GLOBAL PSYCHIATRY ARCHIVES

Case Study

Inhibitory rTMS to the right temporo-parietal junction improves depersonalisation and derealisation

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Abstract

Depersonalization - derealisation disorder (DDD) is a psychiatric condition whereby the individual has persistent or recurrent episodes of depersonalization, derealization or both. Several therapeutic approaches have been suggested for the treatment of DDD. Repetitive transcranial magnetic stimulation (rTMS) is a new non-invasive intervention which has shown promising results in many neuropsychiatric conditions. The role of rTMS as a therapeutic approach in DDD is not extensively investigated. In this paper, we report a case of DDD who presented with depresonlisation and derealisation with prominent varied visual symptoms and benefited from inhibitory rTMS stimulation to the right temporal-parietal junction (TPJ). The patient received 15 sessions of 1 Hz 1200 pulses/session at 110% of resting motor threshold over a period of 3 weeks. The patient reported improvement in several symptom domains of derealisation as well as complete cessation of some of the visual symptoms, such as visual floaters and grid lines in her visual field. Incremental improvement in symptoms were observed from the 10th session to the 15th session. The level of depressive symptoms did not change following rTMS intervention. The case report highlights specificity of the right TPJ stimulation in improvement of DDD symptoms and provide evidence that rTMS should be considered as an intervention approach in DDD.

Keywords: Non-invasive Brain Stimulation, Psychiatric Neuromodulation, Dissociative Disorders, Right TPJ Stimulation.

Introduction

Depersonalization - derealization disorder (DDD) is a psychiatric condition wherein the individual has persistent or recurrent episodes of depersonalization, derealization or both. The symptoms can be detachment from the self and feelings of unreality from their surroundings, being outside observer's own thoughts, feelings, sensations, body or actions. Experience of unreality of individuals or objects in the form of dreamlike, foggy, life less and visually distorted could also be present. The prevalence rate of DDD is around 1% in the general population but increases to 5 to 20% in psychiatric outpatients and 17.5 to 41.9% in psychiatric inpatients (Yang et al., 2023). Despite a high prevalence rate of the condition, it is an under-studied mental disorder. The treatment of the disorder relies on various pharmacotherapies, neuromodulations, and psychotherapies. Repetitive transcranial magnetic stimulation (rTMS) is a new non-invasive intervention which as shown promising results in many neuropsychiatric conditions. In this paper we report a case of DDD who benefited from inhibitory rTMS stimulation to the right temporal-parietal junction (TPJ) who had limited benefit with the ongoing pharmacological and psychological interventions.

The TPJ is a polysensory cortical area that plays a key role in perception and awareness (Papeo et al., 2010). It is the region of the cerebral cortex that borders the temporal and parietal lobes (Rogier et al., 2012). The TPJ is involved in numerous functions including multisensory integration, social cognition, sense of agency and stimulus-driven attention functions (Eddy, 2016).

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Case Study

In this case study, we present a 27-year-old female diagnosed with generalised anxiety disorder and DDD with symptoms primarily related to derealisation who was treated with rTMS. The patient had history of occasional cocaine, ketamine and cannabis use without exhibiting any psychological symptoms. However, at the age of 23 years, after a single usage of magic mushrooms (psilocybin) she experienced panic attacks and an acute episode of derealisation. This subsided within two weeks but a severe relapse occurred two years later following major stressful changes in her life. She experienced chronic symptoms including distorted vision, over processing at the local level (such as increased focus on leaves and branches in a tree, items on shelves in supermarkets or individual tubes in scaffoldings), 'as if she was viewing through a dark filter', having visual floaters and grid lines in her visual field, increased colour intensity perception, and derealisation symptoms. The patient also complained of problems in attention and concentration. No psychotic symptoms or ophthalmologic causes were identified.

At the time of the initiation of rTMS the patient had comorbid anxiety and depressive symptoms for which she was prescribed Duloxetine 120 mg once daily, Olanzapine 7.5 mg once at night and Lorazepam 0.5 mg as and when needed. The patient was also undergoing a course of once weekly cognitive behavioral therapy. The patient reported improvements in some symptoms from the olanzapine which was kept at a steady dosage throughout the treatment. The patient considered a trial of rTMS due to limited response with medication and psychotherapy. Previous work has shown promising results using 1 Hz stimulation over the right TPJ in DDD (Orrù et al., 2021). There is a report of a single case of hallucinogen-persisting perception disorder treated with rTMS over the right TPJ (Creton et al., 2024). Therefore, a 1 Hz stimulation was applied to the right TPJ at a 110% of resting motor threshold. The treatment was carried out for three weeks, with a single train of 1800 pulses per session once a day, five days a week. No side effects were noticed during the treatment.

To track the patient's progress, the following psychometric tests were performed including: the Cognitive Failure Questionnaire (CFQ), Cambridge Depersonalization Scale (CDS), Generalized Anxiety Disorder-7 scale (GAD-7), Patient Health Questionnaire-9 (PHQ-9), and Zung Self Rating Depression Scale (SDS). As the patient complained increased focus on local elements in her surroundings, a Navon type local and global task was also carried out, where the global letters were formed of local letters. The local letters could be same or different to the global letters. The patient was asked to respond by a computer key press if she saw target letters "H" or "O" either in global or local form as fast and as accurately she could. The letters were displayed for 500 ms and a 2000 ms response time was given. A total of 50 random trials were presented. The patient's initial scores on these tests are given in the Table 1.

Table 1: Patient's raw scores before the start of rTMS intervention

Test	*Domain*	*Raw score*
Cambridge Depersonalization Scale (CDS)	Frequency	43
	Duration	82
	Total	125
	Anomalous Body Experience : Frequency	10
	'Emotional Numbing : Frequency	13
	Anomalous Subjective Recall : Frequency	10
	Alienation from Surrounding : Frequency	13
	Anomalous Body Experience : Duration	8
	'Emotional Numbing : Duration	22
	Anomalous Subjective Recall : Duration	16
	Alienation from Surrounding: Duration	23
Cognitive Failure Questionnaire (CFQ)	Total	49
	Forgetfulness	16
	Distractibility	18
	False trigger	11
Generalised Anxiety Disorder -7	GAD-7	3
Patient Health Questionnaire -9	PHQ-9	21
Zung Self Rating Depression Scale (SDS)	SDS	53
Local and Global Task	Global level Target RT (in ms)	916
	Local level Target RT (in ms)	877
	No target RT (in ms)	990
	Global Target no. of errors	1
	Local Target no. of errors	1

RT= Reaction Time, ms= millisecond,

The patient's progress on rTMS intervention was assessed on these tests after 10 sessions and after 15th session. The percentage change scores are given in the Figure 1.

After 15 sessions of rTMS over the right TPJ the patient showed good improvement in several domains. In terms of specific symptoms, the patient reported no more visual floaters and grid lines in her visual field. We observed a good level of overall improvement (44%) on the DDD symptoms as rated on the CDS. We also observed a high degree of improvement (68.2%) on the duration of emotional numbing related experiences, a feature of derealisation. There were small improvements on depersonalization related symptoms

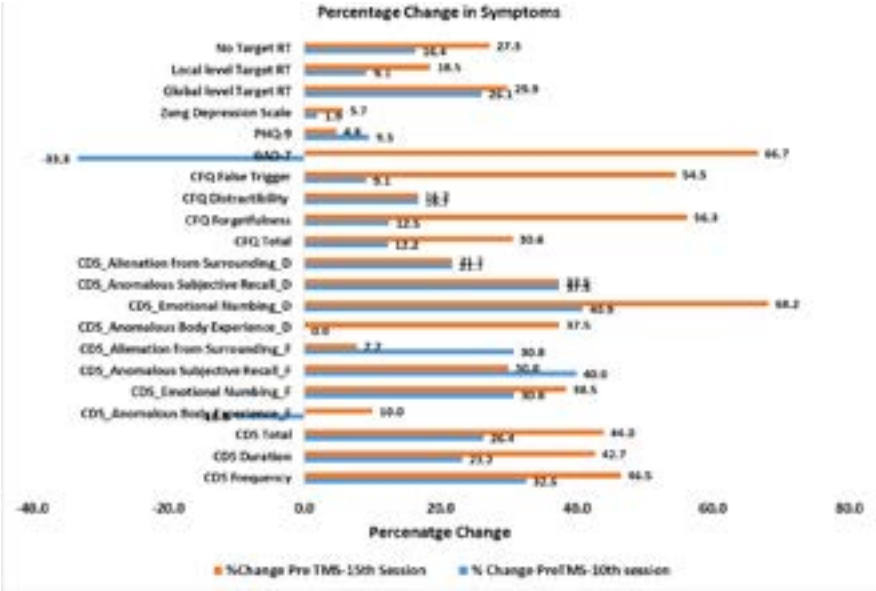

Figure 1: Percentage change shown from pre rTMS intervention to 10th session and after 15th session (post) of stimulation. CDS= Cambridge Depersonalization Scale; CFQ= Cognitive Failure Questionnaire; GAD-7= Generalized Anxiety Disorder-7;), PHQ-9=Patient Health Questionnaire-9. A positive change indicates improvement in symptoms

(such as on the alienation from surrounding part of the CDS). Improvements were also observed on the cognitive symptoms particularly on the symptoms associated with forgetfulness and false triggers (above 54%). The improvement in cognitive symptoms may be associated with the resolution of DDD symptoms. The improvement on all the domains increased from 10th session to the 15th session, suggesting a continued improvement process with increasing number of sessions. The patient discontinued rTMS intervention after 15 sessions due to financial reasons. It is possible that we could have achieved better improvement with continued rTMS sessions beyond 3 weeks.

Discussion

rTMS is increasingly being used in treatment resistant psychiatric conditions as a therapeutic intervention. In a recent systematic review of treatment approaches to DDD, rTMS is proposed as one of the intervention approaches (Wang et al., 2024) where the TPJ and ventrolateral prefrontal cortex (VLPFC) has been suggested as the brain targets for stimulation. In this case report we show that inhibitory rTMS (1 Hz) applied over the rTPJ improves DDD. We used 15 session over 3 weeks and observed an overall 44% improvement. It is likely that we could have achieved further improvement with continued rTMS intervention. Indeed improvement from 51% reduction on the CDS score to 68% reduction was observed in patients who continued their intervention from 3 weeks to 6 weeks (Christopeit et al., 2014).

Previous study has shown a network of brain areas involved in DDD where abnormalities along sequential hierarchical areas, secondary and cross-modal, of the sensory cortex (visual, auditory, and somatosensory) has been reported. These processes were mediated by increased glucose metabolic activity in the sensory cortex in the temporal, parietal, and occipital lobes (Simeon et al., 2000). These findings suggest a crucial problem in multisensory integration in DDD (Murphy, 2023). The TPJ has been implicated in multisensory integration (Papeo et al., 2010; Rogier et al., 2012; Eddy, 2016) as well as out of body experience (OBE), a feature of DDD (Blanke et al., 2005). Blanke et al. (2005) using EEG evoked potential study found a predominantly rTPJ activity in an OBE task. Furthermore, they stimulated rTPJ using single pulse TMS to the rTPJ and intra parietal sulcus (IPS). They found that rTPJ stimulation selectively affected the performance on their OBE task in healthy participants. Considering the specific role of and hyperactivity observed in the rTPJ in DDD, an inhibitory rTMS intervention was planned.

Previous studies have used rTMS to brain regions other than the rTPJ in treating DDD. Keenan and colleagues (Krrnan et al., 1999) used 1 Hz to the dorsolateral prefrontal cortex (DLPFC) to a patient with DDD reported improvement in patient symptoms. Similarly, Jiménez-Genchi (2004) used LDLPFC stimulation in a case of DDD and reported 28% symptom improvement. Karris et al. (2017) reported a case of DDD who had not previously responded to pharmacotherapy and responded to bilateral DLPFC stimulation. In a case series report of 7 patients with medication resistant DDD 1 Hz rTMS was applied to the VLPFC at 110% RMT intensity. Their patients received 2 rTMS sessions per week over 10 weeks.

These patients showed on average 44% reduction in DDD symptoms. They did not show improvement on depression scores (Mevorach et al., 2010). Their findings were similar to what we observed in our patient. We also observed an overall improvement of 44% in DDD symptoms with no change in depressive symptoms. The symptoms of DDD that did not improve were that of colour intensity and local elements perception. Interestingly, though, on the Navon's global local task, the patient's pre rTMS intervention reaction time (RT) was faster for the local elements compared to the RT to the global elements. After the rTMS intervention the RT for the local elements was slower than the global elements. This RT change, however, did not translate into changes in symptoms. It is possible that a different target site for stimulation to reduce the local salient stimulus processing should be considered. The IPS has been proposed to modulate local and global salience processing (Mevorach et al., 2010) which could be a potential target for rTMS intervention. In their work using functional magnetic and resonance imaging (fMRI) and rTMS, Mevorach et al. (2010) showed that the left and right IPS contributes differently to the processing of local and global targets in the presence of salient distractors. They used 5 pulses of 10 Hz stimulation over the left and right IPS and observed that excitatory TMS to the left IPS improves target processing and significant reaction time improvement was observed for distractor processing after right IPS stimulation. These findings suggest the differential role of left and right IPS in modulating target and distractor processing, which could be considered in rTMS intervention for patients with such perceptual symptoms.

This case study demonstrates the usefulness of inhibitory 1 Hz rTMS intervention at the rTPJ in DDD patients and provides evidence for rTMS to be considered as an intervention tool in DDD. The TPJ stimulation may contribute to improvement in specific symptoms of DDD and this change seems to be associated with the number of TMS sessions. The inhibitory rTMS to the rTPJ could have led to reduced hyperactivity that is observed in DDD patients. Although, Jay et al. (2016) considers 20 sessions may be optimal to treat DDD using rTMS, we suggest that more number of sessions my lead to continued improvement and an optimal number of sessions should be worked out in larger studies. As several brain targets have been explored in treating DDD and none of these targets lead to a complete cessation of symptoms, we suggest that additional or combination of brain targets may be considered to fully address the DDD symptoms. For example, Zheng et al. (2022) & Zheng et al. (2025) using meta analysis of fMRI data showed a network of brain regions involved in DDD such as the bilateral medial prefrontal cortex, DLPFC, superior parietal gyrus, superior temporal gyrus, and right VLPFC. These brain regions could be a potential rTMS target for intervention in future studies.

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The manuscript has been co-produced with the patient.

Declaration of interest

SK and TM are directors at Oxford Brain and Mind
No other conflict of interest for any of the authors

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