

CRITICAL REVIEW



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Effectiveness of Repetitive Transcranial Magnetic Stimulation Treatment on Depression

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AJUNI BIRAK¹**ABSTRACT**

Major depressive disorder (MDD) is a prevalent mental health condition often treated with medication that may cause adverse effects, especially in younger individuals. Repetitive transcranial magnetic stimulation (rTMS) is a promising alternative for those who do not respond to traditional medications and methods of therapy. This noninvasive treatment targets brain regions associated with depression, such as the dorsolateral prefrontal cortex (DLPFC), using magnetic pulses to modulate neural activity. Current studies show that rTMS can improve response and remission rates with fewer side effects compared to standard treatments. Its safety profile, combined with its effectiveness for treatment-resistant cases, makes it a promising alternative to antidepressants. While current research on rTMS is limited by varying treatment durations and a lack of long-term data, rTMS presents as a valuable option for managing MDD.

BACKGROUND

MDD is a common neuropsychiatric disorder that affects an estimated 300 million people globally.¹ It is characterized by long-term, persistent sadness or depressive episodes wherein a person may feel empty or irritable. Individuals with MDD may experience a loss of interest in activities, excessive self-criticism, guilt, or suicidal ideation.¹ Scientists have examined physiological differences between the brains of individuals with and without depression, though it remains unclear if these differences are a result or a cause of the disorder.² The brains of patients suffering from depression often exhibit changes in grey matter and neuronal activity.² For example, key prefrontal regions can undergo a reduction in volume, such as the DLPFC, which is involved in mood regulation and executive function.²

The most common method of treating MDD is through the use of medication.³ Antidepressants in particular are currently regarded as the most effective way to treat depression; however, they have been shown to cause side effects, such as dizziness, nausea, insomnia, sexual dysfunction, heart problems, and heightened suicidal thoughts in people under the age of 25.⁴ rTMS is an alternative method that induces changes in brain activity to treat MDD.⁵ rTMS is a subtype of TMS which noninvasively stimulates certain regions of the brain using electromagnetic fields generated by a coil.^{5,6} rTMS therapy generally has fewer side effects than antidepressants and has been shown to decrease the severity of depressive symptoms in patients who did not respond adequately to standard medication and therapies.^{5,7}

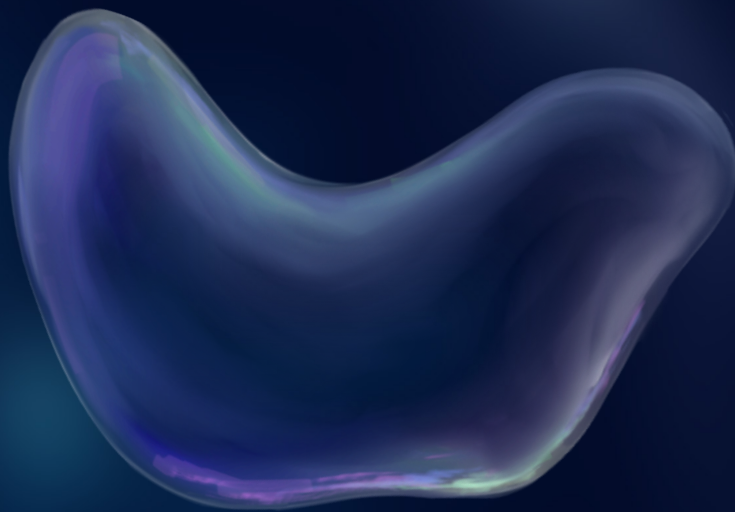
OVERVIEW OF EVIDENCE:**RTMS EFFICACY IN ADOLESCENTS**

Gu et al. conducted a double-blind sham-controlled study examining the safety and efficacy of low-frequency rTMS in 40 adolescents aged 13-17 with MDD over a two week period.⁹ Depressive symptoms, as well as response and remission rates,

were measured using the Hamilton Depression Rating Scale (HAMD) and were compared to initial scores. Response was defined as a decrease of 50% or more in the HAMD score of the last session compared to the initial score, while remission was defined as having an HAMD score of seven or below. Although the study did not reach statistical significance between the active and sham groups, the active group still showed numerically higher response and remission rates, at 70% and 55%, respectively, compared to the sham group, at 60% and 35%, respectively.⁹ Both groups had similar minimal side effects after the trial, which included fatigue, mild headaches, and insomnia.⁹ These results suggest a safe and potentially clinically beneficial application of rTMS in adolescents.⁹

LONG-TERM DURABILITY OF RTMS RESPONSE

In a systematic review and meta-analysis combining data from 23 studies, Senova et al. examined the long-term response rate for rTMS treatment after three, six, and twelve months.¹⁰ The study found that 66.5% of patients maintained their response three months after receiving treatment, while 46.3% sustained their response for 12 months.¹⁰ Although response rates declined over time, nearly half the patients retained clinical benefit for up to one year.¹⁰ While the treatment parameters varied between studies included in the systematic review, the overall results indicated that rTMS could offer a viable, long-term alternative treatment option for MDD.¹⁰



rTMS EFFECTIVENESS IN TREATMENT-RESISTANT DEPRESSION

Gaynes et al. conducted a systematic review on the efficacy of rTMS treatments, focusing on patients who failed two or more medications.⁷ This study found that active rTMS treatment resulted in a decrease in depressive severity and symptoms. Patients receiving rTMS treatments, as opposed to sham treatment, showed remission rates up to five times higher than the placebo, and were also three times more likely to respond to the therapy.⁷ Most studies included in the review evaluated the short-term efficacy of rTMS, with a timeline of four to six weeks, and the treatments were conducted over periods of five days to six weeks.⁷ rTMS resulted in an average decrease of four points on the HAMD scale, providing evidence for the short-term effectiveness of rTMS for those with treatment-resistant depression.⁷

LIMITATIONS

Many of the previously discussed studies were conducted over only a few weeks, with some describing a lack of long-term maintenance treatments past one year. In addition, they provided limited follow-up on the sustained effectiveness of the treatment over extended periods. While rTMS has been generally found to offer short-term relief from depression symptoms and is considered relatively safe during these shorter studies, the absence of comprehensive, long-term follow-up data in the reviewed studies means that the safety and efficacy of rTMS over longer durations cannot be confidently assured.^{7,10,11}

The treatment duration used in different rTMS studies varies by a large margin.^{7,11} For example, in the systematic review conducted by Gaynes et al., studies with treatment durations ranging from one to six weeks were included.⁷ This variation in treatment duration may have influenced the consistency of the reported outcomes. The review indicated that rTMS treatment has overall positive remission and response rates; however, the four trials with the longest treatment period (four to six weeks) had response and remission rates that exceeded the reported results, suggesting that the efficacy of rTMS may be underestimated. This disparity must be further studied to gain a better understanding of the impact of rTMS duration on depression treatment.

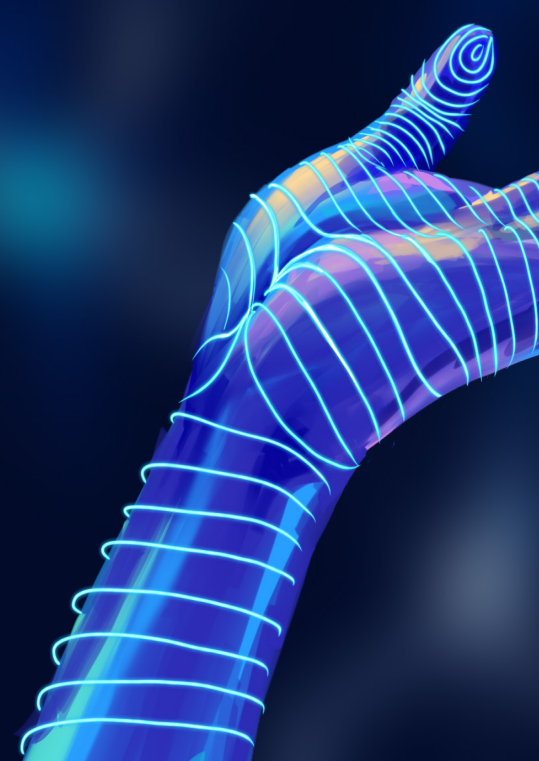
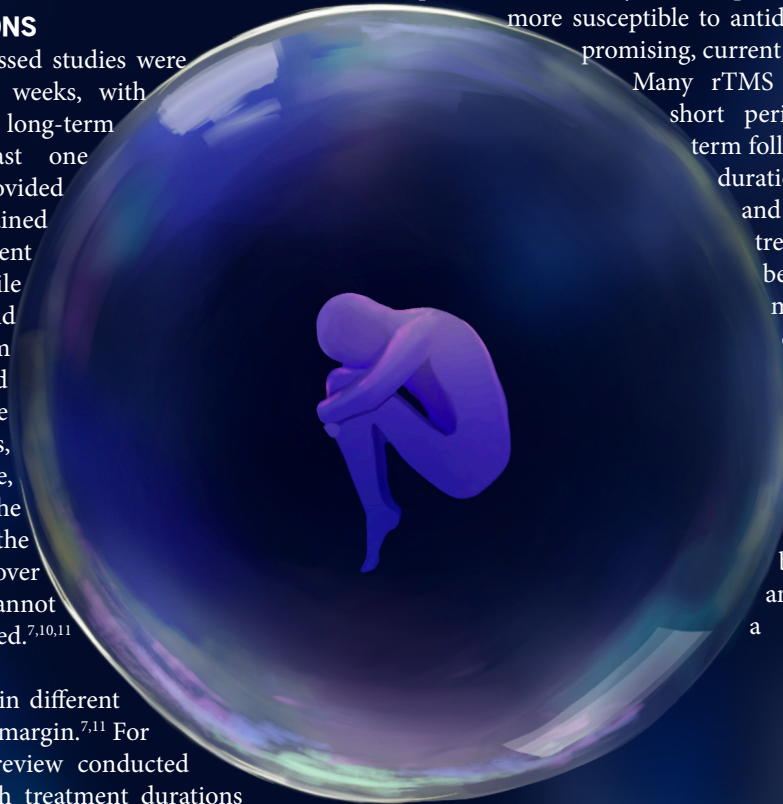
Another limitation to rTMS therapy is the lack of data focusing on older adults (>60 years), despite this population accounting for approximately 18.4% of depressed people in the United States.^{12,13} One review conducted by Overvliet et al. concluded that around 12.5% of older adults experienced adverse effects from rTMS therapy. This is relatively low compared to the adolescent study conducted by Gu et al., which reported rates of adverse side effects ranging from 42.5% to 62.5%.

rates of adverse side effects ranging between 42.5% to 62.5%. This may suggest that rTMS is well-suited to elderly patients. However, it is difficult to generalize these findings as the participants in the studies reviewed by Overvliet et al. took less external medications and had fewer health issues than the average elderly individual.¹³ More research is necessary to determine potential benefits of rTMS therapy for older adults.

CONCLUSION

rTMS is a promising treatment for MDD, particularly in cases where antidepressants have failed. Various studies have shown that rTMS can induce higher response and remission rates compared to sham treatments, effectively reducing depression symptoms. It can also be used alongside other treatments, such as antidepressants and psychotherapy, which enhances its potential for addressing treatment-resistant cases. Furthermore, rTMS presents a clinically viable option for individuals who may be more susceptible to antidepressant side effects. Though promising, current rTMS research has limitations.

Many rTMS studies are conducted over short periods, with insufficient long-term follow-up. Additionally, treatment duration varies widely across studies, and evidence suggests that longer treatment periods may produce better outcomes. In the future, more research is required to determine optimal treatment duration and frequency for varying demographics. As rTMS therapy for depression is explored more thoroughly, addressing these gaps will help optimize its efficacy, broaden its applicability, and improve outcomes for a wider range of patients.



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