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FULL-LENGTH REPORT



Effects of bilateral tDCS over DLPFC on response inhibition, craving, and brain functional connectivity in Internet gaming disorder: A randomized, double-blind, sham-controlled trial with fMRI

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ABSTRACT

Background and aims: Impaired inhibitory control accompanied by enhanced craving is hallmark of addiction. This study investigated the effects of transcranial direct current stimulation (tDCS) on response inhibition and craving in Internet gaming disorder (IGD). We examined the brain changes after tDCS and their correlation with clinical variables. **Methods:** Twenty-four males with IGD were allocated randomly to an active or sham tDCS group, and data from 22 participants were included for analysis. Participants self-administered bilateral tDCS over the dorsolateral prefrontal cortex (DLPFC) for 10 sessions. Stop-signal tasks were conducted to measure response inhibition and participants were asked about their cravings for Internet gaming at baseline and post-tDCS. Functional magnetic resonance imaging data were collected at pre- and post-tDCS, and group differences in resting-state functional connectivity (rsFC) changes from the bilateral DLPFC and nucleus accumbens were examined. We explored the relationship between changes in the rsFC and behavioral variables in the active tDCS group. **Results:** A significant group-by-time interaction was observed in response inhibition. After tDCS, only the active group showed a decrease in the stop-signal reaction time (SSRT). Although craving decreased, there were no significant group-by-time interactions or group main effects. The anterior cingulate cortex (ACC) showed group differences in post- versus pre-tDCS rsFC from the right DLPFC. The rsFC between the ACC and left middle frontal gyrus was negatively correlated with the SSRT. **Discussion and conclusion:** Our study provides preliminary evidence that bilateral tDCS over the DLPFC improves inhibitory control and could serve as a therapeutic approach for IGD.

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KEYWORDS

Internet gaming disorder, transcranial direct current stimulation, stop-signal task, craving



INTRODUCTION

Internet gaming has become a popular leisure activity, leading to growing worldwide concerns about excessive and problematic gaming (Kuss & Griffiths, 2012). Since the American Psychiatric Association included Internet gaming disorder (IGD) in the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) (American Psychiatric Association, 2013), the World Health Organization classified gaming disorder as an addictive disorder in the 11th revision of the International Classification of Diseases and Related Health Problems (ICD-11) (World Health Organization, 2019). These changes reflect the growing scientific research findings that IGD is similar to substance-related and other addictive disorders in terms of neurobiological underpinnings, clinical characteristics, and treatment (Choi et al., 2014; Zheng et al., 2022).

A central feature of IGD, which shares proposed criteria in the DSM-5 and ICD-11, is 'loss of control'. 'Loss of control' characterizes all types of addiction and is linked to reduced inhibitory control, including response inhibition (Jentsch & Pennington, 2014). Response inhibition is the ability to suppress or delay responses to stimuli to meet goal-directed behaviors and is a key feature of self-control and impulsivity (Fujita, 2011; Hofmann, Friese, & Strack, 2009). Impairments in response inhibition have been observed in substance use disorders (SUDs) and gambling disorder using neurocognitive tasks such as Stroop, Go/No-Go, and Stop-Signal task (SST) (Smith, Mattick, Jamadar, & Iredale, 2014). Moreover, several behavioral and neuroimaging studies have shown dysfunctional response inhibition and high levels of impulsivity observed in individuals with IGD (Argyriou, Davison, & Lee, 2017). A meta-analysis to estimate the strength of the association between response inhibition and IGD revealed a medium overall effect size (Cohen's $d = 0.56$) (Argyriou et al., 2017).

Craving is another clinical characteristic of IGD (Dong, Wang, Du, & Potenza, 2017; Niu et al., 2016). It plays a crucial role in the maintenance and relapse risk of addictive behaviors (Kosten et al., 2006). Studies on IGD have shown that patients with IGD reported stronger cravings for playing games (Dong et al., 2017; Niu et al., 2016), and craving-associated functional magnetic resonance imaging (fMRI) alteration were found in patients with IGD but not in recreational gamers (Zeng, Wang, Dong, Du, & Dong, 2022).

A conceptual review of IGD proposed that impaired inhibitory control may lead to the IGD phenotype by the inefficient suppression of heightened cravings for rewarding experiences or gaming, leading to excessive Internet gaming (Dong & Potenza, 2014).

Therefore, enhancing inhibitory control and reducing cravings may benefit individuals with IGD. Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation technique that can alter cortical activation by applying weak direct electrical currents (Naish, Vedelago, MacKillop, & Amlung, 2018). Given the association between hypoactivation of the prefrontal cortex (PFC) and impaired

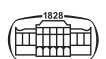
inhibitory control (Luijten et al., 2014), prefrontal tDCS may help improve inhibitory control (Loftus, Yalcin, Baughman, Vanman, & Hagger, 2015; Schroeder, Schwippel, Wolz, & Svaldi, 2020). Accordingly, tDCS has been considered for treating addiction (Coles, Kozak, & George, 2018; Luigjes, Segrave, de Joode, Figuee, & Denys, 2019). tDCS over the dorsolateral PFC (DLPFC) reduces addiction-related behaviors, including alcohol use (da Silva et al., 2013) and cigarette smoking (Mondino et al., 2018), and reduces craving (Jansen et al., 2013). However, research on the effect of tDCS on impaired response inhibition in IGD is limited compared to its impact on craving in addiction. Furthermore, previous studies on problematic online gamers have mainly focused on single-session tDCS (Wu et al., 2021) or were open-label, single-arm trials (Jeong et al., 2020).

Therefore, the present study aimed to evaluate the effects of multi-session tDCS on the primary outcome of response inhibition and secondary outcome of craving in individuals with IGD using a randomized, double-blind, sham-controlled design. Additionally, we explored how tDCS affects alterations in brain functional connectivity and their correlation with clinical variables. We hypothesized that multi-session bilateral tDCS over the DLPFC, compared to sham tDCS, would differentially improve inhibitory control and reduce craving.

METHODS

Participants

The participants recruited from Seoul St. Mary's Hospital's addiction clinics were young adult males aged 19–39 years, as younger people usually play more games than older adults (Mihara & Higuchi, 2017), and there is a higher prevalence of IGD in men (Fam, 2018). Recruitment started in March 2018 and ended in December 2018. The inclusion criteria were active gamers (spending over 50% of their online time gaming) for at least one year, IGD diagnosed according to the DSM-5 criteria by a clinically experienced psychiatrist, and no prior IGD treatment. The exclusion criteria included other psychiatric disorders, including depression, attention-deficit hyperactivity disorder, or alcohol use disorder (AUD), medical or neurological disorders, including epilepsy, history of head trauma and metal in the head or face, psychotropic medication use, or being left-handed. Structured clinical interview (Mini-International Neuropsychiatric Interview-Plus [MINI-Plus]) (Yoo et al., 2006) and Annett's Hand Preference Questionnaire (Annett, 1970) were used to rule out other psychiatric disorders and left-handedness, respectively. Twenty-four eligible participants were included in this study. The sample size was determined based on a previous clinical trial with a similar experimental design in gambling disorder, given the lack of research on the effects of tDCS on response inhibition in IGD. The study (Soyata et al., 2019) estimated the sample size, considering an effect size for the improvement in decision-making and cognitive flexibility ($f = 0.6$), a power of 0.8, and an alpha of



0.05. We adjusted the effect size to $f = 0.3$, considering findings from a meta-analysis of the effects of tDCS on response inhibition (Schroeder et al., 2020). Consequently, the final sample size was determined to be 24 participants.

Procedure

Study design. The CONSORT flow diagram is illustrated in Figs 1 and 2 outlines the randomized, double-blind, and sham-controlled clinical trial. A computer-generated randomization sequence (Research Randomizer version 4.0) (Urbaniak & Plous, 2013) allocated the participants ($n = 12$ per group) to an active or sham group in a 1:1 ratio. The tDCS stimulation protocol was set at baseline using the device station connected to a portable tDCS module. An assistant set the stimulation type (active or sham) so that the experimenter and participant were blinded to the

stimulation condition. Each participant was trained to apply the tDCS module at baseline and self-administered tDCS every weekday over two weeks (10 sessions in total) at home.

Clinical assessments and fMRI scans were performed at baseline (pre-tDCS) and two weeks later (post-tDCS) at the hospital to evaluate the differences in response inhibition, craving, and resting-state brain functional connectivity (rsFC) between the active and sham groups. Pre- and post-tDCS assessments were performed within two days before and after the tDCS sessions. Participants were instructed to refrain from alcohol 24 h before and from smoking and caffeinated beverages one hour before the fMRI scans.

tDCS protocol. A battery-powered portable tDCS module (Ybrain, Seongnam, Republic of Korea) delivered direct current through a pair of electrodes. The anodal and cathodal electrodes were positioned over the F3 (left DLPFC)

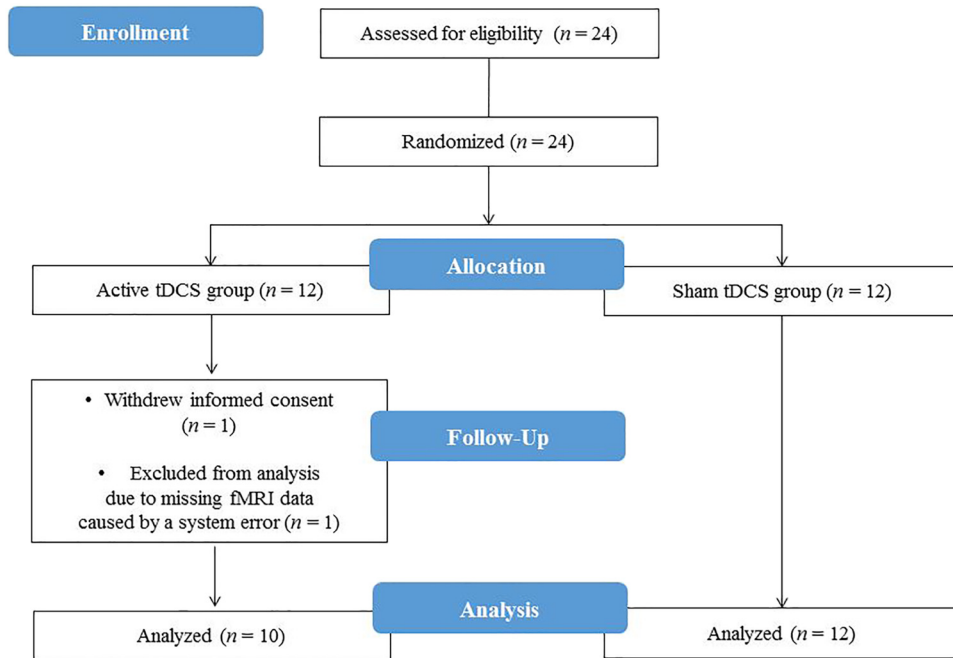


Fig. 1. CONSORT flow diagram of the study

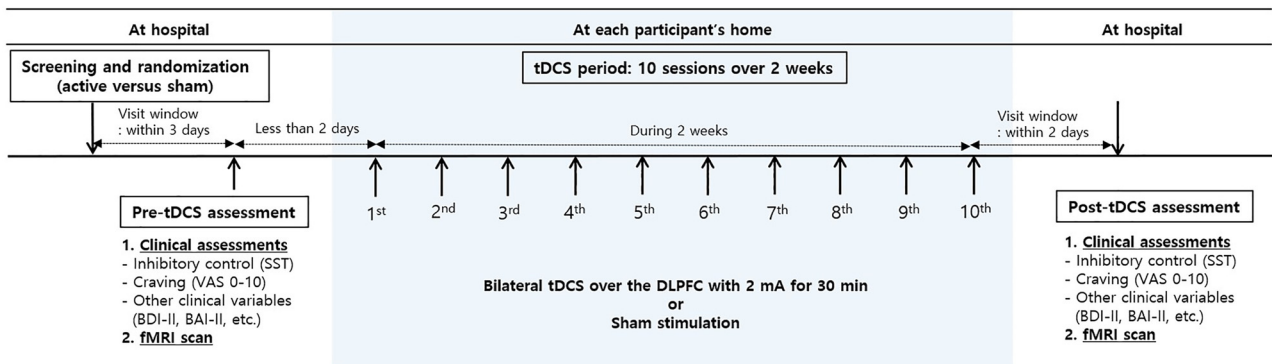


Fig. 2. Flow chart of the study design

tDCS, transcranial direct current stimulation; SST, stop-signal task; VAS, visual analog scale; BDI-II, Beck depression inventory-II; BAI-II, Beck anxiety inventory-II; fMRI, functional magnetic resonance imaging.



and F4 (right DLPFC), respectively, according to the 10–20 international EEG system. A 2 mA constant current was administered for 30 min, featuring a 30-s ramp-up at the start and a 30-s ramp-down at the end of the stimulation. In the sham tDCS condition, the same electrode montage was used with the same ramp-up of 30-s, but the current was switched off after 30-s. This widely used and reliable sham tDCS technique elicits the same cutaneous itching sensation in participants as active tDCS (Jacobson, Javitt, & Lavidor, 2011; Woods et al., 2018). Additional information about the tDCS protocol is found in [supplementary material](#).

Measures

Clinical variables. Sociodemographic data (age, education level, occupation, marital and smoking status, and alcohol consumption) were collected. Participants completed the Alcohol Use Disorders Identification Test (AUDIT) (Kim et al., 2014), Fagerström Test for Nicotine Dependence (FTND) (Ahn et al., 2002), Beck Depression Inventory (BDI)-II (Sung et al., 2008), and Beck Anxiety Inventory (BAI)-II (Beck, Epstein, Brown, & Steer, 1988). Internet gaming characteristics were assessed, including the initiation age of Internet gaming, weekday and weekend gaming hours in the past year, and the Korean version of the Young's Internet Addiction Test (Y-IAT) for IGD severity. The Y-IAT consists of 20 items on a five-point Likert scale (1–5), where higher scores suggest higher levels of addiction, with scores over 50 indicating at risk of addiction (Young & De Abreu, 2010). Participants also underwent the short form of the Korean Wechsler Adult Intelligence Scale-IV to estimate their full intellectual functioning (IQ) (Jung & Baek, 2019).

To evaluate the effects of tDCS on response inhibition and craving, we conducted the SST of the Cambridge Neuropsychological Test Automated Battery (CANTAB) (Wild & Musser, 2014), and participants rated their subjective craving for Internet gaming for the past week on a visual analog scale (VAS) ranging from 0 (no craving at all) to 10 (extreme craving).

The CANTAB has been used in clinical research to measure cognitive functions, and the SST has been widely used to assess response inhibition (Lipszyc & Schachar, 2010). The SST took approximately 14 min, requiring participants to respond to arrow stimuli (go trial) and withhold responses when an audio tone occurred (stop trial). The stop-signal reaction time (SSRT), an outcome measure of SST, reflects the effectiveness of the inhibitory control, with shorter SSRT indicating better response inhibition. Additional information about SST can be found in the [supplementary material](#).

Safety and tolerance of tDCS. To evaluate the safety and tolerance of tDCS, we assessed the most commonly reported adverse events (AEs) in previous studies (Brunoni et al., 2011) after completing the stimulation. Participants were asked to rate five AEs (itching, tingling, burning sensation, headache, and other discomfort) on a VAS ranging from 0 (absent) to 10 (unimaginably severe) based on how strongly they occurred over the past week. AEs were also categorized as 'occurred (VAS >0)' or 'did not occur (VAS = 0)'.

Statistical analyses

Two participants in the active group were excluded from the analysis because one withdrew informed consent after one stimulation session due to a tingling sensation and headache, and the fMRI data of another subject were missing due to a system error. In addition, participants receiving fewer than 7 out of 10 tDCS sessions were planned to be excluded from the analysis; however, no participants were excluded for this reason. Accordingly, 10 participants in the active group and 12 in the sham group were included in the final analysis using per protocol analysis.

Shapiro-Wilk and Levene tests assessed data normality and homogeneity of variance, respectively. Sociodemographic and clinical characteristics and the presence and severity of AEs, were compared between the active and sham groups using appropriate statistics, including the independent *t*-test, Mann-Whitney *U* test, or Fisher's exact test. Changes in behavioral and clinical variables, such as response inhibition (SSRT) and craving (VAS), were analyzed using repeated-measures analysis of covariance. Greenhouse-Geisser correction was applied when sphericity was violated. Statistical significance was set at $p < 0.05$. SPSS (version 24.0, IBM Corp., Armonk, NY, USA) was used for all analyses.

MRI data acquisition and functional connectivity analyses

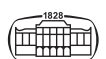
Resting-state fMRI and structural MRI data were acquired for the subjects by using a MAGNETOM Trio 3T MRI system (Siemens Healthineers, Erlangen, Germany). Resting-state fMRI data were preprocessed using tools in SPM12 (<https://www.fil.ion.ucl.ac.uk/spm/>). Details on the acquisition of MRI data and the preprocessing of fMRI data are found in [supplementary material](#).

Seed-to-whole-brain functional connectivity analyses were performed using Conn (<https://web.conn-toolbox.org/>). The bilateral DLPFC and nucleus accumbens (NA) were selected as seed regions. The DLPFC is a brain region related to response inhibition (Loftus et al., 2015), and previous neuroimaging studies have revealed the DLPFC and NA as the two key regions associated with cravings (George & Koob, 2013).

First-level analyses involved correlating the time series from each seed region with the entire brain's voxels, yielding seed-to-whole-brain Fisher-transformed correlation maps. Differences in the images (post – pre) were generated for each subject. Two-sample *t*-tests with IQ as a covariate identified voxels with significant differences in rsFC between the active and sham groups. The results were thresholded at $p < 0.001$ (uncorrected) at the voxel level and $p < 0.05$ (family-wise error correction) at the cluster level. Regression analyses were employed to examine the correlation between changes in rsFC in the surviving cluster and behavioral variables.

Ethics

This study was conducted in accordance with the Declaration of Helsinki. This study was approved by the Institutional Review Board (IRB) of Seoul St. Mary's Hospital (IRB



number: KC17DN5C0751). All participants were informed about the study and provided informed consent.

RESULTS

Sociodemographic and clinical characteristics and Internet gaming patterns at baseline

No significant differences were found in age, marital and employment status, smoking, alcohol use, education years, and IQ between the active and sham groups. Furthermore, the two groups had no significant differences in Internet gaming patterns. Both groups showed at risk of addiction based on the mean Y-IAT (active: 60.1 ± 15.3 , sham: 70.3 ± 14.0) and similar craving VAS scores (active: 6.4 ± 1.6 , sham: 5.7 ± 2.4). In addition, they showed a similar response inhibition capacity for SSRT (active: 211.5 ± 21.8 , sham: 206.7 ± 37.2). No significant differences were observed in the AUDIT, FTND, BDI-II, and BAI-II scores between the two groups (Table 1).

Effect of tDCS on response inhibition and craving

For response inhibition, a significant group-by-time interaction was observed in the SSRT ($F = 4.584$, $p = 0.045$, $\eta_p^2 = 0.186$), indicating that the SSRT between the stimulation conditions differed over time (Fig. 3A). The interaction was still significant after controlling for baseline BDI-II and BAI-II scores ($F = 4.459$, $p = 0.049$, $\eta_p^2 = 0.199$). The active tDCS group showed a decreased SSRT, indicating enhanced response inhibition, while the sham group showed an increased SSRT; however, within-group changes did not reach statistical significance. The active tDCS group, in comparison to the sham group, showed a statistically significant difference in SSRT after stimulation in the between-group analysis ($t = -2.159$, mean: 199.30 vs. 219.09, 95% CI of difference: -38.94 to -0.02 , $p = 0.044$).

The main effect of time (pre- vs. post-stimulation) on craving was statistically significant ($F = 23.955$, $p < 0.001$), indicating decreased craving VAS scores for all participants, regardless of the tDCS condition. However, the interaction between time and stimulation condition was not significant ($F = 0.635$, $p = 0.435$), suggesting that active tDCS had no advantage in reducing craving (Fig. 3B). The craving VAS scores did not exhibit a statistically significant difference between the pre- and post-stimulation conditions for both the active and sham groups. Furthermore, there was no statistically significant difference in reduction of craving VAS scores between the two groups ($t = 0.797$, mean: -1.65 vs. -2.29 , 95% CI of difference: -1.04 to 2.32 , $p = 0.435$).

Group differences in rsFC changes (post-tDCS versus pre-tDCS)

Significant differences in rsFC changes from the right DLPFC post-tDCS versus pre-tDCS were observed in the anterior cingulate cortex (ACC) (peak at MNI coordinates: 2, 18, 34; cluster size: 94 voxels). The active tDCS group

Table 1. Sociodemographic and clinical characteristics of participants at baseline

Variables	Active (<i>n</i> = 10, male)	Sham (<i>n</i> = 12, male)	<i>p</i> -value
Age, mean years (SD)	26.9 (5.2)	27.3 (5.3)	0.974
Marital status, <i>n</i> (%)			0.714
Unmarried	9 (90.0)	11 (91.7)	
Married	0 (0)	1 (8.3)	
Others (divorced)	1 (10.0)	0 (0)	
Employment status, <i>n</i> (%)			0.348
Yes	4 (40.0)	2 (16.7)	
No	6 (60.0)	10 (83.3)	
Years of education, mean years (SD)	15.6 (1.2)	15.6 (1.4)	0.872
K-WAIS-IV estimated full IQ, mean (SD)	108.4 (12.9)	112.8 (9.9)	0.387
Smoking, <i>n</i> (%)			0.172
Non-smoker	5 (50.0)	10 (83.3)	
Current smoker	5 (50.0)	2 (16.7)	
Alcohol, <i>n</i> (%)			>0.999
Non-drinker	1 (10.0)	1 (8.3)	
Drinker	9 (90.0)	11 (91.7)	
AUDIT, mean (SD)	8.8 (9.3)	6.1 (4.3)	0.872
FTND, mean (SD)	1.1 (1.3)	0.7 (1.6)	0.346
Internet gaming-related variables			
Internet gaming initiation age, mean ages (SD)	11.5 (5.2)	12.4 (6.6)	0.724
Weekday average Internet game usage hours, mean hours day (SD)	2.1 (1.4)	3.2 (2.4)	0.203
Weekend average Internet game usage hours, mean hours days (SD)	3.4 (1.6)	5.8 (4.2)	0.107
Y-IAT, mean (SD)	60.1 (15.3)	70.3 (14.0)	0.120
Craving VAS, mean (SD)	6.4 (1.6)	5.7 (2.4)	0.424
BDI-II, mean (SD)	10.7 (7.7)	16.3 (11.9)	0.220
BAI-II, mean (SD)	3.1 (4.7)	4.8 (8.3)	0.497
SSRT, mean ms (SD)	211.5 (21.8)	206.7 (37.2)	0.429

SD, standard deviation; *n*, numbers; K-WAIS, Korean Wechsler Adult Intelligence Scale; IQ, intelligence quotient; AUDIT, alcohol use disorders identification test; FTND, Fagerström test for nicotine dependence; Y-IAT, Young's Internet addiction test; VAS, visual analog scale; BDI, Beck depression inventory; BAI, Beck anxiety inventory; SSRT, stop-signal reaction time.

p-value in the independent t-test, Mann-Whitney U test, or Fisher's exact test

exhibited increased connectivity between the right DLPFC and ACC compared with the sham group (Fig. 4). Apart from that, no regions were observed showing differences in rsFC changes with seed regions (both DLPFC and NA) post-versus pre-tDCS when comparing the two groups.

Exploratory analysis of the relationship between changes in right DLPFC-ACC rsFC and changes in SSRT did not show a significant correlation. However, in the active group,



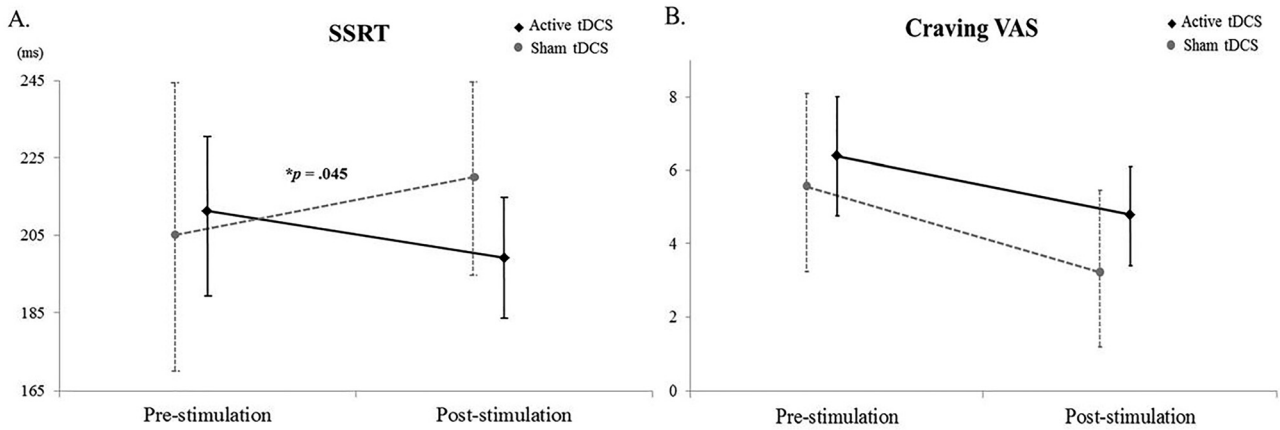
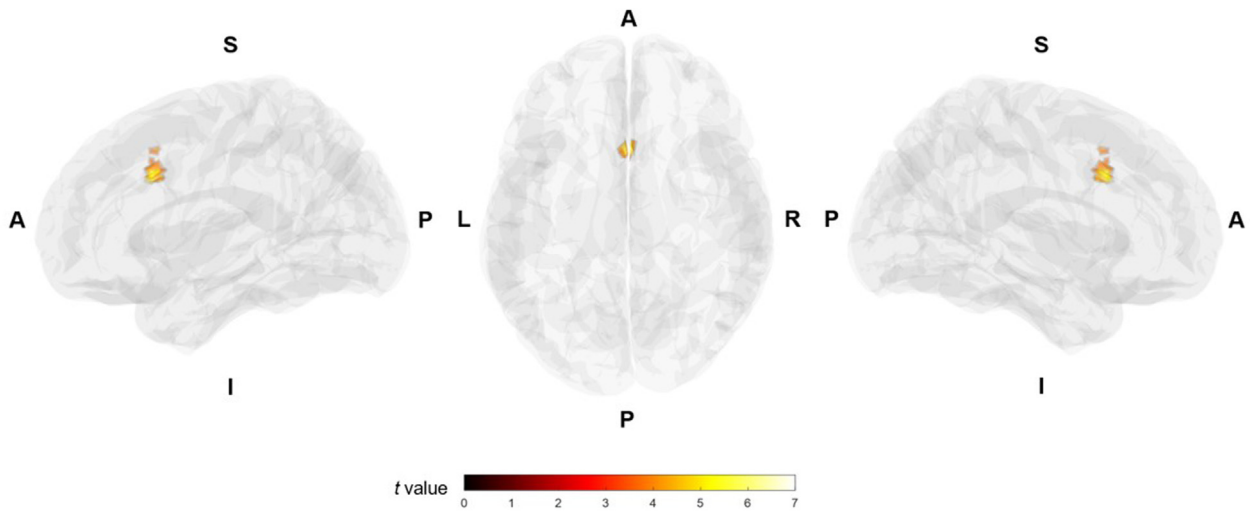


Fig. 3. Changes in the (A) SSRT and (B) craving VAS scores after tDCS

Values are presented as mean ± SD. **p* < 0.05 in group-by-time interaction.

SSRT, stop-signal reaction time; VAS, visual analog scale; tDCS, transcranial direct current stimulation; SD, standard deviation.



Brain region	<i>t</i> value	<i>p</i> value	Coordinates (mm)			Cluster size (voxels)
			<i>x</i>	<i>y</i>	<i>z</i>	
Anterior cingulate cortex (ACC)	6.610	< .001	2	18	34	94

Fig. 4. The figure and table depict the brain regions showing changes in rsFC with the right DLPFC, revealing a significant group difference (voxel-level threshold, *p* < 0.001; corrected FWE < 0.05; voxels >30)

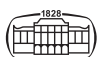
A/P, anterior/posterior; S/I, superior/inferior; L/R, left/right; rsFC, resting-state functional connectivity; DLPFC, dorsolateral prefrontal cortex; FWE, family-wise error.

the connectivity strength between the ACC and left middle frontal gyrus (MFG) was significantly negatively correlated with the SSRT (Fig. 5).

Safety and tolerance of tDCS

There was no significant difference in the average number of tDCS sessions between the active and sham groups (active = 9.3 ± 1.0, sham = 9.0 ± 1.2; *p* = 0.722) and all participants included in the analyses tolerated tDCS well. No significant

differences were observed in the occurrence of AEs between the two groups. Regarding the severity of AEs, itching and burning sensations, headache, and other discomfort, such as skin redness at the application site, did not differ between the two groups. However, the severity of the tingling sensation was significantly higher in the active group than in the sham tDCS group (active = 4.3 ± 2.6, sham = 2.1 ± 1.7; *p* = 0.029). Participants reported that all AEs subsided after tDCS completion and occurred exclusively during tDCS application.



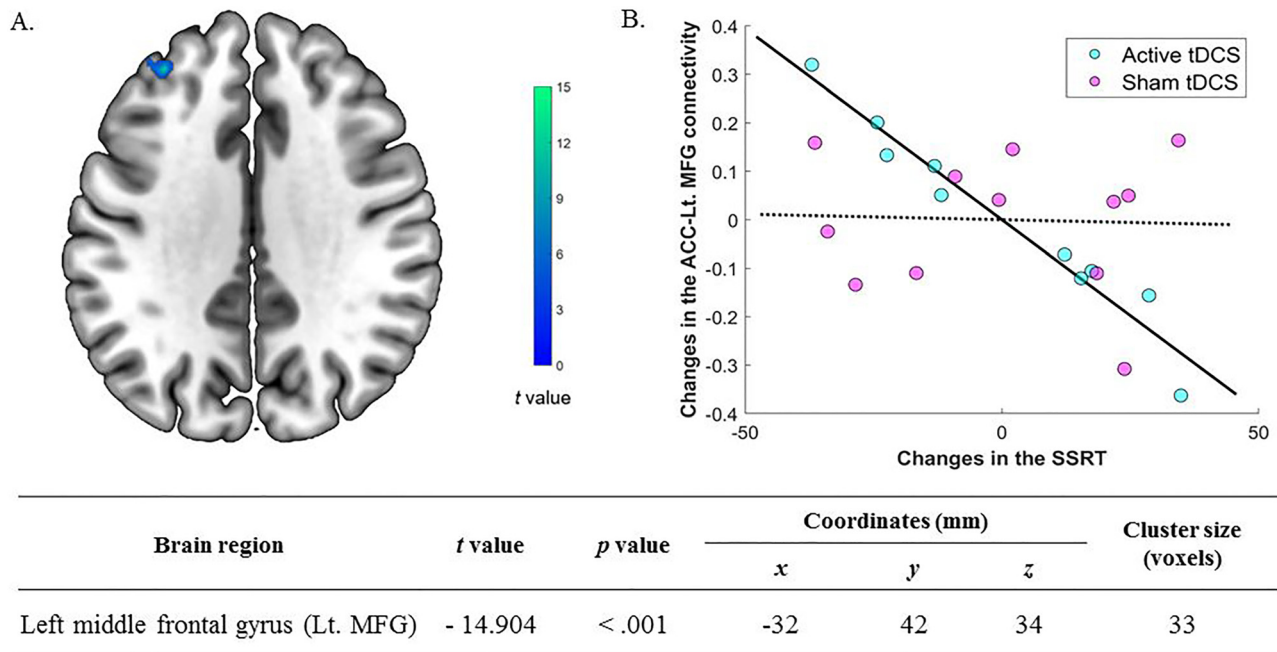


Fig. 5. Fig. 5A and the table depict the brain regions demonstrating a negative correlation between changes in rsFC with ACC and SSRT in the active tDCS group. In Fig. 5B, the relationship between the ACC–Lt. MFG connectivity and SSRT in the active tDCS group is illustrated. The solid line represents the regression line for the active group, and the dotted line represents the regression line for the sham tDCS group rsFC, resting-state functional connectivity; ACC, anterior cingulate cortex; SSRT, stop-signal reaction time; tDCS, transcranial direct current stimulation.

DISCUSSION

This randomized, double-blind, sham-controlled study explored the effect of multi-session bilateral tDCS over the DLPFC on inhibitory control measured by the SST and craving assessed using the VAS in individuals with IGD. Additionally, we investigated the changes in rsFC between the active and sham groups following tDCS and their association with clinical variables.

Regarding the inhibitory control, active tDCS reduced SSRT, indicating improved response inhibition. This aligns with a recent meta-analysis of 45 studies, including 2,668 healthy or clinical populations, that showed the significant effect of tDCS on inhibitory control (Hedge's $g = 0.21$) (Schroeder et al., 2020). However, the effect of tDCS on inhibitory control in addictive disorders remains understudied. In a study (Witkiewitz et al., 2019), patients with AUD received weekly tDCS for eight weeks with mindfulness-based relapse prevention, revealing no additive effects of active versus sham tDCS on the SSRT task. In contrast, another study involving patients with AUD and chronic tobacco users (Weidler et al., 2022) showed a shortened SSRT after active tDCS, but not sham tDCS. However, no differences between stimulation conditions were observed in healthy controls. Additionally, studies conducted among men with IGD demonstrated that a single-session of tDCS over the right DLPFC resulted in enhanced cognitive regulation of craving and improved inhibitory control over

addiction-related cues (Wu et al., 2020, 2021). These inconsistencies in results could be attributed to the heterogeneity of the addiction groups, such as substance type, and the heterogeneity of the stimulation parameters, including electrode montage and stimulation period.

Despite the efficacy of tDCS in enhancing inhibitory control (Chen et al., 2021; Schroeder et al., 2020), the underlying neural changes and mechanisms of action remain unclear. Several neuroimaging studies have shown that the DLPFC is a critical brain region for response inhibition (Chen et al., 2021; Hughes et al., 2014). Hence, many brain stimulation studies, including repetitive transcranial magnetic stimulation and tDCS, have targeted the DLPFC to improve inhibition deficits or reduce cravings in addiction (Martinotti et al., 2019; Schroeder et al., 2020; Zhang, Fong, Ouyang, Siu, & Kranz, 2019). Our study found that the rsFC between the right DLPFC and ACC increased following active tDCS compared to that in the sham group. The connectivity between the ACC and the left MFG, a frontal region containing the left DLPFC, was significantly negatively correlated with the SSRT. The ACC is considered as a hub for regulating cognitive control during the resolution of conflict between relevant and irrelevant information, as well as for monitoring ongoing behavior (Pastötter, Hanslmayr, & Bäuml, 2010; Spunt, Lieberman, Cohen, & Eisenberger, 2012). The ACC has reciprocal connections with the bilateral DLPFC, therefore, when the ACC detects a conflict, it signals the conflict to the DLPFC to implement cognitive

control (MacDonald, Cohen, Stenger, & Carter, 2000). Moreover, the ACC has been proposed to play a role for exerting cognitive control itself when more unpredictable response inhibitions are required (Garavan, Ross, Murphy, Roche, & Stein, 2002). Previous neuropsychological and neuroimaging studies have indicated that the cortical system involving the ACC and the DLPFC is dysfunctional in individuals with SUDs (Forman et al., 2004; Hester & Garavan, 2004; Yücel et al., 2007) and these reduced inhibitory skills are linked to poorer treatment outcomes and relapse (Brewer, Worhunsky, Carroll, Rounsaville, & Potenza, 2008; Streeter et al., 2008). When combined, our findings of increased functional connectivity between these two brain regions and improved inhibitory control ability after tDCS support previous observations that tDCS can enhance response inhibition and provide intriguing insight into the underlying neural mechanisms of action in response inhibition improvement after tDCS.

Recent literature on tDCS in addiction has primarily focused on cravings. A meta-analysis of 32 studies, including 937 patients with SUDs (alcohol, nicotine, or other drugs) or food addiction, revealed a total medium effect size (adjusting Hedge's $g = 0.42$), favoring active over sham tDCS to reduce cravings (Chen, Qin, He, & Zou, 2020). Even among smokers who did not seek treatment for cessation, a study reported a 50% reduction in cigarette cravings after active tDCS, whereas no differences were observed in the sham group (Perri & Perrotta, 2021). In a study involving individuals with gambling disorder, there was a significant reduction in craving through active tDCS (Martinotti et al., 2019), and another study demonstrated an attenuated background craving in males with IGD (Wu et al., 2021). However, contrary to expectations, our study found no significant interaction between time and stimulation conditions, although the active and sham groups experienced decreased craving. Several possible explanations exist for the discrepancy in results between the studies mentioned above and ours. First, the number of participants in our study may have been too small to detect significant differences, although the sample size is approximately 20–40 in most tDCS studies, similar to the present study (Chen et al., 2020). Second, the heterogeneity of the addiction group and tDCS parameters across the studies could also explain the differences in the results, as mentioned previously. Third, the differences can be partly explained by the evaluation of cravings. Previous studies used the VAS to measure craving, as in this study, or various questionnaires, such as the modified version of questionnaire of smoking urges, obsessive-compulsive drinking scale, or food craving questionnaire (Chen et al., 2020). When considering the timeframe over which craving is assessed, certain studies (Rosenberg, 2009), similar to our study, have utilized the approach of reporting craving scores over the past week, while others have focused on the present moment (Rosenberg, 2009). The assessment period of the past week in our study includes the period during which tDCS was administered. Therefore, motivational aspects related to participation in the study, along with the ongoing tDCS factor, might have influenced

the craving assessment. Consequently, this influence could have led to a reduction in craving, even within the sham group. In addition, the present study measured spontaneous craving only rather than cue-induced craving. A previous study suggested that the mechanisms underlying spontaneous and cue-induced craving may differ, and heightened executive control over cue-reactivity could potentially be a mechanism influencing the effects of tDCS in addictive disorders (Wu et al., 2021). Fourth, the decreased craving in the sham tDCS group may be related to placebo effects. Research assessments with a therapist (experimenter) – patient (participant) relationship could create the expectation of therapeutic benefit (Schambra, Bikson, Wager, DosSantos, & DaSilva, 2014). Furthermore, placing tDCS electrodes on the scalp itself may lead to the anticipation of noticeable effects (Jeong et al., 2020).

The impairment of inhibitory control is a key component of addictive disorders (Jentsch & Pennington, 2014) and has been observed in IGD (Argyriou et al., 2017). The present study evaluated the effects of tDCS on response inhibition and craving. Our findings showed that multi-session bilateral tDCS over the DLPFC enhanced response inhibition but did not reduce craving, and this effect may occur by strengthening the connectivity between the ACC and DLPFC.

This study had several limitations. First, the study included a small group of young male participants, mostly university students. Although adolescents and young adult males demonstrate far more addictive Internet gaming use than females (Mihara & Higuchi, 2017; Severo et al., 2020), our results may limit generalizability to other IGD populations. Additionally, we excluded participants with co-occurring psychiatric disorders to ensure group homogeneity. Future studies with larger and more diverse groups of subjects regarding age, sex, and comorbidities are needed to fully elucidate the effects of tDCS in IGD. Second, our study was limited by the lack of a control group, such as non-gamers or recreational gamers, although we used a sham group. Including a control group may have provided a better understanding of the effects of tDCS in IGD. Third, the level of craving was assessed using a self-reported questionnaire, and only spontaneous cravings were assessed. Using a VAS for measuring craving provides an immediate and personalized assessment of subjective experience (Mezinskis, Honos-Webb, Kropp, & Somoza, 2001). However, craving is a complex phenomenon influenced by multiple factors, such as stress and cues (Anton, 1999). Therefore, future research should corroborate various methods to measure multifaceted cravings using physiological measures such as skin conductance responses. Fourth, the long-term effects of stimulation were not examined. A previous study with smokers reported a significant improvement in the Go-/No-Go task reaction time three months after active tDCS compared to sham tDCS (Verveer, Remmerswaal, van Der Veen, & Franken, 2020). Further long-term follow-up assessments are required to explore the lasting effects of tDCS on inhibitory control.



CONCLUSION

This study provides preliminary evidence that multi-session bilateral tDCS over the DLPFC improves inhibitory control in IGD and is a step toward understanding the neural underpinnings of the effect of tDCS on response inhibition. This implies that tDCS might be a promising therapeutic option for IGD by enhancing response inhibition. This study encourages further research on the effects of tDCS in IGD.

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SUPPLEMENTARY MATERIAL

Supplementary data to this article can be found online at <https://doi.org/10.1556/2006.2024.00017>.

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