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RESEARCH ARTICLE

# Modulating behavioral inhibition by tDCS combined with cognitive training

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**Abstract** Cognitive training is an effective tool to improve a variety of cognitive functions, and a small number of studies have now shown that brain stimulation accompanying these training protocols can enhance their effects. In the domain of behavioral inhibition, little is known about how training can affect this skill. As for transcranial direct current stimulation (tDCS), it was previously found that stimulation over the right inferior frontal gyrus (rIFG) facilitates behavioral inhibition performance and modulates its electrophysiological correlates. This study aimed to investigate this behavioral facilitation in the context of a learning paradigm by giving tDCS over rIFG repetitively over four consecutive days of training on a behavioral inhibition task (stop signal task (SST)). Twenty-two participants took part; ten participants were assigned to receive anodal tDCS (1.5 mA, 15 min), 12 were assigned to receive training but not active stimulation. There was a significant effect of training on learning and performance in the SST, and the integration of the training and rIFG–tDCS produced a more linear learning slope. Better performance was also found in the active stimulation group. Our findings show that tDCS-combined cognitive training is an effective tool for improving the ability to inhibit responses. The current study could constitute a step toward the use of tDCS and cognitive training as a therapeutic tool for cognitive control impairments in conditions such as attention-deficit hyperactivity disorder (ADHD) or schizophrenia.

**Keywords** tDCS · Cognitive training · Behavioral inhibition · rIFG · Stop signal task

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## Introduction

Behavioral adjustment corresponding to environmental changes constitutes a critical component of human nature, which is reflected by behavioral inhibition processes (Barkley 1997; Li et al. 2006, 2008; Logan and Cowan 1984). A deficit in inhibiting responses is a characteristic of several psychiatric disorders such as attention-deficit hyperactivity disorder (ADHD; Aron and Poldrack 2005; Barkley 1997), obsessive compulsive disorder (OCD; Rosenberg et al. 1997) and schizophrenia (Hoptman et al. 2004; Kiehl et al. 2000).

Transcranial direct current stimulation (tDCS), a non-invasive brain stimulation technique that modulates cortical excitability via applying a weak electrical current through the scalp, has been successfully used as a tool to improve behavioral inhibition (Beeli et al. 2008; Hsu et al. 2011; Jacobson et al. 2011). Previous work (Jacobson et al. 2011) showed that unilateral anodal tDCS over the right inferior frontal gyrus (rIFG) improved the ability to inhibit responses as assessed by the stop signal task (SST;

Verbruggen et al. 2008). In a follow-up study (Jacobson et al. 2012), resting EEG recorded after applying the same montage as tDCS showed a selective diminution of Theta band activity compared to sham stimulation.

Based on functional imaging and studies using electrophysiology, a network including prefrontal cortical areas and subcortical brain regions has been determined to control behavioral inhibition processes in the SST. Li et al. (2006), for instance, reported that efficient response inhibition was associated with increased cortical activation in superior medial and precentral frontal brain areas. In rats, lesions of the orbitofrontal cortex resulted in increased stop signal response times and lesions of the subthalamic nucleus reduced general stopping accuracy (Eagle et al. 2008). Another brain area shown to be a major component in the inhibition network is the rIFG. For example, Li et al. (2008) showed that successful inhibition was associated with greater activation of multiple cortical areas, including the rIFG and middle frontal gyri. Rubia et al. (2001) also showed common activation foci across different stop task versions in bilateral but predominantly right hemispheric inferior pFC. Similarly, patients with rIFG, but not left IFG (lIFG), lesions show a selective deficit in response inhibition as measured by the SST (Aron et al. 2003).

Cognitive training has been shown to be effective in improving executive functions such as sustained attention (Ben-Yishay et al. 1987) and more complex components of attention (Kerns et al. 1999; Sturm et al. 1997), as well as working memory (Klingberg et al. 2002, 2005), neuropsychological measures (Ethier et al. 1989; Gray et al. 1992; Sohlberg and Mateer 1987), and academic performance (Kerns et al. 1999; Shalev et al. 2007). Several studies have investigated the generalization of attentional cognitive training approaches and found an effect on reading ability (Raskin and Mateer 1993), work performance (Mateer et al. 1990), everyday memory ability (Mateer and Sohlberg 1988), and driving (Sivak et al. 1984). Posner and Rothbart (2005) argued that the generalization of attentional cognitive training is supported by electrophysiological changes as Baribeau et al. (1989), Posner and Rothbart (2005), and Raskin (1998) demonstrated a "normalization" of brain electrical activity following attention training.

Only few previous studies tested for practice effects in response inhibition. Cohen and Poldrack (2008) found that behavioral improvements induced by a single 3-h training session in a motor sequence learning task did not affect the ability to inhibit responses, as indicated by an absence of SSRT differences between the testing sessions. They concluded that increased automaticity is not associated with a loss of control over these automatized movements. Logan and Burkell (1986) trained participants for 6 days using a stop signal paradigm and confirmed Logan and Cowan (1984) findings that stop signal paradigm is relatively stable over practice.

Although the effects of both tDCS and cognitive training have been investigated separately, the effects of the integration of the two methods are only beginning to be explored (Cohen-Kadosh et al. 2010; Reis et al. 2009). In this study, we investigated the effect of cognitive training integrated with rIFG-tDCS on behavioral inhibition and specifically tested whether (1) multiple-session training is effective in improving the ability to inhibit responses and (2) the integration with rIFG-tDCS would further induce/facilitate training-induced improvements. Neither cognitive training alone nor the integration of training with tDCS has been explored with behavioral inhibition.

## Methods

### Participants

Twenty-two healthy adults participated in the study. Participants were randomly assigned to two groups; ten of them (seven women, three men) with a mean age of 23.58 years (SD, 4.16 years) received tDCS (*Anodal* group) during training, and twelve of them (seven women, five men; matched for age) did not receive stimulation (*Control* group) during training. All participants were right-handed, without any known neurological or psychiatric conditions, and/or metallic implements. All were naive to the nature of the experiment and gave a written informed consent before taking part in the study. Inattention and impulsivity were assessed via the Adult ADHD Self-Report Scale (ASRS; Reuter et al. 2006).

### Procedure

Participants came to the laboratory for five consecutive days and performed the stop signal task (SST) for about 8 min each day. Prior to performing the task, the experimental group (*Anodal*) received anodal tDCS (1.5 mA) over the rIFG for 15 min. tDCS was given from the first to the fourth day, but not on the fifth day. The fifth day's test was aimed to investigate the sustainability of the effects of tDCS, 24 h after stimulation had stopped.

### tDCS

A direct current of 1.5 mA for 15 min was induced by two saline-soaked surface sponge electrodes (5 × 7 cm) and delivered by a battery-driven, constant-current stimulator (Magstim®, Whitland, Wales, UK). Previous studies have shown this intensity of stimulation to be safe in healthy volunteers (Iyer et al. 2005).

In the *Anodal* group, the anode electrode was placed over the rIFG, and the cathode electrode was placed over the left orbitofrontal cortex (lOFC). Localization was established using the 10–20 EEG system, in which rIFG was identified as the crossing point between T4-Fz and F8-Cz (Monti et al. 2008). The lOFC electrode was positioned above the left eyebrow (Nitsche and Paulus 2000).

Stop signal task (SST)

We used the STOP-IT program by Verbruggen et al. (2008), which presented one of two symbols (circles and squares) on each trial. Participants responded to the stimuli by pressing the left or right key on a computer mouse as quickly as possible. However, in 25 % of the trials, an auditory stop signal was presented shortly after stimulus onset instructing participants to immediately stop their responses. The time between the stimulus and the stop signal (stop signal delay (SSD)) was adjusted after every stop signal trial. The task was started with an SSD of 250 ms. Following successful stopping, the SSD was increased by 50-ms increments; after unsuccessful stopping, the SSD was decreased by 50-ms increments. The tracking procedure yielded an overall ratio of *p* (response/stop signal) of .5. An auditory "beep" (750 Hz, 75 ms) was used as a stop signal and was randomly presented in 25 % of the trials. The task consisted of 192 trials divided into three blocks with a 10-s break between blocks. Eight practice trials were given at the start of each session, although the experimenter made sure that subjects understood the task and added practice trials when needed. A fixation sign (+) and visual stimuli were presented at the screen center, in a white font on a black background. The distance between participants and the screen was 55 cm, and the stimulus size was 1.5 $cm^2$. The response keys were the right mouse button for circles and the left mouse button for squares. The visual stimulus remained on the screen for 1,250 ms, and the ISI was 2,000 ms.

## Results

ASRS (ADHD Self-Report Scale) values showed that there was no baseline difference in the impulsivity levels between the two groups; an independent *t* test revealed a non-significant difference between the two groups in their ASRS scores (mean ASRS in the Anodal tDCS group was 14.458 (SEM 1.433) and mean ASRS in the control group was 12.450 (SEM 1.094); $t$ (20) = 1.077, $p$ = .294).

The index in the SST is the SSRT that was calculated as mean RT in the go trials minus mean SSD in the stop trials. Since we used a tracking procedure, the overall probability (respond/signal) was about .5 for all subjects (range, 43.8–59.6). In order to investigate whether training combined with tDCS affected behavioral inhibition, we conducted an analysis with the behavioral inhibition measurement, the SSRT (stop signal response time) as the dependent variable. A mixed design analysis of variance (ANOVA) with training days (*day 1, day 2, day 3, day 4*) as a within-subject variable and group (*Anodal, Control*) as a between-subject variable revealed a significant main effect for training days ($F$ (3, 60) = 6.818, $p < .001$), an insignificant main effect for group ($F$ (1, 20) = .998, $p$ = .330), and a significant interaction ($F$ (3, 60) = 2.775, $p$ = .049; Fig. 1a). Additional repeated measures ANOVAs were conducted for each of the experimental groups with training day as a within-subject variable. Analysis revealed a significant main effect ($F$ (3, 7) = 5.322, $p$ = .032) for the *Anodal* group, and an insignificant main effect for the *Control* group ($F$ (3, 9) = 1.702, $p$ = .236).

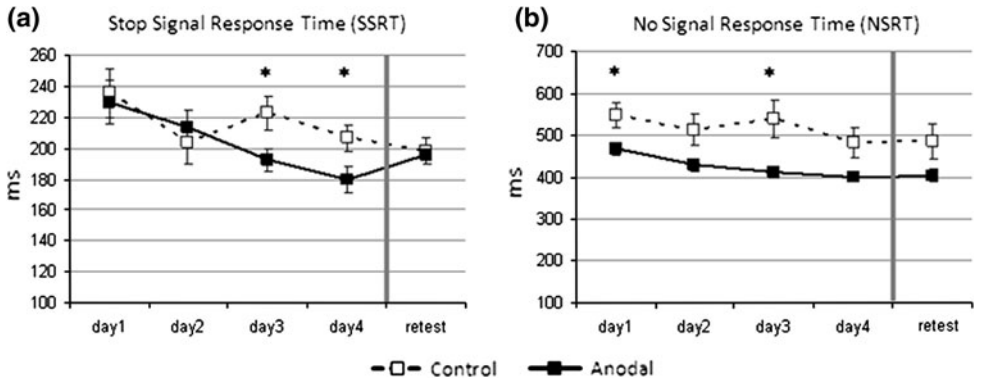


**Fig. 1** The effect of 4 days of cognitive training and tDCS on the performance in the stop signal task and the post-training retest (5th day). **a** The effect on the response inhibition measurement, stop signal response time (SSRT). The x-axis represents the five consecutive days; the y-axis represents time (msec). The performance of the Anodal tDCS group is plotted in *black* (*solid*), the *dashed line* represents the performance of the control group. **b** The effect on the control measurement, no signal response time (NSRT). The x-axis represents the five sequential days; y-axis represents the time (msec). The *solid line* represents the performance of the Anodal group, and the *dashed line* represents the performance of the control group. *Asterisk* represents $p < .05$

Contrast analyses were conducted for each group separately for SSRTs across days; a significant linear trend ($F$ (1, 9) = 17.485, $p$ = .002) was revealed in the *Anodal* group, whereas the analysis with *Control* group revealed an insignificant linear trend ($F$ (1, 11) = 1.896, $p$ = .196).

Additionally, we conducted independent samples $t$ tests to test for SSRT differences between the groups on each of the four training days; analysis revealed that the groups differed on the 3rd and 4th days, with superior performance in the tDCS group ($t$ (20) = .223, $p$ = .825; $t$ (20) = .495, $p$ = .625; $t$ (20) = 2.347, $p$ = .029; $t$ (20) = 2.176, $p$ = .042, for the first, second, third, and fourth day, respectively).

In order to investigate whether the manipulations resulted in generic increases in the speed of processing rather than a selective effect on behavioral inhibition, additional analyses were conducted with the control measurement, the no signal response time (NSRT) as the dependent variable. A mixed design ANOVA with training days (*day 1, day 2, day 3, day 4*) as a within-subject variable and group (*Anodal, Control*) as a between-subject variable revealed a significant main effect for training days ($F$ (3, 60) = 8.671, $p < .001$), a significant main effect for group ($F$ (1, 20) = 5.457, $p$ = .030), and an insignificant interaction ($F$ (3, 60) = 1.658, $p$ = .186; Fig. 1b). Similar analysis of accuracy revealed no significant effects, with high accuracy in both groups (general mean, 91 %; range, 87–94 %).

Further analyses were conducted in order to investigate the long-term effects of the training with and without tDCS. No significant differences were found between training day 4 and the retest in either group (*Anodal* group: $t$ (9) = 1.701, $p$ = .123; *Control group*: $t$ (11) = .944, $p$ = .366; Fig. 1a). A minor increase in SSRT was found in the *Anodal* group, whereas a minor decrease was found in the *Control* group, resulting in no significant differences between groups that extended to the fifth day ($t$ (20) = .230, $p$ = .821).

## Discussion

The ability to inhibit responses is crucial for daily functioning, and a deficit in this process is characterizing several psychiatric disorders (Aron and Poldrack 2005; Barkley 1997; Rosenberg et al. 1997; Hoptman et al. 2004; Kiehl et al. 2000). We aimed here to investigate whether training of behavioral inhibition combining with tDCS could improve this function. We investigated the effect of 4 days of cognitive training integrated with tDCS over rIFG on behavioral inhibition. Results indicate that training effectively improved the ability to inhibit responses and that the combination of training with tDCS generated a greater effect than multiple-session training alone. There was a significant main effect for training day and a significant interaction between training day and group with the SSRT measurement, and additional ANOVAs, conducted for each of the groups, revealed a significant main effect for the training in the *Anodal* group, whereas no significant main effect was found in the *Control* group. This finding in the control group is consistent with previous studies reporting the absence of reliable training effects in response inhibition (Cohen and Poldrack 2008; Logan and Burkell 1986). No significant difference in the ASRS questionnaire was found between the two groups; therefore, the possibility that the reported differences were due to a baseline difference in the subjects' impulsivity levels was excluded.

Average SSRT values in the *Anodal* group were consistently shorter (shorter SSRT indicates better ability to inhibit the responses) compared to the *Control* group on each of the days, apart from the second day; however, this difference reached significance only on the third and the fourth days. With respect to previous work (Jacobson et al. 2011), where a significant difference between anodal and sham stimulation conditions in a within-subject design was found, we assume that the initial insignificant difference observed in this study may have resulted from the application of a between-subject design. The training paradigm of the current study required a between-subject design, which is more susceptible to the rather large inter-individual variability (which was also observed in the previous work), and therefore is less sensitive to the small changes yielded in the dependent variable—the group (*Anodal* group/*Control* group).

In order to investigate whether our manipulation affected cognitive processing in a more general way beyond the ability to inhibit responses, we further analyzed its effect on the control parameter in the SST, the NSRT, that is, the RT in the go trials. There was a significant main effect, which suggests that the training affected also the general ability to discriminate between the two shapes and respond faster. However, there was no significant interaction between the two groups across days, showing that tDCS had no additional effect on these generic improvements.

In order to investigate the long-term effects of the training with and without tDCS, participants did the SST on the fifth day, that is, a retest without brain stimulation. The significant differences between the groups on day 4 did not survive to the retest on day 5, even though there was no significant change within groups between day 4 and retest. This suggests that the beneficial effects of tDCS are rather short-lived. Adjustments of the training and stimulation protocol in the form of a larger number of training sessions and trials as well as a higher stimulation intensity and duration may help to maximize the beneficial effects of

tDCS and thus increase the chances to induce long-lasting improvements. It may also help to stimulate concurrently with participants performing the task (as opposed to the offline protocol used in this study) to increase the reported effects.

One limitation of the current study was that participants of the control group did not receive sham stimulation (a stimulation protocol that is subjectively undistinguishable from the active stimulation protocol but without including real stimulation). It therefore cannot be ruled out that the reported findings may be the result of unspecific effects of brain stimulation compared to no stimulation. However, we would like to point out that participants of the Anodal group were informed that tDCS may or may not affect their performance in either way (positive or negative). We therefore think that unspecific increased or decreased levels of motivation in the Anodal group cannot solely explain the gradual and direction-specific training effects found in the active stimulation group over time.

An alternative interpretation is that tDCS of rIFG has a stronger effect when stop task performance has stabilized after some practice, hence the differences between the groups in day 3 and day 4, but not the first 2 days. This alternative requires future further testing by manipulating number of trials per session; however, even if this is the source of the facilitative tDCS effect, it still supports the superiority of combining tDCS and training over training only. Our findings have both theoretical and practical importance. On the theoretical level, we found that cognitive training improved the ability to inhibit responses and that the integration of rIFG–tDCS with cognitive training yielded a more substantial effect on behavioral inhibition. Furthermore, our findings might also prove the relevance of the development of applied techniques combining cognitive training and tDCS in order to improve behavioral inhibition, which might diminish symptoms of impulsive-based disorders.

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