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Transcranial Direct Current Stimulation Improves Executive Dysfunctions in ADHD: Implications for Inhibitory Control, Interference Control, Working Memory, and Cognitive Flexibility

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Abstract

Objective: This study examined effects of transcranial direct current stimulation (tDCS) over the dorsolateral prefrontal cortex (DLPFC) and orbitofrontal cortex (OFC) on major executive functions (EFs), including response inhibition, executive control, working memory (WM), and cognitive flexibility/task switching in ADHD. **Method:** ADHD children received (a) left anodal/right cathodal DLPFC tDCS and (b) sham stimulation in Experiment 1 and (a) left anodal DLPFC/right cathodal OFC tDCS, (b) left cathodal DLPFC/right anodal OFC tDCS, and (c) sham stimulation in Experiment 2. The current intensity was 1 mA for 15 min with a 72-hr interval between sessions. Participants underwent Go/No-Go task, N-back test, Wisconsin Card Sorting Test (WCST), and Stroop task after each tDCS condition. **Results:** Anodal left DLPFC tDCS most clearly affected executive control functions (e.g., WM, interference inhibition), while cathodal left DLPFC tDCS improved inhibitory control. Cognitive flexibility/task switching benefited from combined DLPFC-OFC, but not DLPFC stimulation alone. **Conclusion:** Task-specific stimulation protocols can improve EFs in ADHD. *(J. of Att. Dis. XXXX; XX(X) XX-XX)*

Keywords

ADHD, executive function deficits, cognitive control, transcranial direct current stimulation (tDCS), prefrontal cortex

Introduction

Attention deficit/hyperactivity disorder (ADHD) is one of the most pervasive neurodevelopmental disorders of childhood (Wilmshurst, 2014), with behavioral symptoms of hyperactivity, inattention, or both (Asherson, 2012). ADHD is characterized by a variety of deficits in cognitive domains such as attention (Barkley, 1997), inhibitory control (Rubia, Smith, Brammer, Toone, & Taylor, 2014), working memory (WM) (Kasper, Alderson, & Hudec, 2012), and executive functions (EFs) (Hudec et al., 2015). Cognitive deficits in ADHD include impaired inhibitory, attentional, and motivational control and timing (Smith, Taylor, Brammer, Toone, & Rubia, 2006), suggesting that ADHD is a disorder of control functions (Nezhad, Khodapanahi, Yekta, Mahmoodikahriz, & Ostadghafour, 2011). EFs deficits are among the most pervasive deficits in ADHD, such that ADHD was labeled as an executive dysfunction disorder, whose symptoms are based on a primary deficit in EFs (Barkley, 1997; Castellanos & Tannock, 2002; Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005).

Executive functioning or executive control encompasses high-level cognitive functions that are essential for goal-directed behavior. Failure of executive control underlies many psychiatric and neurological disorders and has been specifically shown in developmental psychopathologies, especially in ADHD (Pennington & Ozonoff, 1996). Several EF domains underlie symptoms of ADHD. A meta-analysis study about

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the EF concept of ADHD (Willcutt et al., 2005) reported response inhibition and WM as the most consistently impaired domains in ADHD. Similarly, other studies proposed impaired inhibitory processes as the core deficit in ADHD that disrupts other EF domains (Barkley, 1997; Nigg, 2001). However, the heteregenous executive dysfunctions in ADHD should be taken into account in order to have a more realistic picture of ADHD. For example, there are different types of behavioral inhibition (e.g., interference inhibition, prepotent inhibition) captured by different tasks on which ADHD children may perform differently.

Despite explicit heterogeneity in neuropsychological formulation of ADHD (Fair, Bathula, Nikolas, & Nigg, 2012), two major models have been proposed to account for behavioral deficits in ADHD: one is the "cognitive dysfunction or inhibition-based model," suggesting that inhibition-based executive deficits are core deficit in ADHD (Cepeda, Cepeda, & Kramer, 2000; Sonuga-Barke, 2005). According to this model, faulty inhibitory processes, especially those controlling motor responses (Nigg, 2001), lead to failure of executive control, which in turn result in impulsive behavior (Patros et al., 2015) and hyperactivity. The alternative "motivational dysfunction model" emphasizes on impaired reward processing rather than cognitive deficits, suggesting that behavioral deficits in ADHD are a result of deficient resource allocation or reduced arousal (Cepeda et al., 2000; Sonuga-Barke, 2005). These models are aligned with the "prefrontal hypothesis of ADHD" (Seidman, Valera, & Makris, 2005) according to which abnormalities in the frontostriatal circuitry and prefrontal cortex (PFC) are associated with behavioral deficits in ADHD. The dorsolateral PFC (DLPFC) is the primary region involved in inhibition-based models, whereas the orbitofrontal cortex (OFC) is more closely implicated in motivational dysfunction models (Seidman et al., 2005; Sonuga-Barke, 2005). These models also implicate that executive dysfunctions in ADHD involve both, "hot" and "cool" EFs. Dividing EFs into cool and hot is an organizing principle of EFs to distinguish between the control of purely cognitive (i.e., "cold") stimuli versus affective or reward-related stimuli (i.e., "hot") (Ward, 2015). The former is thought to be closely associated with DLPFC functions, whereas the latter is assumed to be closely related, but not limited to OFC activity (Rubia, 2011).

It is, however, of note that these models may downplay neuropsychological heterogeneity, which is more common in atypically developing children like ADHD (Fair et al., 2012). Recent theoretical papers suggest a substantial overlap between ADHD and typically developing children in some neuropsychological measures and neuroconitive mechanisms which are central to ADHD. According to this, only a subset of ADHD children can be considered clinically "affected" on the basis of any one measure or given neurocognitive mechanisms (Nigg, Willcutt, Doyle, & Sonuga-Barke, 2005). Therefore, although the models proposed here help in classification of ADHD subtypes, they may not include other subsets of children with ADHD.

Functional and structural abnormalities in the PFC are well-documented in ADHD and other disorders accompanied by EF impairments such as major depression (Nitsche, Boggio, Fregni, & Pascual-Leone, 2009), obsessive-compulsive disorder (OCD; Gonçalves et al., 2011), and schizophrenia (Callicott et al., 2000). Structural imaging studies found smaller prefrontal volumes in ADHD either in the right or left hemisphere (Bush, Valera, & Seidman, 2005), and dysfunction of DLPFC, ventrolateral PFC (VLPFC), and OFC are often reported in ADHD studies (Seidman et al., 2005). These PFC regions are associated with core cognitive deficits of ADHD; DLPFC and VLPFC are involved in vigilance, selective and divided attention, attention shifting, planning, executive control, and WM (Duncan & Owen, 2000; Elliott, 2003) and the OFC is associated with social disinhibition and impulsivity (Rolls, 2004). Functional imaging studies also revealed abnormalities of frontal regions in children with severe ADHD, including right hypofrontality during response inhibition tasks (Langleben et al., 2001). However, other studies reported mixed results and showed hyperfrontality in ADHD during response inhibition (Schulz et al., 2004).

More specifically, neuroimaging and brain stimulation studies suggest that decreased activity in the right lateral PFC (rLPFC) and right inferior frontal gyrus (rIFG) (Depue, Burgess, Willcutt, Ruzic, & Banich, 2010; Soltaninejad, Nejati, & Ekhtiari, 2015b; Verbruggen, Aron, Stevens, & Chambers, 2010) are responsible for poor inhibitory control. Other studies link poor inhibitory control in ADHD to reduced activation in the presupplementary motor area (pre-SMA) (Hsu et al., 2011) and increased activity in the frontal eye field (FEF) (Juan & Muggleton, 2012). For deficient WM and attentional control functions, left DLPFC (lDLPFC) hypoactivity seems to be involved (Brunoni & Vanderhasselt, 2014; Salehinejad, Ghanavai, Rostami, & Nejati, 2017). In sum, decreased activity in the rLPFC is suggested to be responsible for impaired inhibitory control, which is aligned with overall right hypofrontality in ADHD (Langleben et al., 2001), and decreased activity in the lDLPFC seems to be relevant for impaired WM and executive control.

Recent studies highlight the relevance of noninvasive brain stimulation for modulating cortical excitability (Lefaucheur, 2016; Nitsche et al., 2008). Transcranial direct current stimulation (tDCS) is a brain stimulation technique by which a weak direct current applied on the scalp modulates cortical excitability by shifting resting neuronal membrane potential. Anodal stimulation increases cortical excitability, whereas cathodal stimulation decreases it at the macroscopic level (Nitsche et al., 2009). tDCS has been shown to improve impaired components of EF not only in ADHD (Soltaninejad, Nejati, & Ekhtiari, 2015a) but also in

other disorders accompanied by impaired EF such as depression (Salehinejad, Ghanavai, et al., 2017; Nejati, Salehinejad, Shahidi, & Abedin, 2017) and OCD (Brem, Grünblatt, Drechsler, Riederer, & Walitza, 2014) as well as in healthy populations (Salehinejad, Nejati, & Derakhshan, 2017) depending on the targeted cortical area. Feasibility and safety of tDCS application in children has been documented in previous studies (Andrade et al., 2013; Krishnan, Santos, Peterson, & Ehinger, 2015).

Recent brain stimulation studies on ADHD tried to modulate cortical excitability of regions supposed to be relevant especially for inhibitory control. Hsu et al. (2011) showed that anodal tDCS over the pre-SMA improved inhibitory control, while cathodal tDCS impaired it. In a recently published study, we found that cathodal tDCS over the lDLPFC improved inhibitory control in prepotent response inhibition explored by a Go/No-Go task, while anodal tDCS over the same area impaired it (Soltaninejad et al., 2015a). This was the first tDCS study targeting the lDLPFC for improving inhibitory control. The foundation for this effect might be an indirect increase of cortical activity in the right DLPFC (rDLPFC), which is suggested to enhance inhibitory control (Depue et al., 2010), by cathodal tDCS over the lDLPFC due to transcallosal connections (Kobayashi & Pascual-Leone, 2003; Lindenberg, Nachtigall, Meinzer, Sieg, & Flöel, 2013).

While most of the available brain stimulation studies have focused on inhibitory processes in ADHD, there is lack of evidence about the effectiveness of tDCS with regard to other impaired EF domains in ADHD. Moreover, previous studies have shown mixed results regarding either hypofrontality or hyperfrontality in ADHD (Langleben et al., 2001; Schulz et al., 2004), and the way different PFC regions contribute to different EF domains in ADHD is still incompletely understood. Therefore, this study aims to investigate effects of tDCS of the DLPFC and OFC, which are the most involved PFC regions in ADHD deficits, on some of the significantly impaired executive functioning domains such as response inhibition (measured by the Go/No-Go task), interference control (measured by the Stroop task), WM (measured by the N-back test), and task switching/cognitive flexibility (measured by the Wisconsin Card Sorting Test-WCST) in two experiments. In Experiment 1, we only targeted the DLPFC using anodal/sham tDCS. In Experiment 2, we also targeted the OFC using anodal/cathodal/sham tDCS.

Based on findings of previous tDCS studies discussed above, we have three hypotheses. First, we hypothesized that anodal lDLPFC tDCS would improve WM, measured by the N-back test, and interference inhibition, measured by the Stroop task in ADHD (Hypothesis 1). This was based on the large body of evidence that hypoactivity of the lDLPFC is involved in impaired WM and executive dysfunction in disorders marked with frontal abnormalities. Second, we expected to observe improved prepotent response inhibition via cathodal stimulation of the lDLPFC (supposed to increase activity in the rLPFC) but not after anodal lDLPFC or cathodal rDLPFC tDCS, as these stimulation protocols are supposed to decrease activity in the rLPFC (Hypothesis 2). This was based on the finding suggesting that decreased activity of the rLPFC is responsible for poor inhibitory control in ADHD (Depue et al., 2010; Soltaninejad et al., 2015a). Finally, with regard to cognitive flexibility/task switching, which is measured by the WCST, we expect to observe improved WCST performance after simulation montages involving both DLPFC and OFC (Hypothesis 3). Although the WCST depends on DLPFC activity, performance on it is dependent on feedback and motivational processing that are related to medial regions of the PFC. (Summerfelt, Alphs, Funderburk, Strauss, & Wagman, 1991; Zanolie, Van Leijenhorst, Rombouts, & Crone, 2008). Indeed, the WCST measures some aspects of both hot (e.g., task switching, disinhibition) and cold EFs (i.e., executive control), implicating that it would benefit from activation of both DLPFC and OFC (Cepeda et al., 2000; Rolls, 2004).

Method

Participants

We enrolled 25 children (age $M_1 = 10$, $SD_1 = 2.23$; $M_2 = 9$, $SD_2 = 1.8$) diagnosed with ADHD symptoms according to the *Diagnostic and Statistical Manual of Mental Disorders* 5th ed (American Psychiatric Association, 2013) diagnostic criteria examined by a professional child psychiatrist. We monitored clinical symptoms via the Strengths and Weaknesses of ADHD Symptoms and Normal Behavior (SWAN) Rating Scale (Swanson et al., 2012), and results of this questionnaire confirmed symptoms of ADHD in subjects. Participants who scored 1.67 or higher were selected as participants with ADHD symptoms according to the Swanson, Nolan and Pelham Rating Scale (SNAP)–IV Parent Version Questionnaire (Swanson, Nolan, & Pelham, 1992). The cutoff point for inattentional and hyperactivity/impulsivity subscales were 1.78 and 1.44, respectively. Demographic information is shown in Table 1. Inclusion criteria were (a) not being on ADHD medication (e.g., methylphenidate) during the experiment; (b) being free from present or past history of neurological or psychiatric disorders, epilepsy, seizures, and head injury or loss of consciousness; and (c) moderate to severe ADHD scores on the SNAP rating scale. Both experiments were separate and none of the participants from the Experiment 1 participated in Experiment 2. The study was performed according to the latest version of the Declaration of Helsinki ethical standards and approved by the local institutional review board and the ethical committee of the local university. Given that participants were under legal age, their parents were

Table 1. Demographic Information of Participants.

Variable	Experiment 1	Experiment 2
Gender, male (female)	15 (0)	5 (5)
Age, *M* (*SD*)	10 (2.3)	9 (1.8)
Ritalin use history, yes (no)	15 (0)	10 (0)
SNAP inattention, *M* (*SD*)	1.45 (0.38)	1.82 (0.18)
SNAP, *M* (*SD*)	2.07 (0.48)	2.40 (0.35)
hyperactivity/compulsivity, *M* (*SD*)	1.76 (0.41)	1.87 (0.22)

Note. SNAP = Swanson, Nolan and Pelham Rating Scale.

instructed about experimental procedures. They then gave their informed consent before participation. Participants were free to withdraw from the experiment at any stage.

Experimental Protocol

We conducted a randomized, double-blinded sham-controlled trial. The design was a crossover study in which participants were randomly assigned to a sequence of tDCS treatment. Participants were randomly assigned to each stimulation condition. In Experiment 1 ($N = 15$) participants received anodal and sham tDCS and in Experiment 2 ($N = 10$) they received anodal, cathodal, and sham tDCS. EF domains (response inhibition, interference control, WM, task switching/cognitive flexibility) were assessed right after each stimulation condition in the same session. The order of stimulation conditions and EF tasks were randomized and counterbalanced across participants in both experiments to control for "order effects". Both experimenters and subjects were blind to the study hypothesis.

Procedure

Given that participants were children, we intensified standards and safety aspects of tDCS application in terms of electrode size and current intensity based on evidence from previous studies on children (e.g., Minhas, Bikson, Woods, Rosen, & Kessler, 2012). The tDCS device in use was "ActivaDose II Iontophoresis" Delivery Unit manufactured by Activa Tek, battery-driven with a 9-volt battery as its source. Electrical direct current generated by the stimulator was applied through a pair of saline-soaked sponge electrodes with size of 25 cm^2 (5 × 5) for 15 min. Given that participants are children with smaller head circumference, this electrode size was selected. The current was constant and of 1 mA in intensity, with a 30 s ramp up and down. In both experiments participants received tDCS for 15 min at 1 mA intensity with a 72-hr washout period between tDCS sessions. The stimulation montages of Experiment 1 were (a) anodal F3 (lDLPFC) / cathodal F4 (rDLPFC) tDCS, according to the international electroencephalogram (EEG) 10/20 system, and (b) sham stimulation of the same regions. In Experiment 2, we had three stimulation modalities: (a) anodal F3 / cathodal Fp2 (right OFC) tDCS with cathodal electrode placed at a minimal distance of 6 cm from the anodal electrode to decrease the probability of shunting of current through the scalp (Nitsche et al., 2007), (b) cathodal F3 / anodal Fp2 tDCS, and (c) a sham tDCS which served as control condition. During the sham condition, electrical current was ramped up for 30 s to generate the same sensation as active condition for the participant in the sham group and then turned off without the participants' knowledge (Palm et al., 2013). This method of sham stimulation has been shown to be reliable (Gandiga, Hummel, & Cohen, 2006). All patients were blind to the type of tDCS delivered in each session. A side effect survey was done after tDCS sessions (see Figure 1).

Cognitive Assessment

In this study, we measured response inhibition, interference control, WM, and cognitive flexibility/task switching with the Go/No-Go, Stroop, N-back, and WCST tasks respectively. We need however, to note to similarities and differences between the tasks. While the Go/No-Go and Stroop task rely on a global inhibitory mechanism (Verbruggen, Liefooghe, Notebaert, & Vandierendonck, 2005), each may capture different aspects of response inhibition. For example, some evidence suggests that both tasks measure prepotent response inhibition (Khng & Lee, 2014) however, it has been shown that the two tasks may index different constructs such as the response inhibition and interference control with unique neural contributions (Dimoska-Di Marco, McDonald, Kelly, Tate, & Johnstone, 2011). On the contrary, there are different tasks that capture response inhibition (e.g., Stop Signal Task-SST) and interference control (e.g., Flanker task) differently. It is essential therefore to consider such minor differences in different aspects of each cognitive construct and their respective tasks when interpreting results.

Go/No-Go task. To measure inhibitory control, we used the Go/No-Go task which is a less difficult measure of response inhibition compared with the SST. Participants are presented with stimuli in a continuous stream. They need to make a binary decision on each stimulus by pressing a button (Go) for a specific stimulus and not pressing the same button (No-Go) for a different stimulus. In this study, participants were presented with a plane which appeared on the screen in four directions, up, down, left, and right. They were instructed to press the button aligned with the plane (the Go condition), but to withhold pressing any button when the sound "Beep" was heard (the No-Go condition). Participants were then asked to focus on a cross on the screen and to press the response button "as quickly and

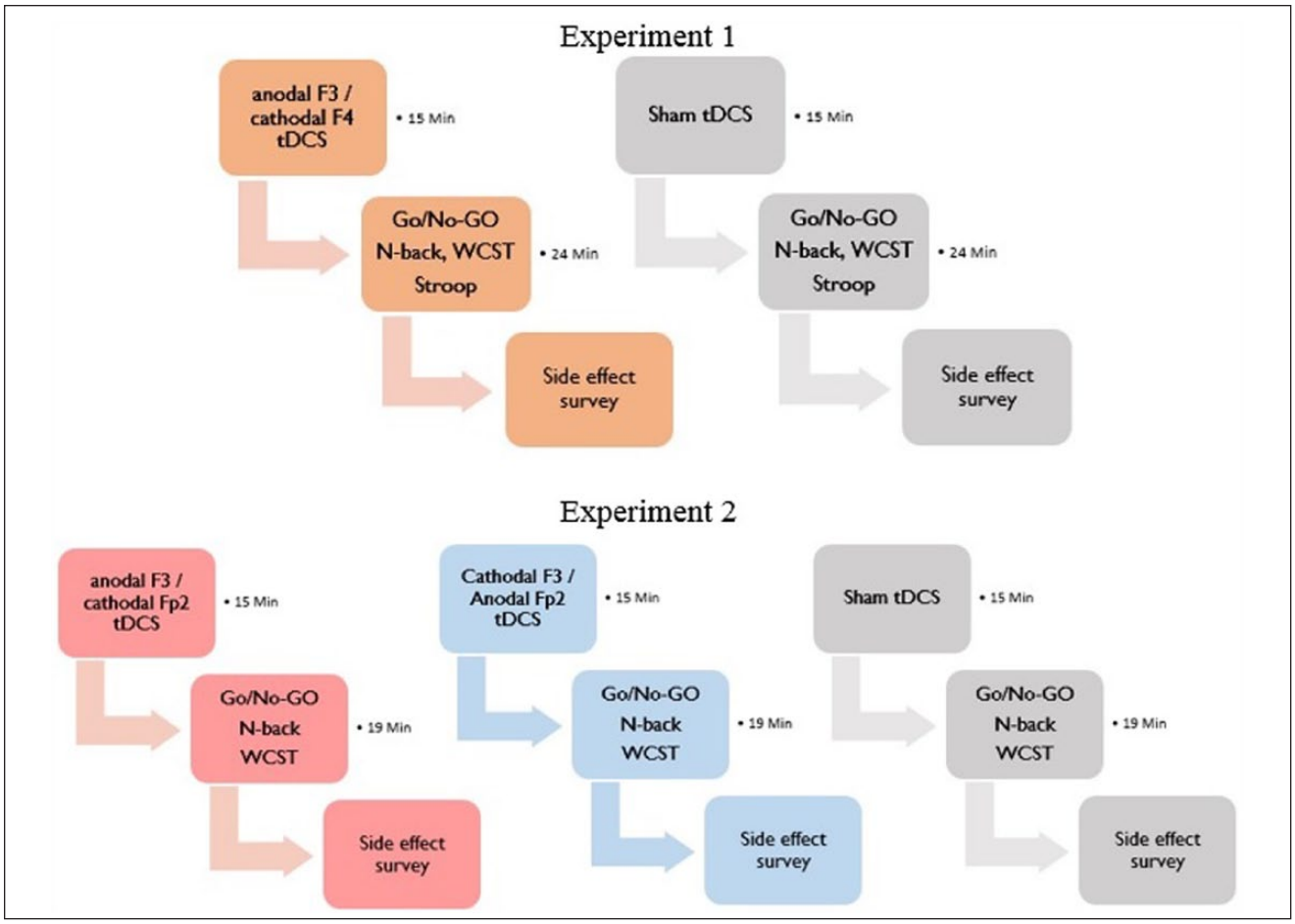

Figure 1. Procedure of tDCS conditions in Experiment 1 (top) and Experiment 2 (bottom).
Note. tDCS = transcranial direct current stimulation; F3 = left dorsolateral prefrontal cortex; F4 = right dorsolateral prefrontal cortex; Fp2 = right orbitofrontal cortex; WCST = Wisconsin Card Sorting Test.

accurately as possible" for all Go stimuli. The task consisted of 50 stimuli that required response execution on 75% of trials, and inhibition of response on the remaining 25%. The planes (7 × 7 cm) were static and black and were presented on a white screen. The task was counterbalanced across runs and participants. Dependent variables were accuracy for the Go and No-Go categories and reaction time (RT) of Go stimuli. The correct response to No-Go stimuli is of specific interest as it examines prepotent response inhibition as an index of inhibitory control. This task takes about 7 min to complete. Details about duration of stimuli, fixation time, and latency of beep are displayed in Figure 2.

It is noteworthy that the Go/No-Go task procedure used in this study resembles the SST paradigm (Logan, 1994). Especially, it is similar to the Stop Signal Reaction Time (SSRT) in that both investigate the ability to inhibit a response (Georgiou & Essau, 2011), but the SST is actually a more difficult variation of the Go/No-Go paradigm. In the standard Go/No-Go paradigm, participants are presented with certain stimuli that are asked to respond and certain stimuli that are asked not to respond to. In contrast, the SST requires participants to respond to stimuli but on some trials they will get a "stop" signal meaning that they need to stop the response they might already have initiated (Morein-Zamir & Sahakian, 2010). In other words, in the Go/No-Go paradigm stimuli are consistently associated with going and stopping than in the stop-signal paradigm where stimuli are inconsistently associated with going and stopping (Verbruggen & Logan, 2008), which is why response inhibition is more difficult in the Stop-signal than Go/No-Go task (Johnstone et al., 2007).

Stroop task. While the Go/No-Go task (specifically the No-Go stimuli) is a measure of prepotent response inhibition, the Stroop task is rather a measure of interference control with unique neural contributions of both tasks specially in ADHD (Dimoska-Di Marco et al., 2011). This is relevant, as different PFC regions are supposed to be involved in interference versus prepotent response inhibition (Vendrell et al., 1995; Wager et al., 2005). The task requires participants to

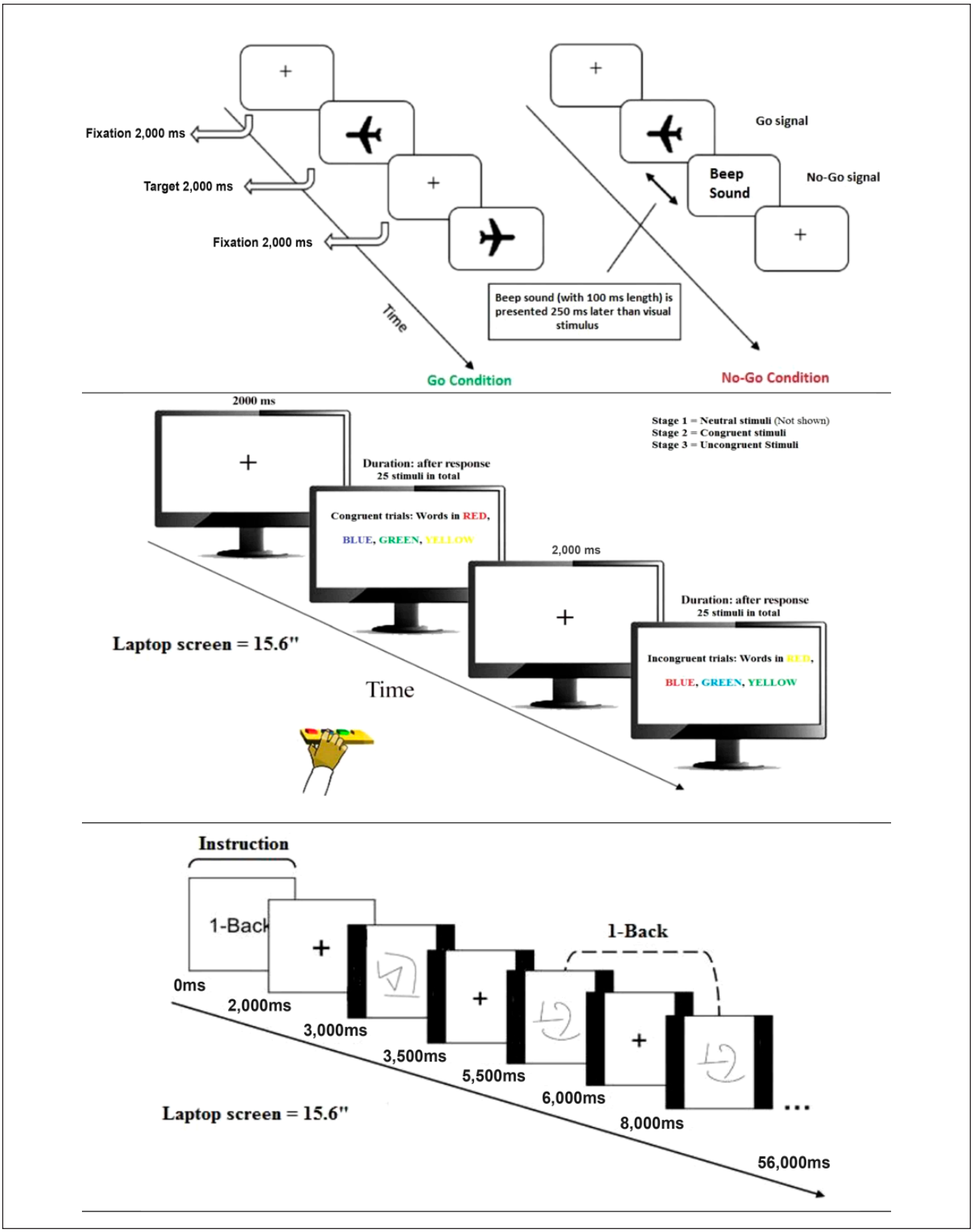

Figure 2. The Go-No-Go (top), Stroop (middle), and N-back (bottom) tasks procedure.

view color names presented in various ink colors (e.g., red, blue, yellow, green) and name the color of the ink. Participants were given four buttons marked with four colors and were instructed to select a color when presented with the word as fast as possible. During the neutral trials, the word is written in black ink (e.g., "red" in black ink) and participant should press the button with the corresponding color; during the congruent trial, the word matches the ink color (e.g., "blue" in blue ink) and in the incongruent trials, the word conflicts with the ink color (e.g., "red" in yellow ink) and participants should respond to the color of the ink and inhibit the word. There were 25 stimuli for each stage with size of 7 (length) × 5 (width) cm of each stimulus and the next stimulus was presented after participants' response. Interference inhibition is measured by the proportion of false answer and RT of the third stage (i.e., incongruent trials) that shows interfering stimuli. Details about duration of stimuli presentation are displayed on Figure 2.

N-Back test. To probe WM performance, we used the visual "N-back" task, which is a widely used test of WM performance (Brewin & Smart, 2005) and is sensitive to the underlying neural basis of WM in the PFC (Owen, McMillan, Laird, & Bullmore, 2005). During the N-back task, participants are presented with a stimulus (letter or picture) one at a time on a screen. Participants are asked to identify the picture that repeats relative to the one presented "*n*" items before its onset. In our study, the target was any picture that was identical to the one it preceded one trial back, which is called "1-back" task. Each participant completed three runs of the task, each run consisted of 30 stimuli, lasting around 6 min in total. The stimuli consisted of 10 different images, which means that each image was randomly repeated three times in each run (Figure 2). Participants were instructed to answer only if the 1-back picture was the same. The task was counterbalanced across runs and participants. We used mean RT of correct responses and the number of correct responses on the 1-back task as measures of WM performance. Stimuli presentation in all three computerized tasks (i.e., Go/No-Go, Stroop, N-back) were controlled by a laptop with a 15.6″ screen (Schneider, Eschman, & Zuccolotto, 2002) at a viewing distance from the monitor of approximately 50 cm.

WCST. The WCST is regarded as the gold standard of EF (Ozonoff, Goodlin-Jones, & Solomon, 2005), which is sensitive to frontal abnormalities (Romine et al., 2004). It is primarily used to measure cognitive flexibility, planning, and set maintenance (Kaland, Smith, & Mortensen, 2008) as well as task-switching abilities (Cepeda et al., 2000). PFC dysfunctions are associated with impaired WCST performance (Merriam, Thase, Haas, Keshavan, & Sweeney, 1999). WCST performance also depends on impulsive responding (Sweitzer, Allen, & Kaut, 2008) and some studies used the WCST as a measure of impulsivity (Leshem & Glicksohn, 2007), implying that other PFC regions than the DLPFC may be involved. Motivational deficits have been suggested as one possible reason of poor performance on the WCST in populations with frontal abnormalities. Previous studies showed that individuals with ADHD consistently exhibit poorer performance in WCST compared with healthy controls (Romine et al., 2004). In this study, we used the WCST to measure cognitive flexibility and task-switching ability that are other domains of EFs. The WCST requires participants to identify the sort criterion of a set of cards based upon "correct" versus "incorrect" feedback given by the examiner. After correctly matching a card according to a stimulus feature (color, form, or number) for 10 consecutive trials, the matching feature changes. Four WCST variables, namely, number of categories, perseverative errors, RT, and total errors were used to measure participant's performances. We used the short version of WCST with 64 cards, which lasts about 7 min.

Statistical Analysis

We used IBM Statistical Package for the Social Sciences (SPSS) for windows, version 24 (SPSS Inc, Chicago, IL, USA) for data analysis. To examine effect of tDCS on EFs, we used repeated measures ANOVA with stimulation condition (anodal F3-cathodal F4 / sham in Experiment 1 and anodal F3-cathodal Fp2 / cathodal F3- anodal Fp2 / and sham in Experiment 2) as within-subject factors. Our data met the ANOVA linear assumptions and the Leven's test was used to examine homogeneity of variances. Mauchly's test was used to evaluate the sphericity of the data before performing the repeated-measures ANOVA for each dependent variable. In case that the assumption of sphericity was violated, the degrees of freedom were corrected using Greenhouse–Geisser estimates of sphericity. A significance level of $p < .05$ was used for all statistical comparisons and Fisher's least significant difference (LSD) post hoc test was used for post hoc analysis.

Results

All participants tolerated tDCS well and no adverse effects were reported except for mild itching or tingling under electrodes. Descriptive statistics including mean and standard deviation of participants' scores on dependent variables are shown in Table 2. Participants' performance on major variables are displayed on Figure 3.

We conducted repeated measures ANOVA in Experiment 1 to examine effects of the tDCS conditions (anodal lDLPFC -cathodal rDLPFC / sham) on participants' performance on the Go-No/Go, WCST, N-back, and Stroop tasks. Results showed no significant differences between tDCS conditions in the Go-No/Go measures of

Table 2. Mean and *SD*s of Cognitive Tasks and ADHD Scores.

		Experiment 1		Experiment 2		
		Anodal F3 / Cathodal F4	Sham	Anodal F3 / Cathodal Fp2	Cathodal F3 / Anodal Fp2	Sham
Tasks	Source	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)	*M* (*SD*)
Go/No-Go	Accuracy Go	93.33 (11.42)	90.90 (19.56)	100 (0.00)	100 (0.00)	98.54 (3.24)
	Time	1.08 (0.21)	1.03 (0.17)	1.33 (0.9)	1.31 (0.13)	1.23 (0.12)
	Accuracy No-Go	19.86 (7.6)	19 (7.80)	22.7 (1.33)	24.2 (1.22)	20.7 (4.39)
N-back	Accuracy	15.26 (8.32)	14.40 (7.42)	21 (2.26)	19.40 (2.27)	17.90 (2.92)
	RT[a]	120.23 (22.48)	175.73 (55.44)	103.39 (24.19)	120.87 (48.60)	162.88 (94.41)
WCST	Perseverative errors	17.60 (3.60)	18 (8.98)	7.8 (2.44)	11.8 (3.29)	14.80 (3.7)
	Category completed	2.46 (0.83)	2.40 (1.05)	5.1 (0.71)	4.5 (0.52)	3.9 (0.73)
	Time[a]	237.30 (79.75)	291.12 (106.70)	123.22 (16.85)	143.10 (30.82)	170.28 (85.94)
	Total errors	29.71 (8.3)	30.73 (9.34)	11 (2.86)	16 (4.32)	21.60 (5.36)
Stroop	Accuracy incongruent	34.93 (15.54)	24.93 (12.01)	NA	NA	NA
	RT	2.87 (2.21)	1.39 (0.44)	NA	NA	NA

Note. F3 = left dorsolateral prefrontal cortex; F4 = right dorsolateral prefrontal cortex; Fp2 = right orbitofrontal cortex; WCST = Wisconsin Card Sorting Test; RT = response time; NA = not administrated. [a]Values are shown in seconds.

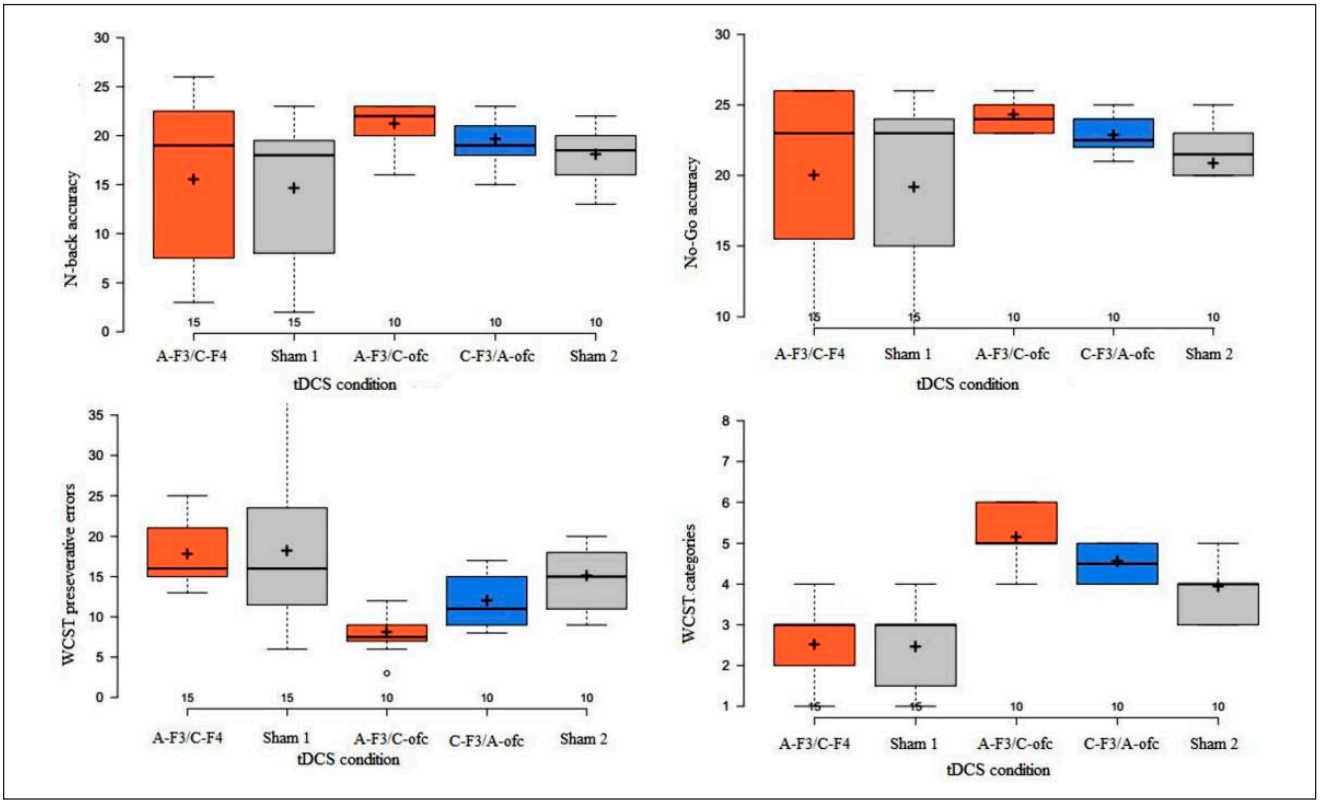

Figure 3. N-back accuracy, No-Go accuracy, perseverative errors, and categories completed after each tDCS condition in both experiments. *Note.* Experiment 1: *N* = 15, Experiment 2: *N* = 10. tDCS = transcranial direct current stimulation; A = anodal tDCS; F3 = left dorsolateral prefrontal cortex; C = cathodal tDCS; F4 = right dorsolateral prefrontal cortex; OFC = orbitofrontal cortex.

Table 3. Exp 1: ANOVA Results for Effects of tDCS Conditions (Anodal F3-Cathodal F4/Sham) on Go/No-Go Task, WCST, N-Back Test, and Stroop Task.

Tasks	Source	*df*	Mean square	*F*	Significance	η_p^2
Go/No-Go	Accuracy Go	1, 14	44.31	0.19	.66	0.01
	Time	1, 14	0.02	2.42	.14	0.15
	Accuracy No-Go	1, 14	5.63	1.02	.32	0.06
Stroop	Accuracy incongruent	1, 14	346.80	9.01	**.01**	0.39
	RT	1, 14	16.46	7.07	**.02**	0.33
N-Back	Accuracy	1, 14	5.63	0.21	.65	0.01
	RT	1, 14	21,561.75	21.01	**.01**	0.62
WCST	Perseverative errors	1, 14	1.20	0.03	.86	0.01
	Category completed	1, 14	0.03	0.06	.81	0.01
	Time	1, 14	21,721.40	7.87	**.01**	0.36
	Total errors	1, 14	7.50	0.15	.69	0.01

Note. Significant results are highlighted ($p \leq .05$) in bold. tDCS = transcranial direct current stimulation; F3 = left DLPFC; F4 = right DLPFC; WCST = Wisconsin Card Sorting Test; RT = response time.

accuracy Go ($F = 0.19$, $p = .66$), accuracy No-Go ($F = 1.02$, $p = .32$), and RT ($F = 2.42$, $p = .14$). These results suggest that anodal lDLPFC/cathodal rDLPFC tDCS did not improve inhibitory control in ADHD, which is in accordance with the second hypothesis. ANOVA results also showed no significant effect of anodal lDLPFC/cathodal rDLPFC tDCS on cognitive flexibility and task switching measured by the WCST regarding perseverative errors, completed categories, and total errors. For WM performance, anodal lDLPFC/cathodal rDLPFC tDCS did not significantly increase the number of accurate responses ($F = 0.21$, $p = .65$). However, RT was significantly reduced after anodal lDLPFC/cathodal rDLPFC tDCS compared with sham stimulation ($F = 21.01$, $p < .01$). Finally, the respective ANOVA showed a significant improving effect of anodal lDLPFC/cathodal rDLPFC tDCS on interference response inhibition measured by the Stroop task outputs of accuracy ($F = 9.01$, $p < .01$) and RT ($F = 7.7$, $p < .02$). In sum, results of Experiment 1 indicated a significant effect of anodal lDLPFC/cathodal rDLPFC tDCS on performance of the Stroop task and N-back speed but not the WCST and Go-No/Go tasks. Results of Experiment 1 are shown in Table 3.

Results of Experiment 2 revealed improving effect of the left DLPFC / right OFC (rOFC) tDCS on most of the EFs. With regard to inhibitory control, the respective repeated-measures ANOVA showed significant differences between stimulation conditions for No-Go accuracy, which is a measure of prepotent response inhibition ($F = 4.48$, $p < .03$). Fisher's LSD post hoc test showed that cathodal lDLPFC/anodal rOFC tDCS (Montage 2) resulted in a significant increase of No-Go accuracy compared to sham stimulation ($p < .01$; $M_{\text{Montage 2}} = 24.2$ vs. $M_{\text{sham}} = 20.7$), suggesting that this electrode arrangement improves prepotent response inhibition in ADHD (Table 4).

In addition, we observed a significant effect of stimulation on WCST performance. Particularly, results showed that in contrast to Experiment 1, anodal lDLPFC/cathodal rOFC tDCS (Montage 1), cathodal lDLPFC/anodal rOFC tDCS (Montage 2) and sham stimulation significantly differed regarding perseverative errors ($F = 10.70$, $p < .01$) and completed categories ($F = 15.67$, $p < .01$). The respective post hoc analyses further showed that both anodal lDLPFC/cathodal rOFC tDCS ($p < .01$; $M_{\text{Montage 1}} = 7.8$ vs. $M_{\text{sham}} = 14.8$) and cathodal lDLPFC/anodal rOFC tDCS ($p < .04$; $M_{\text{Montage 2}} = 11.8$ vs. $M_{\text{sham}} = 14.8$) significantly reduced perseverative errors in ADHD children compared with sham stimulation although the first montage was significantly more effective compared with the second one ($p < .01$; $M_{\text{Montage 1}} = 7.8$ vs. $M_{\text{Montage 2}} = 11.8$). The same pattern of results was observed for completed categories and total errors, and the respective post hoc analysis showed that anodal lDLPFC/cathodal rOFC tDCS ($p < .01$; $M_{\text{Montage 1}} = 5.1$ vs. $M_{\text{sham}} = 3.9$) and cathodal lDLPFC/anodal rOFC ($p < .01$; $M_{\text{Montage 2}} = 4.5$ vs. $M_{\text{sham}} = 3.9$) significantly increased categories completed by ADHD children compared with sham stimulation. Again the first montage was significantly more effective compared with the second one ($p < .01$; $M_{\text{Montage 1}} = 5.1$ vs. $M_{\text{Montage 2}} = 4.5$). These results suggest that increasing activity of the lDLPFC and reduction of rOFC activity is more effective in improving cognitive flexibility, attentional shifting, and task switching compared with sham situation as well as the reversed montage.

Finally, the respective repeated measures ANOVA showed a significant difference between stimulation conditions regarding WM performance for both accuracy

Table 4. Exp 2: ANOVA Results for Effects of tDCS Conditions (Anodal F3-Cathodal Fp2/Cathodal F3-Anodal Fp2/sham) on Go/No-Go Task, WCST, and N-back Test.

Tasks	Source	*df*	Mean square	*F*	Significance	η_p^2
Go/No-Go	Accuracy Go	2, 18	7.02	2.01	.16	0.18
	Time	2, 18	0.02	2.09	.15	0.19
	Accuracy No-Go	2, 18	30.83	4.48	**.03**	0.33
N-Back	Accuracy	2, 18	24.03	9.84	**.01**	0.52
	RT	2, 18	9,346.97	5.89	**.01**	0.39
WCST	Perseverative errors	2, 18	123.33	10.70	**.01**	0.54
	Category completed	2, 18	3.60	15.67	**.01**	0.63
	Time	2, 18	55.80	3.06	.07	0.25
	Total errors	2, 18	281.20	16.67	**.01**	0.64

Note. Significant results are highlighted ($p \leq .05$) in bold. tDCS = transcranial direct current stimulation; F3 = left DLPFC; Fp2 = right orbitofrontal cortex; WCST = Wisconsin Card Sorting Test; RT = response time.

($F = 9.84$, $p < .01$) and RT ($F = 5.89$, $p < .01$). The post hoc LSD test showed that only Montage 1 (anodal lDLPFC / cathodal rOFC tDCS) resulted in a significant increase in accuracy and RT compared with sham stimulation ($p < .04$; $M_{\text{Montage 1}} = 21$ vs. $M_{\text{sham}} = 17.9$; $p < .01$; $M_{\text{Montage 1}} = 103.39$ vs. $M_{\text{sham}} = 162.88$). Interestingly, Montage 1 (anodal lDLPFC/cathodal rOFC tDCS) was significantly superior in increasing working memory accuracy compared with Montage 2 (anodal rOFC/cathodal lDLPFC tDCS) ($p < .03$; $M_{\text{Montage 1}} = 21$ vs. $M_{\text{Montage 2}} = 19.4$).

Discussion

The present study investigated effects of modulating cortical activity of PFC regions, namely, the DLPFC and OFC, on improving executive functioning in ADHD using electrical brain stimulation. According to the prefrontal hypothesis of ADHD (Seidman et al., 2005), behavioral deficits in this disorder are related to abnormal DLPFC (inhibition-based model) and OFC functioning (motivational dysfunction model; Sonuga-Barke, 2005). Despite promising results of tDCS studies in disorders with frontal abnormalities, its application in ADHD has only recently been documented. These studies mostly investigated effects of tDCS on inhibitory process (Bandeira et al., 2016; Hsu et al., 2011; Soltaninejad et al., 2015a). To our knowledge, this is the first tDCS study to investigate the role of the DLPFC and OFC in a broader range of impaired EF domains of ADHD, including inhibitory control, WM, executive control, and cognitive flexibility/task switching.

Regarding inhibitory control, results of the first experiment showed that left anodal/right cathodal DLPFC tDCS does not improve response inhibition in the Go-No/Go task. This tDCS montage should lead to decreased activity of rDLPFC as a result of cathodal rDLPFC tDCS as well as anodal lDLPFC tDCS, the latter likely reducing activity of the contralateral region through inhibitory transcallosal connections (Mishra, Nizamie, Das, & Praharaj, 2010). Reduced response inhibition in ADHD is explained by unsuccessful disengagement in the Go/No-go task, which is necessary for successful performance. For this disengagement, rLPFC activity is crucial, and thus reduction of activity of this area, which was the case in Experiment 1, should not improve performance. Our second experiment however, showed that cathodal lDLPFC/anodal rOFC tDCS significantly improved accuracy of No-Go responses, likely by indirectly activating the rDLPFC via reduction of transcallosal inhibition. Moreover, due to smaller head circumference in children, this might also have affected the rDLPFC, which is close to the rOFC. These findings support the second hypothesis of the study that cathodal lDLPFC tDCS would improve prepotent response inhibition and are in accordance with findings of previous studies showing that decreased activity in the rLPFC is responsible for poor inhibitory control (Aron & Poldrack, 2005; Depue et al., 2010). Our results also replicate findings of a recently conducted tDCS study in which cathodal stimulation of the lDLPFC significantly improved accuracy of No-Go responses (Soltaninejad et al., 2015a). In further accordance with these results, cathodal tDCS over the lDLPFC improved ADHD symptoms in adult ADHD patients (Cachoeira et al., 2017).

In addition to response inhibition, we investigated interference control measured by the Stroop task. We found that left anodal/right cathodal DLPFC tDCS improved both accuracy and RT in the Stroop task. Supporting our first hypothesis, this finding is in accordance with recent brain imaging studies showing activation of both, left and right, but relatively larger activation of the lDLPFC during Stroop task performance (Hyodo et al., 2016; Jiang, Bailey, Xiang, Zhang, & Zhang, 2016). In further accordance, high-frequency repetitive transcranial magnetic stimulation (rTMS)

over the lDLPFC has beneficial effects on both congruent and incongruent trials during Stroop task performance compared with sham stimulation (Vanderhasselt, De Raedt, Baeken, Leyman, & D'haenen, 2006). Our results suggest that increasing activity of the lDLPFC by anodal tDCS leads to enhanced cognitive control over relevant stimuli (naming the color but not the word) by maintaining them in WM. The observation that performance of the Go-No/Go and Stroop tasks are differently altered by DLPFC activation implicates that the activation of this region is task-specific (Pope, Brenton, & Miall, 2015). In other words, these tasks are involved in different aspects of response inhibition and are thus suported by different cortical regions. Moreover, it also suggests that the relevance of the interhemispheric balance for task performance is also task- or domain-specific, as an impact of suggested alterations of interhemispheric balance on performance was only observed for response inhibition, but not other EF domains.

WM is another impaired EF in ADHD. Although children with ADHD exhibit significant WM deficits (Kasper et al., 2012) relative to their typically developing peers, no study has investigated effects of tDCS, which is a robust technique for improving WM, on WM in ADHD (Brunoni & Vanderhasselt, 2014). Our findings show that left anodal/right cathodal DLPFC tDCS (in Experiment 1) significantly improved participants' performance in the N-back task compared with sham stimulation. Interestingly, in the second experiment, both accuracy and RT were improved by stimulation, while only RT benefited in the first experiment. This specifically supports our first hypothesis about improving effects of anodal lDLPFC tDCS on WM. Nonetheless, stronger effect of tDCS from the Experiment 2 could be explained in several ways. One explanation could be opposing effects of cathodal lDLPFC tDCS in Experiment 1, which could reduce increased activity of the lDLPFC. Previous tDCS studies have already shown improved WM performance after anodal stimulation of the lDLPFC (Brunoni & Vanderhasselt, 2014; Fregni et al., 2005). Our findings replicate results of these studies, and suggest decreased activity in the lDLPFC as causally relevant for impaired attentional control and WM in ADHD and other disorders with executive dysfunctions (Banich et al., 2009; Fregni et al., 2005; Nitsche et al., 2009; Salehinejad, Rostami, & Ghanavati, 2015). Another explanation for these results takes the role of inhibitory control for WM performance into account, which was also improved in the second experiment. Inhibition is introduced as the central executive part of WM in Baddeley's model of WM (Hasher, 2006) and improved inhibitory control, which was only observed in the second experiment, could explain why participants' WM was more robustly improved in Experiment 2.

Cognitive flexibility, task switching, and attentional shifting were other EF domains investigated in the present study. The stimulation conditions in Experiment 2, which involved both DLPFC and OFC, significantly improved performance on these EFs compared with the first experiment, supporting our third hypothesis. WCST performance requires EF domains that clearly benefit from DLPFC-related executive functioning such as attentional and executive control (Cepeda et al., 2000) for directing behavior toward achieving a goal (sorting cards based on a criterion). However, when the rule changes, participants need to inhibit the now irrelevant response, which requires inhibition, and to apply a new rule which requires disinhibition. Disinhibition and impulsivity are OFC-related deficits in ADHD (Rolls, 2004). Therefore, stimulation montages that target both regions (i.e., DLPFC and OFC) might be optimal to enhance WCST performance. This also implies that deficits in ADHD are not limited to executive dysfunctions controlled by the DLPFC and are related to DLPFC–OFC interaction rather than imbalanced DLPFC activity marked in other disorders with frontal abnormalities. Additionally, the findings suggest that some but not all EFs in ADHD are dependent to DLPFC-OFC or "hot-cool" interaction.

Regarding the presumed DLPFC–OFC interaction in WCST performance, both tDCS montages (i.e., anodal lDLPFC tDCS/cathodal rOFC tDCS and cathodal lDLPFC tDCS/anodal rOFC tDCS) significantly improved performance on the WCST in ADHD children compared with sham stimulation although the first montage was significantly more effective that the second one. One explanation for the performance-improving effect of cathodal lDLPFC tDCS addresses cognitive flexibility, which is one of the EFs measured by the WCST. Recent tDCS studies showed increased cognitive flexibility after cathodal tDCS of the lDLPFC (Luft, Zioga, Banissy, & Bhattacharya, 2017). Cathodal stimulation of the lDLPFC facilitates disengagement from the current task and engagement in novel ones. This is one of the abilities required to apply new rules in the WCST and might explain why the second montage also improved WCST performance. The improving effect of anodal tDCS of the lDLPFC could then be explained by increased cognitive control and attentional shifting. In other words, reduced DLPFC activity that affects both sustained and transient aspects of attentional control in ADHD (Banich et al., 2009) was increased by anodal tDCS, which would lead to regulation of top-down attentional control which is one of the underlying mechanisms of improved scores of performance on the WCST.

In sum, our study suggests modulation of PFC regions, namely, the DLPFC and OFC, modified performance on EF tasks; accordingly, while lDLPFC activity is more closely related to executive control, WM, and interference control in ADHD, rDLPFC activation is more involved in inhibitory control. Moreover, our findings suggest that cognitive flexibility/task switching and attentional shifting mostly benefit from DLPFC–OFC interactions. Interestingly, our

findings suggest that the effects of activation of PFC regions, especially the DLPFC, are task-specific and domain-specific, benefiting some but not all the EFs domains in a lateralized way (i.e., lDLPFC and rDLPFC involvement in Stroop performance or lDLPFC/rOFC involvement in WCST performance). One initial implication of the findings is that both major models of ADHD (i.e., cognitive dysfunction model, motivational dysfunction model) should be taken into account for addressing executive dysfunctions in ADHD. The "prefrontal hypothesis of ADHD" which includes both models, then might be a better framework for treating executive dysfunctions in ADHD.

Nevertheless, findings of the present study should be interpreted considering what follows. First, executive dysfunctions in ADHD presented in this study should not imply a homogeneous description and single core dysfunction of ADHD deficits. Instead, ADHD is quite a heterogeneous disorder in terms of impaired deficits and neuropsychological measures central to ADHD (Fair et al., 2012). Second, the executive dysfunctions measured in this study should be discussed based on the validity and specificity of tasks given the significant overlap and differences between executive deficits in ADHD.

This study is also an initial step toward developing clinical treatment of ADHD, especially regarding impaired EFs, by electrically stimulating the DLPFC or OFC. A recent study supports this notion by showing beneficial effects of tDCS on ADHD symptoms (Cachoeira et al., 2017). tDCS as a neuromodulation technique, can enhance cerebral plasticity and could then be used as a tool to increase the developmental potential of children (Holt & Mikati, 2011) which can be of special interest in neurodevelopmental disorders such as ADHD. Importantly, our results suggest using task-specific stimulation protocols to ameliorate specific deficits. For example, our findings suggest to use stimulation montages that increase activity in the rDLPFC using either cathodal lDLPFC tDCS (Soltaninejad et al., 2015a) or anodal rDLPFC tDCS for improving impulsive behavior and inhibitory control in ADHD (Beeli, Casutt, Baumgartner, & Jäncke, 2008). Anodal lDLPFC tDCS is also suggested for enhancing WM and executive control as this stimulation protocol increases cortical excitability of the lDLPFC of which its role in WM is well-documented. Finally, anodal lDLPFC tDCS/cathodal rOFC or cathodal lDLPFC tDCS might be beneficial for improving cognitive flexibility, attentional shifting, and impulsivity in ADHD. The latter stimulation protocol might benefit more attentional and behavioral deficits in ADHD by ameliorating attentional deficits (through anodal lDLPFC tDCS) and impulsive behaviors (through targeting OFC).

The present study has some limitations too. First of all, both experiments had a relatively low number of participants, although the total sample size was adequate considering that small sample size has been the case in many studies on ADHD children. Second, the first experiment sample size only included male ADHD children. Third, our design involved only poststimulation assessment, whereas assessment of task performance before and after tDCS provides a better evaluation of tDCS effectiveness. This is of importance given the neuropsychological heterogeneity of patients with ADHD, which necessitates application of more robust designs such as pre- and posttest designs. Finally, although we considered a minimal distance of 6 cm from the anodal electrode with the reference electrode, low focality of tDCS limits interpretability of the stimulation effects regarding specific areas. Future studies should also explore potential long-term effects of tDCS on cognitive deficits in ADHD. Our results do not suggest a simple locus of neural dysfunction of the DLPFC in ADHD. Neuroimaging studies are required to specify accurate localizations of PFC regions involved in respective symptoms to improve targeting of stimulation approaches.

Author Contributions

VN. and MAS. conceived and designed the study. A.N. collected the data. MAS. and VN. analyzed and interpreted the data. MAS. wrote the manuscript. MAN., AHJ. and MAS. critically revised the manuscript.

Declaration of Conflicting Interests

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References

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: American Psychiatric Publishing.

Andrade, A. C., Magnavita, G. M., Allegro, J. V. B. N., Neto, C. E. B. P., Lucena, R. d. C. S., & Fregni, F. (2013). Feasibility of transcranial direct current stimulation use in children aged 5 to 12 years. *Journal of Child Neurology*, *29*, 1360-1365. doi:10.1177/0883073813503710

Aron, A. R., & Poldrack, R. A. (2005). The cognitive neuroscience of response inhibition: Relevance for genetic research in attention-deficit/hyperactivity disorder. *Biological Psychiatry*, *57*, 1285-1292.

Asherson, P. (2012). ADHD across the lifespan. *Medicine*, *40*, 623-627.

Bandeira, I. D., Guimarães, R. S. Q., Jagersbacher, J. G., Barretto, T. L., de Jesus-Silva, J. R., Santos, S. N., . . . Lucena, R. (2016). Transcranial direct current stimulation in children and adolescents with attention-deficit/hyperactivity disorder (ADHD): A pilot study. *Journal of Child Neurology*, *31*, 918-924.

Banich, M. T., Burgess, G. C., Depue, B. E., Ruzic, L., Bidwell, L. C., Hitt-Laustsen, S., . . . Willcutt, E. G. (2009). The neural basis of sustained and transient attentional control in young adults with ADHD. *Neuropsychologia*, *47*, 3095-3104.

Barkley, R. A. (1997). Behavioral inhibition, sustained attention, and executive functions: Constructing a unifying theory of ADHD. *Psychological Bulletin*, *121*, 65-94.

Beeli, G., Casutt, G., Baumgartner, T., & Jäncke, L. (2008). Modulating presence and impulsiveness by external stimulation of the brain. *Behavioral and Brain Functions*, *4*, 1-33.

Brem, S., Grünblatt, E., Drechsler, R., Riederer, P., & Walitza, S. (2014). The neurobiological link between OCD and ADHD. *ADHD Attention Deficit and Hyperactivity Disorders*, *6*, 175-202.

Brewin, C. R., & Smart, L. (2005). Working memory capacity and suppression of intrusive thoughts. *Journal of Behavior Therapy and Experimental Psychiatry*, *36*, 61-68. doi:10.1016/j.jbtep.2004.11.006

Brunoni, A. R., Nitsche, M. A., Bolognini, N., Bikson, M., Wagner, T., Merabet, L., . . . Fregni, F. (2012). Clinical research with transcranial direct current stimulation (tDCS): Challenges and future directions. *Brain Stimulation*, *5*, 175-195. doi:10.1016/j.brs.2011.03.002

Brunoni, A. R., & Vanderhasselt, M.-A. (2014). Working memory improvement with non-invasive brain stimulation of the dorsolateral prefrontal cortex: A systematic review and meta-analysis. *Brain and Cognition*, *86*, 1-9. doi:10.1016/j.bandc.2014.01.008

Bush, G., Valera, E. M., & Seidman, L. J. (2005). Functional neuroimaging of attention-deficit/hyperactivity disorder: A review and suggested future directions. *Biological Psychiatry*, *57*, 1273-1284. doi:10.1016/j.biopsych.2005.01.034

Cachoeira, C. T., Leffa, D. T., Mittelstadt, S. D., Mendes, L. S. T., Brunoni, A. R., Pinto, J. V., . . . Schestatsky, P. (2017). Positive effects of transcranial direct current stimulation in adult patients with attention-deficit/hyperactivity disorder: A pilot randomized controlled study. *Psychiatry Research*, *247*, 28-32. doi:10.1016/j.psychres.2016.11.009

Callicott, J. H., Bertolino, A., Mattay, V. S., Langheim, F. J. P., Duyn, J., Coppola, R., . . . Weinberger, D. R. (2000). Physiological dysfunction of the dorsolateral prefrontal cortex in schizophrenia revisited. *Cerebral Cortex*, *10*, 1078-1092. doi:10.1093/cercor/10.11.1078

Castellanos, F. X., & Tannock, R. (2002). Neuroscience of attention-deficit/hyperactivity disorder: The search for endophenotypes. *Nature Reviews Neuroscience*, *3*, 617-628.

Cepeda, N. J., Cepeda, M. L., & Kramer, A. F. (2000). Task switching and attention deficit hyperactivity disorder. *Journal of Abnormal Child Psychology*, *28*, 213-226. doi:10.1023/a:1005143419092

Depue, B. E., Burgess, G. C., Willcutt, E. G., Ruzic, L., & Banich, M. T. (2010). Inhibitory control of memory retrieval and motor processing associated with the right lateral prefrontal cortex: Evidence from deficits in individuals with ADHD. *Neuropsychologia*, *48*, 3909-3917.

Dimoska-Di Marco, A., McDonald, S., Kelly, M., Tate, R., & Johnstone, S. (2011). A meta-analysis of response inhibition and Stroop interference control deficits in adults with traumatic brain injury (TBI). *Journal of Clinical and Experimental Neuropsychology*, *33*, 471-485.

Duncan, J., & Owen, A. M. (2000). Common regions of the human frontal lobe recruited by diverse cognitive demands. *Trends in Neurosciences*, *23*, 475-483. doi:10.1016/S0166-2236(00)01633-7

Elliott, R. (2003). Executive functions and their disorders: Imaging in clinical neuroscience. *British Medical Bulletin*, *65*, 49-59. doi:10.1093/bmb/65.1.49

Fair, D. A., Bathula, D., Nikolas, M. A., & Nigg, J. T. (2012). Distinct neuropsychological subgroups in typically developing youth inform heterogeneity in children with ADHD. *Proceedings of the National Academy of Sciences of the United States*, *109*, 6769-6774.

Fregni, F., Boggio, P., Nitsche, M., Bermpohl, F., Antal, A., Feredoes, E., . . . Pascual-Leone, A. (2005). Anodal transcranial direct current stimulation of prefrontal cortex enhances working memory. *Experimental Brain Research*, *166*, 23-30. doi:10.1007/s00221-005-2334-6

Gandiga, P. C., Hummel, F. C., & Cohen, L. G. (2006). Transcranial DC stimulation (tDCS): A tool for double-blind sham-controlled clinical studies in brain stimulation. *Clinical Neurophysiology*, *117*, 845-850. doi:10.1016/j.clinph.2005.12.003

Georgiou, G., & Essau, C. A. (2011). Go/No-Go task. In S. Goldstein & J. A. Naglieri (Eds.), *Encyclopedia of child behavior and development* (pp. 705-706). Boston, MA: Springer.

Gonçalves, Ó. F., Carvalho, S., Leite, J., Pocinho, F., Relvas, J., & Fregni, F. (2011). Obsessive compulsive disorder as a functional interhemispheric imbalance at the thalamic level. *Medical Hypotheses*, *77*, 445-447. doi:10.1016/j.mehy.2011.06.004

Hasher, L. (2006). Aging and long-term memory: Deficits are not inevitable. In E. Bialystok & F. I. M. Craik (Eds.), *Lifespan cognition: Mechanisms of change* (pp. 162-177). New York, NY: Oxford University Press .

Holt, R. L., & Mikati, M. A. (2011). Care for child development: Basic science rationale and effects of interventions. *Pediatric Neurology*, *44*, 239-253.

Hsu, T.-Y., Tseng, L.-Y., Yu, J.-X., Kuo, W.-J., Hung, D. L., Tzeng, O. J., . . . Juan, C.-H. (2011). Modulating inhibitory control with direct current stimulation of the superior medial frontal cortex. *NeuroImage*, *56*, 2249-2257. doi:10.1016/j.neuroimage.2011.03.059

Hudec, K. L., Alderson, R. M., Patros, C. H. G., Lea, S. E., Tarle, S. J., & Kasper, L. J. (2015). Hyperactivity in boys with attention-deficit/hyperactivity disorder (ADHD): The role of executive and non-executive functions. *Research in Developmental Disabilities*, *45-46*, 103-109. doi:10.1016/j.ridd.2015.07.012

Hyodo, K., Dan, I., Kyutoku, Y., Suwabe, K., Byun, K., Ochi, G., . . . Soya, H. (2016). The association between aerobic fitness and cognitive function in older men mediated by frontal lateralization. *NeuroImage*, *125*, 291-300. doi:10.1016/j.neuroimage.2015.09.062

Jiang, J., Bailey, K., Xiang, L., Zhang, L., & Zhang, Q. (2016). Comparing the neural correlates of conscious and unconscious conflict control in a masked Stroop priming task. *Frontiers in Human Neuroscience*, *10*, Article 297. doi:10.3389/fnhum.2016.00297

Johnstone, S. J., Dimoska, A., Smith, J. L., Barry, R. J., Pleffer, C. B., Chiswick, D., & Clarke, A. R. (2007). The development of stop-signal and Go/Nogo response inhibition in children aged 7-12 years: Performance and event-related potential indices. *International Journal of Psychophysiology*, *63*, 25-38. doi:10.1016/j.ijpsycho.2006.07.001

Juan, C.-H., & Muggleton, N. G. (2012). Brain stimulation and inhibitory control. *Brain Stimulation*, *5*, 63-69.

Kaland, N., Smith, L., & Mortensen, E. L. (2008). Brief report: Cognitive flexibility and focused attention in children and adolescents with Asperger syndrome or high-functioning autism as measured on the computerized version of the Wisconsin Card Sorting Test. *Journal of Autism and Developmental Disorders*, *38*, 1161-1165. doi:10.1007/s10803-007-0474-1

Kasper, L. J., Alderson, R. M., & Hudec, K. L. (2012). Moderators of working memory deficits in children with attention-deficit/hyperactivity disorder (ADHD): A meta-analytic review. *Clinical Psychology Review*, *32*, 605-617.

Khng, K. H., & Lee, K. (2014). The relationship between Stroop and stop-signal measures of inhibition in adolescents: Influences from variations in context and measure estimation. *PLoS ONE*, *9*(7), Article e101356. doi:10.1371/journal.pone.0101356

Kobayashi, M., & Pascual-Leone, A. (2003). Transcranial magnetic stimulation in neurology. *The Lancet Neurology*, *2*, 145-156.

Krishnan, C., Santos, L., Peterson, M. D., & Ehinger, M. (2015). Safety of noninvasive brain stimulation in children and adolescents. *Brain Stimulation*, *8*, 76-87. doi:10.1016/j.brs.2014.10.012

Langleben, D. D., Austin, G., Krikorian, G., Ridlehuber, H. W., Goris, M. L., & Strauss, H. W. (2001). Interhemispheric asymmetry of regional cerebral blood flow in prepubescent boys with attention deficit hyperactivity disorder. *Nuclear Medicine Communications*, *22*, 1333-1340.

Lefaucheur, J.-P. (2016). A comprehensive database of published tDCS clinical trials (2005-2016). *Neurophysiologie Clinique/Clinical Neurophysiology*, *46*, 319-398. doi:10.1016/j.neucli.2016.10.002

Leshem, R., & Glicksohn, J. (2007). The construct of impulsivity revisited. *Personality and Individual Differences*, *43*, 681-691. doi:10.1016/j.paid.2007.01.015

Lindenberg, R., Nachtigall, L., Meinzer, M., Sieg, M. M., & Flöel, A. (2013). Differential effects of dual and unihemispheric motor cortex stimulation in older adults. *The Journal of Neuroscience*, *33*, 9176-9183.

Logan, G. D. (1994). On the ability to inhibit thought and action: A users' guide to the stop signal paradigm. In D. D. T. H. Carr (Ed.), *Inhibitory processes in attention, memory, and language* (pp. 189-239). San Diego, CA: Academic Press.

Luft, C. D. B., Zioga, I., Banissy, M. J., & Bhattacharya, J. (2017). Relaxing learned constraints through cathodal tDCS on the left dorsolateral prefrontal cortex. *Scientific Reports*, *7*(1), 2916. doi:10.1038/s41598-017-03022-2

Merriam, E. P., Thase, M. E., Haas, G. L., Keshavan, M. S., & Sweeney, J. A. (1999). Prefrontal cortical dysfunction in depression determined by Wisconsin Card Sorting Test performance. *American Journal of Psychiatry*, *156*, 780-782.

Minhas, P., Bikson, M., Woods, A. J., Rosen, A. R., & Kessler, S. K. (2012). Transcranial direct current stimulation in pediatric brain: A computational modeling study. *Conference Proceedings: Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, 2012, 859-862.

Mishra, B. R., Nizamie, S. H., Das, B., & Praharaj, S. K. (2010). Efficacy of repetitive transcranial magnetic stimulation in alcohol dependence: A sham-controlled study. *Addiction*, *105*, 49-55.

Morein-Zamir, S., & Sahakian, B. J. (2010). Stop-signal task. In I. P. Stolerman (Ed.), *Encyclopedia of psychopharmacology* (p. 1285). Berlin, Heidelberg: Springer.

Nejati, V., Salehinejad, M. A., Shahidi, N., & Abedin, A. (2017). Psychological intervention combined with direct electrical brain stimulation (PIN-CODES) for treating major depression: A pre-test, post-test, follow-up pilot study. *Neurology, Psychiatry and Brain Research*, *25*, 15-23. doi: 10.1016/j.npbr.2017.05.003

Nezhad, M. A. S., Khodapanahi, M. K., Yekta, M., Mahmoodikahriz, B., & Ostadghafour, S. (2011). Defense styles in internalizing and externalizing disorders. *Procedia—Social and Behavioral Sciences*, *30*, 236-241. doi:10.1016/j.sbspro.2011.10.047

Nigg, J. T. (2001). Is ADHD a disinhibitory disorder? *Psychological Bulletin*, *127*, 571-598.

Nigg, J. T., Willcutt, E. G., Doyle, A. E., & Sonuga-Barke, E. J. S. (2005). Causal heterogeneity in attention-deficit/hyperactivity disorder: Do we need neuropsychologically impaired subtypes? *Biological Psychiatry*, *57*, 1224-1230. doi:10.1016/j.biopsych.2004.08.025

Nitsche, M. A., Boggio, P. S., Fregni, F., & Pascual-Leone, A. (2009). Treatment of depression with transcranial direct current stimulation (tDCS): A review. *Experimental Neurology*, *219*, 14-19. doi:10.1016/j.expneurol.2009.03.038

Nitsche, M. A., Cohen, L. G., Wassermann, E. M., Priori, A., Lang, N., Antal, A., . . . Pascual-Leone, A. (2008). Transcranial direct current stimulation: State of the art 2008. *Brain Stimulation*, *1*(3), 206-223. doi:10.1016/j.brs.2008.06.004

Nitsche, M. A., Doemkes, S., Karaköse, T., Antal, A., Liebetanz, D., Lang, N., . . . Paulus, W. (2007). Shaping the effects of transcranial direct current stimulation of the human motor cortex. *Journal of Neurophysiology*, *97*, 3109-3117. doi:10.1152/jn.01312.2006

Owen, A. M., McMillan, K. M., Laird, A. R., & Bullmore, E. (2005). N-back working memory paradigm: A meta-analysis of normative functional neuroimaging studies. *Human Brain Mapping*, *25*, 46-59. doi:10.1002/hbm.20131

Ozonoff, S., Goodlin-Jones, B. L., & Solomon, M. (2005). Evidence-based assessment of autism spectrum disorders in children and adolescents. *Journal of Clinical Child & Adolescent Psychology*, *34*, 523-540. doi:10.1207/s15374424jccp3403_8

Palm, U., Reisinger, E., Keeser, D., Kuo, M.-F., Pogarell, O., Leicht, G., . . . Padberg, F. (2013). Evaluation of sham transcranial direct current stimulation for randomized, placebo-controlled clinical trials. *Brain Stimulation*, *6*, 690-695. doi:10.1016/j.brs.2013.01.005

Patros, C. H., Alderson, R. M., Kasper, L. J., Tarle, S. J., Lea, S. E., & Hudec, K. L. (2015). Choice-impulsivity in children

and adolescents with attention-deficit/hyperactivity disorder (ADHD): A meta-analytic review. *Clinical Psychology Review*, *43*, 162-174.

Pennington, B. F., & Ozonoff, S. (1996). Executive functions and developmental psychopathology. *Journal of Child Psychology and Psychiatry*, *37*, 51-87.

Pope, P. A., Brenton, J. W., & Miall, R. C. (2015). Task-specific facilitation of cognition by anodal transcranial direct current stimulation of the prefrontal cortex. *Cerebral Cortex*, *25*, 4551-4558. doi:10.1093/cercor/bhv094

Rolls, E. T. (2004). The functions of the orbitofrontal cortex. *Brain and Cognition*, *55*, 11-29. doi:10.1016/S0278-2626(03)00277-X

Romine, C. B., Lee, D., Wolfe, M. E., Homack, S., George, C., & Riccio, C. A. (2004). Wisconsin Card Sorting Test with children: A meta-analytic study of sensitivity and specificity. *Archives of Clinical Neuropsychology*, *19*, 1027-1041.

Rubia, K. (2011). "Cool" inferior frontostriatal dysfunction in attention-deficit/hyperactivity disorder versus "hot" ventromedial orbitofrontal-limbic dysfunction in conduct disorder: A review. *Biological Psychiatry*, *69*(12), e69-e87. doi:10.1016/j.biopsych.2010.09.023

Rubia, K., Smith, A. B., Brammer, M. J., Toone, B., & Taylor, E. (2014). Abnormal brain activation during inhibition and error detection in medication-naive adolescents with ADHD. *American Journal of Psychiatry*, *162*, 1067-1075.

Salehinejad, M. A., Ghanavai, E., Rostami, R., & Nejati, V. (2017). Cognitive control dysfunction in emotion dysregulation and psychopathology of major depression (MD): Evidence from transcranial brain stimulation of the dorsolateral prefrontal cortex (DLPFC). *Journal of Affective Disorders*, *210*, 241-248. doi:10.1016/j.jad.2016.12.036

Salehinejad, M. A., Nejati, V., & Derakhshan, M. (2017). Neural correlates of trait resiliency: Evidence from electrical stimulation of the dorsolateral prefrontal cortex (dLPFC) and orbitofrontal cortex (OFC). *Personality and Individual Differences*, *106*, 209-216. doi:10.1016/j.paid.2016.11.005

Salehinejad, M. A., Rostami, R., & Ghanavati, E. (2015). Transcranial direct current stimulation of dorsolateral prefrontal cortex of major depression: Improving visual working memory, reducing depressive symptoms. *NeuroRegulation*, *2*, 37-49. doi:10.15540/nr.2.1.37

Schneider, W., Eschman, A., & Zuccolotto, A. (2002). *E-Prime: User's guide.* Psychology Software Incorporated. Pittsburgh, PA, USA

Schulz, K. P., Fan, J., Tang, C. Y., Newcorn, J. H., Buchsbaum, M. S., Cheung, A. M., . . . Halperin, J. M. (2004). Response inhibition in adolescents diagnosed with attention deficit hyperactivity disorder during childhood: An event-related fMRI study. *American Journal of Psychiatry*, *161*, 1650-1657. doi:10.1176/appi.ajp.161.9.1650

Seidman, L. J., Valera, E. M., & Makris, N. (2005). Structural brain imaging of attention-deficit/hyperactivity disorder. *Biological Psychiatry*, *57*, 1263-1272. doi:10.1016/j.biopsych.2004.11.019

Smith, A. B., Taylor, E., Brammer, M., Toone, B., & Rubia, K. (2006). Task-specific hypoactivation in prefrontal and temporoparietal brain regions during motor inhibition and task switching in medication-naive children and adolescents with attention deficit hyperactivity disorder. *American Journal of Psychiatry*, *163*, 1044-1051.

Soltaninejad, Z., Nejati, V., & Ekhtiari, H. (2015a). Effect of anodal and cathodal transcranial direct current stimulation on DLPFC on modulation of inhibitory control in ADHD. *Journal of Attention Disorders*, 1-8. Advance online publication. doi:10.1177/1087054715618792

Soltaninejad, Z., Nejati, V., & Ekhtiari, H. (2015b). Effect of transcranial direct current stimulation on remediation of inhibitory control on right inferio frontal gyrus in attention deficit and hyperactivity symptoms. *Rehabilitation Medicine*, *3*(4), 1-9.

Sonuga-Barke, E. J. S. (2005). Causal models of attention-deficit/hyperactivity disorder: From common simple deficits to multiple developmental pathways. *Biological Psychiatry*, *57*, 1231-1238.

Summerfelt, A. T., Alphs, L. D., Funderburk, F. R., Strauss, M. E., & Wagman, A. I. (1991). Impaired Wisconsin card sort performance in schizophrenia may reflect motivational deficits. *Archives of General Psychiatry*, *48*, 282-283. doi:10.1001/archpsyc.1991.01810270094019

Swanson, J., Nolan, W., & Pelham, W. (1992). *The SNAP-IV Rating Scale*. Irvine: University of California.

Swanson, J. M., Schuck, S., Porter, M. M., Carlson, C., Hartman, C. A., Sergeant, J. A., . . . Wigal, T. (2012). Categorical and Dimensional Definitions and Evaluations of Symptoms of ADHD: History of the SNAP and the SWAN Rating Scales. *The International journal of educational and psychological assessment*, *10*(1), 51-70.

Sweitzer, M. M., Allen, P. A., & Kaut, K. P. (2008). Relation of individual differences in impulsivity to nonclinical emotional decision making. *Journal of the International Neuropsychological Society*, *14*, 878-882. doi:10.1017/S1355617708080934

Vanderhasselt, M.-A., De Raedt, R., Baeken, C., 'Leyman, L. D., & D'haenen, H. (2006). The influence of rTMS over the left dorsolateral prefrontal cortex on Stroop task performance. *Experimental Brain Research*, *169*, 279-282. doi:10.1007/s00221-005-0344-z

Vendrell, P., Junqué, C., Pujol, J., Jurado, M. A., Molet, J., & Grafman, J. (1995). The role of prefrontal regions in the Stroop task. *Neuropsychologia*, *33*, 341-352.

Verbruggen, F., Aron, A. R., Stevens, M. A., & Chambers, C. D. (2010). Theta burst stimulation dissociates attention and action updating in human inferior frontal cortex. *Proceedings of the National Academy of Sciences of the United States*, *107*, 13966-13971.

Verbruggen, F., Liefooghe, B., Notebaert, W., & Vandierendonck, A. (2005). Effects of stimulus–stimulus compatibility and stimulus–response compatibility on response inhibition. *Acta Psychologica*, *120*, 307-326.

Verbruggen, F., & Logan, G. D. (2008). Response inhibition in the stop-signal paradigm. *Trends in Cognitive Sciences*, *12*, 418-424. doi:10.1016/j.tics.2008.07.005

Wager, T. D., Sylvester, C.-Y. C., Lacey, S. C., Nee, D. E., Franklin, M., & Jonides, J. (2005). Common and unique components of response inhibition revealed by fMRI. *NeuroImage*, *27*, 323-340.

Ward, J. (2015). *The student's guide to cognitive neuroscience*. New York, NY: Psychology Press.

Willcutt, E. G., Doyle, A. E., Nigg, J. T., Faraone, S. V., & Pennington, B. F. (2005). Validity of the executive function theory of attention-deficit/hyperactivity disorder: A meta-analytic review. *Biological Psychiatry*, *57*, 1336-1346. doi:10.1016/j.biopsych.2005.02.006

Wilmshurst, L. (2014). *Essentials of child and adolescent psychopathology*. Hoboken, New Jersey: John Wiley.

Zanolie, K., Van Leijenhorst, L., Rombouts, S. A. R. B., & Crone, E. A. (2008). Separable neural mechanisms contribute to feedback processing in a rule-learning task. *Neuropsychologia*, *46*, 117-126. doi:10.1016/j.neuropsychologia.2007.08.009

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