Brain Stimulation 17 (2024) 107–108

Contents lists available at ScienceDirect

Brain Stimulation

journal homepage: www.journals.elsevier.com/brain-stimulation

Treatment of Hallucinogen-Persisting Perception Disorder: A case report on repetitive transcranial magnetic stimulation targeting the right temporoparietal junction

Dear Editor, Hallucinogen-Persisting Perception Disorder (HPPD) is a psychiatric condition characterized by recurrent perceptual distorsions or visual hallucinations following drug usage. Symptoms include heightened colors, distorted perception, halos, pareidolia, macropsia or micropsia [1]. Two subtypes of HPPD are recognized: type 1, involving brief re-experiences of substance intoxication, is usually benign and non-distressing [2]. Type-2 encompasses long-lasting, highly distressing visual distorsions and often includes depersonalization, derealization, anxiety or depression [1]. The epidemiology, phenomenology, and treatment of HPPD remain poorly understood [2] and long-term prognosis is unpredictable [1]. The temporoparietal junction (TPJ) plays a pivotal role for embodiment, multisensory integration, self-processing and awareness [3]. Studies have suggested the efficacy of repetitive transcranial magnetic stimulation (rTMS) targeting the TPJ in treating depersonalization and derealization [4]. In 2021, Orru and al. published a review on patients with depersonalization-derealization disorder treated with TPJ-focused TMS, yielding promising results [5]. TMS of the temporoparietal junction has also been explored in the treatment of refractory auditory verbal hallucinations in schizophrenia [6]. While TMS of the left TPJ demonstrated significant positive outcome, TMS of the right TPJ did not outperform sham treatment [6].

Hereby, we present a case of a 29-year-old male diagnosed with type-2 HPPD successfully treated with TMS. The patient had no noteworthy medical or chirurgical history. Initially, he reported sporadic cannabis use at the age of 17 and occasional use of cocaine, LSD or MDMA intake a couple times a year by age 23 without exhibiting HPPD symptoms. However, after a singular LSD usage at 26, he experienced panic attacks, peculiar dreams, muscular spasms, and asthenia for several months, ultimately recovering spontaneously. A more severe relapse occurred one year later, following the use of cannabis, LSD and ecstasy. Persistent visual disturbances, including visual snow in the external visual field and fluctuating derealization, became a daily struggle. Chronic symptoms emerged five years later, encompassing visual field distorsion, permanent visual snow, photophobia, palinopsia, and persistent derealization and depersonalization after a week of cannabis and MDMA use. Nonspecific symptoms also occurred such as anxiety, panic attacks, insomnia and depressive symptoms. Despite ceasing all drug use, symptoms persisted without attenuation. No psychotic symptoms or neurological/ophthalmologic causes were identified.

The patient underwent various treatments including pharmacological intervention (2 mg clonazepam, 100 mg lamotrigine, and escitalopram for comorbid generalized anxiety), and cognitive-behavioral therapy, yielded no improvement in HPPD symptoms. Based on previous research on depersonalization-derealization disorder [3,5], a low frequency rTMS of the right TPJ was administered using a cool DB-80 coil. The patient received a course of 1Hz stimulation of right TPJ at 110% motor threshold intensity, 20 min per session, twice daily for five days, within a one-week period delivering a total of 12 000 pulses. The patient reported no adverse effects. Efficacy was evaluated using the Cambridge Depersonalization Scale (CDS) (State-Version) [7] (Fig. 1) consisting of 22 items rated between 0 and 100%. Before initiating rTMS, 17 items were rated at 0% and none surpassed this level throughout the treatment. Of the remaining five items, scores decreased from 195% to 150%. The patient subjectively noted an improvement in his visual disturbances including attenuation of palinopsia, photophobia and visual snow, along with reduced insomnia and anxiety. The stability of outcomes on visual disturbances, depersonalization, derealization, and nonspecific symptoms persisted for four months following the rTMS course.

Following the positive outcome from the initial rTMS course, maintenance courses were administered at four to six-month intervals over a two-year period. The patient consistently reported a reduction in visual distortions, derealization and depersonalization after each subsequent rTMS session, ultimately leading to remission. Additional symptoms such as insomnia, anxiety and depressive symptoms gradually resolved, reaching full remission. The patient did not undergo any other pharmacological or non-pharmacological interventions during this period. Furthermore, he reported no side effects associated with the rTMS sessions. As of the current date, the patient remains in remission from both HPPD and general anxiety.

To the best of our knowledge, this case constitutes the first use of rTMS targeting the right TPJ in a patient suffering from type-II HPPD. While we acknowledge the possibility that treating the patient's general anxiety may have contributed to the amelioration of his HPPD symptoms, available evidence does not strongly support this hypothesis. Despite possessing an anxious personality, the patient had not sought consultation nor experienced functional impairment due to anxiety before the onset of HPPD. The diagnosis of general anxiety disorder occurred years after the initiation of HPPD and resolved before the cessation of HPPD symptoms. In the context of prior research on rTMS in depersonalization-derealization disorder and auditory verbal hallucinations, we faced the choice of targeting either the right or left TPJ. We opted for the right TPJ, as the patient did not exhibit schizophrenia nor auditory verbal hallucinations. While the primary anticipated outcome was a reduction in depersonalization and derealization, we observed a concurrent decrease in visual disturbances, encompassing palinopsia, photophobia, visual field distorsions, and visual snow. Although the possibility of spontaneous resolution of HPPD cannot be ruled out, the patient's symptoms remained stable for months before the initiation of rTMS, and their incremental reduction following each maintenance course suggests potential treatment efficacy.

Considering acceptability and tolerance of rTMS, the functional

https://doi.org/10.1016/j.brs.2023.12.015
Received 14 November 2023; Received in revised form 28 December 2023; Accepted 29 December 2023
Available online 5 January 2024
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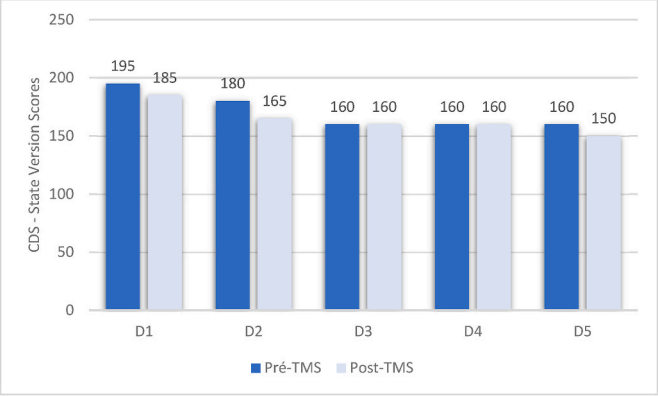

Fig. 1. Cambridge Depersonalization Scale (State Version) scores (%) before and after each session of the initial rTMS course.

disability associated with HPPD, and the partial effectiveness of pharmacological treatments for this indication, further investigations are warranted to explore the feasibility and efficacy of rTMS in the treatment of HPPD.

CRediT authorship contribution statement

Sylvain Creton: Investigation, Methodology, Writing – original draft, Writing – review & editing. **Gaëlla Boulanger:** Writing – review & editing. **Thomas Pereon:** Writing – review & editing. **Jean-Marie Batail:** Supervision, Validation, Writing – review & editing. **Dominique Drapier:** Investigation, Methodology, Validation, Visualization, Writing – review & editing.

Declaration of competing interest

Jean-Marie BATAIL has served as a scientific consultant for Magnus Medical. The other authors declare no conflicts of interests.

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