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EFFICACY

OF TRANSCRANIAL MAGNETIC STIMULATION (RTMS) IN THE TREATMENT OF DEPRESSION. A CASE OF STUDY

EFICACIA DE LA ESTIMULACIÓN MAGNÉTICA TRANSCRANEAL (EMTR) EN EL TRATAMIENTO DE LA DEPRESIÓN. UN ESTUDIO DE CASO

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ABSTRACT

Major depressive disorder (MDD) is a disabling psychiatric condition with a high prevalence of treatment resistance, often requiring alternative neuromodulation approaches. Repetitive Transcranial Magnetic Stimulation (rTMS) has emerged as a non-invasive technique targeting fronto-limbic circuits, particularly the left dorsolateral prefrontal cortex (DLPFC), to modulate effective and cognitive regulation. We present a single-case clinical study of a 39-year-old female patient with moderate MDD who received 16 sessions of high-frequency (10 Hz) rTMS over four weeks. Depressive symptoms were assessed using the Hamilton Depression Rating Scale (HAM-D) at baseline, post-intervention, and six-month follow-up. Scores improved from 17 to 5 post-treatment, and remained at 13 at follow-up, indicating sustained therapeutic response. The patient reported enhanced energy, motivation, and social reintegration. This case suggests the potential clinical utility and tolerability of rTMS in modulating affective networks in depression, while emphasizing the need for cautious interpretation given the single-case design. The treatment also yielded significant psychosocial benefits, facilitating the patient's social reintegration and functional recovery. Qualitative reports and family observations noted marked improvements in energy, motivation, and emotional availability, enabling her to resume work responsibilities and social activities. These functional gains demonstrated notable durability, with sustained social participation and occupational performance maintained at the six-month follow-up, despite a mild symptomatic recurrence. This underscores that rTMS contributed not only to symptom reduction but also to restoring the patient's social world and daily functioning.

Keywords:rTMS, Depression, Dorsolateral prefrontal cortex, Neuromodulation, Affective regulation, Treatment-resistant depression, Case study.

RESUMEN

El trastorno depresivo mayor (TDM) es una condición psiquiátrica incapacitante con una alta prevalencia de resistencia al tratamiento, lo que a menudo requiere enfoques alternativos de neuromodulación. La estimulación magnética transcraneal repetitiva (EMTr) ha surgido como una técnica no invasiva que actúa sobre los circuitos fronto-límbicos,

particularmente en la corteza dorsolateral prefrontal izquierda (DLPFC), para modular la regulación afectiva y cognitiva. Presentamos un estudio clínico de caso único de una paciente de 39 años con TDM moderado, quien recibió 16 sesiones de EMTr de alta frecuencia (10 Hz) durante cuatro semanas. Los síntomas depresivos fueron evaluados mediante la Escala de Hamilton para la Depresión (HAM-D) al inicio, tras la intervención y en el seguimiento a seis meses. Las puntuaciones mejoraron de 17 a 5 después del tratamiento, y se mantuvieron en 13 en el seguimiento, lo que indica una respuesta terapéutica sostenida. La paciente reportó mayor energía, motivación y reintegración social. Este caso sugiere la utilidad clínica y la tolerabilidad potencial de la EMTr en la modulación de redes afectivas en la depresión, al tiempo que enfatiza la necesidad de una interpretación cautelosa debido al diseño de caso único. El tratamiento también produjo beneficios psicosociales significativos, facilitando la reintegración social y la recuperación funcional de la paciente. Los informes cualitativos y las observaciones familiares señalaron mejoras notables en energía, motivación y disponibilidad emocional, lo que le permitió reanudar sus responsabilidades laborales y actividades sociales. Estas ganancias funcionales demostraron una durabilidad notable, manteniéndose una participación social y un desempeño ocupacional sostenidos en el seguimiento a los seis meses, a pesar de una recurrencia sintomática leve. Esto destaca que la EMTr contribuyó no solo a la reducción de síntomas, sino también a restaurar el mundo social y el funcionamiento diario de la paciente.

Palabras clave: EMTr, Depresión, Corteza prefrontal dorsolateral, Neuromodulación, Regulación afectiva, Depresión resistente al tratamiento, Estudio de caso.

INTRODUCTION

Major depressive disorder (MDD) is defined as a mental condition characterized by persistent sadness, anhedonia, chronic fatigue, appetite disturbances, concentration difficulties, and recurrent thoughts of death or suicide (American Psychiatric Association [APA], 2014). Its etiology is multifactorial, involving genetic, neurobiological, psychological, and environmental components (Lascano-Arias et al., 2025; Rutakumwa et al., 2023).

Globally, more than 280 million people suffer from depression, making it one of the leading causes of social disability (Bahamón et al., 2023; Yildirim et al., 2022). Gender disparities are also notable, with women reporting higher prevalence of depressive symptoms compared to men. In Latin America, the prevalence of depression is estimated at 22% (Huang et al., 2023), while in Ecuador, approximately 25% of the population is believed to exhibit depressive symptomatology (Ministerio de Salud Pública [MSP], 2024). Despite ongoing advancements in psychopharmacology and psychotherapy, approximately 30% to 50% of patients with MDD fail to respond adequately to conventional treatment, thereby qualifying as having treatment-resistant depression (TRD).

In this clinical context, several innovative therapeutic strategies have been developed in recent years, particularly for individuals with TRD (Li et al., 2020; Moreta-Herrera et al., 2025). Among them, repetitive transcranial magnetic stimulation (rTMS) has emerged as a promising, non-invasive technique that uses focused magnetic fields to stimulate specific cortical regions. High-frequency stimulation applied to the left dorsolateral prefrontal cortex (DLPFC), a region functionally associated with affective regulation, has shown positive clinical outcomes (González-Chacón & González-Chacón, 2022). Recent studies have demonstrated the effectiveness of rTMS in alleviating depressive symptoms, including accelerated protocols that produce faster symptom remission (Cao et al., 2023).

Other novel interventions include the use of ketamine, an NMDA receptor antagonist with rapid antidepressant effects in patients with TRD (Conejo-Cerón et al., 2021), and esketamine, an enantiomer of ketamine, which has received FDA approval for intranasal administration in TRD, demonstrating significant reductions in depressive symptoms in controlled trials (Daly et al., 2018).

Additionally, psychedelic-assisted therapies, such as those employing psilocybin, have been explored for their therapeutic potential in depression. A recent clinical trial reported significant symptom reduction in TRD patients treated with psilocybin (Carhart-Harris et al., 2021). Furthermore, neurosteroidal treatments, such as zuranolone, a positive allosteric modulator of GABA-A receptors, have shown efficacy in postpartum depression, offering short-term oral treatment with promising results (Deligiannidis et al., 2021).

Of all these, rTMS stands out due to a robust and growing body of research supporting its efficacy and safety in TRD. Since its approval by the U.S. Food and Drug Administration (FDA) in 2008, rTMS has become established as a non-invasive and well-tolerated therapeutic alternative (Coutinho et al., 2018). A recent meta-analysis concluded that active rTMS is significantly more effective than sham stimulation in reducing depressive severity and improving both response and remission rates.

Moreover, rTMS has demonstrated clinical benefits across diverse populations, including older and younger adults, with response rates ranging between 29% and 66.3%

(Ortiz-Cruz et al., 2021). Its favorable tolerability is well documented, with minimal adverse effects reported. A comprehensive meta-analysis by (Wei et al., 2017a) including 18 studies and 1,396 patients, indicated that combining rTMS with antidepressant medication yields significantly better clinical outcomes than pharmacotherapy alone. Depressive scale scores were significantly lower in the rTMS group at both 2 weeks (MD = -4.68) and 4 weeks (MD = -5.53), with no notable differences in tolerability or safety between groups.

In a multicenter observational study applying high-frequency rTMS to the left DLPFC, response rates of 53.5% and remission rates of 42.8% were observed, reinforcing the effectiveness of rTMS in real-world clinical settings (Kong & Gozani, 2018). With respect to safety, rTMS carries a low risk of adverse effects, most commonly transient headaches or localized scalp discomfort. The absence of anesthesia requirements and its suitability for outpatient administration render rTMS an attractive alternative to electroconvulsive therapy (ECT), especially in community-based treatment environments (Klomjai et al., 2015).

These findings support the increasing use of rTMS as an effective and safe intervention, both as monotherapy and in combination with conventional treatments. It is particularly valuable in patients who have shown limited or no response to antidepressant medications or structured psychotherapy. Nevertheless, despite the promising evidence, several gaps remain in the clinical integration of rTMS, especially in Latin American contexts where its incorporation into routine psychiatric care is still limited. While multicenter trials and meta-analyses have established its efficacy under controlled conditions, there is a critical need to examine its applicability, functional outcomes, and symptomatic responses in real-world, resource-constrained settings.

The Present Study

The present study is grounded in the need to generate contextualized, empirical evidence regarding the clinical and functional effects of rTMS. This includes not only validated quantitative symptom reduction, but also improvements in emotional, functional, and adaptive outcomes. Although case reports inherently limit generalizability, they offer nuanced, phenomenological insights into therapeutic change that are often overlooked in randomized clinical trials.

This study aims to evaluate the clinical response and functional impact of high-frequency rTMS in a female patient diagnosed with moderate MDD. It assesses changes in depressive symptoms via the Hamilton Depression Rating Scale (HAM-D), as well as subjective reports on well-being, daily functioning, and perceived recovery. The hypothesis is that a 16-session protocol of high-frequency rTMS applied to the left DLPFC will result in a significant reduction in depressive symptomatology, accompanied by functional and self-reported improvements in quality of life.

In line with the theoretical and empirical literature, this case study contributes to the broader field of translational psychiatry by examining the real-world utility of rTMS as a neuromodulatory intervention in an underrepresented population and clinical setting.

MATERIALS AND METHODS

Case Presentation

The clinical case involves a 39-year-old female patient, single, residing in an urban area, with incomplete university education and employed in the administrative sector. She sought psychological assistance at a university-based mental health service, reporting an eight-month history of symptoms consistent with a moderate major depressive episode.

Primary symptoms included persistent sadness, anhedonia, initial insomnia, reduced appetite, constant fatigue, concentration difficulties, and feelings of worthlessness. While the patient denied suicide attempts, she reported occasional passive suicidal ideation. Additionally, she experienced nonspecific somatic symptoms, such as tension-type headaches and functional gastrointestinal discomfort, that worsened under work-related stress.

Her psychopathological history revealed prior engagement in cognitive-behavioral therapy for three months, with no sustained or clinically significant improvement. At the time of referral for neuromodulation, she was not undergoing pharmacological treatment. However, she had previously been prescribed selective serotonin reuptake inhibitors (SSRIs), which were discontinued early due to gastrointestinal side effects and poor adherence.

The initial assessment included administration of the Hamilton Depression Rating Scale (HAM-D), yielding a score of 17, indicative of moderate depression (Hamilton, 1960). This was supported by a structured clinical interview based on DSM-5 diagnostic criteria, which confirmed the diagnosis of major depressive disorder, current moderate episode, with no psychotic features or seasonal pattern.

The diagnostic evaluation combined the HAM-D with a structured DSM-5 interview. Differential diagnoses such as bipolar disorder and anxiety disorders were considered and ruled out: no history of manic or hypomanic

episodes was reported, and anxiety symptoms did not reach diagnostic threshold. The persistence of core depressive symptoms with moderate functional impairment supported the diagnosis of moderate MDD. Prognostically, poor response to prior treatments, low social support, and occupational stress were identified as risk factors, which justified referral to rTMS.

The patient voluntarily consented to participate in the repetitive transcranial magnetic stimulation (rTMS) protocol, signing an informed consent form. No neurological contraindications or personal or family history of epilepsy were identified that would preclude rTMS treatment.

From a psychosocial perspective, the patient reported a limited family support network, characterized by distant relationships with her parents and siblings. This lack of emotional containment increased her perceived loneliness and contributed to the persistence of depressive symptoms, in line with evidence highlighting social support as a protective factor in depression.

Occupationally, the patient described high job demands in her administrative role, including workload pressure, strict deadlines, and extended hours, which exacerbated fatigue, concentration difficulties, and insomnia. Additional stressors included financial strain and uncertainty regarding job stability, both of which were identified by the patient as major contributors to her emotional distress.

Socially, she reported a restricted interpersonal circle, with limited recreational activities and scarce community integration. The reduction in social interactions amplified her isolation and reduced opportunities for external emotional support. This adverse psychosocial context, marked by low family cohesion, occupational overload, and limited community support, appears to have played a crucial role in symptom chronicity and in the lack of sustained response to prior psychotherapeutic and pharmacological interventions.

Nevertheless, despite these limitations, the patient demonstrated strong motivation to engage with the rTMS protocol. She actively collaborated with the clinical team and consistently recorded her progress in a structured diary. This resilient attitude likely facilitated adherence to treatment and contributed to the positive short-term outcomes observed.

rTMS Intervention

The intervention consisted of a standard high-frequency (10 Hz) rTMS protocol, targeted at the left dorsolateral prefrontal cortex (DLPFC), a region implicated in emotional regulation. This stimulation frequency and cortical target were selected based on their well-established efficacy in the treatment of moderate to severe major depressive disorder. Multiple clinical trials and meta-analyses have supported the use of 10 Hz stimulation over the left DLPFC, showing consistent antidepressant effects and high tolerability, particularly in treatment-resistant populations (González-Chacón & González-Chacón, 2022; Wei et al., 2017b).

The decision to apply the protocol over a four-week period, with 16 sessions in total, reflects conventional clinical practice and is supported by international guidelines for rTMS administration in depression. While accelerated protocols of rTMS have shown comparable efficacy with faster symptom improvement (e.g., protocols with a higher number of sessions per week), recent studies have reported that such intensive protocols, although effective, require increased logistical resources, may elevate patient burden, and often demand stricter clinical supervision. In this specific clinical setting, a conventional four-week schedule was preferred to ensure optimal adherence, continuous safety monitoring, and feasibility within the institutional infrastructure (Prodi et al., 2024). This timeline aligns with previous studies on rTMS efficacy and allows for a comprehensive evaluation of both short-term and long-term treatment effects and front-limbic modulation, central to the neurocircuitry of depressive disorders. Stimulation was delivered using a clinically certified neuromodulator device, calibrated to 100% of the resting motor threshold of the first dorsal interosseous muscle.

A total of 16 sessions were administered over four consecutive weeks, at a rate of four sessions per week. Each session lasted approximately 37 minutes, during which 3,000 magnetic pulses were delivered in 10-second trains followed by 50-second inter-train intervals, consistent with established clinical parameters for rTMS in depression

Throughout the treatment course, the patient was clinically monitored during each session for both symptomatic response and safety. Vital signs, including blood pressure, heart rate, and oxygen saturation, were systematically assessed immediately before and after stimulation using a calibrated digital sphygmomanometer and pulse oximeter. In addition, the patient was observed continuously for any acute changes in alertness, discomfort, or neurological symptoms during stimulation. Adverse events were documented in accordance with standardized safety checklists, and clinical staffs were trained to implement immediate response protocols in the unlikely event of severe reactions, such as seizure activity or syncope. This structured monitoring ensured adherence to best clinical practice and provided reassurance regarding the safety and tolerability of the rTMS sessions.

The patient was instructed to maintain a structured clinical diary, recording daily information on mood, energy levels, sleep patterns, and cognitive performance. Additionally, brief weekly clinical interviews were conducted to monitor treatment progression and provide emotional support as needed. At the conclusion of the intervention, depressive symptoms were re-assessed using the HAM-D, allowing for pre-post comparative analysis of treatment outcomes

Assessment Instruments

To evaluate the patient's depressive symptoms, the Hamilton Depression Rating Scale (HAM-D) was administered at three time points: pre-treatment, post-treatment, and six-month follow-up. The HAM-D is a clinician-administered instrument used to assess the severity of depression, covering mood, insomnia, somatic symptoms, anxiety, and psychomotor changes. It has demonstrated high internal consistency (α = 0.80–0.90) and widespread validation across clinical and research populations (Table 1).

Table 1. Quantitative instruments used in the EMT case study.

Instrument	What measures	Consistency	Validation	Cut-off points
HAM-D	It measures the severity of depressive symptoms. It evaluates symptoms such as mood, insomnia, feelings of guilt, anxiety, and somatic symptoms.	High internal consistency (α = 0.80 and 0.90) (Hamilton, 1960).	Validated in diverse populations, with an accepted in both research and clinical practice.	<7: No Depression 7-17: Mild to moderate depression 18-24: Moderate to severe depression >24: Severe depression
α = Cronbach's alpha				

Source: own work

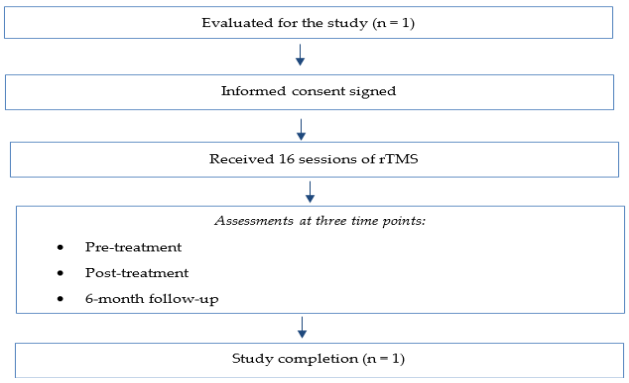
This scale was chosen due to its robust psychometric properties and clinical utility in monitoring treatment outcomes in major depressive disorder.

Study Process

Figure 1 presents a CONSORT-style flow chart illustrating the entire process followed for this single participant, from the initial evaluation to the final follow-up. The flowchart provides a clear visual representation of how the participant was assessed for eligibility, included in the study, received the intervention (rTMS), and was followed through three key evaluation points: pre-treatment, post-treatment, and at six-month follow-up (Figure 1).

In addition to the flowchart, Table 2 presents a clinical timeline that outlines the key stages of the patient's therapeutic process. This timeline includes major events, clinical evaluations, rTMS sessions, and relevant observations across the full course of care, from baseline to follow-up. It serves to contextualize the intervention and highlight the patient's trajectory over time.

Fig 1. CONSORT-style Flowchart of the Participant's Study Process, from Initial Evaluation to Follow-up.



Source: own work

Table 2. Clinical Timeline of the Patient's Treatment Process.

Time Point	Clinical Activity / Observation
Week 0	Initial psychiatric evaluation. HAM-D administered (score = 17). Informed consent signed. No pharmacotherapy in use.
Week 1 (Sessions 1–4)	Start of rTMS treatment. Mild headache reported during initial sessions. Clinical diary initiated.
Week 2 (Sessions 5–8)	Weekly clinical interview conducted. Notable improvement in mood and energy. No adverse events.
Week 3 (Sessions 9–12)	Continued symptom reduction. Patient reports improved sleep, concentration, and affective stability.
Week 4 (Sessions 13–16)	Final rTMS sessions administered. Post-treatment HAM-D score = 5. Patient expresses functional improvement.
Month 6 (Follow-up)	Follow-up evaluation. HAM-D score = 13. Mild symptom recurrence. Patient remains functional with stable mood overall.

HAM-D = Hamilton Depression Rating Scale.
Source: own work.

RESULTS AND DISCUSSION

Quantitative Analysis

The patient's depressive symptoms were assessed using the Hamilton Depression Rating Scale (HAM-D) at three time points: prior to treatment (pre), immediately after completing the intervention (post), and at six-month follow-up (Table 3).

Table 3. HAM-D scores over time

Instrument	Pre-intervention	Post-intervention	Tracking
HAM-D*	17	5	13
*= Overall score. HAM-D: Hamilton Scale for Depression			

Source: own work.

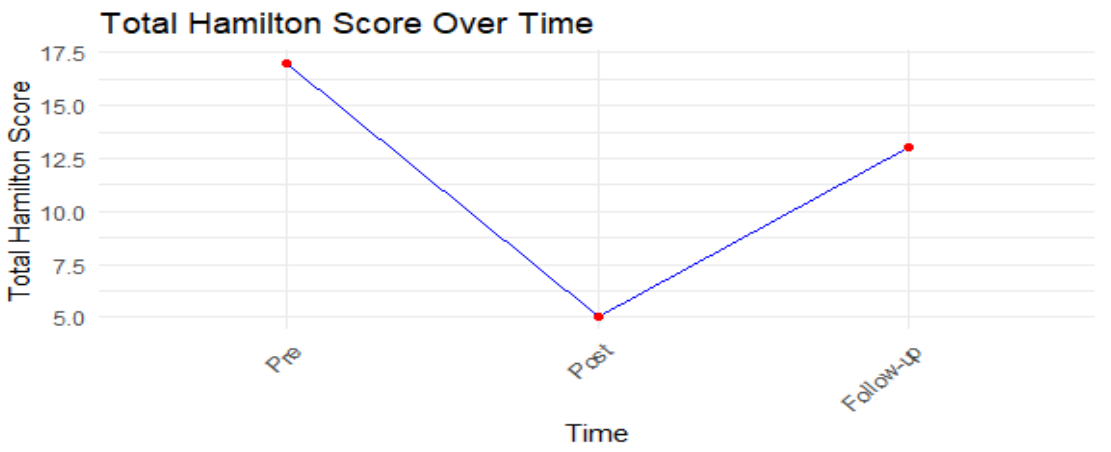
At baseline, the HAM-D score was 17, placing the patient in the range of moderate depression. This score justified the initiation of neuromodulatory intervention. Upon completion of the 16-session high-frequency rTMS protocol, the patient's HAM-D score decreased to 5, indicating near-complete remission and a transition to a non-depressive clinical status. The 12-point reduction observed exceeded the typical threshold for clinical improvement.

The significant reduction in depressive symptoms, evidenced by the HAM-D score decreasing from 17 (moderate depression) to 5 (near remission) after 16 rTMS sessions, provided the patient with the foundational emotional stability necessary for social re-engagement. This clinically significant improvement directly translated into increased energy and motivation, allowing her to initiate contact with friends and family, thereby breaking the cycle of social withdrawal that characterized her pre-treatment state.

At the six-month follow-up, the score increased slightly to 13, suggesting the return of mild depressive symptoms. Although this change indicates some symptom re-emergence, the overall progress compared to baseline reflects sustained therapeutic benefit over time.

The Figure 2 illustrates the trajectory of HAM-D scores across three key assessment points: baseline (pre-treatment), immediately post-treatment, and 6-month follow-up. A significant reduction in the HAM-D score was observed following treatment, with the patient moving from a moderate depression classification (score = 17) to near remission (score = 5). However, at the 6-month follow-up, a slight increase in symptoms was noted (score = 13), suggesting a mild recurrence of depressive symptoms. Despite this, the score remained substantially lower than baseline, reflecting overall clinical improvement with partial maintenance of therapeutic benefits.

Fig 2. Evolution of HAM-D scores over time.



Source: own work.

This case study illustrates a notable reduction in depressive symptoms, suggesting potential therapeutic benefits of high frequency rTMS in moderate depression. The clinical improvement, evidenced by a 12-point decrease in the HAM-D score, exceeded the minimum threshold of 7 points considered indicative of a clinically relevant response (González-Chacón & González-Chacón, 2022). These findings align with prior evidence supporting the efficacy of rTMS in treatment-resistant depression, with response rates ranging from 29% to 66.3% depending on patient characteristics and symptom severity (Kong & Gozani, 2018; Wei et al., 2017a).

The neuromodulatory effects of rTMS on the left DLPFC, a region central to affective regulation and executive function, contributed to improved cognitive clarity and emotional control. The patient noted enhanced concentration and decision-making abilities, which empowered her to navigate social interactions and occupational demands more effectively. This cognitive improvement underpinned her successful reintegration into her administrative work and bolstered her confidence in social settings.

Qualitative Analysis

Complementary to the quantitative assessment, a qualitative analysis was conducted using semi-structured interviews and the patient's self-reported clinical journal. The patient described a progressive emotional improvement, characterized by increased energy, reduced fatigue, and improved affective regulation. She resumed previously abandoned activities, improved her performance at work, and experienced a renewed sense of social engagement.

Qualitative reports from the patient's clinical diary highlighted that the alleviation of core symptoms like anhedonia and chronic fatigue was pivotal for her functional recovery. She reported a renewed capacity for pleasure and interest in social activities, which facilitated her return to previously abandoned community and recreational events. This restoration of social motivation is a critical outcome, as it addresses the behavioral activation component essential for sustained recovery from depression.

The patient also reported enhanced concentration and decision-making capabilities, which translated into increased motivation to resume academic pursuits. Furthermore, she noted greater emotional availability in her interpersonal relationships and a reduction in social withdrawal.

Family members supported these observations, reporting noticeable improvements in her emotional state and social participation. During follow-up, the patient maintained a generally stable emotional condition, though she reported slight fluctuations in mood and energy levels, corresponding to the mild increase observed in the HAM-D score.

Family observations corroborated the patient's self-report, noting a marked transformation in her interpersonal demeanor. They described her as being "more present" and emotionally available, indicating that the therapeutic benefits of rTMS extended beyond intrapsychic symptom relief to positively impact relational dynamics and family cohesion. This

external validation underscores the treatment's role in repairing the social dysfunction associated with depressive episodes.

From the patient's perspective, the rTMS intervention was perceived not only as clinically effective but also as transformative in her daily life. She emphasized improvements in energy, motivation, and emotional stability, which facilitated her reintegration into both professional and personal roles. The patient described the treatment process as tolerable, reporting only mild and transient discomfort during the first sessions, and highlighted the importance of feeling actively engaged in her recovery through the use of a structured clinical diary.

Caregivers also provided valuable insights, noting marked changes in her mood, social interactions, and overall functionality. Family members expressed that the patient appeared "more present" in daily activities and showed a renewed capacity to maintain interpersonal relationships. They further reported a reduction in her emotional withdrawal and an increase in proactive communication. These perspectives underscore not only the symptomatic relief achieved through rTMS but also its broader impact on family dynamics and the patient's subjective sense of recovery.

Although a follow-up assessment at six months showed a mild symptom recurrence (HAM-D score of 13), the patient maintained a significantly higher level of social functioning compared to her baseline. This suggests that while the intense antidepressant effect may attenuate over time, the functional and psychosocial gains achieved—such as sustained work performance and active social circles—exhibit greater durability, highlighting a valuable dissociation between symptom relapse and social disability.

Functional gains also emerged as a key outcome. The patient reported significant improvements in energy, concentration, and motivation, translating into greater engagement in social and occupational roles. This functional recovery aligns with previous studies emphasizing rTMS's impact not only on symptom reduction but also on psychosocial functioning and quality of life (Klomjai et al., 2015). The patient resumed social connections and academic goals, suggesting broader therapeutic benefits beyond symptom alleviation.

The intervention's favorable safety and tolerability profile, with only transient mild headaches reported, were crucial for the patient's consistent adherence to the protocol. This positive experience allowed her to engage fully in the treatment process without the burden of significant side effects, thereby supporting her overall journey toward recovery and enabling her to focus her regained energy on rebuilding her social life and personal goals.

Interpretation of Results

The data from this single case suggests possible early effects of rTMS in reducing depressive symptoms and contributing to functional improvements. These preliminary findings should be interpreted with caution, as they cannot be generalized beyond the individual level. The immediate post-treatment decline in symptom severity and qualitative enhancements in energy, cognition, and social functioning suggest a strong therapeutic effect. Recent studies have proposed accelerated rTMS protocols that produce faster symptom remission with comparable efficacy to standard protocols. However, the four-week protocol used in this case was selected to balance treatment intensity and patient tolerance, particularly in clinical settings where patient safety and adherence are critical. Future research should consider exploring the potential benefits of shorter, more intensive rTMS protocols in patients with treatment-resistant depression. While the follow-up revealed some symptom recurrence, the overall improvement remained significant.

These findings indicate possible effectiveness of high-frequency rTMS as a neuromodulation-based intervention, although conclusions remain limited by the single-case design. They also highlight the importance of longitudinal monitoring and, when necessary, maintenance strategies to sustain long-term benefits.

However, several limitations warrant discussion. First, as a single case report, generalizability is inherently limited, and the absence of a control group precludes causal inferences. The lack of a sham or comparator condition was not an oversight but rather an inherent feature of the case report design, which aims primarily to provide preliminary, descriptive evidence and generate hypotheses for future research. Case reports are not intended to establish efficacy but to highlight clinical observations that may inform subsequent controlled investigations.

Another limitation is the potential impact of interindividual variability. Patient-specific factors, such as metabolic conditions or adherence to previous treatments, can significantly influence outcomes. For example, patients with metabolic disturbances or comorbid medical conditions may show reduced responsiveness to neuromodulatory interventions, which complicates the generalization of treatment outcomes. Similarly, individual differences in neurobiological plasticity, stress reactivity, and treatment adherence may contribute to heterogeneous clinical

trajectories. These factors highlight the importance of developing stratified approaches that consider patient-specific moderators of treatment response.

This underlines the need for randomized controlled trials (RCTs) with larger samples to clarify variability in treatment response and to establish evidence-based maintenance strategies. Although previous studies suggest rTMS effects can last several months (Cao et al., 2023; Klomjai et al., 2015), the slight symptom resurgence at follow-up in this case highlights the need for ongoing monitoring and maintenance strategies.

Systematic Adverse Event Reporting

Adverse events were systematically recorded during the rTMS protocol. To ensure a structured and comprehensive reporting of these events, we followed a checklist based on the identification of event types, frequency, duration, severity, and any necessary interventions or outcomes (Table 4).

Table 4. Systematic Adverse Event Reporting During rTMS Treatment

Category	Description
Type of Adverse Event	Mild headache, scalp discomfort during the initial sessions
Frequency and Duration	Occurred in the first 3 sessions, subsided after treatment
Severity	Mild: No significant interference with daily activities
Intervention/Response	No medical intervention required, symptoms resolved spontaneously
Outcome and Resolution	Events resolved without additional treatment, no lasting effects

Source: own work.

An important consideration in the interpretation of this case involves the evaluation of potential differential diagnoses. Bipolar disorder represents a critical diagnostic alternative, as depressive episodes are often the first clinical presentation and may be indistinguishable from unipolar depression without careful longitudinal assessment. Although the patient did not report a history of manic or hypomanic episodes, ongoing monitoring remains essential to exclude a bipolar spectrum disorder, particularly given its therapeutic implications.

At the 6-month follow-up, the patient experienced a slight resurgence in depressive symptoms, including suicidal ideation, as indicated by an increase in the HAM-D score. This rebound is consistent with prior research showing that rTMS, while effective in the short term, may lose its effects over time without additional support or maintenance strategies.

Additionally, the patient was not on pharmacological treatment during the rTMS protocol, limiting comparisons with standard antidepressant therapy. While rTMS combined with pharmacotherapy has shown promising outcomes (Li et al., 2020), further studies are needed to clarify potential synergistic effects.

A further limitation was the absence of neurobiological or neuroimaging data. Although rTMS is known to influence synaptic plasticity, BDNF levels, and neuroinflammatory markers (Klomjai et al., 2015), objective measures of brain function such as fMRI or EEG were not included. Incorporating such tools in future research could enhance understanding of rTMS's mechanisms and support clinical findings with biological evidence.

Clinical Implications and Future Directions

Although the present case involves an adult patient, future investigations should also consider safety aspects in younger populations, as cortical excitability thresholds and tolerability may differ in adolescents. Developing brains present lower cortical excitability thresholds, and high-intensity stimulation may increase risks such as discomfort, headaches, or, in rare cases, seizures. For this reason, international guidelines emphasize cautious parameter selection, adherence to safety thresholds, and close monitoring in younger populations. While not applicable to the present case, these considerations underscore the need for age-specific safety protocols in future studies.

Despite these limitations, this case reinforces the utility of rTMS as a non-invasive intervention for major depression, particularly in treatment-resistant cases. Its ability to induce rapid symptomatic and functional improvements makes it a valuable therapeutic option, especially for patients who have not responded to conventional pharmacological or psychotherapeutic approaches (Daly et al., 2018).

Future research should include randomized controlled trials (RCTs) with larger samples to compare rTMS efficacy against standard treatments and explore long-term maintenance protocols. The combined use of rTMS and pharmacotherapy also merits further investigation to evaluate additive effects. Lastly, integrating neurobiological biomarkers could offer greater insight into rTMS's therapeutic mechanisms and help personalize treatment. Tools such as fMRI, EEG, and inflammatory or neuroplasticity markers could identify patient profiles most likely to benefit and guide individualized rTMS protocols.

CONCLUSIONS

This case study supports the clinical value of high-frequency repetitive transcranial magnetic stimulation (rTMS) as an effective and well-tolerated intervention for moderate major depression. The patient exhibited a clinically significant reduction in depressive symptoms, accompanied by functional and subjective improvements. These findings are consistent with previous research highlighting rTMS as a promising therapeutic alternative for patients with limited response to conventional treatments.

Although positive, the results must be interpreted with caution due to the limitations inherent to single-case designs, including the lack of generalizability and the absence of a control group. The partial return of symptoms at six-month follow-up underscores the need for long-term monitoring and the possible implementation of maintenance protocols.

This study highlights the importance of integrating functional outcomes and patient-reported experiences into treatment evaluation, and it calls for future research using controlled designs and neurobiological markers to better understand rTMS mechanisms and optimize patient-specific protocols.

Notably, the social and functional gains demonstrated considerable durability, as evidenced by sustained improvements in work performance and social engagement even at the six-month follow-up, despite a mild symptomatic recurrence. This dissociation between symptom fluctuation and preserved social functioning underscores that rTMS can provide a foundational neuromodulatory effect that supports lasting psychosocial rehabilitation. These outcomes highlight the importance of evaluating depression treatments not only through symptom scales but also through their tangible impact on restoring a patient's social world and quality of life.

In summary, rTMS shows preliminary potential as a non-invasive neuromodulatory approach in clinical psychiatry, warranting further investigation in controlled studies.

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