THE EFFECT OF TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS) ON COGNITIVE FUNCTIONING IN INDIVIDUALS WITH ATTENTION DEFICIT/ HYPERACTIVITY DISORDER (ADHD)

Noa Beiman, Renana Eitan, Doron Todder, Eldad Keha, and Eyal Kalanthroff

Abstract

Objective: Attention deficit/hyperactivity disorder (ADHD) is among the most prevalent neurodevelopmental disorders in children, often persisting into adulthood. It is characterized by two symptom domains: impulsivity and inattention, both associated with underlying neural and cognitive deficiencies. This study is the first to investigate the potential effects of transcranial direct current stimulation (tDCS) targeting the left DLPFC on cognitive functions related to both symptom domains in adults with ADHD compared to typically developed controls.

Method: This pre-registered clinical trial enrolled 55 participants, 25 of whom were diagnosed with ADHD. Participants completed a series of cognitive tasks before and after receiving either tDCS or sham treatment.

Results: In the ADHD group, tDCS treatment improved measures associated with inattention, but not measures related to impulsivity. In the control group, tDCS treatment had no benefits.

Conclusions: The discrepancy in treatment response observed between inattentive and impulsive symptoms has implications for understanding the neurobiological mechanisms of ADHD. Our findings offer new evidence supporting the positive impact of tDCS on cognitive functions linked to inattention.

Key words: attention-deficit/hyperactivity disorder (ADHD),transcranial direct current stimulation (tDCS), impulsivity, attention, cognition

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Attention Deficit/Hyperactivity Disorder (ADHD) is one of the most common neurodevelopmental disorders among children and often persists into adulthood (Kessler et al., 2005). ADHD is characterized by pervasive and persistent symptoms of inattention and impulsivity/hyperactivity (APA, 2022). Over the years, these symptoms have been associated with deficit in several neuropsychological cognitive functioning, such as inhibitory control (Lijffijt et al., 2005; Schachar et al., 1995), interference control (Homack & Riccio, 2004; Lansbergen et al., 2007), visuospatial attention (Cohen & Kalanthroff, 2019), and sustained attention (Cortese et al., 2006; Epstein et al., 2003; Nichols & Waschbusch,

2004). Consistently, therapeutic approaches to ADHD have been trying to focus on these cognitive deficits, with the goal of achieving better control over attentional processes (Solanto et al., 2010; Steele et al., 2006). In the current study, we aim to focus on one such therapeutic tool, namely transcranial Direct Current Stimulation (tDCS), and investigate its effects on various cognitive functions in individuals with and without ADHD.

ADHD is characterized by two symptom domains: inattention and impulsivity/hyperactivity (APA, 2022). Inattention is mainly manifested in distractibility and concentration difficulties. From a cognitive perspective, inattention is often linked to deficits in sustained attention

- the ability to maintain constant level of attention to a task over long periods of time (Avisar & Shalev, 2011). The most common task to measure sustained attention is the continuous performance task (CPT), which requires participants to detect a rare target among rapidly presented non-targets (Conners et al., 2000). This task, or similar ones, is commonly used for ADHD diagnosis and research (e.g., Huang-Pollock et al., 2012; McGee et al., 2000) due to the significant evidence that individuals with ADHD exhibit low levels of sustained attention (Cortese et al., 2006; Epstein et al., 2003), which manifests mainly in higher omission rates (number of missed targets divided by number of target trials; Advokat et al., 2007). ADHD inattentiveness is also related to reduced or deficient working memory, which is often considered a core deficit in ADHD (Alderson et al., 2013; Brown, 2009). Specifically, deficits in the ability to hold and manipulate information in the short-term memory might make it difficult for individuals with ADHD to engage in a task, as they may lose crucial information necessary for its completion (Wiest et al., 2022). Working memory is commonly assessed using the *N*-back task (Kerns et al., 2001; Willcut et al., 2005). Evidence from the *N*-back task show that individuals with ADHD make more omission errors compared to typically developed controls (Ehlis et al., 2008).

The second ADHD symptom domain, impulsivity, is broadly defined as acting without foresight, encompassing various aspects of behavior. In individuals with ADHD, impulsivity is often manifested as the inability to withhold a response (APA, 2013; Logan et al., 1997). Interestingly, in the CPT and N-back tasks mentioned above, omission rates reflect inattention while commission rates (number of false alarm responses divided by number of non-target trials) reflect impulsivity (Acosta-Lopez et al., 2021; Allenby et al., 2018; Conners et al., 2000). Furthermore, it has been suggested that deficits in two additional cognitive mechanisms underlie ADHD impulsivity: inhibitory control and interference control (Barkley, 1997, 1999). Inhibitory control refers to the ability to stop an ongoing thought or behavior that is inappropriate or irrelevant in a specific context. It is commonly measured using the stopsignal task (Senkowski et al., 2023). The suppression of a no-longer required response supports goal-directed behavior, while impulsive behavior would reflect in erroneous responses to stop signal trials and poorer task performance (Winstanley et al., 2006). Children and adults with ADHD were found to be significantly slower and less efficient in inhibiting their responses in this task, compared to typically developed controls (Lijffijt et al., 2005; Oosterlaan et al., 1998; Schachar et al., 1995). A second mechanism associated with impulsivity is interference control, which refers to the ability to suppress irrelevant or distracting information from the environment to achieve and maintain goal-directed behavior (Coghill et al., 2014; Willcutt et al., 2005). Interference control is widely measured using the Stroop task (Van Mourik et al., 2005). Individuals with ADHD often exhibit impaired Stroop performance, which is typically characterized by a larger interference effect compared to typically developed controls (Homack & Riccio, 2004; Lansbergen et al., 2007). Table 2 summarizes the different tasks and measurements that are associated with the different ADHD symptom domains.

A historical controversy regarding the relationship between the ADHD symptom domains is reflected in the changes to the disorder's definition over the past four decades. While in the DSM-III the definition of the disorder included both a hyperactive type and a non-hyperactive type (APA, 1980), mainly referring to the potential existence of impulsive symptoms without hyperactivity, in the DSM-V (APA, 2013), the subtypes have been reconceptualized as "presentations", reflecting the increasing evidence that symptoms often change within individuals across circumstances and across lifetime (Harvey et al., 2015; Lahey et al., 2005; Manly et al., 2001), and that all ADHD "presentations' generally share similar neuropsychological profiles (Chhabildas et al., 2001; Geurts et al., 2005; Solanto et al., 2007), as well as similar responses to treatment (Toplak et al., 2009). While the evidence concerning the differentiation of ADHD subtypes remains inconclusive, the differentiation between inattentive and impulsive symptoms may be useful. For example, reading difficulties are linked predominantly to inattention (Paloyelis et al., 2010; Willcutt et al., 2007), while oppositional behaviors are linked to impulsivity (Wood et al., 2009). In addition, inattentive and impulsive symptoms have distinct relations with co-occurring neuropsychological deficits (Kuntsi et al., 2014).

Despite notable discrepancies in this area of study (APA, 2022; Segal et al., 2025), neurological studies found potential markers for ADHD in the brain, in areas related to the cognitive mechanisms mentioned above (McCarthy et al., 2014). Specifically, a meta-analysis of 55 fMRI studies revealed significant hypoactivation in bilateral attention networks, including the dorsolateral prefrontal cortex (DLPFC), in individuals with ADHD compared to typically developed controls (Cortese et al., 2006). Along with other cognitive functions, the DLPFC is thought to be associated with working memory (Bédard et al., 2014), sustained attention (Christakou et al., 2013), inhibitory control (Blasi et al., 2006), and interference control (Alvarez & Emory, 2006) - the main cognitive functions associated with ADHD. Thus, it seems that the DLPFC might be an important target for treatment in individuals with ADHD.

Transcranial direct current stimulation (tDCS) is a brain stimulation method, by which a weak direct current applied on the scalp modulates cortical excitability by shifting resting neuronal membrane potential (Brunoni et al., 2012). Anodal stimulation increases cortical excitability, while cathodal stimulation decreases it. TDCS is considered safe, has almost no essential side effects (Andrade et al., 2014; Krishnan et al., 2015), and has proven to be helpful in reducing clinical symptoms in various disorders (Bennabi & Haffen, 2018; Brunelin et al., 2012; Garcia-Gonzalez et al., 2021; Lapenta et al., 2018), including ADHD (Brauer et al., 2021). In addition, over the past twenty years, tDCS has been researched both in clinical and general populations, producing notable improvements across various cognitive functions (Begemann et al., 2020; Chen et al., 2022; Hsu et al., 2015; Satorres et al., 2022). Nevertheless, the evidence regarding tDCS efficacy in enhancing cognitive functioning in ADHD is mixed and inconsistent (Berger et al., 2021). Despite employing similar tDCS protocols, different studies have yielded varying results. For example, using the CPT, Allenby and colleagues (2018) found that after one tDCS session, individual with ADHD demonstrated improvement in commission rates but not in omission rates. However, Jacoby and Lavidor (2018) did not find any effect for the tDCS treatment in both these measures. In the N-back task, Nejati et al., (2020) found faster RTs in individuals with ADHD after a tDCS session compared to prior, with no effect on accuracy rates. Conversely, when using the same task with ADHD adolescents, Sotnikova and colleagues (2017) found faster RTs and reduced RT variability, but lower accuracy rates after tDCS. In the stop-signal task, Dubreuil-Vall and colleagues (2020)

found increased no-stop RTs (RT for non-stop-signal trials) in individuals with ADHD after a tDCS session. However, Allenby and colleagues (2018) did not find any effects on the performance in the stop-signal task following tDCS in individuals with ADHD. In the Stroop task, Nejati and colleagues (2020) found ADHD participants to present increased accuracy after tDCS session, while Soltaninejad and colleagues (2019) did not find any effects for tDCS in this population. Finally, Berger and colleagues (2021) recently showcased that while tDCS reduced clinical symptoms in children with ADHD, another form of transcranial electric stimulation (tES), namely tRNS, resulted in even greater symptom improvement. The positive effects of tRNS were further validated in subsequent studies (Dakwar-Kawar et al., 2022, 2023). It should be noted, that although all studies mentioned above employed the same anodal stimulation brain area (DLPFC), and tested individuals with ADHD, tDCS protocols and study designs did vary across the different studies, posing a challenge to render comparisons between them. Additionally, some of the studies did not conduct comparisons with typically developed controls, making the investigation of the unique treatment effect on ADHD challenging. Therefore, further investigation of tDCS potential effects on ADHD cognitive functioning is required. Assessing the treatment's effects across a variety of tasks within a single study, and compared to typically developed controls, remains notably important.

The goal of the current study was to examine the effects of a single tDCS session, aimed at the left DLPFC, on broad spectrum cognitive functions related both to inattentiveness (sustained attention and working memory) and to impulsivity (inhibitory control and interference control; see table 2) among adults diagnosed with ADHD in comparison to typically developed controls, in a pre-registered (Clinical Trials.gov identifier: NCT04697316) randomized, single-blind, controlled, pretest-posttest design. We hypothesized that performance in all cognitive tasks will be enhanced following the tDCS session, while sham treatment was expected to yield lesser, or no cognitive improvement. Furthermore, we predicted a greater improvement in the ADHD group compared to the control group, due to a possible ceiling effect in the control group (Hsu et al., 2015).

Method

Participants

Twenty-five participants diagnosed with ADHD and 30 typically developed controls participated in the study in return for a small monetary compensation (~50 USD). All participants were university and college students, between the ages of 18-30, were right-handed, and had no history of any psychiatric disorder or neurological condition (other than ADHD for the ADHD group). Participants were recruited by means of advertisements on campus and online platforms. Participants in the ADHD groups were diagnosed with ADHD by the ELAH Institute for the Diagnosis of Learning Disabilities and Attention Deficits at the National Institute for Testing and Evaluations (NITE; established by the associated heads of the universities in Israel; see below) within 2 years prior to the experiment. ADHD participants who reported taking stimulants prescribed for ADHD were allowed to participate but were asked to refrain from medication on the day of the experiment and until completing all study procedures. ADHD and controls were randomly assigned into one of two groups in a single-blind design: tDCS treatment (N ADHD = 12, N control = 15) or sham treatment (N ADHD = 13, N control = 15). A power analysis using G*Power 3.1 (Faul et al., 2007) indicated that the current sample allowed for examination of the two-way interactions (group X treatment) at a power > 80% to test small to medium effects size (0.40 based on Salehinejad et al., 2020), with a Type I error (α < .05). The parameters that were used were as follows: Cohen's f effect size of 0.40, 4 groups, 2 measurements.

Clinical diagnosis

The ELAH institute's ADHD diagnosis includes a psychiatric interview, 2 self-report questionnaires, and 20 computerized tests that assessed cognitive functions, language (reading and writing), arithmetic thinking, attention, memory, perception, and general processing speed. ADHD diagnosis was determined based on the comprehensive and converging evidence and was compatible with DSM-V criteria. In addition, all participants in the ADHD group had a previous diagnosis of ADHD before the age of 12 (given by a certified psychiatrist or neurologist in their community), scored ≥ 7 on part A of the adult ADHD self-report scale at the time of the experiment, and did not report any other psychiatric diagnosis or neurological condition. Control participants completed an in-person interview with a clinical psychologist to rule out ADHD or other psychiatric or neurological disorders. As part of this interview, control participants were asked if they were ever diagnosed with ADHD or any other psychiatric or neurological condition, ever sought diagnosis or treatment for ADHD or any psychiatric disorder or were ever suspected of having ADHD. In addition, all control participants scored < 4 in the ASRS. The full demographic and clinical characteristics of the sample are presented in table 1.

Table 1. Demographic and clinical characteristics of the sample (N=55)

Total sample (N=55)	Mean	SD	Range
Age	23.04	2.20	18-30
7.80	23.01	2.20	10 00
	N	%	
Males	20	36.36	
Females	35	63.63	
ADHD group (N=25)			
Age	23.16	2.27	18-27
ASRS	13.20	2.63	7-18
	N	%	
Males	7	28	
Females	18	72	
Control group (N=30)			
Age	22.93	2.18	20-30
ASRS	2.93	2.80	0-9
	N	%	
Males	13	43.33	
Females	17	56.67	

Note. SD=standard deviation. ADHD = attention deficit/ hyperactivity disorder. ASRS = adult ADHD self-report scale. No significant differences were found between the groups, except for higher ASRS scores in the ADHD group (see Results section).

Procedure

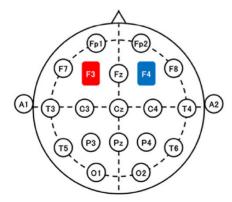
The study was approved by the institutional review board (IRB) of the Jerusalem Mental Health Center (approval number 20-19). The study was pre-registered. After a brief screening to ensure eligibility participants were invited to the lab to sign an inform consent and to complete the study's procedures. First, participants eligibility was confirmed, and clinical assessments and self-report questionnaires (including a demographic questionnaire and the ASRS) were administered. Next, participants completed the computerized tasks before completing the tDCS/sham session followed by a second administration of the tasks. Task order was counterbalanced across participants but remained identical in both administrations (pre & post treatment). For the tasks, participants were seated in a quiet room, in front of a HP EliteDisplay E240 LED 23.8-inch monitor. Data collection and stimulus presentation were controlled by an HP Elite 800G3TWR computer with an Intel i7-8700 4.20GHz processor. Each task began with a practice block, which included feedback for accuracy and reaction time (RT). Practice trials were not included in the analyses. Tasks completion was approximately 60 minutes (including breaks). Next, tDCS or sham treatment was administered (see Tools and Materials for further detail). Afterwards, participants repeated all cognitive tasks (with no practice blocks) in the same order as at pre-treatment. Approximately 5 hours and 24 hours after the end of the experiment, participants received expected follow-up phone calls in which they were asked about possible side effects. At the 5-hours' time-point, three participants (all from tDCS group) reported experiencing a mild headache after the treatment, which subsided within a couple of hours. No adverse side effects were recorded at the 24-hours' time point. As part of the first phone call (5h), the experimenter confirmed that participants did not use Methylphenidate or any equivalent drug. As part of the second phone call (24h), the experimenter asked participants to speculate whether they were assigned to the experimental or the sham control group.

Tools and Materials

TDCS device

Model 1300A 1x1 Transcranial Direct Current (tDCS) Low-Intensity Stimulator and accessories were used. TDCS protocol was conducted according to Metzuyanim-Gorlick and Mashal (2016). To stimulate the left DLPFC, the anode electrode was placed over F3

Figure 1. TDCS electrodes locations



Note. Anodal electrode in red and cathodal electrode in blue.

and the cathode was placed over F4 (see **figure 1**). Each stimulation was applied for 20 min at 2mA intensity. For the sham treatment, stimulation stopped after 30 seconds. Current was renewed for 2 seconds at the end of the session to mimic the tDCS stimulation.

Adult ADHD Self-Report Scale (ASRS)

An 18-item self-report measure that assesses the severity of ADHD symptoms and was used to verify the ADHD diagnosis (for example: "how often do you feel overly active and compelled to do things, like you were driven by a motor?"). Participants were asked to rate the frequency of ADHD symptoms on a five-point likret scale ranging from 0 - "never" to 4 - "very often". A sum score of 4 or higher in part A of the ASRS is consistent with ADHD diagnosis (For further details see: Kessler et al., 2005). The ASRS has excellent test-retest reliability (.89) and good internal consistency (.85; Konfortes, 2010). Cronbach's alpha in the current sample was α =.93.

Tasks

Continuous Performance Task (CPT). The CPT (Conners et al., 2000) is a computerized task aimed to assess sustained attention. The task included 100 trials. Each trial started with an 800ms fixation (a black plus sign at the center of the screen). Next, a random English letter was presented at the center of the screen for 1150ms or until keypress. In 10% of the trials, the letter "X" was presented (target stimulus). Participants were instructed to respond by pressing the "Z" key as quickly as possible for any letter presented, except for the letter "X". When the letter "X" was presented, participants were instructed to press the "/" key. Participants were instructed to use the index finger of both hands. Omission errors (pressing "Z" in response to the letter "x") and commission errors (pressing "/" in response to any letter except for the letter "x") were calculated.

N-back Task. The N-back task (Jaeggi et al., 2010) is a computerized task aimed to as assess working memory. The N-back task is a sequential letter task in which stimuli are single letters presented in a random sequence on a neutral gray background. The task included 120 trials. Each trial started with an 800ms fixation (a black plus sign at the center of the screen) followed by the presentation of a single letter at the center of the screen for 1150ms. For maximal randomization, a sampling with replacement was used for the N-back letters, so each letter had an equal chance of appearing in any given trial. Participants were instructed to respond by pressing the space bar only if the letter that is currently presented was identical to the letter presented two trials earlier (2-back). Omission errors (failing to press the space bar when the letter presented was identical to the letter presented two trials ago) and commission errors (pressing the space bar when the letter presented was not identical to the letter presented two trials ago) were calculated.

Stop-Signal Task. The stop-signal task (Verbruggen & Logan, 2008) is a computerized task aimed to assess inhibitory control. The task included 120 trials. Each trial started with an 800ms fixation (a black plus sign at the center of the screen). Next, a visual go stimulus ("X" or "O") was presented at the center of the screen for 1500ms or until a keypress. Participants were instructed to press the "S" key if they saw a circle, and the "L" key if they saw an X, using the index fingers of both hands. The instructions stated to press the correct key as quickly and accurately as possible and emphasized not to wait for a potential stop-signal. On a

random selection of 25% of the trials, an auditory stop signal ('beep'; 750 Hz, 75ms) was delivered after the go stimuli, signaling the participants to withhold their reaction. The duration between the go and stop-signals (stop-signal delay; SSD) was initially set at 250ms and was subsequently adjusted by a staircase tracking procedure: after each successful stopping the SSD was extended by 50ms (making it harder to stop) and after each unsuccessful stopping the SSD was shortened by 50ms (making it easier to stop). Stop-signal reaction time (SSRT) is defined as the as the time needed for successful inhibition at 50% of the times and is considered a hallmark of inhibitory control (Verbruggen & Logan, 2008). SSRT was calculated using the integration model (Verbruggen & Logan, 2008), such that no-stop RTs were determined by the nth RT, that is, n (number of no-signal trials) \times p (response/signal), and SSRT was then calculated as nth RT - median SSD.

Stroop Task. The Stroop task (Stroop, 1935) is a computerized task aimed to assess interference control. The task included 80 trials. Each trial started with an 800ms fixation (a black plus sign at the center of the screen). Next, a target stimulus which could be a colorword or a meaningless letter string, was presented at the center of the screen for 2000ms or until keypress. The ink color and the meaning of the word stimuli could be either congruent (e.g., the word "GREEN" written in green), incongruent (e.g., "RED" written in green) or neutral ("XXXX" written in green). Congruent and incongruent stimuli were four color words that could appear in four different colors each (green, blue, yellow, and red). This yielded 12 incongruent stimuli

and 4 congruent stimuli. Neutral stimuli appeared in the same four colors, yielding four different neutral stimuli. Participants were instructed to identify the

ink color of the stimulus and to ignore its meaning. RTs for each condition (congruent, incongruent, neutral) were measured from the stimulus onset to response, and two effects were calculated: interference effect (*mean RT of incongruent trials*) and facilitation effect (*mean RT of neutral trials*) and facilitation effect (*mean RT of neutral trials*) and the stimulus (Kalanthroff & Henik, 2013; Kalanthroff et al., 2018; Littman et al., 2019).

Results

The raw data of the current study is available online https://data.mendeley.com/datasets/j6g4vsmk4z/1. Full sample characteristics by group can be found in **table 1**. A two-way analysis of variance (ANOVA) confirmed no significant age differences between the groups, as there was no main effects for group (F(3,51)=.14, p=.71), treatment (F(3,51)=.04, p=.84), and no significant two-way interaction (F(3,51)=.05, p=.82). Additionally, a chi-square test to compare group differences in gender proportion revealed no difference between the four groups $(\chi^2(3)=3.39, p=.34)$.

For each task measure, a difference effect (post-treatment minus pre-treatment) was calculated. The difference was then subjected to a two-way ANOVA, with group (ADHD vs. control) and treatment (tDCS vs. sham) as between subject measures. The complete descriptive statistics is presented in **table 3**.

Table 2. Summary of outcome measures by task and their association to ADHD symptom domain

Task	Cognitive Function	Measure	Symptom Domain
СРТ	Sustained attention	Omission rate	Inattention
CPT	Sustained attention	Commission rate	Impulsivity
<i>N</i> -back	Working memory	Omission rate	Inattention
<i>N</i> -back	Working memory	Commission rate	Impulsivity
Stop-signal	Inhibitory control	SSRT	Impulsivity
Stroop	Interference control	Facilitation effect	Impulsivity
Stroop	Interference control	Interference effect	Impulsivity

Note. CPT = continuous performance task. SSRT = stop signal reaction time.

Table 3. Descriptive statistics of tasks measures by group and treatment

	ADHD				Control			
	tDCS		sham		tDCS		sham	
	pre- treatment	post- treatment	Pre- treatment	post- treatment	pre- treatment	post- treatment	pre- treatment	post- treatment
CPT OR	0.75 (0.12)	0.63 (0.22)	0.59 (0.25)	0.69 (0.24)	0.70 (0.26)	0.62 (0.26)	0.62 (0.23)	0.44 (0.18)
CPT CR	.03 (.03)	.02 (.02)	.03 (.06)	.04 (0.11)	.02 (.02)	.02 (.02)	.02 (.01)	.02 (.04)
N-back OR	0.34 (0.20)	0.17 (0.14)	0.37 (0.21)	0.40 (0.26)	0.23 (0.13)	0.21 (0.13)	0.33 (0.18)	0.29 (0.13)
N-back CR	.08 (.07)	.06 (.06)	0.11 (.08)	.09 (.07)	.08 (.07)	.08 (.09)	0.1(.05)	.09 (.09)
SSRT	240.28 (67.25)	263.78 (96.16)	317.23 (124.96)	275.03 (82.63)	251.93 (58.48)	242.06 (70.15)	253.83 (72.68)	227.05 (58.93)
Stroop FE	-9.51 (72.52)	19.32 (46.68)	43.84 (59.82)	4.16 (105.36)	24.46 (67.45)	28.12 (58.41)	34.68 (71.88)	29.50 (51.51)
Stroop IE	85.58 (97.26)	87.90 (87.87)	37.66 (68.59)	43.23 (87.97)	27.66 (51.45)	1.21 (60.12)	27.35 (88.74)	16.36 (76.65)

Note. Mean and standard deviation (in brackets) of all measures from all tasks, before and after treatment by group and treatment. CPT= continuous performance task. SSRT = stop signal reaction time. tDCS = transcranial direct current stimulation. ADHD = attention deficit/hyperactivity disorder. OR = omission rate. CR = commission rate. FE = facilitation effect. IE = interference effect.

Continuous Performance Task (CPT)

The data of one participant (ADHD sham group) was not fully recorded due to a technical error. Participants with 100% omission rate both at pretreatment and at post-treatment were excluded from the analysis. Three participants were excluded for this reason (one participant from the control tDCS group, one participant from the control sham group, and one participant from the ADHD tDCS group). Thus, the final sample included 51 participants.

Omission rates and commission rates were calculated for each participant in each time-point. Subsequently, the difference between the two timepoints was subjected to a two-way ANOVA with group and treatment as between-subject factors. For omission rate, the analysis yielded a significant main effect for group, F(1,47)=4.31, p=.04, but no significant effect for treatment, F(1,47)=0.24, p=.63. A significant interaction was found, F(1,47)=8.00, p<.01, =0.15 (see figure 2, left upper panel). Planned comparisons using independent sample t-tests revealed that while in the control group there was no significant difference between the \overrightarrow{tDCS} and sham groups, t(1,47)=1.27, p=.21, in the ADHD group there was a significant difference between the groups, t(1,47)=-2.66, p=.01, Cohen's d=1.11, indicating significantly enhanced performance after the treatment in the tDČS group but not in the sham group.

For commission rate, the results yielded no significant main effect for group, F(1,47)=0.16, p=.69, no main effect for treatment, F(1,47)=1.11, p=.30, and the two-way interaction was not significant, F(1,47)=0.95, p=.33.

N-back Task

Omission rates and commission rates were calculated for each participant in each time-point. Subsequently, the difference between the two timepoints was subjected to a two-way ANOVA with group and treatment as between subject factors. For omission rate, the analysis yielded no significant main effect for group, F(1,51)=3.49, p=.07, η_p^2 or for treatment F(1,51)=0.71 p=.40. However, a si treatment, F(1,51)=0.71, p=.40. However, a si interaction was found, F(1,51)=5.65, p=.02, (see figure 2, right upper panel). Planned comparisons using independent sample *t*-tests revealed that while in the control group there was no significant difference between tDCS and sham, t(1,51)=0.38, p=.70, in the ADHD group there was a significant difference between tDCS and sham, t(1,51)=-2.87, p<.01, Cohen's d=1.15, indicating significantly enhanced performance after the treatment in the tDCS group but not in the sham group.

As in the CPT task, the analysis of commission rate yielded no significant main effect for group, F(1,51)=1.05, p=.31, no main effect for treatment, F(1,51)=.06, p=.81, and the two-way interaction was not significant, F(1,51)=0.13, p=.72.

Stop-Signal Task

Stop-signal reaction time (SSRT) is defined as the as the time needed for successful inhibition at 50% of the times and is considered a hallmark of inhibitory control (Verbruggen & Logan, 2008). Since SSRT is an estimation of the time needed for a participant to stop on 50% of the trials, if a participant's success in inhibiting responses to stop trials was significantly different from 50%, the SSRT would not be valid and the participant

should be excluded from further analysis (Verbruggen & Logan, 2008); (see also Verbruggen et al., 2008). Two participants (one participant from the ADHD sham group and one participant from the control sham group) were excluded due to the latter criterion. Thus, the final sample included 53 participants.

SSRTs were calculated using the integration model (Verbruggen & Logan, 2008) for each participant in each time-point. Subsequently, the difference between the two time-points was subjected to a two-way ANOVA with group and treatment as between subject factors. The analysis yielded no significant main effect for group, F(1,49)=0.11, p=.74, no main effect for treatment, F(1,49)=2.36, p=.13, and the two-way interaction was not significant, F(1,49)=0.79, p=.38 (see **figure 2**, left lower panel).

Stroop Task

Participants with extreme RTs (> 3 SD from their group mean) were excluded from the analyses (Kalanthroff et al., 2013). Two participants were excluded for this reason (one from the control tDCS group, and one from the control sham group). Thus, the final sample included 53 participants.

Mean RTs of correct responses were calculated for each participant for each condition. Outlier trials, with RTs > 2.5 SDs from participant's mean in each condition were excluded from analysis (2.7% of total trials). Facilitation effect and interference effect were calculated for each participant in each time point. Subsequently, the difference between the two timepoints was subjected to a two-way ANOVA with group and treatment as between-subject factors. For the facilitation effect, the analysis yielded no significant main effect for group, F(1,49)=.03, p=.87, no main effect for treatment, F(1,49)=1.87, p=.18, and the twoway interaction was not significant, F(1,49)=1.11, p=.30. For the interference effect, the analysis yielded no significant main effect for group, F(1,45)=0.44, p=.51, no main effect for treatment, F(1,49)=.02, p=.89, and the two-way interaction was not significant, F(1,49)=0.21, p=.65 (see **figure 2**, right lower panel).

Discussion

The current pre-registered clinical trial aimed to investigate the effects of anodal tDCS treatment to the left DLPFC, on several cognitive functioning, divided into measures that are more associated with inattentiveness and measures that are more associated with hyperactivity/impulsivity (see table 2). The results indicated that a single session tDCS treatment, compared to sham, led to improvement in the performance of ADHD patients, only in the measures that are associated with inattention: CPT omission rate, which reflects sustained attention, and N-back omission rate, which reflects working memory. Similar improvement was not evident in the control group. For the measures associated with hyperactivity/impulsivity, a single session tDCS treatment did not lead to any improvement, compared to the sham condition, in both groups. Namely, in both groups there was no difference between the pre- and post-treatment performance between the tDCS and sham groups in CPT commissions, N-back commissions, SSRT, and Stroop interference and facilitation, reflecting no effect of tDCS on inhibition and interference control. Notably, despite the provision of several breaks, participants with ADHD exhibited reduced performance in the sham condition across

CPT

N-back

OCS

N-back

OCS

Sham

OCS

ADHD

Control

Stop-signal

Stroop

Stop-signal

Stroop

ADHD

Stop-signal

Stroop

Figure 2. Improved performance in inattention tasks after tDCS treatment in ADHD participants

Note. Key results from all four tasks. The changes (post-treatment – pre-treatment) in omission rate (number of missed targets divided by number of target trials) in the CPT (left upper panel) and the N-back (right upper panel) tasks, stop-signal SSRT (nth RT – median SSD) (left lower panel) and Stroop interference effect (mean RT of incongruent trials – mean RT of neutral trials) (right lower panel) as a function of group and treatment. Downward bars indicate enhanced performance post treatment, while upward bars indicate poorer performance post treatment. Significant differences are marked with a star. Error bars are one standard error from the mean. CPT= continuous performance task. SSRT=stop signal reaction time. tDCS = transcranial direct current stimulation. ADHD = attention deficit/hyperactivity disorder.

most tasks and measures in the post-treatment phase compared to the pre-treatment phase. This finding could be attributed to fatigue and difficulty in maintaining attention throughout the lengthy experiment, which is expected in these participants. This further emphasizes the contribution of tDCS to measures in which these participants exhibited improved performance following the treatment. Importantly, these results do not necessarily support the notion of 'subtypes' in ADHD but rather refers to the different symptom domains that characterize the disorder and could present within the same individual (APA, 2013; Kuntsi, et al., 2014).

Our current protocol utilized anodal stimulation targeting the left DLPFC, a brain region known for its involvement in various cognitive functions, with sustained attention being particularly prominent (Barbey et al., 2013; Christakou et al., 2013). Our results show that anodal tDCS stimulation to this area resulted in enhanced performance in sustained attention and working memory tasks in adults with ADHD. Nevertheless, previous tDCS studies have yielded mixed results. For example, while our results are consistent with Bandeira and colleagues (2016), who, using the visual attention span task (TAVIS-3), found decrease in omission errors after a left DLPFC anodal stimulation in children with ADHD, our results are inconsistent with other studies which used the CPT and either did not find higher accuracy rates after anodal tDCS to the left DLPFC (Jacoby & Lavidor, 2018), or found enhanced accuracy which was attributed to fewer commission errors (and not fewer omission errors as

we found; Allenby et al., 2018). For working memory, our results are in line with previous tDCS studies that found enhanced *N*-back accuracy after anodal tDCS of the left DLPFC (Baumert et al., 2020; Mulquiney et al., 2011), but are inconsistent with other studies that have not found a similar effect (Nejati et al., 2020; Sotnikova et al., 2017). Our protocol also employed cathodal stimulation of the right DLPFC, decreasing right DLPFC cortical excitability. This resulted in null effects in all impulsivity measures. This finding is consistent with previous studies who found no improvement in the stop-signal task (Allenby et al., 2018) nor in the Stroop interference effect (Baumert et al., 2020) after anodal stimulation of the left DLPFC. Our results may also be in line with previous evidence pointing to better stop-signal performance after anodal stimulation of the right DLPFC (Friehs & Frings, 2018) or after cathodal stimulation of the left DLPFC (Friehs & Frings, 2019), because these configurations include activation of the right DLPFC, in contrary to our configuration. As can be seen, the literature regarding the effect of tDCS on cognitive functioning in ADHD is mixed. This heterogeneity in outcomes might be attributed to the varying study designs including task designs, studied populations, tDCS session duration, and stimulation intensity (Dedoncker et al., 2016; Farhat et al., 2022). The current study provides a consistent design to several tasks allowing clear comparisons between them. It is also important to emphasize that while most studies have focused on children with ADHD, this research shifts attention to adults. Since treatment guidelines for

adults are often drawn from pediatric studies despite significant developmental differences, this study seeks to address this gap by advancing knowledge on treatments specifically tailored for the adult ADHD population.

The difference in treatment response observed in our study between the two ADHD symptom domains, raises intriguing implications for their underlying nature. The results of the current study suggest that inattentive and impulsive symptoms may stem from differing neurobiological mechanisms, with the current tDCS configuration aligning more closely with the pathways associated with inattentive symptoms. As mentioned above, substantial evidence supports the relevancy of left DLPFC activation for inattention related measures such as sustained attention and working memory (Barbey et al., 2013; Christakou et al., 2013). At the same time, previous evidence highlights the role of right DLPFC along some other right frontal areas, for decreasing impulsivity (Mitchell & Potenza, 2014), which might explain our null results in impulsivity related measures, considering our protocol employed cathodal stimulation of the right DLPFC, decreasing cortical excitability in this area. For example, Steele and colleagues (2013) found right DLPFC activation to be associated with successful inhibitory control. Kerns and colleagues (2004) found a positive correlation between Stroop accuracy and right DLPFC activation, and other studies showed decreased risk-taking behaviors after anodal stimulation of the right DLPFC, both in the general population (Fecteau et al., 2007) and in a clinical population (Gilmore et al., 2018). This is also consistent with findings regarding Atomoxetine, which was found to effectively reduce measures of impulsivity in ADHD (Mitchell & Potenza, 2014; Robinson et al., 2008), and has been associated with increased right DLPFC activation (Araki et al., 2015; Cubillo et al., 2014). Another intriguing direction emerges from neuroimaging research, indicating that inattention may be associated with the DLPFC, while impulsivity may be linked to other brain regions such as the orbital frontal cortex (OFC) and the anterior cingulate cortex (Makris et al., 2009). Taken together, these findings underscore the complexity of symptomatology within ADHD, emphasizing the need for a nuanced approach that accounts for the underlying contributors of both symptom domains. Future research should consider the potential variation in the underlying neurophysiological nature of each symptom domain, when customizing interventions targeted for inattention or impulsivity. This is important because, as our findings indicate, a single approach may not be effective for both symptom domains. Further investigation into the distinct neural and physiological underpinnings of each symptom domain are required to advance the understanding of their origins and to refine tailored interventions that comprehensively address the complexity of ADHD cognitive phenotype.

Since no advantage for tDCS was observed in control participants, it seems our protocol might exhibit a distinct characteristic of cognitive enhancement that exclusively manifests within the clinical population – adults with ADHD. In the current study, control participants displayed some improvement in most tasks and measures, both in the tDCS and sham groups, with no difference between the two conditions. This indicates that while ADHD participants exhibited a fatigue effect, as discussed above, control participants exhibited a practice effect. One plausible consideration is that this practice effect could have led to a ceiling effect, potentially masking any improvement effect that

could have arisen from the treatment. Another potential explanation for the lack of effect in the control group, relates to the fact that in the current study, the measures that were affected by the tDCS treatment in the ADHD group were all accuracy related. A meta-analysis which evaluated 61 tDCS studies testing the performance in N-back and Go/No-Go tasks, revealed that while neuropsychiatric participants demonstrated increased accuracy after a single-session anodal tDCS, control participants were found to respond faster, but not more accurately (Dedoncker et al., 2016). Notably, even if the current study failed to identify an effect of tDCS on typically developed adults due to ceiling effect or lack of sensitive measures, our results clearly indicate that a single session tDCS treatment to the DLPFC has very little, if at all, noticeable effect on typically developed

Few limitations of the current study should be considered. The current study employed a betweensubject design to avoid the potential carryover effects that can emerge in crossover studies. Nevertheless, it is important to acknowledge that this design renders our results more sensitive to individual differences. This limitation should be considered especially given the high heterogeneity in ADHD (Wolfers et al., 2020). In addition, our goal was to conduct a comprehensive investigation which tests various cognitive domains within the same participants. As mentioned above, this extensive battery might have led to fatigue effects, particularly in the ADHD groups. This effect might actually mask some of the benefits of the tDCS treatment in those individuals. Finally, in their noteworthy work, Nigg et al. (2005) reviewed the literature on cognitive functioning in ADHD and made two key observations: (a) there is a significant overlap between the performance distributions of individuals with ADHD and those without it in all studies, and (b) a big portion of individuals with ADHD exhibits performance within the normal range. In fact, while they found that individuals with executive functions deficiencies were indeed more likely to have ADHD, they also found that only a minority of individuals with ADHD display these deficits. The idea that individuals with ADHD could be divided into two distinct groups, with and without executive function deficits, is also reflected in the influential dual pathway model of ADHD (Sonuga-Barke, 2002). This notion posits a significant limitation to the research on cognitive enhancement in ADHD as it might indicate that only ADHD patients who exhibit cognitive deficits, would benefit from treatment aimed to enhance cognitive functioning (Lambek et al., 2018). It might also suggest that the effect of such cognitive enhancement will transfer to reduction in ADHD symptom severity, only in this group. Future research is needed in order to test these hypotheses.

In summary, the current pre-registered study was the first to investigate the effect of anodal tDCS treatment targeting the left DLPFC on cognitive functions associated with both ADHD symptom domains, namely, inattention and impulsivity, in a before/after randomized clinical trial design, in ADHD adults compared to controls. While previous studies yielded mixed results, potentially due to variance in task administration, the current study was the first to conduct various tasks using identical and standardize administration. Results revealed that a single session of tDCS treatment improved the performance of ADHD patients in measures of sustained attention and working memory, compared to a sham condition, consistent with previous evidence supporting the role of the left DLPFC in these cognitive functions. We observed null effects in measures of impulsivity, highlighting previous evidence suggesting the possible role of the right DLPFC, along other brain regions, in inhibiting impulsive behavior. The discrepancy in treatment response between inattentive and impulsive symptoms raises implications for the underlying neurobiological mechanisms of ADHD. We suggest a nuanced approach to understanding ADHD symptomatology and call for further research into the distinct neural underpinnings of each symptom domain. Most importantly, our results provide novel evidence for the beneficial effect of tDCS on cognitive functions associated with inattention. This finding is particularly significant as it substantiates the therapeutic potential of anodal tDCS in addressing attentional deficits, a fundamental symptom domain of ADHD, while providing a targeted and non-invasive treatment option. By demonstrating the specific efficacy of tDCS in enhancing cognitive functions associated with inattention, this study lays a foundation for future research into personalized neurostimulation interventions and their implications for the management of ADHD symptoms in adult populations.

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