

Gambling disorder and bilateral transcranial direct current stimulation: A case report

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Introduction: Gambling disorder (GD) is a major public health concern with currently no validated and efficacious treatments approved. In this single case study, we report the short- and long-term effect of bilateral transcranial direct current stimulation (tDCS) of dorsolateral prefrontal cortex (DLPFC) on craving and impulse control in a subject with GD. **Methods:** The patient is a 26-year-old Caucasian male with an 8-year history of GD as well as alcohol and cocaine misuse. Treatment consisted of twice-a-day stimulation for 10 days. According to the literature, both the left (to control craving) and the right (to control emotional impulses) DLPFC were stimulated. Patients subsequently received tDCS once a week for 3 months and then once every 2 weeks for another 3 months. **Results:** After 10 days of treatment, the subject reported improved psychiatric symptoms (depression, anxiety, and impulsivity), as well as reduced gambling craving symptom severity. After 3 and 6 months of treatment, the clinical picture further improved. **Discussion:** This is the first report of tDCS effectiveness in a single case study of GD. Therapeutic effects, both on the addictive behavior and on psychiatric comorbid symptomatology, were lasting and continued over 6 months of tDCS maintenance treatment. Future case–control studies are required to test the efficacy of this tool in patients with GD.

Keywords: transcranial direct current stimulation, gambling disorder, dorsolateral prefrontal cortex

INTRODUCTION

Gambling disorder (GD) is characterized by persistent and recurrent maladaptive gambling behavior. The latest fifth edition of the *Diagnostic and Statistical Manual Mental disorders* (DSM-5) reconsiders GD as a behavioral addiction (BA), and includes it in the diagnostic category of Substance-Related and Addictive Disorders. This follows from recent findings suggesting that pathophysiological models for substance-use disorders (SUDs) may be relevant to GD as well. Indeed, disturbances in brain reward system function provide a common substrate that drives compulsivity in GD and other addictive disorders (Leeman & Potenza, 2012; Pettorruso, Martinotti, et al., 2014). Brain reward circuitry involves the dopaminergic system, including the mesolimbic pathway, which projects from the ventral tegmental area (VTA) to the nucleus accumbens, and the mesocortical pathway, which projects from the VTA to the prefrontal cortex (PFC; Koob & Volkow, 2016; Pettorruso, De Risio, et al., 2014). The latter, particularly the dorsolateral PFC (DLPFC), plays a critical role in the addictive cycle, comprising reinforcement learning, craving, and inhibitory control. Importantly, preclinical and

neuroimaging studies have shown that loss of inhibitory control, resulting from damage to the PFC, is crucial in addictive behaviors (Balodis et al., 2012; Moccia et al., 2017).

Although GD is a major public health concern, associated with high relapse rates and significant disability, there are currently no validated and efficacious treatments approved by the Food and Drug Administration (Lupi et al., 2014). Recently, transcranial direct current stimulation (tDCS) has been explored in the field of SUDs and BAs (Lupi et al., 2017; Sauvaget et al., 2015). The few studies that have been conducted suggest a possible role in craving reduction, especially following stimulation of the DLPFC (Lupi et al., 2017; Tortella et al., 2015). Specifically, the left DLPFC seems to modulate craving (Hayashi, Ko, Strafella, & Dagher, 2013), whereas the right DLPFC regulates inhibitory control of emotional impulses (Pripfl, Neumann, Köhler, & Lamm, 2013). Therefore, we hypothesized that

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bilateral DLPFC tDCS would reduce gambling craving and behavior in a subject with GD.

CLINICAL CASE MANAGEMENT

The patient is a 26-year-old Caucasian male with an 8-year history of GD as well as alcohol and cocaine misuse. His gambling activities initially involved sports betting, with long-term/delayed reward. He then turned to online gaming (mainly online poker), with a daily activity of more than 4 hr and daily expenses up to 1,000 Euros. He lived with his partner and his 2-year-old child. His relationship failed as a result of considerable debts related to his gambling activities.

The patient was assessed by a trained psychiatrist (GM, first author), to evaluate comorbid DSM-5 diagnoses. From a clinical viewpoint, he exhibited cyclothymic, anxious, and borderline personality traits, with mild, rapid mood swings (subthreshold for a diagnosis of a mood disorder), exacerbated by alcohol and cocaine use. He displayed high levels of impulsivity and aggressiveness. No psychotic features were present. He reported frequent insomnia, worsened during periods of intense gambling and cocaine abuse. He had previously undergone both psychopharmacological (300 mg/die bupropion, 60 mg/die duloxetine, 1,000 mg/die valproate, and 300 mg/die quetiapine) and psychotherapeutic treatments, with limited success and frequent gambling relapses. Medication had been prescribed following current guidelines or literature data when guidelines were absent/insufficient (Dell’Osso et al., 2012; Di Nicola et al., 2014; Elias & Kleber, 2017).

The patient received tDCS after down-titration of psychotropic medication, which was discontinued due to poor response. The patient gave written informed consent for the procedure and subsequent case publication.

STIMULATION PROCEDURE AND PSYCHOMETRIC ASSESSMENT

tDCS modulates cortical activity using a continuous weak electric current induced by electrodes placed on the scalp, causing focal, prolonged, and reversible shifts in cortical excitability.

The stimulation procedure that we followed has been previously used for SUDs and emotional dyscontrol (Lupi et al., 2017). Safety guidelines were also followed (Nitsche et al., 2005). tDCS was delivered by a battery-driven constant current stimulation with a maximum output of 5 mA (HDCStim class IIa; Model: HDCeEN-05, Newronika s.r.l., Milano, Italy). The current was transmitted by two 25-cm² rectangular sponge electrodes placed on the head and kept in place with rubber straps. Treatment consisted of twice-a-day stimulation (1.5 mA) for 10 consecutive days at 1-hr intervals. The first stimulation was applied over the left DLPFC to control craving, whereas the second stimulation was applied over the right DLPFC to control emotional impulses. Both stimulations lasted 20 min each. Positions F3 and F4 of the International 10/20 EEG system

were used to localize the left and right DLPFC, according to the Beam F3-System (Beam, Borckardt, Reeves, & George, 2009; Herwig, Satrapi, & Schönfeldt-Lecuona, 2003). During left DLPFC anodal stimulation, the anodal electrode was placed over F3 and the cathodal electrode over F4. During right DLPFC anodal stimulation, the anodal electrode was placed over F4 and the cathodal electrode over F3.

After 10 days of treatment, the patient subsequently received tDCS once a week for 3 months and then once every 2 weeks for another 3 months, following the same procedure (two consecutive stimulations at 1.5 Hz, over the left and right DLPFC, respectively).

Patient assessment was performed upon admission, after 10, 100, and 190 days of tDCS.

The following psychometric scales were used:

- South Oaks Gambling Screen, to screen for gambling behavior;
- Brief Psychiatric Rating Scale, to assess overall psychopathological burden;
- Hamilton Depression Rating Scale, to assess depressive symptoms;
- Hamilton Anxiety Rating Scale, to assess anxiety symptoms;
- Barratt Impulsiveness Scale, to assess trait impulsivity;
- Visual Analogue Scale for Craving – Global Score: 1–10, to assess severity of gambling craving;
- Pathological gambling Yale Brown Obsessive Compulsive Scale, to assess obsessive–compulsive symptoms related to gambling behavior;
- Gambling Symptom Assessment Scale, to assess gambling symptom severity.

Ethics

The study procedures were carried out in accordance with the Declaration of Helsinki. The institutional review board of the University of Chieti approved the study. The subject was informed about the study and provided informed consent.

RESULTS

Table 1 presents scores on psychometric scales at baseline and follow-up visits. After 10 days of treatment, psychiatric symptomatology significantly improved, as did gambling severity and craving levels. Both the patient and his family members reported that gambling behaviors ceased. After 3 and 6 months of treatment, we observed a further improvement on overall psychopathological symptoms as well as continued absence of craving. The patient remained completely abstinent from cocaine and alcohol for the entire study period. Mood swings decreased in frequency and intensity, as measured by the appropriate psychometric scales. No adverse reaction or side effect was observed during the entire study period. The patient reported a positive state of mind right after the tDCS stimulation procedures, characterized by a feeling of relaxation and well-being. He also described a therapeutic effect on sleep, with shortening of sleep onset latency on the days of tDCS stimulation.

Table 1. Psychometric evaluations at baseline and after 10, 100, and 190 days of tDCS treatment

	T0	T1 10 days	T2 100 days	T3 190 days	Δ change (%) (T3-T0)/T0
No. of tDCS applications	–	20	44	68	–
SOGS	14	–	–	–	–
BPRS	45	28	26	26	–42.2
HAM-D	14	11	5	5	–64.3
HAM-A	23	10	8	8	–65.2
BIS-11	72	57	51	55	–23.6
VASc	8	0	0	0	–100.0
PG-YBOCS	16	8	6	6	–62.5
G-SAS	26	10	8	8	–69.2

Note. Δ changes between baseline (T0) and end of treatment (T3) are reported in percentage. SOGS: South Oaks Gambling Screen; BPRS: Brief Psychiatric Rating Scale; HAM-D: Hamilton Depression Rating Scale; HAM-A: Hamilton Anxiety Rating Scale; BIS-11: Barratt Impulsiveness Scale; VASc: Visual Analogue Scale for Craving – Global Score: 1–10; PG-YBOCS: Pathological gambling Yale Brown Obsessive Compulsive Scale; G-SAS: Gambling Symptom Assessment Scale.

DISCUSSION

To the best of our knowledge, this is the first report of tDCS effectiveness in GD. We observed a significant impact on gambling craving and behavior after 10 days of right and left DLPFC tDCS. Preclinical and clinical studies have provided strong evidence that compulsivity, impaired self-control, and behavioral inflexibility reflect underlying PFC dysregulation. We hypothesize that bilateral DLPFC modulation prompts a shift back to a precompulsive status, in which higher order executive functions (i.e., decision-making) temper compulsive behavior (Greenwood, Blumberg, & Scheldrup, 2018).

Although two previous studies found that tDCS did not affect gambling task performance or risk propensity in healthy subjects (Boggio et al., 2010; Minati, Campanhã, Critchley, & Boggio, 2012), tDCS is plausibly more effective in GD patients in whom loss of control over the addictive behavior reflects underlying prefrontal dysregulation that sustains dysfunctions in cognitive control, compared to healthy subjects in whom risk propensity may be mediated by different neurobiological substrates (Moccia et al., 2017).

In light of the distinct functions of the right and left DLPFC, we hypothesize that our findings are possibly a result of a synergistic effect exerted by the bilateral stimulation. As observed for other addictive behaviors, a concurrent modulation of craving phenomena (i.e., left DLPFC) and inhibitory control of emotional impulses (i.e., right DLPFC) possibly allowed the drastic cessation of gambling behavior (Hayashi et al., 2013; Lupi, Sepede, Cinosi, Martinotti, & Di Giannantonio, 2018; Pripfl et al., 2013).

Given the overall clinical improvement we observed, it is also possible that tDCS improved comorbid mood and anxiety symptoms, indirectly contributing to cessation of compulsive gambling. Indeed, it is important to consider that tDCS has been increasingly tested for the treatment of other psychiatric disorders, showing particularly promising results for major depression (Fregni et al., 2015; National Institute for Health and Care Excellence, 2015; Nitsche & Paulus, 2011).

The results from the present case suggest that DLPFC tDCS is a safe and promising treatment option for GD worthy of further exploration in large, randomized controlled trials. tDCS shows potential as its probes affected brain circuits in GD, and has the unique therapeutic advantage of directly targeting and remodeling impaired circuits. Future studies should also focus on determining the optimal stimulation target, montage, frequency, magnitude, and address long-term tDCS effects in the clinical setting.

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Authors' contribution: GM directly evaluated the patient, followed him up during all the study period, and wrote the manuscript. EC tested the patient with the psychometric instruments and performed the stimulation procedure. ML developed the tDCS experimental procedure. LDR collaborated in both the evaluation and the writing procedures. MP prepared the literature review and tried to define the rationale of the study. MDG coordinated the study.

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