

# Response Inhibition Induced in the Stop-signal Task by Transcranial Direct Current Stimulation of the Pre-supplementary Motor Area and Primary Sensoriomotor Cortex

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**Abstract.** [Purpose] This study examined whether transcranial direct current stimulation (tDCS) of both the pre-supplementary motor area (pre-SMA) and primary sensoriomotor cortex (M1) alters the response time in response inhibition using the stop-signal task (SST). [Methods] Forty healthy subjects were enrolled in this study. The subjects were randomly tested under the three: the pre-SMA tDCS, M1 tDCS, and Sham tDCS conditions. All subjects performed a SST in two consecutive phases: without or after the delivery of anodal tDCS over one of the target sites (pre-SMA or the M1) and under the Sham tDCS condition. [Results] Our findings demonstrated significant reductions in the stop processing times after the anodal tDCS over pre-SMA, and change response times were significantly greater under the pre-SMA tDCS condition compared to both the M1 tDCS condition and the Sham tDCS condition. There was no significant major effect after delivery of the tDCS for the go processing times observed among the three conditions. [Conclusion] Anodal tDCS of the pre-SMA or M1 during performance of the SST resulted in enhancement of the volitional stop movement in inhibitory control. Our results suggest that when concurrently applied with the SST, tDCS might be a useful adjuvant therapeutic modality for modulation of the response inhibition and its related dynamic behavioral changes between motor execution and suppression.

**Key words:** Transcranial direct current stimulation, Stop signal task, Response inhibition

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## INTRODUCTION

Response inhibition is usually attributed to suppression of an inappropriate action in executive control<sup>1)</sup>. Deficits in response inhibition are thought to be a key component of some neurological and psychopathological disorders<sup>2, 3)</sup>. Many studies have investigated the cognitive processes of the elective response between motor execution and suppression using the stop-signal task<sup>4, 5)</sup>.

The stop-signal task (SST) is based on the stop-signal paradigm that is most suitable for the study of response inhibition and is appropriate for the measurement of response times in both motor execution and suppression<sup>6, 7)</sup>. The SST initiates the 'go process' or the 'stop process', which is generated by the display of each stimulus<sup>7)</sup>. When performing the SST, the go process is associated with activation of the cortico-basal ganglia-thalamocortical circuit, whereas the stop process is associated with activation of the fronto-basal ganglia circuit<sup>8-10)</sup>. Previous studies have reported that the pre-supplementary motor area (pre-SMA) is especially involved in the initiation of self-paced actions and the mediation of motor suppression<sup>11-13)</sup>. In addition, the primary motor cortex (M1) is also involved in volitional suppression

as well as movement preparation since they are mediated by its motor programming circuits<sup>5, 14)</sup>.

Recently, transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS), which are known as modulators of cortical excitability, have been used to facilitate skill acquisition during the performance of a motor task<sup>15-17)</sup>. In the stimulation of cortical neurons by TMS or tDCS, the excitability of cortical neurons is increased at the anode, and decreased at the cathode. Decreased cortical excitability and increased intracortical inhibition have been demonstrated; however, the details of change in cortical excitability during performance of the SST are not fully understood. Despite evidence for a neural contribution to motor execution by M1 or the pre-SMA, no evidence of the contribution to response inhibition in the functional role of either area has been reported. Therefore, the objective of the present study was to determine whether application of anodal tDCS to M1 or the pre-SMA contributes to response inhibition during performance of the SST after delivery of tDCS.

## SUBJECTS AND METHODS

### Subjects

Forty healthy participants with no neurological or psychiatric history were recruited. Participants were excluded

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if they had prior exposure to other sequence-learning studies or externally-stimulated experiments of the cerebral cortex, such as transcranial magnetic stimulation (TMS) or transcranial direct current stimulation (tDCS). All participants provided their written informed consent prior to participation in this experiment. Ethical approval was obtained from the research ethics committee of Yeungnam College in accordance with the ethical standards of the Declaration of Helsinki. Subjects were randomly tested under the M1-tDCS, pre-SMA tDCS and Sham tDCS conditions, on separate day.

### Methods

Direct current was delivered by a battery-driven constant DC current stimulator (Phoresor II Auto Model PM 850, IOMED, USA) and transferred through a water-soaked pair of surface sponge electrodes (35 cm<sup>2</sup>). To stimulate the primary motor cortex (M1), the center of the anode electrode was placed over C3 or C4 (international 10/20 electroencephalographic system), which is well known as the neural representational area of the motor function of the hand<sup>18, 19</sup>. To stimulate the pre-supplementary motor area (pre-SMA), the center of the anode electrode was placed 4 cm anterior to Cz (international 10/20 electroencephalographic system) on the central midline, which is the neural representational area of conflict resolution or monitoring in motor function<sup>20</sup>. This site of pre-SMA localization was used in a previous study<sup>20</sup>. The cathodal electrode was placed over the contralateral supraorbital area.

The stop signal task (SST) was performed using a computer and stimulus presentation software (STOP-IT, Universiteit Ghent, Belgium). It consisted of Go (75% of all trials) and Stop (25% of all trials) trials. The Go signal, such as a square (■), circle (●), diamond (◆), or triangle (▲) was presented randomly on a monitor during conduct of the Go trials. The Stop signal, the shape of an X, was displayed following a variable delay (the Stop-Signal Delay, SSD) subsequent to the overlapping figure signal. The SSD was primarily set to 250 msec and was continuously adjusted with the tracking procedure in order to obtain a probability of responding of 50%. That is, when the participant successfully stopped, the SSD increased by 50 msec, whereas, when the stop was unsuccessful, the SSD decreased by 50 msec. This setting reflected the response inhibition, which describes the probability of responding to a given SSD according to the stop-signal paradigm. The Stop-Signal Reaction Time (SSRT), which corresponds to the latency of the stopping process, was estimated by subtracting the mean SSD from the mean No-Signal Reaction Time (NSRT) during conduct of the Go trials. The analysis program (ANALYZE-IT, Universiteit Ghent, Belgium) provides descriptive statistics, including mean NSRT, probability of responding, and SSD, and provides reliable SSRT estimations<sup>21</sup>.

All participants were seated in front of a table with the non-dominant hand on the response keys, which consisted of the left, right, up, and down arrow keys. Following the visual stimulus on the front of the computer monitor, participants were instructed to press the button as quickly as possible according to the corresponding stimulus dur-

ing conduct of the Go trials. In the Go trials, each stimulus shape was paired with a single correct response key (square, circle, diamond, and triangle with the left, right, up and down arrow keys, respectively). However, the participants were told not to press any buttons in response to the stop stimulus during conduct of the Stop trials. In the SST, the presented stimuli lasted for 1,250 msec, and a default inter-stimuli interval of 2,000 msec was provided. A fixation cross was presented at the center of the monitor for the null (baseline) period until the start of the next trial. Each trial began with the presentation of the fixation cross, which was replaced by the Go trial stimulus after 250 msec. If a button was pressed prior to exhibition of the Go signal, this trial was excluded from the analysis, and if the wrong button was pressed in response to the signal, it was also excluded from the analysis.

All participants performed the SST, which consisted of one block of 132 trials (Go trials: 99, Stop trials: 33), during two consecutive tDCS phases: the pre-tDCS phase and the post-tDCS phase. Participants first performed only the SST test without delivery of tDCS for acquisition of baseline parameters: SSRT and NSRT. After the pre-tDCS phase, participants received tDCS over one of the target sites (M1 or the pre-SMA) and one with no tDCS depending on the condition being tested. Participants then performed the final SST test in the post-tDCS phase. Each participant was tested pre- and post-tDCS under the three conditions (i.e. the M1, pre-SMA, and Sham tDCS). The time interval between each condition was at least 24 hours. A constant current of 1mA intensity was applied for 10 minutes. All participants felt the current as a mild itching sensation or senselessness under the electrodes, depending on the sensitivity of the individuals, who were blinded to the tDCS condition. For the Sham tDCS condition, electrodes were placed in the same positions as for anodal M1 stimulation; however, the stimulator was turned off after 5 seconds, as previously described. Thus, participants in the Sham tDCS condition initially felt a mild itching sensation for one second and believed that they were receiving tDCS in all procedures, but received no current for the remainder of the procedure.

Analysis of variance (ANOVA) was used for analysis of demographic data, including sex and age. All data were analyzed in terms of the means of SSD, SSRT and NSRT, only when the correct movement responses to the Go and Stop signal occurred. The untrimmed mean reaction time in the Go trials was estimated initially (NSRT), and the mean SSD was then subtracted from this value for calculation of the SSRT in the Stop trials. The effect of tDCS under the three conditions was determined using a 2 (factors: M1-tDCS, pre-SMA tDCS, and Sham tDCS) × 2 (test phase: pre-tDCS, post-tDCS) ANOVA with repeated measures on the two dependent variables, SSRT and NSRT. SPSS, version 18.0 was used to conduct all statistical analyses, and  $p < 0.05$  was accepted as statistically significant.

## RESULTS

Among the three groups, there was no significant dif-

**Table 1.** Changes in response times to visual stimuli among the SST test phases (mean  $\pm$  SD)

	M1 tDCS		Pre-SMA tDCS		Sham tDCS		Test	Condi- tion	Interaction (Test $\times$ Condition)
	pre	post	pre	post	pre	post			
SSRT (msec)	387.05 $\pm$ 64.35	339.50 $\pm$ 45.74	382.25 $\pm$ 58.57	301.62 $\pm$ 42.97	385.04 $\pm$ 47.97	351.75 $\pm$ 33.90	0.000*	0.036*	0.004*
NSRT (msec)	890.08 $\pm$ 88.46	854.08 $\pm$ 117.64	885.58 $\pm$ 84.75	887.92 $\pm$ 106.34	886.75 $\pm$ 86.79	880.43 $\pm$ 115.47	0.261	0.777	0.382

NSRT: no-signal reaction time, SSRT: stop-signal reaction time, \* $p < 0.05$

ference in terms of sex (22 males, 18 females) or age (22.97  $\pm$  2.21 years) affecting accomplishment of the SST. Table 1 shows the processing times of both the Go and Stop trials (i.e. the NSRT and SSRT) under each condition during the test phases. In the SSRT, the results of the univariate analysis showed a large main effect of the test phase ( $p < 0.05$ ), condition ( $p < 0.05$ ), and test-by-condition interaction ( $p < 0.05$ ), suggesting that the response times of the stop-signal were lower after delivery of tDCS, compared to those under the sham condition. The results of the post-hoc comparisons showed a significant decrease of the SSRT under the pre-SMA condition, compared to both the M1 and the sham conditions ( $p < 0.05$ ). In the NSRT, the test phase ( $p > 0.05$ ), condition ( $p > 0.05$ ), and test-by-condition interaction ( $p > 0.05$ ) showed no major effects, suggesting that the response times of no-signal were similar under the three conditions.

## DISCUSSION

The main finding of our study was a significant enhancement of the stop movement of the non-dominant hand during performance of the SST after delivery of anodal tDCS of the pre-SMA, but not under the sham condition. In addition, performance of the SST after application of anodal tDCS to M1 resulted in a significant reduction in the stop process time; however, there was no significant difference, compared to the sham condition. Under all tDCS conditions, there were no significant changes in the go processing times. Therefore, improvement in the stop process could be due to enhanced inhibitory control through the effect of direct stimulation after delivery of tDCS to the pre-SMA.

Previous studies have reported the role of the pre-SMA in control of volitional action<sup>4, 11, 22, 23</sup>. These studies confirmed the critical role of the pre-SMA in inhibiting competition with single motor plans in situations of response conflict. In addition, many studies have also reported that M1 plays a vital role in rapid processing between motor execution and suppression in the active stop process<sup>5, 24, 25</sup>. Although go and stop processes, which work alternatively on each other in the SST, are the functional separation between response execution and suppression, they are operated according to the motor executive commands originating from M1. Therefore, to demonstrate an improvement in inhibitory control of stimulation to the pre-SMA and M1, we attempted an experimental design which performed a comparison with the sham condition.

Our findings demonstrated enhancement of the stop

movement after application of anodal tDCS to the pre-SMA, and are in line with those of other studies demonstrating short SSRT in the SST and other aspects of the cognitive process induced shown by tDCS<sup>10, 11</sup>. Previous neuroimaging studies have suggested greater activity in the pre-SMA in association with more efficient response inhibition by shortened SSRT<sup>4, 8, 12</sup>. These results imply that response inhibition is improved by facilitation of functional connections between the pre-SMA and the basal ganglia, which are known as a braking system for constant responses, indicating activation of the pre-SMA prior to initiation of a planned action. In addition, the increased activation of the pre-SMA influenced the stop process, but not the go process, and it appears to be especially crucial for cancelling responses<sup>22, 23</sup>. Other studies have suggested that goal-directed actions can be automatically started and guided to completion by information in the task environment<sup>26, 27</sup>. Accordingly, both the goal of the stop movement and the attention of the stop signal would expedite the stop process and facilitate initiation of response inhibition.

Many studies of tDCS have suggested that application of anodal tDCS to M1 during performance of a motor task involving hand movements resulted in enhanced motor performance and cortical excitability by recruitment of more cortical neurons<sup>28, 29</sup>. The present results showed a reduction of response time compared to the sham condition. They are compatible with the results of prior studies using non-invasive neurostimulation, and motor execution was improved by the after-effect following tDCS due to enhancement of cortical excitability. Our results show that after delivery of tDCS to M1, only the response times of the stop process decreased, but the response time of the go process did not. Previous studies have suggested that the efficiency of response inhibition improves the preparation of the go process before display of the stop-signal, and it can reduce the length of the response time during the stop process<sup>26, 27</sup>. Therefore, sufficient preparation resulted in shortened response times of the stopping process, even though relatively reduced cortical activation was shown in imaging results.

In conclusion, application of anodal tDCS to the pre-SMA or M1 during performance of the SST resulted in enhancement of the volitional stop movement in inhibitory control. Many studies of the SST have shown that the stop process generated by the stop-signal is like a focal emergency brake for inhibitory control, which can suppress the excitability of the whole motor system<sup>30, 31</sup>. Therefore, application of anodal tDCS to the pre-SMA or M1 is a useful adjuvant intervention modality for modulation of response

inhibition and its related dynamic behavioral changes. The most important limitation of this study was that the subjects were not clinical patients. Thus, further studies for the development of clinical applications in mediation of inhibitory control will be needed.

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