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Case Series

EEG-Spectra-Guided Personalized rTMS in PTSD with Co-occurring Psychiatric Disorders: A Case Series

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Abstract

Personalized repetitive Transcranial Magnetic Stimulation (PrTMS®) offers an individualized approach to neuromodulation through customized treatment protocols. This case series aims to explore therapeutic outcomes of PrTMS® in two patients with post-traumatic stress disorder (PTSD), based on standardized rating scale scores and spectral EEG-guided alpha brainwave activity optimization. Participants diagnosed with PTSD received PrTMS® treatments informed by quantitative rating scales and weekly spectral EEG measurements. Weekly psychometric assessments showed an improvement in symptoms, as quantified by PCL-5 (Posttraumatic Stress Disorder Checklist for DSM-5), GAD-7 (Generalized Anxiety Disorder 7-item scale), PHQ-9 (Patient Health Questionnaire-9), and SCI (Sleep Condition Indicator) questionnaires. Specifically, PCL-5 scores demonstrated an average reduction of 20.5 points by the midpoint of treatment (4 weeks), while GAD-7 and PHQ-9 scores decreased by 7 and 8.5 points, respectively, at the end of 7 weeks. Mean SCI scores increased by 6 points by the end of the 7 week-treatment period. While previous studies have also highlighted the role of spectral EEG-directed personalized PrTMS in the treatment of PTSD, ongoing research is needed in order to understand the long-term efficacy of PrTMS®.

Keywords: Personalized Repetitive Transcranial Magnetic Stimulation (PrTMS®); Repetitive Transcranial Magnetic Stimulation (rTMS); Neuromodulation; PTSD (Post-Traumatic Stress Disorder); Spectral EEG; Spectral Electroencephalogram; PCL-5 (Post-Traumatic Stress Disorder Symptom Severity Checklist for DSM-5); Alpha Brainwave Activity

Introduction

Post-traumatic stress disorder (PTSD) has widely been seen to be a diverse and complex disorder, the pathophysiology of which continues to be explored. Previous research has suggested that PTSD may arise from underlying nervous system dysfunction and has even been examined in relation to metabolic disorders [1]. Hallmark symptoms of PTSD such as intrusive thoughts, anxiety attacks, flashbacks, and nightmares, greatly affect the quality of life of those affected [2]. It is common for PTSD to coexist with conditions like major depressive disorder, generalized anxiety disorder and sleep disorders, thus compounding the challenges faced by individuals [3].

The etiology of PTSD has been suggested to be polygenic [4], with the effects of long-term trauma contributing to the manifestation of neurochemical imbalances [5]. Research has shown PTSD may also arise due to genetic influences, particularly involving dopamine dysregulation [4,6-8]. Reward Deficiency Syndrome (RDS) is a condition linked to impaired dopamine function, and has been implicated in the pathogenesis of disorders including PTSD, depression, anhedonia, compulsive behaviors, addiction, ADHD, and autism [9-14]. It is noteworthy that genetic variations correlating with PTSD such as the DRD2 A1 allele, have been categorized as a subtype of RDS [12]. Previous studies have emphasized the potential of genetic testing, such as the Genetic Addiction Risk Severity (GARS) score, in identifying individuals at higher risk for developing PTSD [4][7]. It has been suggested that targeted early intervention could support neurochemical balance and stress resilience, thus improving outcomes [5].

Repetitive Transcranial Magnetic Stimulation (rTMS) has shown promise as a non-invasive modality in mitigating symptoms of PTSD, as evidenced in studies conducted by Yesavage et al. and Kozel., *et al*. [15][16]. rTMS has been shown to target neural circuits involved in fear processing and emotional regulation. Studies have previously shown a decrease in PTSD symptoms following prefrontal TMS application [17] and rTMS directed at the right dorsolateral prefrontal cortex (rDLPFC) [18]. rTMS also has been noted to improve memory, executive function, and cognitive function in PTSD patients [19]. The treatment is generally well-tolerated, with transient side effects such as mild headache and scalp discomfort at the treatment site [20]. Less common are severe side effects such as seizures, the overall risk of which has been found to be less than 1% [21].

Personalized repetitive Transcranial Magnetic Stimulation (PrTMS®), an advancement in rTMS, individualizes patient treatment protocols based on spectral EEG mapping of the brain. This treatment method involves visualizing brain electrical activity

through spectral EEG and administering standardized psychometric tests. These results are then used to create a personalized treatment plan for the patient. The PeakLogic™ software uses this information to generate patient treatment protocols to ensure optimal patient response to therapy. Treatment across multiple cortical areas using lower intensities is a fundamental component of PrTMS® [22].

PrTMS® has shown promising outcomes in autism spectrum disorder, concussion, PTSD, sleep quality, anxiety, and depression [22-26]. A recent study by Makale et al. examined the effects of PrTMS® in treatment-resistant PTSD among combat veterans [22]. Our case series aims to further investigate the therapeutic outcomes of PrTMS® in PTSD co-occurring with psychiatric disorders.

Case Presentations

Case 1

Patient is a 63-year-old Caucasian female with a significant past medical history that included opioid use disorder, reflex sympathetic dystrophy syndrome, fibromyalgia, chronic sciatica, peripheral neuropathy, osteoarthritis, scoliosis, and hepatitis C. Her psychiatric history was significant for major depressive disorder (MDD), generalized anxiety disorder (GAD), and post-traumatic stress disorder (PTSD). She endorsed a history of sexual, physical, and emotional abuse by her step-father during childhood. Although the patient reported a significant substance use history of alcohol, methamphetamine, cannabis, and heroin, she endorsed a long period of sobriety lasting 23 years. Her medication history included buprenorphine medication assisted treatment (MAT) along with fluoxetine and hydroxyzine. She denied any past psychiatric hospitalizations, suicide attempts, or self-harm.

Case 2

Patient is a 57-year-old Caucasian female with a primary diagnosis of PTSD and MDD linked to developmental trauma. The patient's psychiatric history began at age 19, following early childhood experiences of systematic abuse. She served in the Marine Corps, during which she sought therapy for trauma-related symptoms. She reported receiving benefit from consistent psychotherapy. At time of presentation, she had been receiving eye movement desensitization and reprocessing (EMDR) therapy for 14 months. The patient reported three episodes of attempted suicide. Her first experience of suicidal ideation was at age 9, when she ingested a bottle of her father's prescription medication. The second episode took place at age 37, involving ingestion of unidentified pills requiring emergency responder intervention. The third episode occurred at age 47, following an overdose of diazepam tablets and self-administration of ipecac syrup to induce vomiting. The patient's current medications included bupropion extended release augmented with aripiprazole. The patient denied a present history of suicidal ideation.

Methods and Materials

Subjects

The participants were chosen based on an initial clinical diagnosis of PTSD comorbid with psychiatric disorders including GAD, MDD, and sleep disorders. Participants received treatments 5 days a week, for 7 weeks. Written informed consent was obtained from each participant as part of the research study.

Spectral EEG data collection

Weekly spectral EEGs were recorded using a CGX high impedance dry electrode headset. Electrodes were placed in accordance with the 10-20 system.

Psychometric questionnaire administration

PrTMS® treatment response was systematically monitored with psychometric questionnaires. The Post-traumatic Stress Disorder Symptom Severity Checklist (PCL-5), Patient Health Questionnaire-9 (PHQ-9), Generalized Anxiety Disorder-7 (GAD-7), and Sleep Condition Indicator (SCI) were administered to each patient on a weekly basis throughout the course of treatment.

Personalized repetitive transcranial magnetic stimulation (PrTMS®) treatment

PrTMS® was delivered by a trained technologist using the PeakLogic® software installed in the Apollo TMS Therapy System. The FPz (Prefrontal Zero), Fz (Frontal Zero), Cz (Central Zero), F3 (Left Dorsolateral Prefrontal Cortex), and F4 (Right Dorsolateral Prefrontal Cortex) locations (shown in Figure 1) were targeted on the scalp for approximately 30 minutes per day, 5 days per week, for a treatment duration of 7 weeks. Customized stimulus frequency and amplitude protocols were generated each week based on a computerized algorithm (PeakInput™) utilizing data obtained from weekly spectral EEGs and standardized rating scores.

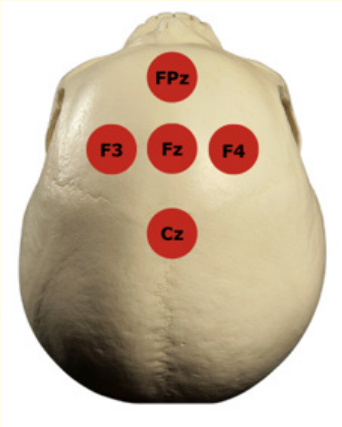

Figure 1: PrTMS® Treatment Locations.

Results

Patient 1

Figure 2: PCL-5 Scores of Patient 1.

Test Scores	9/19/2023	9/27/2023	10/3/2023	10/12/2023	10/19/2023	10/25/2023	11/01/2023
PCL-5	51	46	38	18	25	N/A	N/A
GAD-7	17	15	11	12	13	12	6
PHQ-9	14	7	5	6	12	4	2
SCI	11	15	16	16	17	25	23

Table 1: Neurocognitive Survey Scores of Patients 1.

Patient 2

Test Scores	5/29/2023	6/5/2023	6/14/2023	6/19/2023	6/26/2023	7/7/2023	7/17/2023
PCL-5	74	70	64	66	65	63	57
GAD-7	18	17	17	16	15	18	15
PHQ-9	26	25	25	24	25	22	21
SCI	7	6	6	8	8	1	7

Table 2: Neurocognitive Survey Scores of Patient 2.

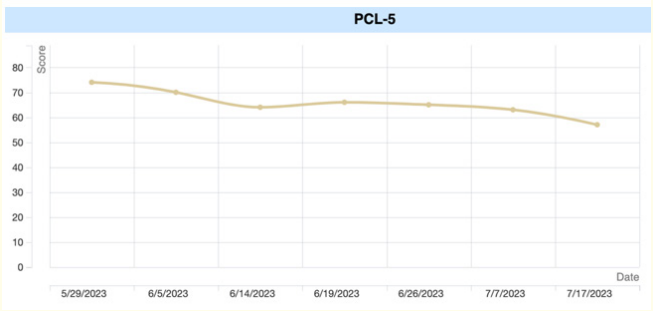

Figure 3: PCL-5 Scores of Patient 2.

Discussion

Alpha brain wave activity stabilization

The optimal frequency range for alpha brainwaves is between 8 and 12 Hz. Dysregulated alpha brainwave activity has been correlated with PTSD symptomatology [28]. Clancy et al. explored the disruptions in the default mode network (DMN) and alpha wave activity in individuals with PTSD. They found that alpha brainwave activity within the optimal frequency range supports DMN functioning, which correlates with deficits in both alpha wave

oscillations and DMN activity in PTSD, manifesting as symptoms such as sensory issues and hypervigilance [28]. Makale et al. further investigated the interconnection between the DMN and alpha activity. They concluded that PTSD may be triggered and sustained by disruptions in the synchronization and communication of alpha oscillatory activity, which typically support these functions [22].

These findings provide a foundation for the PrTMS® approach in improving PTSD symptoms through spectral EEG-guided alpha wave activity optimization. Systematic spectral EEG monitoring is used to assess patient response to PrTMS®, and to optimize the patient's treatment protocol [22]. rTMS has been demonstrated to enhance neural synchronization in alpha frequency bands, utilizing lower electric field strengths relative to conventionally employed motor threshold intensities [27]. This principle is the basis of PrTMS® which customizes intensity of magnetic stimulation based on spectral EEG changes. Both patients in our study demonstrated an improvement in alpha brainwave activity optimization across the treatment period.

Psychometric quantitative rating scales

PCL-5 scores of our patients demonstrated an average reduction of 20.5 points by the midpoint of the treatment duration at 4 weeks. A decrease in PCL-5 scores was previously seen in a study conducted by Parks et al., where 299 patients treated over a period of 6-9 weeks displayed an average reduction of 23 points [29]. Makale., *et al*. also reported favorable outcomes with PrTMS® treatment in veterans diagnosed with PTSD, demonstrating a statistically significant change from baseline at weeks 4 and 6. [22]. A mean decrease of 7 points on GAD-7 and 8.5 points on PHQ-9, and a mean increase of 6 points on SCI, was observed in our study at the end of the 7-week treatment period.

Limitations

A limitation of this case series is the small sample size, which restricts the ability to generalize the results. Another limitation is the absence of PCL-5 scores for patient 1 during the final two weeks of treatment, resulting from technical errors with the software in obtaining and saving the data. The use of patient-reported psychometric assessments may have led to potential subjective response bias. To mitigate this, spectral EEG measurements were utilized to support psychometric findings.

Conclusion

Personalized neuromodulation approaches such as PrTMS® continue to demonstrate promising potential in improving treatment outcomes. Complex co-occurring psychiatric disorders such as PTSD may require global TMS coil placements in order to recruit additional neural circuits, which may not be accomplished with standard left dorsolateral prefrontal cortex placement. Spectral EEG analysis is an important assessment tool along with standardized rating scales in quantifying symptoms and effectively measuring treatment outcomes. Additional research, including multicenter randomized trials, is required to understand the role of spectral EEG in the treatment of complex psychiatric disorders and the long-term efficacy of PrTMS®.

Author Contributions

The original draft of this manuscript was written by KM, SK, SM, JB, CV, and KS. Review and additional editing of the manuscript were conducted by MO, KB, DB, KL, RB, EM, and KS.

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Conflict of Interest Statement

There are no conflicts of interest declared by the authors regarding publication of this paper. This manuscript has been read and approved by all authors.

Declaration of Patient Consent

The authors confirm that written informed consent has been obtained from the study participants for publication of this research.

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