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Improving Working Memory in Adolescents with Substance Use Disorder through Anodal Stimulation of the Left Dorsolateral Prefrontal Cortex

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ABSTRACT

Substance abuse is among the most prevalent and costly health challenges worldwide. Standard medical treatments are often not curative, and relapse is common. The present study aimed to investigate the effectiveness of transcranial direct current stimulation (tDCS) in improving working memory among adolescents with substance use disorder. This quasi-experimental study employed a pretest–posttest design with a follow-up. The statistical population included all male adolescents (aged 18–21) with substance use disorder in Ardabil County, Iran. A total of 40 male adolescents with substance use disorder were recruited from rehabilitation centers supervised by the Welfare Organization, based on inclusion and exclusion criteria, and were randomly assigned to an experimental group (n = 20) and a control group (n = 20). Data were collected using the N-Back neurocognitive task. The treatment protocol involved 15-minute sessions of anodal stimulation over the F3 region and cathodal stimulation over the F4 region at an intensity of 1.5 mA. Data were analyzed using repeated-measures ANOVA in SPSS v.22. The results revealed a significant difference between groups, indicating that anodal stimulation led to improved working memory in the experimental group compared to the control group. These findings suggest growing evidence for the therapeutic potential of tDCS in addiction treatment, particularly for adolescents, and provide empirical support for the optimism surrounding this intervention.

1. INTRODUCTION

From a neurobiological perspective, addiction is considered a brain disorder, in which dysfunction in the neural circuits associated with reward and motivation leads to maladaptive behaviors such as drug craving and relapse [1].

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The unprecedented advances in neuroscience have given rise to neuropsychological models that integrate neurobiological evidence with findings from psychological and psychosocial neuroplasticity, thereby providing more comprehensive explanations of addictive behaviors [2]. All existing models assume that addiction is linked to deficits in top-down cognitive control (executive functioning), which ultimately influences the key stages of the addiction cycle, psychosocial outcomes, and treatment effectiveness [3].

Chronic cocaine use has been associated with cognitive impairments across several domains, with strong evidence of deficits in executive functions such as sustained attention, response inhibition, working memory, and decision-making. Persistent impairments in executive functioning have also been documented among individuals using opioids, methamphetamines, and alcohol [4].

Executive dysfunction during adolescence has been linked to an increased risk of engaging in addictive behaviors, including cigarette smoking, alcohol consumption, video gaming, and binge eating [5]. Exposure to nicotine during adolescence may exacerbate executive dysfunction by disrupting the maturation of neural connectivity between limbic signaling pathways and inhibitory control mechanisms, thereby increasing impulsivity [6]. Although addiction remains a major societal concern, recent advances in cognitive and affective neuroscience have deepened our understanding of this debilitating disorder. Emerging insights across multiple disciplines conceptualize addiction as a compulsive cycle of drug-seeking behavior driven by dysregulated neurocognitive processes [7].

The key processes implicated in addiction include attentional bias, automaticity, reward processing, emotion regulation, stress reactivity, and inhibitory control. Studies have shown that these processes are mediated by substantial individual differences in integrated cortico-limbic and striatal functional and anatomical networks, which contribute to the initiation, maintenance, and reinstatement of addictive behaviors [8].

A growing body of research highlights the critical role of executive dysfunction in substance use disorders. Among the various factors linked to addiction, neuropsychological deficits are particularly important, as substance dependence impairs cognitive functions such as problem-solving, planning, organization, new learning, visuospatial abilities, cognitive flexibility, and memory skills [9]. Extensive studies have confirmed the relationship between executive dysfunction and addiction, a relationship that constitutes the core of many theoretical models of addiction [10]. Substance dependence has been associated with both functional and structural impairments of the prefrontal cortex, leading to reduced frontal activity [11]. Moreover, the prefrontal cortex has been implicated in craving responses to nicotine [12], alcohol [13], opioids [14], and cocaine [15]. Drug craving has been shown to coincide with increased prefrontal cortical activity when individuals are exposed to substance-related cues. This brain region is closely interconnected with executive functions and the reward circuitry [16].

Consequently, interventions that activate the dorsolateral prefrontal cortex (DLPFC) may provide a novel therapeutic approach for addiction [17]. In recent years, there has been a growing interest in non-invasive brain stimulation techniques for the treatment of addiction [18]. One such method is transcranial direct current stimulation (tDCS), a technique that applies low-intensity electrical currents (1–2 mA) through the scalp [19].

tDCS is capable of modulating deeper cortical regions, such as the anterior cingulate cortex (ACC), which appears to play a role in attentional biases toward drug-related cues. Based on this evidence, it has been hypothesized that tDCS targeting the DLPFC—a region critically involved in cognitive control—can modulate ACC activity in individuals with substance use disorder, thereby altering the processing of drug-related cues [20]. Another study demonstrated that stimulation of the DLPFC enhances executive functioning in individuals with substance use disorder [21].

Given these considerations, and in light of the growing optimism regarding non-invasive brain stimulation as a treatment for substance use disorder, the present study was designed to examine the effectiveness of tDCS in improving working memory among adolescents with substance use disorder.

2. MATERIALS AND METHODS

This study employed a clinical trial design with a pre-test, post-test, and follow-up, including a control group. The statistical population consisted of all adolescent substance users in Ardabil City. Participants were selected through convenience sampling based on inclusion criteria (age range 18–21 years; diagnosis of substance use disorder according to DSM-5 criteria; male gender) and exclusion criteria (use of psychiatric medications due to possible interference with the effectiveness of tDCS; diagnosis of bipolar or psychotic disorder according to DSM-5; intracranial implants such as shunts, stimulators, or electrodes, or the presence of any other metallic objects near the head that could not be removed, e.g., in the oral cavity; and history of epilepsy or seizures).

A total of 40 adolescent males with substance use disorder, recruited from rehabilitation camps under the supervision of the Welfare Organization, were randomly assigned to an experimental group (n = 20) or a control group (n = 20). Although previous research indicates that a sample size of 12–15 per group is sufficient, a larger sample was chosen to account for possible attrition. Random assignment was carried out using a random number table. Ultimately, due to attrition, the final analysis was conducted on 16 participants in the experimental group and 16 in the control group.

3. INSTRUMENTS

3.1. tDCS Device

The transcranial direct current stimulation device used in this study was the *ActiveDose* model manufactured by ActivaTek (USA). The device is powered by a 9-volt alkaline battery, with dimensions of 15.5 × 9.8 × 4.8 cm and a weight of 0.18 kg. It can deliver a maximum current intensity of 4 mA (DC). Constant electrical current is applied through electrodes of opposite polarity (anode and cathode) placed on the scalp. Electrodes were carbon-based and conductive, and physiotherapy pads (7 × 5 cm) were used. These pads were placed inside sponges soaked in 9% sodium chloride solution to enhance electrical conductivity and prevent excessive heat generation. The device allows adjustment of current intensity, electrode size, and stimulation duration.

3.2. N-Back Task

The *N-Back* task was used to assess working memory. In this test, a series of visual stimuli are sequentially presented on a computer screen. Participants are required to respond under two different working memory load conditions. In the low-load condition, the participant presses the target key whenever the current stimulus matches the immediately preceding one. In the high-load condition, the participant compares the current stimulus with the one presented two trials earlier and presses the key if they match. The main outcome variables of the task are the number of correct and incorrect responses [22]. The N-Back task has demonstrated strong reliability and is widely used in both clinical and experimental research. Its validity has also been confirmed through comparison with other working memory measures [23].

4. RESULTS

Table 1. Descriptive statistics (mean and standard deviation) of study variables by group and measurement stage

Test	Variable	Time	Control Group M (SD)	tDCS Group M (SD)
N-Back Test	Accuracy	Pre-intervention	73.93 (14.34)	74.43 (9.52)
		Post-intervention	72.31 (13.68)	86.00 (8.45)
		Follow-up	71.62 (11.88)	85.68 (7.53)
	Reaction Time	Pre-intervention	154.81 (30.48)	153.87 (18.43)
		Post-intervention	154.43 (29.68)	128.93 (22.27)
		Follow-up	154.75 (29.11)	120.68 (24.99)

As shown in Table 1, descriptive statistics (mean and standard deviation) of the study variables are presented separately for each group across the three measurement stages (pre-intervention, post-intervention, and follow-up).

Table 2. Results of repeated measures ANOVA for working memory scores in the experimental and control groups

Test	Variable	Source	df	F	p	η²	Pairwise Comparisons
N-Back Test	Accuracy	Time	1.61	9.34	0.001	0.237	tDCS > Control (p < 0.016)
		Group	1	6.54	0.016	0.179	
		Time*Group	1.61	18.61	0.001	0.383	
	Reaction Time	Time	2.00	28.99	0.001	0.492	tDCS > Control (p < 0.030)
		Group	1	5.15	0.030	0.140	
		Time*Group	2.00	28.43	0.001	0.492	

As shown in Table 2, the repeated measures ANOVA indicated that the within-group factor (time) was significant for both components of working memory. In addition, both the between-group effect (group) and the interaction effect (time × group) were statistically significant. Pairwise comparisons further revealed that the tDCS treatment group showed significantly greater improvement in working memory compared to the control group.

5. DISCUSSION AND CONCLUSION

The present study aimed to examine the effects of anodal transcranial direct current stimulation (tDCS) over the left dorsolateral prefrontal cortex (DLPFC) on working memory in adolescents with substance use disorder. The results revealed a significant improvement in working memory in the experimental group compared to the control group. These findings are consistent with previous research in this area [24, 25]. In support of the effectiveness of tDCS on working memory, earlier studies have reported enhancement of cognitive performance, including working memory [26]. Similarly, other research has demonstrated that direct brain stimulation significantly improves visuospatial, verbal, and auditory working memory [27].

The effectiveness of tDCS can be explained by the role of the left DLPFC in mediating executive functions, which are considered higher-order cognitive processes that control and regulate more basic or automatic functions. This region has been linked to complex cognitive processes such as decision-making, selective attention, working memory, strategic memory, conceptual reasoning, goal selection, planning, sequencing, monitoring, and the use of feedback in task performance [28]. Substance use appears to be associated with deficits in executive functioning, cognitive flexibility, general intellectual ability, learning, processing speed, and working memory, as well as with overall brain atrophy and structural and biochemical abnormalities in prefrontal regions [29]. Application of tDCS over the left DLPFC has been shown to increase parasympathetic activity while reducing sympathetic activity. Thus, enhanced activation of this region may contribute to reduced craving in individuals with substance use disorder [30].

Another explanation concerns the role of dopamine in working memory. Studies suggest that dopamine release in prefrontal regions increases during working memory tasks [31]. Enhanced cortical excitability in the prefrontal cortex promotes dopamine release, which in turn improves working memory performance. Moreover, anodal tDCS is likely to increase the level of glutamate—an amino acid associated with working memory, memory recognition, and stimulus–response learning [32].

Overall, the findings of this study demonstrate that tDCS significantly improves working memory in adolescents with substance use disorder. Recently, anodal stimulation of the left DLPFC has been increasingly recognized as a promising intervention for the treatment of substance use disorders. Current evidence supports both the safety and therapeutic potential of this method in children and adolescents. As the first study to investigate this approach in adolescents with substance use disorder, our findings further support its clinical applicability. It is therefore recommended that tDCS be incorporated as an intervention in addiction rehabilitation centers and clinical treatment programs. Future research should also examine the combined use of tDCS with other psychological interventions to maximize its therapeutic effects. Furthermore, while the follow-up in the present study lasted three weeks, longer follow-up periods are suggested to assess the durability of treatment outcomes.

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Declaration

We acknowledge that we used ChatGPT to enhance the academic writing of our manuscript while ensuring the originality and integrity of our work.

Transparency Statement

The data supporting this study are available upon reasonable request to the corresponding author, subject to ethical and confidentiality considerations.

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Declaration of Interest

The authors declare that they have no competing interests.

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