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Case Report

rTMS for Recurrent Major Depressive Disorder and Generalized Anxiety Disorder Comorbid with Heart Failure, Renal Disease, Type 2 Diabetes, and HIV: A Case Report

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Abstract

Repetitive transcranial magnetic stimulation (rTMS) is an FDA-approved modality for treatment-resistant major depressive disorder (MDD). This case report aims to explore the therapeutic outcomes of rTMS in a patient with multiple co-occurring non-psychiatric diseases, including heart failure, renal disease, type 2 diabetes, and human immunodeficiency virus (HIV) infection. Quantitative psychometric assessments were administered weekly via PHQ-9 (Patient Health Questionnaire-9) and GAD-7 (Generalized Anxiety Disorder 7-item scale), which revealed symptom reduction by more than 50% by midpoint of treatment (week 5), and more than 80% improvement from week 6 onward. Quality of life improvements such as improved diet, exercise, ability to function in daily life, and overall sense of well-being were also noted based on weekly administration of the Quality of Life Enjoyment and Satisfaction Questionnaire Short Form (Q-LES-Q-SF). Further, large-scale, randomized and blinded studies are recommended to validate our preliminary observations on the efficacy and safety of rTMS in patients with co-occurring diseases involving moderate to severe multi-organ dysfunction.

Keywords: *Repetitive Transcranial Magnetic Stimulation (rTMS); Dorsolateral Prefrontal Cortex (DLPFC); Neuromodulation; MDD (Major Depressive Disorder); PHQ-9 (Patient Health Questionnaire-9); GAD-7 (Generalized Anxiety Disorder-7 Item Scale); Motor Threshold (MT)*

Introduction

This study focuses on repetitive Transcranial Magnetic Stimulation (rTMS) as a modality to treat recurrent Major Depressive Disorder (MDD) and Generalized Anxiety Disorder (GAD) in a patient with multiple comorbid systemic medical conditions. rTMS is a brain stimulation technique in which the patient is seated with a wire coil placed on the scalp that generates repetitive magnetic pulses to induce an electrical field, resulting in modulation of cortical excitability and depolarization of underlying brain regions [1]. Research has shown efficacy of rTMS for treatment-resistant depression by targeting the Left Dorsolateral Prefrontal Cortex (DLPFC), as well as a robust clinical effect for GAD via low-frequency stimulation of the Right Dorsolateral Prefrontal Cortex [2,3,21]. The treatment is typically safe and well-tolerated, with the most frequent side effects being transient scalp discomfort and mild headaches, while severe side effects, such as seizures, are very rare, with the likelihood projected to be under 1% [4,5].

Case History

We report the case of a 54-year-old male with recurrent MDD and GAD, who was diagnosed with type 2 diabetes in 1997. His diabetes was complicated by neuropathy and nephropathy, resulting in end-stage renal disease requiring hemodialysis in 2016, and eventual renal transplant in 2019. In 2021, he suffered a pulmonary embolism which required anticoagulants for prophylaxis. He also suffered from hypertension and coronary artery disease, which resulted in heart failure (HF) in 2024. He underwent cardiac stent placement in the same year. He is prescribed antiretroviral therapy (ART) with bictegravir, emtricitabine, and tenofovir for human immunodeficiency virus (HIV-1) infection diagnosed in 1991. The patient reported a history of systematic emotional neglect and sexual trauma dating back to his early childhood. He reports onset of depressive episodes at age 11.

At the time of presentation, the patient's symptoms were consistent with recurrent severe MDD without psychotic symptoms, and passive suicidal ideations without plan or intent. In addition, he also received a diagnosis of GAD in light of symptoms consistent with the disorder. The patient underwent trials of multiple antidepressants of different classes, including selective serotonin reuptake inhibitors (SSRIs), duloxetine, bupropion, and augmentation with antipsychotics, including quetiapine, ziprasidone, and cariprazine. rTMS was recommended in late 2024 to alleviate his symptoms due to lack of response from multiple medication trials.

Methods and Materials

Subject

The participant was selected based on an initial clinical diagnosis of MDD refractory to 2 antidepressants of different classes, as well as comorbid HF, renal disease, type 2 diabetes, and HIV. The subject did not have any contraindications to TMS, such as ferromagnetic implants within 12 inches of the head, cardiac pacemaker, implantable cardioverter defibrillator, and history of epilepsy or brain lesions [1]. The subject was recommended 36 rTMS treatments based on clinical findings demonstrating enhanced and sustained remission of depressive symptoms in patients who completed this number of treatments [17]. The subject experienced early symptom remission which prompted him to discontinue rTMS after 27 treatment sessions.

Repetitive transcranial magnetic stimulation (rTMS) treatment

rTMS was administered by certified neurotechnologists using the Stimware® software installed in the Apollo TMS Therapy System. Using the 10 - 20 system, the F3 (Left Dorsolateral Prefrontal Cortex) and F4 (Right Dorsolateral Prefrontal Cortex) locations corresponding to Brodmann areas (BA) 8 and 9 were approximated on the scalp [6]. The motor threshold (MT) was determined at a location in the primary motor cortex which elicited contralateral thumb twitch at the lowest intensity. Treatment parameters for left DLPFC stimulation included a frequency of 10 Hz, 3000 pulses, 40 pulses per train, 75 trains per session, and an intertrain interval of 11 seconds. For right DLPFC treatment, a continuous train of 700 pulses at 1 Hz was administered per session. The Left and Right DLPFC were approximated

5.5 cm anterior to the motor cortex, and each treatment was targeted at these locations for 18 minutes and 34 seconds, and 11 minutes and 40 seconds, respectively [18,19]. Motor evoked potential (MEP) was 38%. Treatment intensity was capped at 100% of the MT, which the patient tolerated throughout the treatment course without discomfort, headache, or seizure. The patient was treated for 27 sessions over 8 weeks.

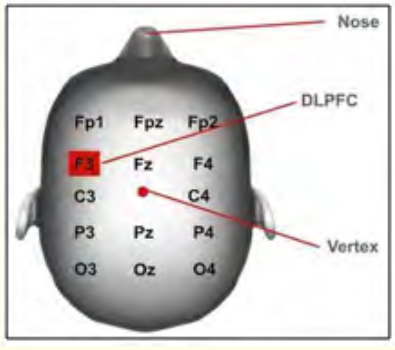

Figure 1: *rTMS treatment locations.*

Psychometric questionnaire administration

rTMS treatment response was systematically monitored using standardized psychometric questionnaires. The Patient Health Questionnaire-9 (PHQ-9) and Generalized Anxiety Disorder-7 (GAD-7) were administered weekly throughout the course of treatment. The Quality of Life Enjoyment and Satisfaction Questionnaire Short Form (Q-LES-Q-SF) was administered weekly to assess quality of life changes [7].

Results

	1/6/25	1/14/25	1/22/25	1/29/25	2/05/25	2/12/25	2/21/25	3/3/25	3/10/25
PHQ-9	19	12	9	10	9	2	2	3	0
GAD-7	12	15	11	10	6	2	2	2	1
Q-LES-Q-SF: Raw Scores	-	26	34	37	34	43	47	51	53
Q-LES-Q-SF: %Maximum	-	21%	36%	41%	36%	52%	59%	66%	70%

Table

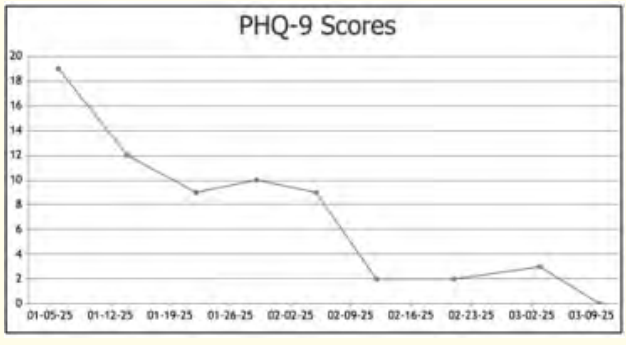

Figure 2: *PHQ-9 scores.*

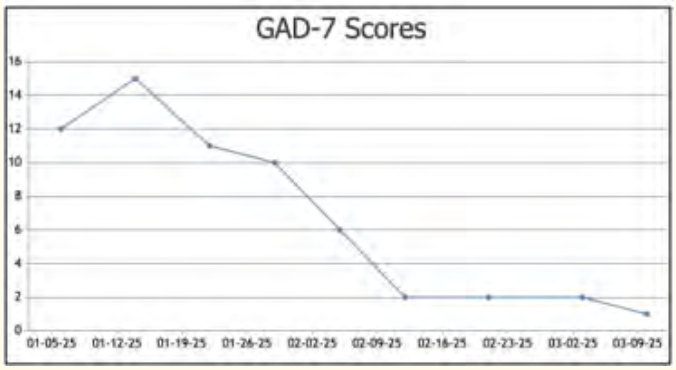

Figure 3: *GAD-7 scores.*

Discussion

Studies have established a bidirectional relationship between MDD and HF, renal disease, diabetes, and HIV. A meta-analysis in 2016 [8] determined the prevalence of depression in patients with HF to be 29%. Likewise, a retrospective cohort study conducted by Bobo., *et al.* [9] revealed that individuals with depression had increased risk of newly diagnosed HF (HR 2.08, 95% CI 1.89 - 2.28), and those with HF had increased risk of newly diagnosed depression (HR 1.34, 95% CI 1.17 - 1.54). A meta-analysis in 2022 [10] revealed the pooled odds ratio (OR) of diabetic nephropathy predicting depression to be 1.46 (95% CI 1.27 - 1.67), and the OR of depression predicting diabetic nephropathy to be 1.22 (95% CI 1.13 - 1.31). In addition, a systematic review by Graham., *et al.* [11] revealed that patients with depression had approximately 40% increased susceptibility to type 2 diabetes. The bidirectional relationship includes shared mechanisms such as inflammation and oxidative stress, compounded by psychosocial factors such as social support and lifestyle choices [12]. Higher odds of ischemic heart disease (OR = 1.38) and chronic kidney disease (OR = 1.53) were also reported in patients with treatment-resistant depression (TRD) compared to those with non-TRD MDD, resulting in higher frequency of emergency room visits and inpatient stays [13]. As a result of recurrent depressive episodes throughout his life, this patient reported periods of increased appetite and hyperphagia, resulting in excessive consumption of processed foods. This lifestyle contributed to the pathophysiology of coronary artery disease, insulin resistance, and renal disease, requiring cardiac stent placement, transmetatarsal amputation due to diabetic gangrene, hemodialysis, and renal transplant. These health-related stressors consequently resulted in worsening of MDD and GAD. HIV neuropathogenesis has also been implicated in the progression of depressive symptoms, owing to neuroinflammation, low central dopaminergic activity, and decreased levels of brain-derived neurotrophic factor (BDNF) attributed to gp120-mediated neurotoxicity [14].

Furthermore, individuals with depression comorbid with anxiety tend to be resistant to standard antidepressant medication regimens. Patients with depression also tend to become more disabled and dysfunctional when anxiety symptoms come into effect. These patients tend to endure greater disease severity and prolonged symptom duration, resulting in greater challenges in work, psychological well-being, and quality of life compared to those without comorbidities. The clinical risks of depression and anxiety comorbidities include increased risk of psychiatric hospitalization, disabilities, and suicide, as well as decreased medication compliance and increased healthcare utilization [22].

By his 27th treatment session, the patient had achieved 100% reduction in PHQ-9 score and a 91.7% reduction in GAD-7 score, as evidenced by improved mood, sleep, energy, concentration, diet, motivation, and interest, as well as remission of GAD symptoms such as nervousness, irritability, restlessness, racing thoughts, and excessive worry [15,16]. Q-LES-Q-SF scores also showed improvement

from 21% to 70% of the maximum, attributed to increased satisfaction related to mood, work, household and leisurely activities, social relationships, ability to function in daily life, and overall sense of well-being. The promising results of this single case study may be attributed to adaptive neuroplasticity induced by bilateral stimulation of the DLPFC and recruitment of multiple cortical neural networks [20].

To the best of our knowledge, the efficacy of rTMS is largely understudied in patients with medical conditions involving moderate to severe multiorgan dysfunction. A study in 2023 involving 7215 patients who received an acute course of rTMS revealed PHQ-9 improvements averaging 3% per rTMS session in the first 10 sessions, and 1% improvement per session thereafter [17]. However, as patients with any non-psychiatric comorbidities were excluded from the study, the results could not be generalized to these patient populations.

Limitations

The use of rTMS in treating recurrent MDD and GAD comorbid with multi-systemic medical diseases was limited to a single case study. The efficacy and safety of rTMS in this population must be studied using large-scale, randomized and blinded trials in order to validate findings. Other limitations include potential response bias due to the use of self-reported psychometric assessments, and absence of Q-LES-Q-SF score for the patient's first treatment session.

Conclusion

We report safe and successful treatment of MDD and GAD using rTMS in a patient with HF, renal disease, type 2 diabetes, and HIV. As a result, the patient reported improved quality of life and ability to accomplish daily activities and health-related tasks. Antidepressant and anxiolytic effects of rTMS resulted in 50% symptom reduction by the midpoint of treatment (week 5), followed by remission from week 6 onward. Further systematic studies must be conducted in order to generalize results.

Author Contributions

KS conceptualized the study. The original draft of this manuscript was written by MO, KM, SM, and KS. Review and additional editing of the manuscript were conducted by CV, AM, VR, KB, and RB.

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Conflict of Interest Statement

The authors report no potential conflicts of interest regarding the publication of this paper. This manuscript has been read and approved by all authors.

Declaration of Patient Consent

Written informed consent was obtained from the patient to publish this paper. Participation in the study adhered strictly to patient privacy and HIPAA guidelines. The participant understood the potential risks and benefits of the interventions. rTMS was administered by certified neurotechnologists under the supervision of a board-certified psychiatrist.

Bibliography

1. Mann SK and Malhi NK. "Repetitive Transcranial Magnetic Stimulation". StatPearls Publishing (2023).

2. Baeken C., et al. "Repetitive transcranial magnetic stimulation treatment for depressive disorders: current knowledge and future directions". *Current Opinion in Psychiatry* 32.5 (2019): 409-415.

3. Parikh TK., et al. "Repetitive transcranial magnetic stimulation for generalized anxiety disorder: a systematic literature review and meta-analysis". *International Journal of Neuropsychopharmacology* 25.2 (2022): 144-146.

4. O'Reardon JP., et al. "Efficacy and safety of transcranial magnetic stimulation in the acute treatment of major depression: A multisite randomized controlled trial". *Biological Psychiatry* 62.11 (2007): 1208-1216.

5. Stultz DJ., et al. "Transcranial magnetic stimulation (TMS) safety with respect to seizures: A literature review". *Neuropsychiatric Disease and Treatment* 16 (2020): 2989-3000.

6. Herwig U., et al. "Using the international 10-20 EEG system for positioning of transcranial magnetic stimulation". *Brain Topography* 16.2 (2003): 95-99.

7. Endicott J., et al. "Quality of life enjoyment and satisfaction questionnaire: a new measure". *Psychopharmacology Bulletin* 29.2 (1993): 321-326.

8. Sokoreli I., et al. "Depression and anxiety as predictors of mortality among heart failure patients: Systematic review and meta-analysis". *Heart Failure Reviews* 21.1 (2016): 49-63.

9. Bobo WV., et al. "Bi-directional association between depression and HF: An electronic health records-based Cohort Study". *Journal of Comorbidity* 10 (2020).

10. Fang T., et al. "Bidirectional association between depression and diabetic nephropathy by meta-analysis". *PLOS One* 17.12 (2022): e0278489.

11. Graham EA., et al. "Measures of depression and risk of type 2 diabetes: A systematic review and meta-analysis". *Journal of Affective Disorders* 265 (2020): 224-232.

12. Liu Y., et al. "Bidirectional relationship between diabetes mellitus and depression: Mechanisms and epidemiology". *World Journal of Psychiatry* 14.10 (2024): 1429-1436.

13. Adekkanattu P., et al. "Comorbidity and healthcare utilization in patients with treatment resistant depression: A large-scale retrospective cohort analysis using Electronic Health Records". *Journal of Affective Disorders* 324 (2023): 102-113.

14. Fabrazzo M., et al. "Bidirectional relationship between HIV/HBV infection and comorbid depression and/or anxiety: a systematic review on shared biological mechanisms". *Journal of Personalized Medicine* 13.12 (2023): 1689.

15. Mahajan S., et al. "Personalized repetitive transcranial magnetic stimulation (PrTMS®) coupled with transcranial photobiomodulation (tPBM) for co-occurring traumatic brain injury (TBI) and post-traumatic stress disorder (PTSD)". *Acta Scientific Neurology* 8.3 (2025): 20-27.

16. Mohankumar K., et al. "EEG-spectra-guided personalized rTMS in PTSD with co-occurring psychiatric disorders: a case series". *Neurology* 8.2 (2025): 03-09.

17. Hutton TM., et al. "Dosing transcranial magnetic stimulation in major depressive disorder: Relations between number of treatment sessions and effectiveness in a large patient registry". *Brain Stimulation* 16.5 (2023): 1510-1521.

18. Carpenter L., et al. "Comparison of clinical outcomes with two transcranial magnetic stimulation treatment protocols for major depressive disorder". *Brain Stimulation* 14.1 (2021): 173-180.

19. Cristancho P., et al. "Crossover to bilateral repetitive transcranial magnetic stimulation: a potential strategy when patients are not responding to unilateral left-sided high-frequency repetitive transcranial magnetic stimulation". *The Journal of ECT* 35.1 (2019): 3-5.

20. Han X., et al. "Effects of repetitive transcranial magnetic stimulation and their underlying neural mechanisms evaluated with magnetic resonance imaging-based brain connectivity network analyses". *European Journal of Radiology Open* 10 (2023): 100495.

21. Narwal K., et al. "Efficacy of right sided low frequency repetitive transcranial magnetic stimulation in treatment resistant anxiety disorders". *Brain Stimulation* 15.5 (2022): 1331-1332.

22. Lewandrowski KU., et al. "Genetic and regulatory mechanisms of comorbidity of anxiety, depression and ADHD: A GWAS meta-meta-analysis through the lens of a system biological and pharmacogenomic perspective in 18.5 M subjects". *Journal of Personalized Medicine* 15.3 (2025): 103.

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