

## Repetitive Transcranial Magnetic Stimulation (rTMS) for Decreasing Gambling Craving in Patients with Gambling Disorder: A Call for Advanced Clinical Investigations

Chidiebere Emmanuel Okechukwu

Sapienza University of Rome, Rome, Italy

### Abstract

Gambling disorder (GD) is an addictive behavioral disorder that alters the frontostriatal neural circuitry and prefrontal control of reward-associated brain areas. An intrusion between prefrontal cortex and the mesolimbic reward pathway has been proposed as the major mechanism behind the pathogenesis of GD. Repetitive transcranial magnetic stimulation (rTMS) is a noninvasive treatment that utilizes magnetic fields to stimulate nerve cells linked to mood and behavioral control; this stimulation is usually applied either on the left or right side of the dorsolateral prefrontal cortex of the brain. rTMS selectively modulates the activities of brain circuits and possess the ability to overturn the alterations in the neurocircuitry of the brain linked to the pathophysiology of GD. rTMS adjusts impulsivity, cognitive/attentional control, cognitive plasticity, and decision-making, which are crucial in decreasing gambling craving and relapse. However, innovative clinical investigations are needed to analyze and establish the impact of rTMS on gambling craving and cessation, using a larger sample size.

**Keywords:** gambling craving; gambling disorder; repetitive transcranial magnetic stimulation; neuroregulation; neurotherapy

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**\*Address correspondence to:** Chidiebere Emmanuel Okechukwu, Department of Public Health and Infectious Diseases, Sapienza University of Rome, Piazzale Aldo Moro 5, 00185, Rome, Italy. Email: [chidiebere.okechukwu@uniroma1.it](mailto:chidiebere.okechukwu@uniroma1.it)

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**Edited by:** Rex L. Cannon, PhD, SPESA Research Institute, Knoxville, Tennessee, USA

**Reviewed by:** Rex L. Cannon, PhD, SPESA Research Institute, Knoxville, Tennessee, USA  
Mark S. Jones, DMin, University of Texas at San Antonio, San Antonio, Texas, USA

Gambling disorder (GD) is a complicated behavioral addiction that affects the frontostriatal neural circuitry and prefrontal control of reward-associated brain areas, a discrepancy between prefrontal cortex (PFC) and the mesolimbic reward pathway has been proposed as the major mechanism behind the pathogenesis of GD (Pettoruso et al., 2020). There is an elevated functional connectivity between the regions of the PFC and mesolimbic reward pathway in GD patients (Pettoruso et al., 2020). The distorted connection between prefrontal structures and the mesolimbic reward system in GD is similar to the pathophysiological mechanism implicated in substances use disorders (Pettoruso et al., 2020). GD is a growing public health issue, and its aftereffects are family issues, substance misuse, suicidal ideation, suicide, and criminal activities such as robbery and drug smuggling to raise cash for

gambling (Okechukwu, 2019). Individuals with GD often encounter financial difficulty and abject poverty because of relentless gambling (Okechukwu, 2019). Moreover, mood disorders such as major depressive disorder, generalized anxiety disorder, and personality disorder are associated psychiatric comorbidities of GD (Okechukwu, 2019).

Repetitive transcranial magnetic stimulation (rTMS) is a noninvasive treatment that utilizes magnetic fields to stimulate nerve cells linked to mood and behavioral control, this stimulation is usually applied either on the left or right side of the dorsolateral prefrontal cortex (DLPFC) of the brain (Lefaucheur et al., 2014). High-frequency rTMS of the left DLPFC appears to be effective, and low-frequency rTMS of the right DLPFC has possible effectiveness (Lefaucheur et al., 2014). According to the study

conducted by Gay et al. (2017), they found that patients with GD had decreased gambling craving following a single session of high frequency rTMS delivered to their left DLPFC after viewing a gambling video, using a MagPro X100 stimulation system.

A key advantage of rTMS is that it selectively modulates the activities of brain circuits and possesses the ability to overturn the alterations in the neurocircuitry of the brain linked to the pathophysiology of GD (Pettoruso et al., 2021). rTMS significantly modulates impulsivity, cognitive/attentional control, decision-making, and cognitive plasticity, which are crucial in decreasing gambling craving and relapse (Zucchella, Mantovani, Federico, Lugobani, & Tamburin, 2020). rTMS has been shown to adjust dopaminergic and glutamatergic neurotransmission, and both transmissions are altered in GD patients (Pettoruso et al., 2019). rTMS causes a decrease in dopamine transporter availability in striatal regions, leading to modulation in dopaminergic pathways; this implies that rTMS has the potential to modulate brain functioning, and neural circuits associated with GD (Pettoruso et al., 2019).

Neuroimaging findings have shown similar activation defects in regions of the mesolimbic reward system in patients with GD and substance use disorders (Limbrick-Oldfield, Van Holst, & Clark, 2013). Some patients with GD often abuse cocaine (Cowlshaw, Merkouris, Chapman, & Radermacher, 2014). However, rTMS is effective in lowering cocaine use and sleep disruption (Gómez Pérez et al., 2020).

Providing 5-Hz rTMS therapy for 2 weeks significantly reduced craving and impulsivity, and improved functional connectivity between left DLPFC with ventromedial prefrontal cortex, and ventromedial prefrontal cortex with right angular gyrus in patients with cocaine use disorder (Garza-Villarreal et al., 2021). Moreover, clinical improvements were observed in patients with comorbid gambling and cocaine use disorder who had undergone a high-frequency left-DLPFC-rTMS stimulation. including diminished cocaine craving and intake and decrease in the craving to gamble. There was also improvement in sleep quality and decrease in anxiety and depression among the patients (Cardullo et al., 2019).

In conclusion, GD is an addictive behavioral disorder, in which dysfunctions in the prefrontal neural activity have been proposed as the underlying pathophysiological mechanism.

Therefore, targeting the PFC for the treatment of GD using rTMS is a promising therapeutic innovation. rTMS seems to decrease gambling craving, enhance mood control, and improve cognitive function in patients with GD. rTMS could emerge as a reliable adjunct therapy in support of cognitive-behavioral therapy for the treatment of GD. However, advanced clinical investigations are needed to scrutinize and establish the impact of rTMS on gambling craving and cessation, using a larger sample size.

### Author Disclosure

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