

Exploring the Therapeutic Potential of Repetitive Transcranial Magnetic Stimulation (rTMS) in Ophthalmic Comorbidities

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ABSTRACT

Symptomatic vitreous opacities (SVO) and macular degeneration (MD) are associated with elevated rates of depression and anxiety, yet the psychological burden of these ophthalmic conditions often persist despite standard pharmacologic treatment. We present three cases—two with MD and one with SVO—of treatment-resistant major depressive disorder treated with repetitive transcranial magnetic stimulation (rTMS) targeting the dorsolateral prefrontal cortex (DLPFC). Each patient completed 36 sessions of bilateral DLPFC rTMS over 6–8 weeks following failed antidepressant trials. PHQ-9 and GAD-7 scores were tracked weekly, with all three patients demonstrating substantial symptom reduction (PHQ-9 decreases of 70–93.8%; GAD-7 decreases of 83.3–100%) and no adverse events. To our knowledge, based on a targeted literature search, no prior published cases have evaluated rTMS for depression in the context of SVO/MD. These preliminary observations suggest rTMS may serve as an effective adjunctive treatment for psychiatric symptoms in patients with chronic visual disturbances and co-occurring psychological distress, warranting further investigation in larger cohorts.

Keywords: Symptomatic Vitreous Opacities (SVO), Macular Degeneration (MD), Repetitive Transcranial Magnetic Stimulation (rTMS), Generalized Anxiety Disorder 7-item scale (GAD-7), Patient Health Questionnaire-9 (PHQ-9)

Introduction

This study focuses on using repetitive transcranial magnetic stimulation (rTMS) as a therapeutic alternative to treat symptoms of depression following pharmacological psychiatric interventions. Myodesopsias, commonly referred to as vitreous floaters, are a frequent perception of spots, strands, or

other mobile opacities within the visual field (Ramovecchi *et al.*, 2021). Although often benign, symptomatic myodesopsias can become persistent and bothersome, interfering with visual attention and quality of life in affected individuals. Macular degeneration, a progressive degenerative condition affecting the central retina, is similarly associated with significant declines in visual function and has been independently linked to increased rates of depression and anxiety among affected patients. While treatments exist within ophthalmologic medicine, many neuropsychiatric side effects commonly persist among patients (Brody *et al.*, 2001). Mental health disturbances appear to be prevalent among individuals with symptomatic vitreous opacities (SVO) and macular degeneration (MD), with patients consistently demonstrating elevated scores on standardized measures of depression, anxiety, and perceived stress, including the PHQ-9 and GAD-7. Despite preserved visual acuity, these elevated psychological symptom scores are associated with poorer mental health-related quality of life, highlighting the substantial psychological burden experienced by patients with ophthalmic conditions (Leung *et al.*, 2026).

rTMS is a noninvasive brain stimulation technique in which a wire coil positioned over the scalp generates repetitive magnetic pulses that induce an electrical field in the underlying cortex, thereby modulating cortical excitability and neuronal activity (Mann and Malhi 2023). Research has demonstrated the efficacy of rTMS in the management of treatment-resistant depression, particularly through stimulation of the left dorsolateral prefrontal cortex (DLPFC). Low-frequency stimulation of the right DLPFC has also demonstrated robust clinical effects in patients with generalized anxiety disorder (GAD) (Parikh *et al.* 2022; O'Reardon *et al.* 2007). Overall, rTMS is considered a safe and well-tolerated treatment, with the most common adverse effects consisting of transient scalp discomfort and mild headaches. More serious adverse events, including seizures, are exceedingly rare, with the estimated risk occurring in fewer than 1% of patients (Odrón *et al.* 2025; Herwig *et al.* 2003).

Case History

Patient 1:

The patient is a 46 year old adult who reported a history of major depressive disorder (MDD) diagnosed several years ago, with symptoms persisting and progressively worsening over approximately five years. Prior to treatment, the patient experienced low energy, diminished interest and motivation, difficulty concentrating, depressed mood, racing thoughts, feeling on edge, and difficulty relaxing, which contributed to difficulty falling and staying asleep. The patient also experienced symptomatic vitreous opacities (SVO), which were clinically noted to co-occur with, and were considered by the treating clinician as potentially relevant to, the patient's overall visual and psychological burden. Ophthalmologic evaluation

prior to rTMS initiation confirmed mild, bilateral vitreous opacities, with uncorrected visual acuity of 20/60 in the right eye and 20/60-2 in the left eye; anterior and posterior segment examination was otherwise unremarkable, with normal intraocular pressures and normal retinal, macular, and optic nerve findings bilaterally. The patient was managed with observation alone, and ophthalmologic re-evaluation was not repeated during the rTMS course, precluding assessment of interval change in ocular findings. The patient failed an adequate trial of an antidepressant medication regimen that included bupropion, aripiprazole, mirtazapine, and quetiapine. At the time of psychiatric evaluation, the patient further reinforced feeling the aforementioned depressive symptoms. The patient reported a remote history of suicidal thoughts approximately three to four years prior and noted continued improvement through approximately four years of therapy. The patient elected to undergo rTMS targeting the dorsolateral prefrontal cortex (DLPFC) to further address depressive symptoms and improve interest and enjoyment in daily activities, sleep quality, energy, stress tolerance, and anxiety.

Patient 2:

The patient is a 61 year old female with a history of recurrent major depressive disorder (MDD) since childhood, with prior severe episodes at ages 9–10, in 2016, and at ages 23–24, and a comorbid diagnosis of PTSD related to childhood trauma. Prior to treatment, she reported depressed mood, anhedonia, poor concentration, low energy, worthlessness, and racing thoughts, alongside excessive worry, intrusive memories, and hypervigilance, with associated insomnia. The patient also carried a diagnosis of dry age-related macular degeneration, intermediate dry stage, bilaterally, with associated small parafoveal cysts in the left eye, managed by a retinal specialist. Best-corrected visual acuity was 20/40-2 in the right eye and 20/70-2 (improving to 20/40+2 with pinhole) in the left eye, with optical coherence tomography demonstrating no macular edema or subretinal fluid and drusen-associated retinal pigment epithelial changes without hemorrhage. Additional ophthalmologic findings included chronic, symptomatic vitreous degeneration with possible posterior vitreous detachment bilaterally (no retinal tears or detachment on scleral depressed examination), bilateral early cataracts managed with observation, and keratoconjunctivitis sicca attributed to dry eye. The patient was managed with observation and nutritional supplementation per AREDS guidelines, with no treatment indicated for any of these findings at the time of evaluation, and required ophthalmology clearance prior to neuromodulatory treatment. Ophthalmologic re-evaluation was not repeated during the rTMS course, precluding assessment of interval change in ocular findings. She had failed trials of bupropion and trazodone. On evaluation, she continued to endorse depressive and anxiety symptoms, with exam notable for psychomotor retardation and depressive

ruminations, though denied any suicidal or homicidal ideation. She met criteria for treatment-resistant recurrent MDD and elected to pursue rTMS targeting the DLPFC.

Patient 3:

The patient is a 64 year old female with longstanding, treatment-resistant major depressive disorder since her mid-teenage years, with prior severe episodes in her 20s after her husband's death by suicide, and marked worsening in the past few months. She reported depressed mood, anhedonia, fatigue, worthlessness, hopelessness, and insomnia. She carried a diagnosis of bilateral macular degeneration and had undergone bilateral cataract surgery three years prior, ophthalmic conditions considered by the treating clinician as clinically relevant to her overall psychological burden. She was followed by a retinal/ophthalmology specialist with routine surveillance visits occurring one to two times yearly, most recently approximately one month before psychiatric evaluation. Ophthalmology clearance was obtained prior to initiation of neuromodulatory treatment, confirming no contraindication to rTMS; detailed quantitative ophthalmologic findings, including visual acuity, disease staging, and imaging results, were not available for inclusion in this report, and no change in ophthalmologic status was reported during the rTMS treatment course. She had failed fluoxetine, escitalopram, duloxetine, and quetiapine, and remained symptomatic on bupropion, sertraline, trazodone, and methylphenidate. On evaluation she presented with depressed mood and constricted affect, with a remote interrupted suicide attempt in her 20s but no current suicidal ideation. She met criteria for treatment-resistant recurrent MDD and elected to pursue rTMS targeting the DLPFC.

Methods

rTMS Protocol

rTMS was administered by certified neurotechnologists using Stimware® software integrated with the Apollo TMS Therapy System. The F3 and F4 locations corresponding to the left and right dorsolateral prefrontal cortices (DLPFC), respectively, were approximated on the scalp using the international 10–20 EEG system and corresponded approximately to Brodmann areas 8 and 9 (Jasper, 1958). Motor threshold (MT) was determined over the primary motor cortex as the lowest stimulation intensity capable of eliciting a contralateral thumb twitch (Cole *et al.*, 2020). The left DLPFC was stimulated at 10 Hz with 3,000 pulses per session, delivered in 40-pulse trains across 75 trains with an 11-second intertrain interval (Fig. 1). Right DLPFC stimulation consisted of a continuous 1-Hz train of 700 pulses per session. Both DLPFC treatment sites were located approximately 5.5 cm anterior to the motor cortex, with stimulation durations

of 18 minutes and 34 seconds for the left DLPFC and 11 minutes and 40 seconds for the right DLPFC, respectively (Cole *et al.*, 2020; Mahajan *et al.*, 2026).

This bilateral stimulation approach—high-frequency stimulation of the left DLPFC paired with low-frequency stimulation of the right DLPFC—reflects a sequential bilateral rTMS strategy used clinically to address depression with comorbid anxiety, grounded in the prefrontal asymmetry model of affective disorders, which posits relative hypoactivity of the left DLPFC and relative hyperactivity of the right DLPFC in depression, with each hemisphere differentially implicated in mood- and anxiety-related symptom clusters. Bilateral DLPFC stimulation combining left high-frequency and right low-frequency parameters has been recognized by the Canadian Network for Mood and Anxiety Treatments (CANMAT) as a second-line rTMS approach for treatment-resistant depression (Milev *et al.*, 2016; Chou *et al.* 2021). The specific pulse parameters used in this series reflect a locally adapted protocol rather than a single standardized published regimen; the left-sided parameters approximate previously reported sequential bilateral protocols, while the right-sided low-frequency, continuous-train parameters were selected based on established low-frequency inhibitory dosing for right DLPFC stimulation in generalized anxiety disorder (Parikh *et al.*, 2022).

Motor threshold (MT) was individually established for each patient prior to treatment initiation, measured via motor evoked potential (MEP) at 52% for Patient 1, 73.5% for Patient 2, and 64.5% for Patient 3. Treatment intensity was initiated at a percentage of each patient's MT and gradually titrated upward over the course of treatment until reaching a ceiling of 100% of MT, consistent with tolerability-based titration approaches described in prior sequential bilateral protocols. Specifically, Patient 1 began at 75% of MT (39% stimulator intensity), Patient 2 began at 70% of MT (51% stimulator intensity), and Patient 3 began at 80% of MT (51% stimulator intensity). All three patients tolerated stimulation well throughout the full treatment course, with no reported discomfort, headaches, or seizures at any point. Each patient completed a total of 36 rTMS sessions targeting the DLPFC: Patient 1 over an 8-week period, and Patients 2 and 3 each over a 6-week period.

Concomitant psychotropic medication regimens for each patient remained unchanged throughout the course of rTMS treatment. No new medications were initiated, discontinued, or dose-adjusted during the 6–8 week treatment period for any of the three patients, including Patient 3, who remained on a stable regimen of bupropion, sertraline, trazodone, and methylphenidate throughout treatment. No changes to psychotherapy or ophthalmologic treatment occurred during the observation period for any patient.

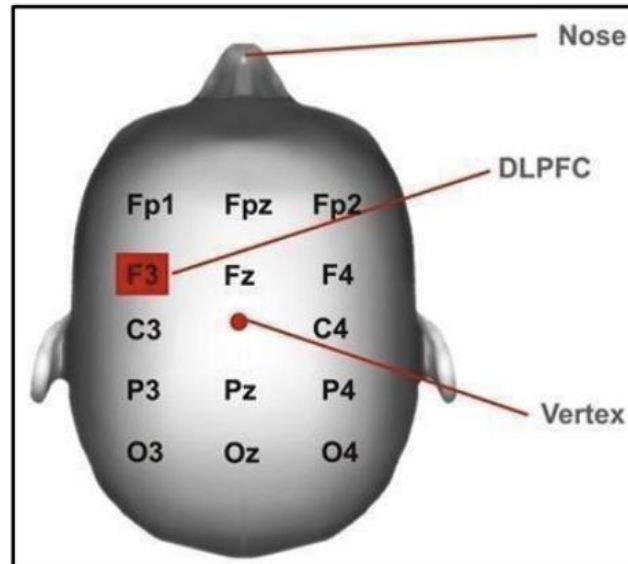


Figure 1: rTMS Treatment Locations

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. Patients selecting a low score indicates a lack of negative symptoms, and a high score indicates an increase in negative symptoms. A lower score would imply a reduction in symptom severity, thus indicating an improvement in depressive and anxiety symptom burden following rTMS treatment (Mahajan *et al.*, 2026; Ong *et al.*, 2022).

Results

Psychometric Questionnaire Results

Across all three patients, notable reductions in both PHQ-9 and GAD-7 scores were observed, signaling improved clinical signs and symptoms following rTMS treatment. Patient 1's PHQ-9 score decreased by 70% (20 to 6) and GAD-7 score decreased by 83.3% (12 to 2) over 8 weeks of treatment. Patient 2's PHQ-9 score decreased by 90% (20 to 2) and GAD-7 score decreased by 100% (16 to 0) over 6 weeks of treatment. Patient 3's PHQ-9 score decreased by 93.8% (16 to 1) and GAD-7 score decreased by 100% (5 to 0), also over 6 weeks of treatment. Reference [Fig. 2](#) and [Table 1-3](#) for psychometric questionnaire results in graphical and numerical forms. Scores reported as N/A indicate that the corresponding data were not obtained due to technical difficulties during data collection. Collectively, these

results demonstrate that by the end of treatment, all three patients achieved substantial improvements in reducing depressive and anxiety symptoms.

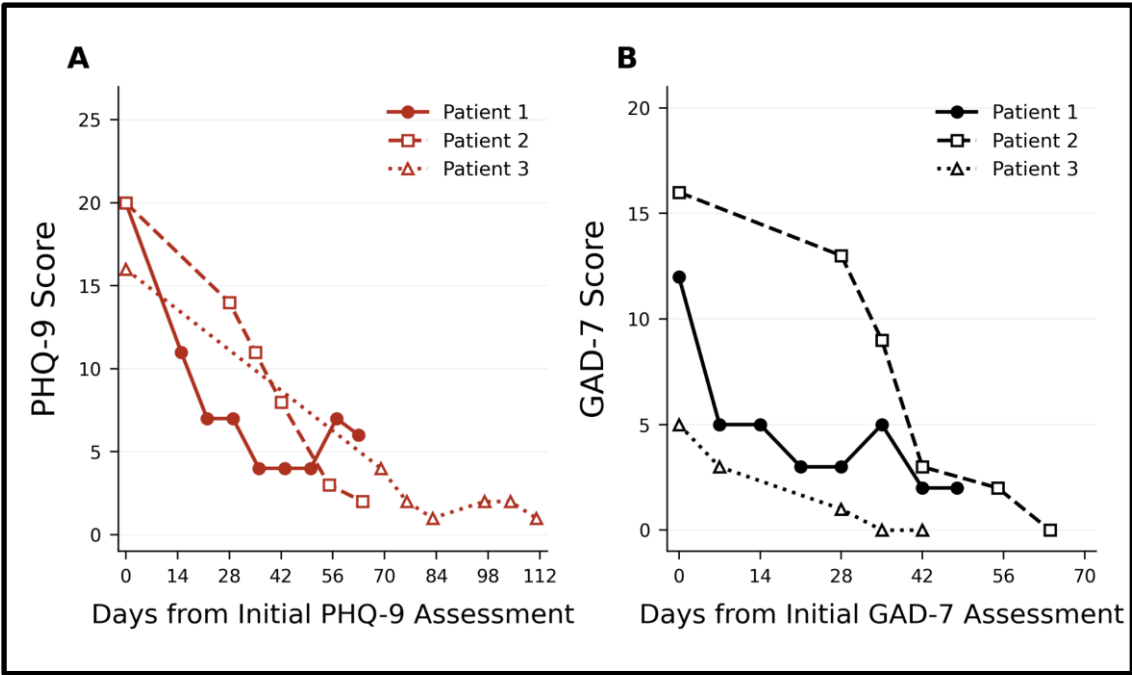


Figure 2: PHQ-9 & GAD-7 Scores.

PHQ-9 and GAD-7 Assessment Scores		
Patient 1 April-June 2026		
Assessment Date	PHQ-9 Score	GAD-7 Score
04/13/2026	20	N/A
04/28/2026	11	12
05/05/2026	7	5
05/12/2026	7	5
05/19/2026	4	3
05/26/2026	4	3
06/02/2026	4	5
06/09/2026	7	2
06/15/2026	6	2

Table 1: Patient 1 Tabulated PHQ-9 & GAD-7 Data.

PHQ-9 and GAD-7 Assessment Scores		
Patient 2 December 2025-February 2026		
Assessment Date	PHQ-9 Score	GAD-7 Score
12/23/2025	20	16
01/20/2026	14	13
01/27/2026	11	9
02/03/2026	8	3
02/16/2026	3	2
02/25/2026	2	0

Table 2: Patient 2 Tabulated PHQ-9 & GAD-7 Data.

PHQ-9 and GAD-7 Assessment Scores		
Patient 3 December 2025-April 2026		
Assessment Date	PHQ-9 Score	GAD-7 Score
12/18/2025	16	N/A
02/25/2026	4	5
03/04/2026	2	3
03/11/2026	1	N/A
03/25/2026	2	1
04/01/2026	2	0
04/08/2026	1	0

Table 3: Patient 3 Tabulated PHQ-9 & GAD-7 Data.

Discussion

To our knowledge, no prior peer-reviewed reports have evaluated rTMS specifically for depression occurring in the clinical context of SVO/myodesopsias or macular degeneration; however, this observation is based on a targeted PubMed/Google Scholar search using combinations of "repetitive transcranial magnetic stimulation," "rTMS," "myodesopsia," "macular degeneration," "symptomatic vitreous opacities," and "depression," rather than a systematic literature search, and should be interpreted with appropriate caution. To date, published literature on rTMS for psychiatric symptoms in the context of chronic, non-psychiatric medical comorbidities remains limited to a small number of case reports and reviews in other

conditions, such as fibromyalgia (Conde-Antón *et al.*, 2023); however, these reports do not address ophthalmic disease or evaluate rTMS as a treatment for the psychological burden associated with pre-existing SVO or MD.

Traditional pharmacologic treatment of depression can yield mixed results, particularly in chronic or treatment-resistant cases. Although antidepressants benefit many patients, medication-specific effects vary across individuals and placebo response is substantial in clinical trials (Fournier *et al.* 2010; Undurraga and Baldessarini, 2012). In patients with ophthalmic conditions such as SVO or MD, pharmacotherapy may improve mood symptoms but does not address the persistent attentional and emotional burden associated with floaters. In addition, psychotropic medications may have ocular adverse effects that warrant attention and coordination with ophthalmology (Undurraga and Baldessarini, 2012). A meaningful proportion of patients experience incomplete response despite antidepressant treatment, supporting the use of individualized or adjunctive interventions such as rTMS (Mrazek *et al.*, 2014). In these cases, depressive and anxiety symptoms persisted despite several psychiatric medications, while PHQ-9 and GAD-7 scores improved markedly following rTMS.

Accordingly, these cases should be viewed as preliminary, hypothesis-generating evidence rather than evidence that rTMS directly treats the underlying vitreous pathology. Although a single case cannot establish causality, the magnitude and temporal relationship of the improvements to treatment support further study of rTMS in patients with visual conditions that impose a chronic cognitive and emotional burden. The findings suggest that rTMS may be a useful adjunctive treatment for depressive and anxiety symptoms in patients with chronic visual disturbances and co-occurring psychological distress and reduced quality of life.

Limitations

This use of rTMS for depressive and anxiety symptoms in patients with symptomatic vitreous opacities or macular degeneration was limited to three isolated patients. The potential benefits of bilateral DLPFC rTMS in patients with SVO or MD need to be studied with larger sample sizes to confirm its effectiveness in reducing psychiatric symptoms associated with persistent visual disturbances. Nevertheless, the marked reductions in PHQ-9 and GAD-7 scores provide preliminary evidence warranting further investigation (Mahajan *et al.*, 2025).

Another limitation was the utilization of self-reported psychometric questionnaire scores, including the PHQ-9 and GAD-7, which may have introduced self-reporting or expectancy bias

(Mohankumar *et al.*, 2025). Nevertheless, the reductions in these scores were accompanied by clinical observations of improved mood, anxiety, sleep, energy, motivation, and engagement in daily activities, supporting the clinical relevance of the reported improvement.

Conclusion

rTMS is being researched as a therapeutic alternative to traditional psychiatric interventions and treatments. Our study shows promising preliminary observations for treating depressive and anxiety symptoms in patients with comorbid ophthalmic conditions such as SVO and macular degeneration. Following the conclusion of rTMS treatment, the patients reported major decreases in PHQ-9 and GAD-7, in combination with improved, clinically observed symptom reduction. Further systematic studies need to be conducted with a larger cohort of patients subject to randomization in order to generalize the results across populations. Quantitative neuroimaging methods in combination with spectral EEG data analysis are recommended for future studies to validate our preliminary observations.

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Conflict of Interest Statement: The authors report no conflicts of interest.

Consent: This report describes a retrospective review of de-identified clinical data from three patients treated in routine clinical practice. In accordance with institutional policy and 45 CFR 46.102(l), retrospective case reports and small case series (3 patients and under) of this nature do not constitute human subjects research and were therefore exempt from institutional review board review. No prospective interventions, randomization, or research-specific procedures were undertaken; all treatments described were delivered as part of standard clinical care. Written informed consent for treatment and for publication of anonymized clinical information was obtained from each patient. All data were de-identified prior to analysis, and patient privacy and HIPAA requirements were observed throughout. This ensured that the subjects understood the potential risks and benefits of diagnostic testing and treatment interventions. rTMS treatments were administered under the supervision of a board-certified psychiatrist by certified neurotechnologists.

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