Article

Transcranial Direct Current Stimulation Improves Reward Processing in Children With ADHD

Journal of Attention Disorders
1–9

DOI: 10.1177/1087054720923094
journals.sagepub.com/home/jad
SAGE

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Abstract

Objective: Individuals with ADHD have deficits in reward processing and related cognitive tasks such as delay discounting and risky decision-making. The ventromedial prefrontal cortex (vmPFC) and dorsolateral prefrontal cortex (dlPFC) are two distinct cortical areas that are involved in reward processing. **Methods:** Twenty children with ADHD received transcranial direct current stimulation (tDCS) in three separate sessions with one of three montages each, including anodal/cathodal tDCS over the left dlPFC and right vmPFC respectively, the reversed montage, and a sham stimulation condition. During stimulation, in each session, participants performed the balloon analogue risk taking and chocolate delay discounting tasks. **Results:** A significant effect of stimulation condition on emotional processing was observed. Specifically, anodal tDCS over the right vmPFC, coupled with cathodal tDCS over the left dlPFC, reduced risky decision-making and delay discounting. **Conclusion:** These results imply that the left dlPFC and right vmPFC are involved in reward processing in children with ADHD. This finding is discussed in the light of the delay aversion theory of ADHD. *(J. of Att. Dis. XXXX; XX(X) XX-XX)*

Keywords

ventromedial prefrontal cortex, dorsolateral prefrontal cortex, transcranial direct current stimulation, reward processing, risky decision-making, delay discounting, ADHD

Introduction

The delay aversion theory suggests that individuals with attention deficit-hyperactivity disorder (ADHD) cannot tolerate delays because of impaired time perception, representing an executive function and respective negative emotions associated with waiting, which cannot be easily controlled, which involves motivational factors (Sonuga-Barke, 2003; Sonuga-Barke et al. 2003). Thus, individuals with ADHD prefer an immediate small reward to a larger remote one and show a steeper discount of delayed rewards due to altered sensitivity to reinforcement (Luman et al., 2010; Wilson et al., 2011). In accordance, numerous studies have found a stronger preference of immediate smaller rewards over delayed larger ones in individuals with ADHD (Antrop et al., 2006; Bitsakou et al., 2009; Coghill et al., 2014; Marco et al., 2009; Mies et al., 2019; Solanto et al., 2001). Moreover, the intensity of hyperactive/impulsive symptoms in ADHD is positively correlated with the rate of discounting (Scheres & Hamaker, 2010).

The respective alteration of the evaluation of the time factor in ADHD affects not only tolerance to delay but impairs also other higher cognitive functions, such as decision-making. Particularly, risky decision-making, characterized by choosing a smaller immediate reward, and not a larger remote one, is affected in ADHD, by preferring positive short- to long-term consequences (Coghill et al., 2014; Dekkers et al., 2016; Drechsler et al., 2008, 2010; Huber & Kunz, 2007; Matthies et al., 2012; Reynolds, 2006).

At the level of the brain, the potential competition of immediate and delayed choices can be tracked back to two distinct neural systems involved in reward processing and cognitive control (Ballard & Knutson, 2009; McClure et al., 2004). As shown by a functional magnetic resonance imagining (fMRI) study in heathy adults, immediate reward is associated with activation of the ventral striatum, the medial orbitofrontal cortex (mOFC), the medial prefrontal cortex (mPFC), and the posterior cingulate cortex (PCC), whereas delayed reward is associated with activation of the dorsolateral prefrontal cortex (dlPFC), the ventrolateral prefrontal cortex (vlPFC), and the lateral orbitofrontal cortex (lOFC).

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The former structures could be considered as reward processor and the latter one as cognitive control system (McClure et al., 2004). Furthermore, gray matter volumes in the dlPFC and inferolateral frontal cortex correlate inversely with delay discounting rates (Bjork et al., 2009).

Knowledge about the involvement of these areas in reward delay processing offers the option to modulate the respective cortical areas through brain stimulation, and modulate respective performance. Non-invasive brain stimulation (NIBS) techniques, such as transcranial electrical stimulation (tES) and transcranial magnetic stimulation (TMS), provide an opportunity to modulate cortical excitability and an activity to alter cognitive functions. tES applies an electrical current to the brain that alters cortical excitability (Nitsche & Paulus, 2000). In particular, transcranial direct current stimulation (tDCS) alters neuronal resting membrane potentials, and depending on the stimulation, polarity enhances or reduces excitability of the cortical target at a macroscopic level. Beyond acute effects, tDCS induces plasticity of glutamatergic synapses (Nitsche et al., 2008).

Furthermore, tDCS is used for amelioration of symptoms and improvement of performance in psychiatric disorders (Kuo et al., 2014). In particular, in individuals with ADHD, anodal tDCS over the left dlPFC improved clinical symptoms (Allenby et al., 2018; Soff et al., 2017), and some cognitive functions, such as memory consolidation (Prehn-Kristensen et al., 2014), inhibitory control (Munz et al., 2015; Soltaninejad et al., 2015, 2019), selective attention (Bandeira et al., 2016), working memory and interference control (Nejati et al., 2017; Sotnikova et al., 2017), and sustained attention (Allenby et al., 2018).

In a previous study of our group, anodal tDCS over the left dlPFC combined with cathodal tDCS over the right vmPFC, as compared with the reversed electrode positions, reduced risky decision-making and delay discounting in healthy adults (Nejati et al., 2018). This electrode montage does not allow to identify the specific role of cathodal tDCS over the right vmPFC, or anodal tDCS over the left dlPFC. Since a seesaw interaction between dlPFC and vmPFC has been suggested for the central-executive and default mode network (Fox et al., 2005), one might, however, speculate that both areas interact for respective effects on reward processing. With respect to underlying executive functions, this concept is supported by results of another study of our group, where we compared the effects of bilateral anodal/cathodal tDCS over the dlPFC with those of dlPFC/vmPFC stimulation. Here, only the latter electrode montages improved executive functions in children with ADHD. Specifically, working memory and cognitive flexibility were improved with anodal tDCS over the left dlPFC, coupled with cathodal tDCS over the right vmPFC, and inhibitory control was improved with the reversed electrode montage (Nejati et al., 2017). Thus, combined stimulation of dlPFC and vmPFC might be a well-suited protocol to alter executive functions. The polarity-dependent difference of effects with respect to specific tasks might be due to the respective motivational/emotional/social demands of specific executive functions. For instance, prepotent inhibitory control, as measured by the go/no-go task, has a social- or context-dependent demand that involves the vmPFC (Chen et al., 2009; Elliott et al., 2004; Goldstein et al., 2001; Kelly et al., 2004).

In sum, executive and motivational concepts of ADHD are contributing to the delay aversion theory. Individuals with ADHD are characterized by a higher amount of risky decision-making and steeper delay discounting. These impairments are assumed to be based on both impaired cognitive control and reward processing. The dlPFC and vmPFC are two main components of reward processing that handle cognitive control and motivational demands of reward, respectively.

Given the role of cognitive control, especially inhibitory control, in risky decision-making and delay discounting (Najarzadegan et al., 2016; Nejati, 2013) and in accordance with our previous study, which showed an improvement of inhibitory control via anodal tDCS over the right vmPFC combined with cathodal tDCS over the left dlPFC (Nejati et al., 2017), we expected that in ADHD patients, anodal tDCS over the right vmPFC combined with cathodal tDCS over the left dlPFC improves risky decision-making and delay discounting, whereas this effect was not expected for the reversed electrode montage, or sham stimulation.

In this study, we aimed to explore these hypotheses in children with ADHD. We expected to improve reward processing in children with ADHD through stimulation of the respective cortical areas.

Materials and Methods

Participants

Twenty right-handed children with ADHD, age range between 6 and 12 years ($M = 8.60 \pm 1.56$, 16 boys, four girls), participated in the study. All participants were diagnosed with ADHD according to the *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; DSM-5; American Psychiatric Association, 2013) diagnostic criteria by a professional child psychiatrist. We used G*power (Faul et al., 2013) to determine the required sample size. Based on a power of 0.95, an alpha level of .05, and a medium effect size ($f = 0.40$) suggested for tDCS studies (Minarik et al., 2016), the required sample size for our design was 16. We added four more participants to compensate for dropouts and unforeseen variability. Five participants had moderate ADHD, with a score between 34 and 60, and 15 participants had severe ADHD with a score higher than 60 in Conner's rating scale, parent version (Conners et al., 1998). This questionnaire has 26 questions with a 4-point Likert-type response, with a grade ranging from 26 to 104. The higher the grade, the more severe the symptoms. This scale was validated for the Iranian population (Hooshyari et al., 2008). Table 1 presents the demographic parameters of the participants in detail.

Table 1. Demographic Characteristics of Participants.

Variables	*M* (*SD*)/description
Age	8.60 (1.56)
Education	2.7 (1.65)
ADHD score	75.75 (17.60)
ADHD subtype	4ADHD-I, 16ADHD-C
Gender	4F/16M

Note. ADHD-I: inattentive ADHD; ADHD-C: combined ADHD.

Participants were unaware of the stimulation protocol and aims of the study. None of the participants received medication (e.g., methylphenidate) during the study. Participants either never received respective medication before, or stopped intake at least 1 month before the start of the study. None of the participants had a presence or past history of head trauma or other neurological or psychiatric disorders. Participants were screened for psychiatric and neurologic comorbidities based on their medical records in the psychology clinic. All participants had normal or corrected-to-normal vision. The procedures were in accordance with the ethical standards of the Helsinki Declaration of 1975, as revised in 1983. This study was approved by the ethical committee of Shahid Beheshti University.

Chocolate delay discounting task (CDDT)

The delay discounting task is a monetary reward task that provides a choice between a small immediate and large delayed reward. The respective delay duration and amount of the delayed reward is increased during task performance. The individual turning point of decision, which depends on the trade-off between immediate small rewards and larger but delayed reward, makes this task suitable for the assessment of reward processing. In this study, we used chocolate images (Figure 1), instead of monetary choices, because for the children participants of this study, chocolate is a well-suited primary reward (Reuben et al., 2010). This task has been used earlier in children with ADHD as an intervention-sensitive task (Nejati, 2020). The immediate small reward was one chocolate bar, whereas the big rewards were two, five, 10, and 20 chocolate bars, promised to be available in 1 day, 2 days, 3 days, 5 days, 1 week and 1 month, respectively. The main variable of this test is rate of discounting (K) which is calculated by the function $V_i = A_i/(1 + K_iD_i)$. In this function, V_i is the present value and the delayed reward is A_i at delay D_i (Kirby, 1997). The K_s as the main variable were calculated separately for each situation and the mean of K_s was calculated as K_{mean}. Performing this task took about 5 min for our participants.

Balloon analogue risk-taking task (BART)

This task has been developed for assessment of risky decision-making (Lejuez et al., 2002). It requires decision-making under risk and reward/punishment anticipations (Chan et al., 2008). This task has been used for the assessment of risk taking in children with ADHD or clinically impulsive samples with and without brain stimulation (Alizadehgoradel et al., 2020; Gilmore et al., 2018; Nejati, 2020). In this task, in each trial a balloon is presented to the participant on a computer screen, and the task of the participant is to pump it up by pressing a respective button. Each button press increases the size of the balloon and earns an amount of virtual monetary reward, 1,000 RLS in this study, in a temporary box. The balloon can explode at any size, and larger balloons are associated with a greater risk for explosion. If the balloon explodes, the accumulated monetary reward in the temporary box is lost. Money can be transferred from the temporary to a permanent box by pressing the button of "collecting money" (Figure 1). In this case, the balloon disappears and the participant starts with the next one in the next trial. The task consists of 30 trials and takes about 5 min. The measures of this test are the following: (a) adjusted value (AV), the number of pumps of balloons which did not explode, (b) unadjusted value (UV) or the overall number of pumping (maximum pumping), and (c) the number of successfully pumped balloons (SPB).

tDCS protocol

The foc.us v2 transcranial stimulator, which was tested for reliability via an oscilloscope and ampere meter, and showed stable current strength, was used for brain stimulation. An electrical direct current of 1 mA generated by the stimulator was applied through a pair of saline-soaked sponge electrodes with a size of 24 cm^2 (4 × 6) for 15 min. In this study, we conducted tDCS in three sessions, with electrodes placed according to the 10–20 electroencephalogram (EEG) international system, including (a) anodal vmPFC (Fp2)/cathodal dlPFC (F3), (b) anodal dlPFC (F3)/cathodal vmPFC (Fp2), and (c) sham stimulation with one electrode over the left dlPFC and the other over the right vmPFC. For sham stimulation, electrical current was ramped up for 30 s to generate the same sensation as the active condition, and then turned off without participants' awareness (Palm et al., 2013).

Procedure

After signing the written consent form by the parents of participants, the examiner explained the task instructions. The stimulation sessions were performed in a quiet room with a week interval to prevent carry-over effects. The order of stimulation was counterbalanced across participants, who were unaware of stimulation type. The order of sessions in the participants was randomized according to Consort guidelines. We designed the predefined sequences for our three sessions and dedicated a number to each sequence. Then participants who were blinded to the respective sequences drew a number, and the order of interventions was conducted in accordance with the sequence indicated by that number.

Figure 1. Left: balloon analogue risk-taking task (BART) and right: chocolate delay discounting task (CDDT).

About 5 min after the beginning of stimulation, participants performed the BART and chocolate delay discounting tasks, which lasted for about 10 min. Both, tDCS and behavioral tasks were performed by one researcher/author (A.S.K.). After each stimulation session, a side-effect checklist was completed. None of the participants had severe side effects. Blinding was successful based on participants' guesses about real or sham conditions after the respective experimental sessions, 47.0% correct, $\chi^2(1) = 1.04$, $p = .308$.

Data Analysis

This study had a single-blind, complete crossover design. Data analyses were conducted using the statistical package SPSS for Windows, version 21. Normality and homogeneity of variance of the data collected from each stimulation condition were confirmed using the Levin test. To explore the effect of tDCS on task performance, repeated-measure one-factorial analyses of variance (ANOVAs) were conducted for the within-subject factor "Stimulation condition" (three different montages). The measures of delay discounting task (K), and the balloon analogue risk-taking task (AV, unadjusted value [UAV], and SPB) served as dependent variables. Mauchly's test of sphericity was conducted to test for sphericity of the data, and degrees of freedom were corrected using the Greenhouse–Geisser method, if required. Post hoc analyses were carried out by Fisher's least significant difference (LSD) test. A significance level of $p < .05$ was used for all statistical comparisons.

Results

All participants performed the tasks appropriately and tolerated tDCS well. Participants reported some degree of mild and tolerable itching, tingling, and burning sensation under the electrodes during approximately the first 30 s of stimulation in each tDCS condition. Table 2 shows the descriptive statistics of respective measures of both tasks. We conducted repeated measures ANOVAs to examine effects of the tDCS conditions on performance on the delay discounting and BART tasks (Figures 2 and 3). The ANOVAs showed significant differences between tDCS conditions in the delay discounting measures of K_{10}

Table 2. Descriptive Statistics (Mean, Standard Deviation) of Cognitive Task Performance.

Tasks	Source	Sham *M* (*SD*)	AvmPFC/CdlPFC *M* (*SD*)	AdlPFC/CvmPFC *M* (*SD*)
DDT	K_{mean}	3.95 (2.91)	2.69 (2.69)	3.91 (3.20)
	K_2	0.50 (0.40)	0.53 (0.39)	0.60 (0.40)
	K_5	1.86 (1.70)	1.73 (1.48)	1.76 (1.62)
	K_{10}	5.42 (3.57)	3.30 (3.67)	4.17 (3.88)
	K_{20}	10.42 (7.70)	5.35 (6.02)	9.11 (8.17)
BART	AV	18.49 (11.69)	16.68 (11.12)	17.79 (8.95)
	UV	17.57 (10.53)	16.06 (10.25)	17.30 (8.38)
	SPB	24.30 (2.97)	26.10 (2.38)	25.25 (2.93)

Note. A = anodal; C = cathodal; vmPFC = ventromedial prefrontal cortex; CdlPFC = dorsolateral prefrontal cortex; K = the constant of delay discounting; DDT = delay discounting task; BART = balloon analogue risk-taking task; AV = adjusted value; UAV = unadjusted value; SPB = successfully pumped balloon.

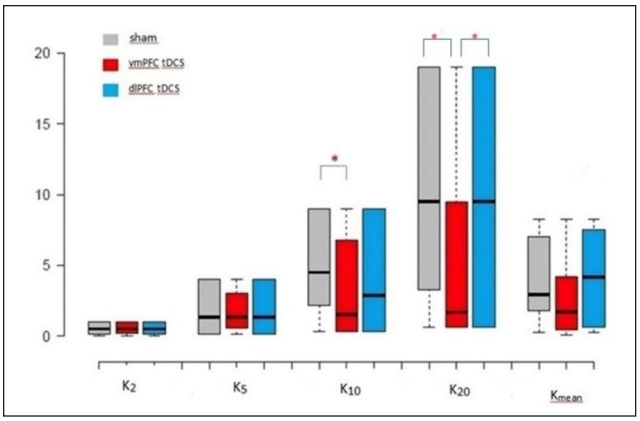

Figure 2. Shown are the effects of tDCS on different variables of the delay discounting task.
Note. vmPFC = ventromedial prefrontal cortex; dlPFC = dorsolateral prefrontal cortex; K = the index of delay discounting in different values. *Significant pairwise comparisons between stimulation conditions based on the results of post hoc tests. The horizontal bars are showing the means and the error bars the range of variables.

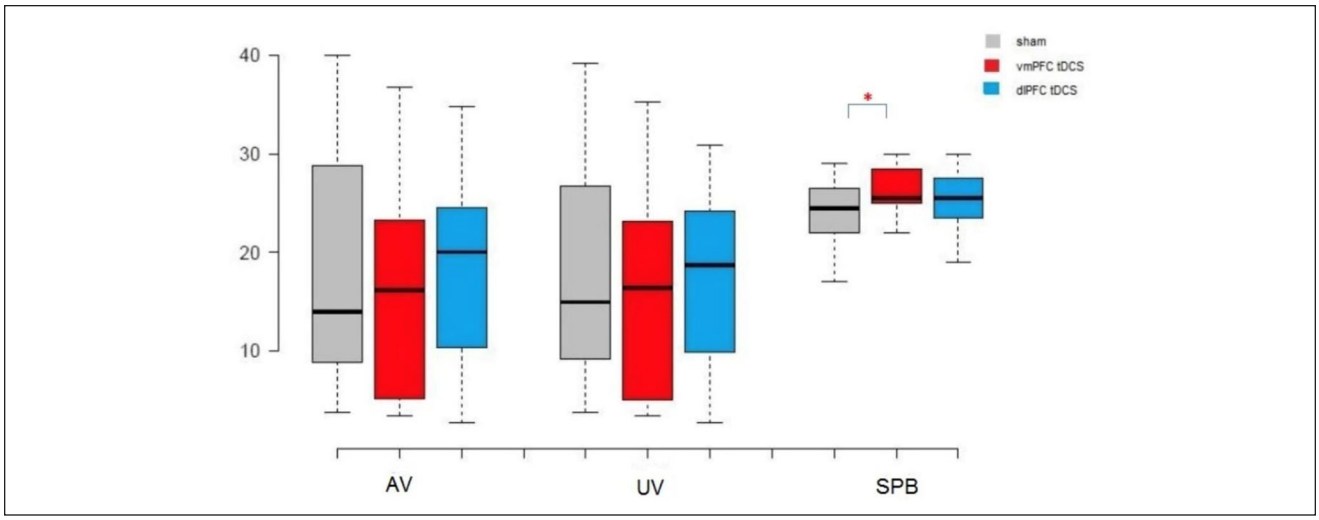

Figure 3. Shown are the effects of tDCS on the different variables of the balloon analogue risk-taking task.
Note. vmPFC = ventromedial prefrontal cortex; dlPFC = dorsolateral prefrontal cortex; AV = adjusted value; UC = unadjusted value; SB = successfully pumped balloons.
*Significant pairwise comparisons between stimulation conditions based on the results of post hoc tests. The horizontal bars are showing the mean and the error bars the range of variables.

Table 3. Results of the Repeated Measures ANOVAs for Effects of tDCS Conditions (Sham/Anodal vmPFC-Cathodal dlPFC/Anodal dlPFC-Cathodal vmPFC).

Tasks	Source	*df*	MS	*F*	*p*	η_p^2
DDT	K_{mean}	1.67	12.16	3.49	.05	0.15
	K_2	1.86	0.04	0.46	.62	0.03
	K_5	1.74	0.15	0.11	.86	0.00
	K_{10}	1.74	26.07	4.17	**.02**	0.18
	K_{20}	1.96	140.66	5.91	**.001**	0.23
BART	AV	1.91	24.24	0.62	.53	0.04
	UV	1.82	19.77	0.63	.52	0.04
	SPB	1.56	20.68	6.88	**.001**	0.26

Note. Significant values ar in bold-face. DDT = delay discounting task; BART = balloon analogue risk-taking task; tDCS = transcranial direct current stimulation; MS = mean square; η_p^2 = partial eta squared.

($F = 4.17$, $p = .02$) and K_{20} ($F = 5.91$, $p = .001$), but non-significant differences for the K_{mean} ($F = 3.49$, $p = .05$), K_2 ($F = 0.55$, $p = .55$), and K_5 ($F = 0.09$, $p = .86$) conditions (Table 3).

Results of the LSD post hoc analyses for K_{20} revealed that anodal vmPFC/cathodal dlPFC differed significantly from sham ($p = .006$) and anodal dlPFC/cathodal vmPFC ($p = .019$). Furthermore, for K_{10}, anodal vmPFC/cathodal dlPFC differed significantly from sham stimulation ($p = .023$). These results suggest that increasing activity of the right vmPFC and reduction of left dlPFC activity led to better performance of the delay discounting task in ADHD children.

For the BART task, the respective ANOVA results showed no significant effect of tDCS on risk-taking behavior with respect to the adjusted (AV; $F = 0.44$, $p = .63$) and unadjusted values (UV; $F = .42$, $p = .65$). However, the repeated measures ANOVA showed significant differences between stimulation conditions for successfully pumped balloons (SPB), which is the number of balloons that did not explode, and a measure of risk-taking behavior ($F = 6.88$, $p = .001$; Table 3).

Results of the LSD post hoc analyses revealed a significant difference between anodal vmPFC/cathodal dlPFC and sham stimulation ($p < .001$), indicating a significant decrease of risk-taking behavior in ADHD children. The order of sessions was integrated as covariate in the analysis for both tests. No significant effect was found for the order of sessions in any of the variables.

Discussion

The results of this study show that anodal tDCS over the right vmPFC coupled with cathodal tDCS over the left dlPFC, as compared with the reversed electrode positions and sham stimulation, increases the tendency to choose delayed gains and to make more conservative decisions in ADHD patients.

With respect to the cognitive theories of ADHD, the executive function theory cannot easily explain this tDCS-induced risky decision-making and delay discounting alteration. This concept assumes that the dlPFC, an area relevantly involved in executive functions, is hypoactive in individuals with ADHD, and that this hypoactivity causes functional deficits (Emond et al., 2009; Seidman et al., 2006). The results of this study, however, show no beneficial effect of anodal tDCS over the left dlPFC, coupled

with cathodal tDCS over the right vmPFC, on both tasks under study. This argues against a relevant contribution of hypoactivity of the left dlPFC to increased risky decision-making and delay discounting on its own in these patients. Impaired right vmPFC functionality is another possible mechanism suggested to be involved in respective clinical symptoms and cognitive dysfunctions. The motivational theory states that impaired reward processing in individuals with ADHD origins from altered activation of the vmPFC (Cubillo et al., 2012; Fassbender et al., 2009; Rubia et al., 2009; Yang et al., 2019). However, the specific role of the vmPFC in reward processing is a matter of debate. On one hand, hyperactivity of the vmPFC is considered to be relevant and explained as a consequence of weakened inhibitory effects of the dlPFC on the vmPFC (Fassbender et al., 2009). On the other hand, hypoactivity of the vmPFC has been shown in other studies and considered as foundation of impaired reward processing (Yang et al., 2019). The correlational nature of neuroimaging studies, which this assumption is based upon, makes it difficult to come to definite conclusions, which can, however, be obtained by interventional approaches. The results of this study suggest that excitability enhancement of the vmPFC, coupled with inhibition of the dlPFC, improved the performance of reward processing while the reversed electrode polarities did have no effects. This finding suggests that reward processing as a hot executive function is dependent on right vmPFC activation and left dlPFC deactivation, and that pathologically reduced activity of the right vmPFC is relevant for respective deficits.

In detail, the results of this study show that anodal tDCS over the right vmPFC coupled with cathodal tDCS over the left dlPFC reduced delay discounting, as compared with the other intervention conditions. These effects were only present for the largest amounts of the future value, which was the selection of one chocolate now versus 10 or 20 chocolates later. With lower amounts of delayed rewards, however, none of the interventions were efficient. This suggests that in this study, anodal tDCS over the right vmPFC, combined with cathodal tDCS over the left dlPFC, has shifted the subjective value of larger delayed rewards, or enabled participants to make more rational decisions. A similar pattern of results has been found in healthy individuals with anodal and cathodal tDCS over the right and left dlPFC, respectively (Hecht et al., 2013). Furthermore, a neuroimaging study found higher activation of the medial OFC for high-incentive versus low-incentive rewards in adults with ADHD, as compared with healthy controls (Wilbertz et al., 2012).

This structural discrimination of the reward processing system fits well to the delay aversion theory of ADHD which attribute impaired reward processing to vmPFC hypoactivity. Furthermore, the results of this study showed that cathodal tDCS over the left dlPFC, coupled with anodal tDCS over the right vmPFC reduces risky decision-making. Based on the experimental design of this study, we cannot attribute this result clearly to the excitatory role of anodal tDCS over the right vmPFC or the inhibitory role of cathodal tDCS over the left dlPFC, or a combined effect. All of these concepts are supported by the results of other neurostimulation studies. Confirmative evidence comes from studies, which showed that applying cathodal tDCS over the left dlPFC reduced risk taking in healthy adults (Wen et al., 2019), and anodal tDCS over the right vmPFC enhanced conservative decision-making and cognitive impulse control (Ouellet et al., 2015).

Some limitations of this study should be taken into account. We used combined montages for stimulation, which tackled two areas which have potential relevance for the cognitive processes under study, and thus, we cannot make clear statements about the specific role of each area for performance of these tasks. Future studies should thus probe area-specific stimulation protocols. In this line, a further issue that should be addressed in future studies is clarification of the kind of interaction between vmPFC and dlPFC in reward processing with respect to competition or cooperation.

In this study, we introduced a new tDCS montage for individuals with ADHD, on the grounds of the motivational theory and the neural correlates of deficient reward processing. In this study, we applied a single-session and online stimulation condition with neuropsychological assessment.

We used a 2-point checklist to report side effects (present/absent). It would be advantageous to use a several-point Likert-type checklist in future studies to be able to quantify side effects. Furthermore, the researcher performing the tDCS was not blinded for the study allocation. This study was an exploratory study, with a relatively small sample size, which proposes a new tDCS montage for an understudied construct in children with ADHD. Repetitive stimulation sessions with follow-up are proposed for future studies to explore the suitability of this intervention for clinical application.

Author Contributions

VN. conceived and designed the study. ASK. collected the data. MAN. and VN. analyzed and interpreted the data. VN. wrote the manuscript. MAN. critically revised the manuscript.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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