelve neurologically healthy volunteers (6M, 6 F; 26.9 +/- 11.4 years) participated in the study. Testing was performed in two sessions, separated by a minimum of 48 hours, for all participants. Written informed consent was obtained before beginning testing; the study was conducted in accordance with University of Ottawa Research Ethics Board, and conformed to the most recent version of the Declaration of Helsinki.

Apparatus

Participants were seated facing a computer monitor at eye level, approximately 50 cm away. The right forearm was placed in a custom-made manipulandum with a padded concave armrest with the right shoulder flexed and abducted approximately 15˚. Two Velcro straps were used between the wrist and elbow to secure the arm in place. The wrist was semi-pronated with the palm facing inward in a neutral position (neither flexed nor extended), and the hand was secured to a separate swivelling rest, with the axis of rotation at their wrist. As such, participants' wrist movements were restricted to flexion and extension.

Task

Participants performed an anticipation-timing task involving a targeted wrist extension coincident with a clock hand arriving at a predefined location. A circle similar to a clock face (10 cm in diameter) was displayed with the numbers 1 through 10 evenly spaced around its perimeter starting at the 12 o'clock position (see Coxon et al. 2006 for a figure showing a similar display). At the beginning of each trial, a tone sounded and the words "Get Ready" appeared at the center of the screen below the circle, indicating to the participant that their wrist should be at the neutral home position (neither flexed nor extended). The "Get Ready" disappeared after 1000 ms and a clock hand began rotating clockwise around the circle, starting at the number 1 and completing the rotation in 1000 ms. Participants were to perform a 20˚ wrist extension movement as quickly and accurately as possible coincidently with the arrival of the clock hand at the number 8 (which was indicated by a red arrow). Participants were instructed that occasionally the clock hand would stop before reaching the target location and that on these trials they should try to inhibit their movement if possible. After each trial, participants were given feedback regarding their timing accuracy and awarded points based on timing performance to encourage accuracy. Points were given when displacement onset occurred

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within ±15 ms of the clock hand arriving at the target (1 point per ms below 15), and were subtracted when displacement onset occurred more than 50 ms early or late. Accuracy feedback and a running total of points awarded were displayed for 3 sec, followed by the beginning of the next trial. Throughout all trials, participants were notified if their movement amplitude error was greater than 10˚ and were also verbally encouraged to time their movements as accurately as possible with the goal.

In each session participants performed 20 practice trials which were followed by a pre-tDCS testing block. The pre-tDCS block consisted of 160 anticipation-timing trials, in which on 25% of trials, the clock hand stopped 80, 110, 140, 170 or 200 ms prior to arriving to the target position. These "stop trials" occurred randomly throughout the test, and 8 stop trials occurred for each stop time. After completion of the pre-tDCS block, the direct current stimulation was applied (see below), followed by an 8-minute rest interval. A post-tDCS testing block of another 160 trials (including 25% stop trials) was then performed. This sequence was repeated for the second testing session. Each anticipation-timing testing block lasted for approximately 16 minutes.

Transcranial direct current stimulation (tDCS)

Two electrodes were placed on the scalp in order to stimulate the desired area. The stimulating or "active" electrode (small sponge electrode, 1.5cc, 7.8 cm^2, Ionto+ Inc.) was placed 1.8 cm anterior to the measured location of Cz (based on the international 10-20 system for EEG electrode placement). The location for the active electrode was determined by mapping the centroid of the SMA based on Talairach space onto standardized head coordinates [18]. A similar location for SMA has been previously identified using TMS [19]. The active electrode was self-adhesive, however additional foam underwrap was used to ensure optimal contact. The "return" electrode was a self-adhesive carbon-foam electrode (Ionto+ Inc.) measuring 39 cm^2, placed centrally on the forehead directly above the eyebrows. Electrical stimulation was delivered using a Dupel iontophoresis constant current delivery device (Empi Inc.). Current was set at 1 mA and was delivered for 10 minutes (current density at the active electrode was thus 0.128 mA / cm^2). The relatively large return electrode allowed the current density to be sufficiently low as to be functionally inert with respect to the underlying cortical tissue [15].

In each of the two testing sessions participants received either the anodal or cathodal stimulation between pre- and post-tDCS testing blocks. Polarity order was balanced between participants. Participants and the experimenter conducting the trials were unaware of stimulation polarity. Testing sessions were conducted a minimum of 48 hours apart in order to ensure a complete washout of any residual tDCS effects. Previous investigation has shown that using similar stimulation parameters, tDCS effects are greatest 10-25 minutes following stimulation [20]; as such, in order to test during that timeframe, participants waited 8 minutes as a rest interval between the end of stimulation and the post-tDCS block.

Recording equipment

Surface electromyographic (EMG) data were collected from the muscle bellies of the right extensor carpi radialis longus (ECR) and right flexor carpi radialis (FCR) using bipolar preamplified (gain = 10) surface electrodes (Delsys Bagnoli DE-2.1) connected via shielded cabling to an external amplifier system (Delsys Bagnoli 16). The recording sites were lightly scrubbed with a pumice gel in order to decrease electrical impedance. Electrodes were placed parallel to the muscle fibres, and attached using double-sided adhesive strips. A grounding electrode was placed on participants' right lateral epicondyle. A potentiometer attached to the central axis of the manipulandum was used to collect wrist angular position data. On each trial, raw bandpassed (20-450Hz) EMG and unfiltered position data were digitally sampled at 1 kHz (National Instruments PCI-6052E via BNC-2090) for 2000 ms using a customized program written with LabVIEW software (National Instruments Inc.) and stored for offline analysis. Data collection was initiated by the computer 500 ms prior to the clock hand starting its rotation.

Data reduction

All trials were classified as Full Go, Partial, or Full Stop responses. A "movement" was defined to have occurred when a change of more than 0.2˚of angular displacement from the starting position was detected. "Full Go" responses were defined as trials when peak displacement was greater than 10°. Partial responses were trials where a movement was detected of less than 10˚. Peak displacement was the maximal angular excursion from the home position, while time to peak displacement was the time from displacement onset to peak displacement. Movement final position was defined as the first point at which angular velocity fell below and remained below 8˚/s for at least 150 ms, any secondary corrections after the first endpoint were ignored. Movement time was defined as the time from displacement onset to final position. Surface EMG burst onsets in wrist extensors and flexors were defined as the point at which the EMG first began a sustained rise above baseline levels. In brief, the location of this point was determined by first displaying the raw EMG pattern on a computer monitor with a superimposed line indicating the point at which the level of EMG activity in a rectified and filtered (25 Hz, dual pass, lowpass 2nd order elliptic filter) trace increased to more than 2 standard deviations above baseline (mean of 100 ms of EMG activity starting at clock hand movement). Onset was then verified by visually locating and manually adjusting (if necessary) the onset

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mark to the point at which the activity first increased. This method allowed for correction of errors due to the strictness of the algorithm [21, 22]. Peak EMG amplitudes were defined as the largest amplitude in EMG, rectified and filtered with a 25 Hz low pass elliptic filter, recorded within an interval of 100 ms following EMG burst onset.

Statistical analysis

Control trial data were analyzed using 2 (polarity: anodal vs. cathodal) x 2 (block: pre-tDCS vs. post-tDCS) Repeated Measures Analysis of Variance (RM ANOVA) tests. Stop trial data were analyzed using 2 (polarity) x 2 (block) x 5 (stop time, 80-200ms) RM ANOVAs. Partial eta squared (η_p^2) is reported to provide an estimate of the proportion of the variance that can be attributed to the tested factor. Prior to analysis, proportion variables were corrected for normalcy using an arcsine square root transformation. Greenhouse-Geisser corrected degrees of freedom were used to correct for violations of the assumption of sphericity. Differences where the probability of committing a Type I error was less than .05 were considered to be significant. Simple effects tests and Tukey's HSD post-hoc tests were administered where appropriate to determine the locus of any differences. Uncorrected student's t-tests were used to examine between-day differences in grouped pre- or post-tDCS variables.

Results

Probability of response in stop trials

Full-Go responses

The probability of participants performing a full non-cancelled response (i.e., not successfully inhibiting the planned movement after receiving a stop signal) was compared before and after stimulation. Analysis showed a main effect for block, $F(1,11) = 10.245$, $p = .008$, $\eta_p^2 = .482$, as well as a main effect for stop time, $F(4,44) = 124.830$, $p < .001$, $\eta_p^2 = .919$. As seen in Figure 1, the probability of erroneously responding increased as the stop-signal latency decreased. More relevant, however, was a significant interaction between polarity and block, $F(1,11) = 8.332$, $p = .015$, $\eta_p^2 = .431$. As expected, simple effects test showed a main effect of stop time for both anodal stimulation, $F(1,11) = 100.587$, $p < .001$, $\eta_p^2 = .901$, and for cathodal stimulation, $F(1,11) = 83.196$, $p < .001$, $\eta_p^2 = .883$, indicating that as the stop-signal was presented with less time prior to the timing goal, participants were less likely to be able to inhibit their response. However, a main effect of block was found for anodal tDCS, $F(1,11) = 17.241$, $p = .002$, $\eta_p^2 = .610$, indicating that participants were more likely to have a non-cancelled response post-stimulation than pre-stimulation (Fig. 1A). On the other hand, for cathodal stimulation the main effect of block was not significant, $F(1,11) = 3.188$, $p = .102$, $\eta_p^2 = .225$ (Fig. 1B). No other main effects or interactions were found.

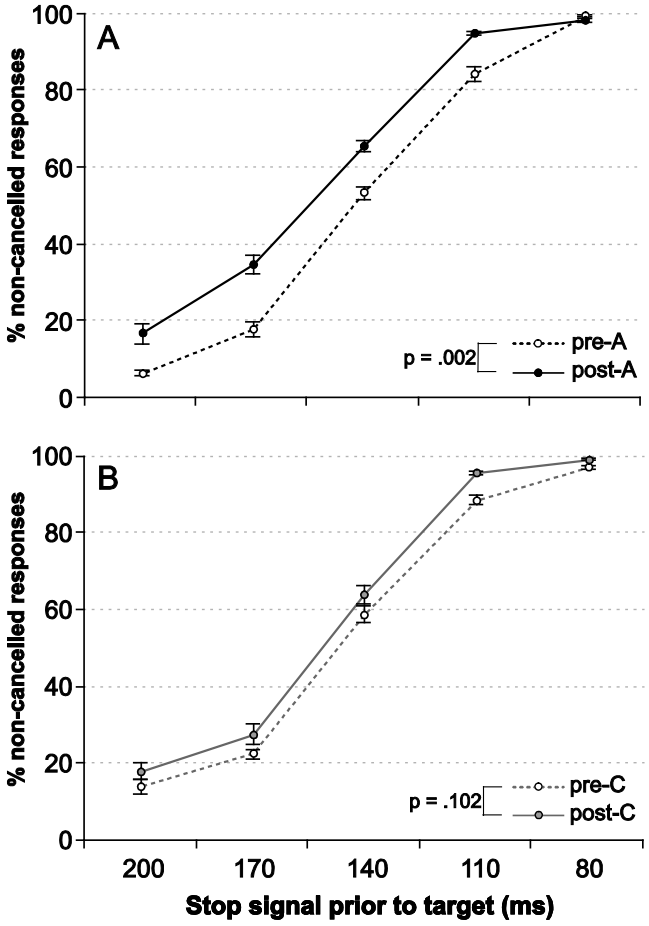

Figure 1. Percentage (±SE) of non-cancelled (i.e., "go") responses as a function of stop-signal latency (ms prior to target), for pre- and post-anodal (A) and cathodal (B) tDCS trial blocks. A (Black) = anodal stimulation; C (grey) = cathodal stimulation; pre- / post- refer to pre-tDCS and post-tDCS blocks respectively. Note a significant main effect of block (i.e., higher percentage of non-cancelled responses post-tDCS) for anodal but not cathodal tDCS.

Partial responses

The proportion of partial responses observed at each stop time was analyzed between polarities and testing blocks. There was no main effect of stimulation polarity ($p = .601$) or testing block ($p = .141$), and there was no interaction between the factors ($p = .396$). There was a main effect of stop time, $F(4,44) = 25.637$, $p < .001$, $\eta_p^2 = .700$. Tukey's post-hoc tests showed that participants were more likely to produce a partial response when the pointer stopped 170 ms prior to the target (32.1% of trials) compared to when it stopped 80 or 100 ms (1.5 and 7.4% of trials respectively) ($p < .05$). In addition, they were more likely to produce a partial response when the pointer

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stopped at 140 ms prior to the target (26.0% of trials) compared to 80 ms ($p < .05$). Finally there were no interactions between stop time and any of the other factors.

Timing of response

For control trials (no stop-signal), the time at which participants responded with respect to the timing goal was analyzed between blocks and polarities. Data are presented in Figure 2. A main effect was found for block, $F(1,11) = 5.740$, $p = .036$, $\eta_p^2 = .343$, however, this was overshadowed by a significant interaction between polarity and block, $F(1,11) = 5.649$, $p = .037$, $\eta_p^2 = .339$. Post-hoc t-tests performed on all control trials showed that following anodal stimulation participants initiated their response significantly earlier ($p < .001$) with respect to the timing goal compared to pre-tDCS (mean difference of 12.6 ms). No difference was observed for cathodal stimulation ($p > .05$) with a mean pre- to post-tDCS difference of 2.6 ms (Fig. 2). Importantly, a significant difference in time of responding was noted between pre-tDCS blocks (i.e. cathodal vs. anodal pre-tDCS blocks) whereby participants initiated the movement 5.7ms later in the pre-tDCS block prior to anodal stimulation compared to the pre-tDCS block prior to cathodal stimulation ($p < .001$). However, a significant difference was also found between time of responding between the post-tDCS blocks (cathodal vs. anodal) whereby participants initiated the movement 4.33 ms *earlier* following anodal stimulation compared to post-cathodal stimulation ($p = .003$).

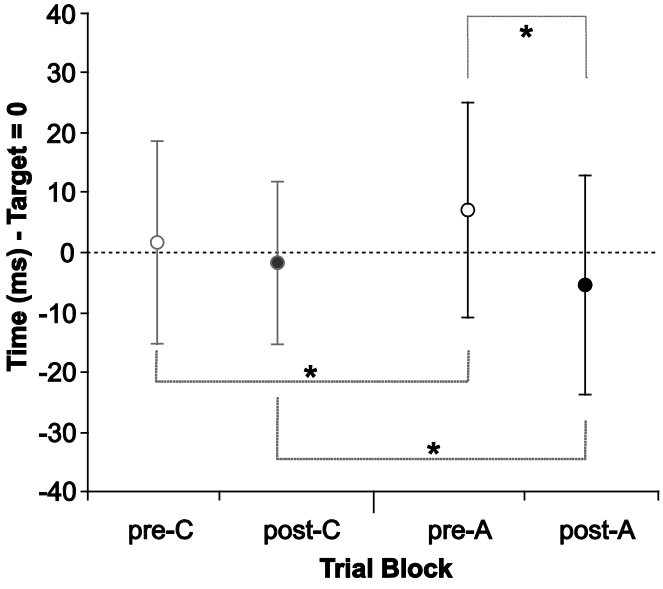

Figure 2. Mean (±SD) time of response onset for each trial block. Dashed line represents the anticipation timing target (0 ms); early and late responses with respect to the target are represented by positive or negative times, respectively. C (grey) = cathodal stimulation; A (Black) = anodal stimulation; pre- / post- refer to pre-tDCS and post-tDCS blocks respectively. Asterisks indicates a significant ($p < .01$) difference between stimulation polarities and times of interest.

In order to determine if any changes in performance observed could be attributed to learning within a block of trials, each block of 160 trials (pre- and post for each polarity) was broken into 4 bins of successive trials (e.g. trials 1-40, 41-80, 81-120, 121-160) and means calculated for time of movement onset. These data were then analyzed using a 2 (polarity) x 2 (block: pre-tDCS vs. post-tDCS) x 4 (trial bin) RM ANOVA. While there was main effect of block and an interaction between block and polarity (see above), there was no main effect found for trial bin ($p = .765$), and no interactions involving trial bin (all p values $> .785$).

Task performance

No significant main effects or interactions were observed for final position or movement time in control trials ($p > .05$). However, while there were also no significant effects of polarity or time on peak velocity and peak displacement, there was significant main effect for block (pre-tDCS vs. post-tDCS) found for both *time to* peak velocity, $F(1,11) = 8.378$, $p = .015$, $\eta_p^2 = .432$, and for *time to* peak displacement, $F(1,11) = 7.451$, $p = .020$, $\eta_p^2 = .404$, indicating that at least the initial part of the movement was made faster in the post-test for both polarities.

Discussion

In this experiment motor performance in an anticipation-timing task that included the occasional stop-signal was investigated following tDCS applied over the SMA. Little kinematic feedback was provided during the experiment (the predominant emphasis was on movement timing accuracy), but participants were nevertheless competent in performing the task. Although accuracy was unaffected following tDCS, participants did perform the initial part of their movement faster post-tDCS compared to pre-tDCS (time to peak velocity and time to peak displacement, see Table 1); however, because these differences occurred independent of tDCS polarity it is likely that this effect was due to practice and/or increased familiarity with the movement task rather than tDCS itself. In comparison, relatively strong effects of tDCS on stopping ability and response timing were observed. Specifically, while no significant effects were observed following cathodal tDCS, anodal tDCS resulted in earlier response initiation on control trials and a decreased probability of stopping on stop trials. Although a decrease in the probability of stopping may suggest that anodal tDCS led to a decrease in inhibitory function, the observation that responses were initiated earlier during control trails suggests that stopping ability may have been compromised by an effective decrease in the stop-signal latency.

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Table 1.

Mean (SD) values for kinematic variables observed both pre- and post-tDCS in both stimulation conditions

	Anodal Stimulation		Cathodal Stimulation	
Kinematic Variable	**pre-tDCS**	**post-tDCS**	**pre-tDCS**	**post-tDCS**
Peak velocity (deg/s)	320.95 (122.26)	336.47 (144.23)	350.90 (117.35)	325.97 (98.05)
Time to peak velocity (ms)	67.61 (26.87)	52.23 (27.43)*	65.61 (21.18)	60.46 (16.55)*
Peak displacement (deg)	18.90 (5.91)	19.90 (6.26)	21.62 (4.76)	19.39 (2.91)
Time to peak displacement (ms)	116.46 (34.37)	102.94 (32.76)*	118.62 (30.67)	110.47 (26.63)*
Final position (deg)	14.76 (6.25)	16.04 (5.50)	17.41 (4.93)	15.61 (3.57)
Movement time (ms)	166.98 (27.93)	165.76 (22.86)	173.08 (29.23)	165.50 (30.77)

** Significant ($p < .05$) difference compared to pre-tDCS block*

A previous study utilizing a stop-signal reaction time (SSRT) task also found that applying anodal tDCS over the region of the SMA affected stopping probability [16]. Specifically, while no changes were observed in "go" reaction times or in stop-signal reaction times, the authors did find that non-cancelled response rates (i.e., trials where participants received a stop-signal but were unable to inhibit the movement) were significantly altered: Anodal tDCS decreased non-cancelled rates (i.e., increased stopping probability), while cathodal tDCS increased non-cancelled rates (i.e., compromised stopping ability). Given that a change in stopping performance was observed in this previous SSRT task, it was expected that similar results would be observed in the current study where an anticipation-timing stop-signal task was used. That is, similar changes in stopping ability should be observed if the SMA was involved in inhibitory control in a similar way during both tasks. However, we observed a result opposite to that reported by Hsu et al. [16]. More precisely, while cathodal tDCS did not significantly affect the rate of non-cancelled responses (Fig. 1B), anodal tDCS led to an *increase* in the rate of non-cancelled responses (Fig. 1A) whereby participants made movements on stop trials more often, and were thus less successful at inhibiting the planned response. It therefore appears that in the current study anodal tDCS applied over the SMA diminished participants' ability to inhibit the planned action [cf. 16]. Although an increased percentage of partial responses was observed for the 140 and 170 ms stop times (compared to 80 ms), this pattern of results has been reported previously [e.g., 6]. More importantly, however, the probability of observing partial responses was unaffected by the application of tDCS.

The different effect of tDCS applied over SMA seen in the current study compared to that reported by Hsu et al. [16] may be explained by differences in task demands leading to changes in the activation balance between movement-related processes and inhibitory processes [6, 23]. There is a fundamental difference in the relative timing of stimuli for initiating and inhibiting a response in SSRT tasks compared with anticipation-timing tasks. In stop-signal tasks a "go" stimulus is always presented first followed by a stop-stimulus on a relatively small proportion of trials, but anticipation-timing tasks require participants to anticipate the arrival of the "go" stimulus, which may or may not occur (i.e., the clock hand may stop prior to arriving to the target). As such, anticipation-timing tasks do not involve any temporal uncertainty regarding the movement, while the time at which the movement must be executed during a stop-signal task is only known when the "go" stimulus is presented. The differences in temporal uncertainty between these two types of tasks have been suggested to result in changes in the timing of movement preparation [2, 4], and may have affected the activation balance between the movement production and inhibition processes [23].

Rather than increasing the inhibitory activity in SMA, it is possible that anodal tDCS led to increased preparatory-related activity, as significantly earlier response onsets were observed with respect to the target post-tDCS (Fig. 2). It has been well documented that the SMA is strongly involved in preparation for action. For example, movement-related neurons in the SMA have been shown to increase in firing activity throughout the preparatory time interval with peaks in firing rate occurring near the onset of movement [24]. Increasing the excitability of the SMA using anodal tDCS may have led to earlier movement initiation through an increase in this motor preparatory activity. Effectively, this early response initiation decreased the stop-signal latency with respect to the target: The interpretation of a stop-signal latency relies on the assumption that participants are, on average, initiating their movement on control trials coincidently with the clock hand arriving at the target. Thus, if participants are initiating their movements late on average in control trials, the effective stop-signal latency on stop trials is longer [see 1]; conversely, if participants initiate their movements early, the effective stop-signal latency is shorter. It is quite possible that the reason participants showed an increased likelihood of non-cancelled responses following anodal stimulation is due to this average earlier movement onset and effectively shorter stop-signal latency. As seen in Fig. 2, a similar trend towards earlier response initiation in the post-stimulation test was seen for both cathodal and anodal tDCS, though this difference was small following cathodal tDCS and was only significant for anodal tDCS ($p < .01$).

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Given this common trend for both polarities, it is possible that another factor contributed to the observed earlier responses, such as practice or even placebo effects. However, we feel that this is explanation is unlikely since an analysis showed that little learning was occurring within each block of trials (at least for response onset time) and thus the changes observed were more likely a result of the application of tDCS. Finally, anodal tDCS may have in fact led to a decrease in direct inhibitory control in the SMA [13]. If this is true, then the decreased probability of inhibition seen post-anodal tDCS may in fact reflect decreased inhibitory control, and may not be a consequence of the earlier responses.

One limitation of our results stems from the fact that there appears to be no significant differences in stopping probability between post-anodal and post-cathodal trials (Fig. 1). This may be interpreted to suggest that there was in fact no effect of tDCS. However, given that data collection for each polarity took place on separate days, it may be difficult to justify between-polarity comparisons, as the main question concerned how performance was affected following tDCS in a particular session. Indeed, pre-tDCS stopping probability appears to have differed between polarities making the interpretation of stopping results between polarities challenging. Some insight might be gained if it is accepted, as argued above, that differences in stopping probability stemmed from differences in response onset time in control trials. Analysis of grouped data showed that even though there were differences in time of responding (with respect to the target) in the pre-tDCS blocks, we only observed a *change* in time of response onset following anodal stimulation (Fig. 2). This data shows that although there were different initial levels of performance between pre-tests, there was a large change in performance following anodal-tDCS that resulted in a significantly decreased time of responding (both compared to pre-tDCS as well as to post-cathodal tDCS). At the same time there was no significant change in performance between pre-tDCS and post-tDCS trials with cathodal stimulation suggesting that anodal tDCS did indeed have an effect on time of responding, effectively reducing stop-signal latency.

There is some controversy regarding the specific role the SMA has in the stopping of movement. Recently, researchers found that participants with a higher GABA concentration in SMA showed a weaker inhibition of automatic priming effects in a subliminal prime-mask reaction time (RT) task. If the SMA was involved in implementing inhibition directly, more GABA would be expected to lead to a stronger inhibition of the prime. However, the authors found that increased GABA was correlated with decreased inhibition of the prime. This finding was interpreted as evidence that the SMA was involved in the production of inhibition (i.e., starting the inhibition process) and that increasing its activity led to greater inhibition of the inhibitory activity, or in other words, a decreased inhibition of the effect of the prime [25]. Importantly, in the same study, stop signal RT did not correlate with SMA GABA concentration, further suggesting the SMA is not directly involved in the implementation of inhibitory motor activity [25]. As the SMA-proper may be more involved in the production of the inhibitory response [25], it is possible that in the current experiment up-regulating SMA may have acted to inhibit the production of the inhibitory response, leading to an increased probability of, and/or earlier "go" response. In contrast, a recent study showed that disrupting processing in the pre-SMA using suprathreshold TMS diminished stopping ability in a stop-signal paradigm. This result suggests that at least the pre-SMA can play a critical role in implementing stopping [13]. The different results found in these studies highlight the functional differences between the pre-SMA and SMA, though they both are thought to contribute to inhibition [11].

It is important to note that the pre-SMA was said to have been specifically targeted in the study by Hsu et al. [16] as opposed to the SMA-proper in the current study, though the low focality of tDCS may not allow for such a distinction. That is, the current experiment aimed to modulate the excitability of the SMA, but likely also affected the pre-SMA. Given their functional distinction [26], modulating both areas may have caused interactions that ultimately altered the behavioural effects. An inherent weakness of tDCS the way it is employed currently is the potential for current spread over cortical areas not intended for stimulation [15]. Though the active electrode was placed over the SMA-proper, other motor areas may have been affected, which may have been responsible for the earlier movement initiation times seen following anodal tDCS stimulation. It has also been suggested that remote cortical areas may be affected by tDCS due to dense connectivity with the targeted brain area [27]. The primary motor cortex (M1) is not only situated directly posterior to the SMA, but also has been shown to have both dense anatomical and strong effective connectivity with the SMA [28]. While anodal tDCS applied over premotor cortex has been shown to lead to a decrease in intracortical inhibition in M1, single pulse motor evoked potentials were unaffected [27]. Thus, although unlikely, the excitability of M1 or other brain regions may have been modulated along with SMA either by unintended current spread or remote activation, but because we did not monitor these areas it cannot be stated with any degree of certainty. Recent studies suggest that a 4x1 electrode montage (high-definition tDCS) may be effective in generating more focal changes in cortical excitability [20, 29].

Conclusion

In this experiment, tDCS was applied over the area of the SMA, and the effects on motor performance during an anticipation-timing task were investigated. While

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significant effects were not seen following cathodal tDCS, anodal tDCS resulted in earlier response initiation in control trials and a decreased probability of a successful withholding of movement on stop trials. We suggest that anodal tDCS resulted in early response initiation leading to an effectively reduced stop-signal time. This decreased stop-signal latency may have resulted in the decreased probability of inhibition, rather than a decrease in inhibitory control. From a motor control perspective, the dynamic nature of the environment often requires one to be able to react to stimuli, to act concurrently with events, or even to withhold actions; therefore it is not surprising that the brain-behaviour relationships and consequently structure-function relationships are complex. In this respect, tDCS appears to be a promising neuromodulation technique for inhibitory processing, offering a potential intervention for clinical populations with inhibitory deficits including attention-deficit/hyperactivity disorder [30], obsessive compulsive disorder [31], Tourette's syndrome [32], and Parkinson's disease [33, 34]. However, our results suggest that further research is required in order to identify the neuromodulatory target that produces the best possible improvements in inhibitory control.

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