



AKADÉMIAI KIADÓ

# Psychedelic-assisted therapy for people with gambling disorder?

PEDRO ROMERO<sup>1</sup> , ANDREA CZAKÓ<sup>1,2</sup> ,  
WIM VAN DEN BRINK<sup>3</sup>  and ZSOLT DEMETROVICS<sup>1,2\*</sup> 

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<sup>1</sup> Centre of Excellence in Responsible Gaming, University of Gibraltar, Gibraltar, Gibraltar

<sup>2</sup> Institute of Psychology, ELTE Eötvös Loránd University, Budapest, Hungary

<sup>3</sup> Amsterdam University Medical Centers, Department of Psychiatry, Amsterdam, The Netherlands

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## VIEWPOINT



### ABSTRACT

Gambling disorder is a severe mental health and behavioural problem with harmful consequences, including financial, relationship and mental health problems. The present paper initiates discussion on the use of psychedelics combined with psychotherapeutic support as a potential treatment option for people living with a gambling disorder. Recent studies have shown promising results using psychedelic-assisted therapy (PAT) to treat anxiety, depression, post-traumatic stress disorder, and various substance use disorders. Considering the similarities in the underlying psychosocial and neurobiological mechanisms of gambling disorder and other addictive disorders, the authors suggest that psychedelic-assisted therapy could be effective in treating gambling disorder. The paper also underscores the need for further research into the viability and effectiveness of psychedelic-assisted therapy for gambling disorder.

### KEYWORDS

psychedelics, gambling disorder, psychedelic-assisted therapy, behavioural addictions, gambling

## EARLY EXPERIENCES WITH THE THERAPEUTIC USE OF CLASSIC PSYCHEDELICS

Classic psychedelics (5HT<sub>2A</sub>-agonists), such as lysergic acid diethylamide (LSD), psilocybin, and dimethyltryptamine (DMT), are powerful psychoactive substances that alter perception, mood, and cognition. They are generally considered physiologically safe and do not cause abuse or dependence (Nichols, 2016), especially when used in clinical settings. Some of these compounds have been used for millennia by humans for multiple purposes, not only for religious and spiritual ceremonies but also for medicinal purposes (Schultes, Hofmann, & Rätsch, 2001). Both direct and indirect evidence underlines the use of natural psychedelics from the Neolithic period and Ancient Indo-European, Egypt and pre-Columbian civilisations (Carod-Artal, 2013; Samorini, 2019; Wasson, Hofmann, & Ruck, 2008). In the 1950s and 1960s, LSD was widely researched with over a thousand studies involving 40,000 participants exploring its effectiveness in the treatment of multiple conditions (Daws et al., 2022). Political and legal issues stopped psychedelic research in the 1960s but it resurged in the 1990s and blossomed in the last 20 years (Carhart-Harris & Goodwin, 2017).

Since then, there has been a renaissance in psychedelic research motivated by developments in neuroscience, political and social changes, the need for new mental health treatments, decriminalisation and regulation, and a better understanding of drug use safety. Recent research indicates the potential of psychedelic-assisted therapy (PAT) to treat treatment-resistant mental disorders, including various substance use disorders (Andersen, Carhart-Harris, Nutt, & Erritzoe, 2021). While atypical psychedelics (e.g., MDMA, ketamine) also show

\*Corresponding author.  
E-mail: [Zsolt.Demetrovics@unigib.edu.gi](mailto:Zsolt.Demetrovics@unigib.edu.gi)



positive results (Mitchell et al., 2021; Sessa et al., 2021; Walsh et al., 2022), we will focus here on classic psychedelics, e.g. LSD, psilocybin, and DMT.

## HOW DO CLASSIC PSYCHEDELICS WORK?

There are multiple, partly overlapping hypotheses on how psychedelics work. First, the Entropic Brain hypothesis (Carhart-Harris, 2018; Carhart-Harris et al., 2014) is based on the assumption that people living with mental disorders often show rigid cognitive processes. Psychedelics, by increasing the entropy of the brain, help to process information and emotions differently from the usual functioning and thereby help the person to gain new insights and facilitate the therapeutic process. Second, the Default Mode Network (DMN) hypothesis (Carhart-Harris & Friston, 2010) suggests that psychedelics disrupt the functioning of specific brain regions, allowing profound changes in emotion and perception. The disruption of this channel allows a different type of memories and provides new insights that can be integrated with already existing memories (Daws et al., 2022). Third, the psychedelic state model suggests that psychedelics create a different state of consciousness rather than disrupting the functioning of specific brain regions. This different state of consciousness is characterised by heightened introspection, emotions, creativity, insight into abstract thinking, and a sense of unity (Bayne & Carter, 2018; Carhart-Harris et al., 2014). The fourth model of Relaxed Beliefs Under Psychedelics (REBUS) (Carhart-Harris & Friston, 2019) suggests that the key mechanism by which psychedelics produce their effect is the reduction of the strength of prior beliefs and assumptions. Fifth, the Self-entropic broadening theory suggests that psychedelics can lower the person's self-focus, leading to positive changes in well-being (Dourron, Strauss, & Hendricks, 2022). In the sixth model, the 5-HT<sub>2A</sub> receptor hypothesis, the therapeutic effects of psychedelics are supposed to be mediated through their interaction with serotonin 5-HT<sub>2A</sub> receptors in the brain, leading to a cascade of neural effects that may facilitate therapeutic insights and promote emotional processing in individuals with mental disorders (Vollenweider & Kometer, 2010). In the seventh model, increased neuroplasticity may also contribute to the (long-term) effectiveness of PAT as a systematic review (de Vos, Mason, & Kuypers, 2021) pointed out that the administration of a psychedelic produces rapid changes in plasticity. In a recent review, the different models are described at a biochemical, neural, and psychological dimension, offering the opportunity to understand these compounds at different conceptual levels (Van Elk & Yaden, 2022).

## RECENT PROMISING RESULTS

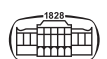
The new wave of psychedelic research has produced promising results, especially in treating hard-to-treat conditions (Schlag, Aday, Salam, Neill, & Nutt, 2022) such as

(treatment-resistant) substance use disorders, post-traumatic stress disorder, and depressive disorders. In addition, psychedelics have shown remarkable effects in assisting patients with existential end-of-life distress (Kelmendi et al., 2016; Schimmers et al., 2022; Yaden et al., 2022).

A factor that may have contributed to the recent success of research with PAT is the carefully designed studies that also consider set (e.g., personality, expectations) and setting (e.g., physical environment, music, patient-therapist relation) and make use of preparation, and integration sessions (Guss, Krause, & Slosower, 2020; Mithoefer, 2015). Preparation sessions allow participants to discuss their history and situation with clinicians, set their intentions, and understand what to expect during the psychedelic sessions. The limited number of dosing sessions take place in a safe and comfortable environment, with usually two clinicians present to provide a safe and holding environment. Finally, integration sessions help participants make sense of their psychedelic experience and integrate it into their lives. PAT uses a psychedelic compound to enhance the talking therapy's effectiveness.

Research in treating major depressive disorder with PAT has produced encouraging results. In a recent randomised, waiting list-controlled clinical trial with two psilocybin sessions, 71% of participants had clinically significant responses, with 54% in remission at week 4 (Davis et al., 2021). In a double-blind randomised placebo controlled trial, a single moderate dose of psilocybin combined with psychotherapy led to an absolute decrease in symptoms, with 54% meeting remission criteria 14 days after the intervention (von Rotz et al., 2023). Similarly, in a double-blind randomized controlled trial, depressed patients treated with a single dose of 25 mg, 10 mg or 1 mg (placebo) psilocybin, the 25 mg group showed significant reductions in depression severity up to 6 weeks after the psilocybin session (Goodwin et al., 2022). In a recent RCT comparing 25 mg psilocybin with 100 mg niacin (placebo) similar positive results were obtained in patients with major depression (Raison et al., 2023).

Some of the most consistently encouraging outcomes of PAT have been obtained in patients with a substance use disorder. A meta-analysis of six randomised placebo control trials in patients with 'alcoholism' from the 1960s and 1970s, showed that a single dose of LSD had significant effects on reduced drinking and abstinence up to six months (Krebs & Johansen, 2012). In a small pre-post study ( $n = 15$ ) with three psilocybin sessions for tobacco dependence, 80% of participants were still abstinent at six months follow-up (Johnson, 2022; Johnson, Garcia-Romeu, Cosimano, & Griffiths, 2014, 2017). Similarly, a small ( $n = 10$ ) pre-post study with two psilocybin sessions in alcohol dependent patients showed reduced drinking lasting up to 6 months. Recently, the first randomised clinical trial in alcohol dependent patients comparing 12 weeks motivational enhancement therapy/cognitive behavioral therapy (MET/CGT) plus two psilocybin sessions with 12 weeks MET/CGT plus two diphenhydramine (placebo) sessions produced a robust decrease in alcohol intake lasting at least 6 months (Bogenschutz et al., 2022).



Overall, studies on PAT are very promising in the treatment of a range of mental health conditions, including substance use disorders, with the added benefit of being administered on a few occasions compared to many current long-term pharmacological treatments with high drop-out rates and persistent side effects (Arana, 2000; Bet, Hugtenburg, Penninx, & Hoogendijk, 2013; Dols et al., 2013). Contrary to popular belief, the use of psychedelics in clinical settings proved to be safe (Schlag et al., 2022). Nonetheless, there are also risks associated with PAT. Classic psychedelics can increase blood pressure and heart rate, presenting risks for those with heart conditions and there are contraindications for people with certain pre-existing conditions (e.g. psychosis, epilepsy, serious cardiovascular disorder) or taking certain medications (e.g. SSRIs, MAO-inhibitors). Participants may experience adverse effects such as anxiety, confusion, headaches, and fatigue. Rare but serious issues like psychotic episodes, depressive reactions, or Hallucinogen Persisting Perception Disorder (HPPD), which causes lasting perceptual disturbances, are also concerns. These risks highlight the importance of careful patient screening and monitoring in therapeutic settings (Ley et al., 2023; Schlag et al., 2022; Strassman, 1984).

Although these results are promising, we need to be mindful that the number of participants in these studies is small and additional research is needed in this field.

## THE USE OF CLASSIC PSYCHEDELICS IN GAMBLING DISORDER

Gambling disorder (GD) is a serious mental and behavioural problem with a lifetime prevalence of 0.4%–1% (American Psychiatric Association, 2013). The harmful consequences of GD include financial problems, relationship difficulties, mental health issues, and heightened morbidity and mortality rates (Cowlshaw & Kessler, 2016). Individuals with GD exhibit significantly higher suicidality than the general population (Karlsson & Håkansson, 2018). The prevalence of comorbid disorders in GD is very high, with 64% of people with GD having three or more co-occurring conditions. The most common comorbid disorders linked to harmful and disordered gambling include anxiety, mood, and substance use disorders (Fong, 2005; Gartner, Bickl, Härtl, Loy, & Häffner, 2022; Kessler et al., 2008; Moreira, Azeredo, & Dias, 2023).

The currently available psychotherapeutic and pharmacotherapeutic options for GD (Dowling et al., 2015) are similar to those for the treatment of substance use disorders. The most common treatments include cognitive-behavioural therapy (CBT), cognitive therapy, exposure therapy, imaginal desensitisation, motivation enhancement therapy (MET), and couple's therapy. CBT is more effective, in addressing thoughts and behaviours associated with gambling. Pharmacological treatments like nalmefene and naltrexone may reduce gambling severity, but they have higher dropout rates than the various psychotherapies (Eriksen et al., 2023; Ioannidis et al., 2023; Ribeiro, Afonso, & Morgado, 2021). Although probably effective, many patients do not respond

to these interventions. Current therapeutic options have low to moderate effectiveness, with treatment dropout rates up to 51% (Roberts, Murphy, Turner, & Sharman, 2020) and one-year relapse rates reaching 58% (Müller et al., 2017). For this reason, exploring novel approaches to treating GD could improve the prognosis for people affected by harmful gambling.

Based on the above summary, psychedelic-assisted therapy presents an intriguing approach that has so far shown promising results in addressing substance use disorders that share many symptoms and etiological features with GD (American Psychiatric Association, 2013; Rash, Weinstock, & Van Patten, 2016; Wareham & Potenza, 2010). Considering the similarities in the underlying neurobiological mechanisms in these disorders and the existence of proposals to integrate psychedelic-assisted therapy for GD (Re et al., 2019) it seems realistic that PAT could be effective in the treatment of gambling disorder as well as other behavioural addictions, such as gaming disorder, compulsive sexual behaviour disorder, and eating disorders (Johnson, 2022; Peck et al., 2023; Richard & Garcia-Romeu, 2023; Zafar et al., 2023). Moreover, PAT's potential to target disorders frequently comorbid with GD also supports the above position. Future research should study this potential, including different gambler populations with different background characteristics and comorbid histories. While atypical psychedelics are not the focus of this position paper, we would like to mention that encouraging results are seen in the treatment of patients with different substance use disorders (alcohol, cocaine, cannabis) using ketamine or MDMA (e.g., Dakwar et al., 2020; Sessa et al., 2021; Walsh et al., 2022). Of special interest for this report is the case study of a 44-year-old man with chronic GD, who after 4 sessions of intravenous ketamine recovered, and this improvement continued for the subsequent 6 months with no gambling behaviour and only fleeting thoughts of gambling (case of ketamine including a case study for GD and MDMA) (Grant & Chamberlain, 2020). With this in mind, we certainly should be open to exploring the application of (classic) psychedelics for the treatment of gambling problems.

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as an independent consultant. He is also Chief of Safer Gambling partnerships for the Scottish charity betblocker.org which provides free gambling blocking software for people living with gambling problems. Betblocker is mainly funded by UKGC LCCP RET and donations from operators in licensed jurisdictions. PR is also a former Non-Executive Director for ESG Gaming not-for-profit, registered and regulated Community Interest Company. None of the above-listed funding sources are related to this article. ZD is Editor-in-Chief of the Journal of Behavioral Addictions.

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