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# Review of Transcranial Magnetic Stimulation as a Treatment Modality for Depression in the Indian Population

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## ABSTRACT

Transcranial Magnetic Stimulation, commonly referred to as "TMS", is a rapidly growing noninvasive treatment modality that uses magnetic pulses to stabilize and stimulate nerve cells in the brain. It is commonly used to combat neuropsychiatric disorders, such as depression, obsessive compulsive disorders and cognitive impairments. TMS treatment is often viewed as an alternative option for those who showcase resistance to traditional over the counter or prescribed medications. Although viewed as a significant step forward in the psychiatric industry, the popularity of TMS is still growing and its latest advances are not prevalent among most regions of India. Apart from this, there are uncertainties surrounding the efficiency of TMS. These uncertainties have ultimately paved the way for ongoing research evaluating its efficacy, long term effects and overall processes. In this article we will explore the benefits and limitations of TMS treatment, review how it compares to other options, as well as its future in the Indian medical sector.

## Introduction

One of the biggest challenges plaguing the Indian population today is the increase in prevalence of neuropsychiatric disorders, namely depression. In India, the National Mental Health Survey 2015-16 revealed that nearly 15% Indian adults need active intervention for one or more mental health issues and one in 20 Indians suffers from depression. It is estimated that in 2012, India had over 258 000 suicides, with the age-group of 15-49 years being most affected. Although various depression treatments ranging from pharmacotherapy to psychotherapy are available in India, the vast majority of treatment-resistant patients are beginning to prefer non-invasive treatment options. The primary issue surrounding pharmacotherapy options such as SSRI's (selective serotonin reuptake inhibitors) are their extensive list of side effects, as well as their "delayed time to take effect" (Jaiswal, 2023). Additionally, treatment options such as electroconvulsive therapy are less popular due to the invasive nature of the therapy and associated adverse cognitive effects (Jaiswal, 2023). Trans cranial magnetic stimulation (TMS) on the other hand is gaining popularity as a treatment modality for depression .There is growing evidence to support its use in patients with depression as a monotherapy or as an adjunct to pharmacotherapy (Somani, 2019) However, current challenges such as the long term benefits, access to care, identifying patients that would benefit from TMS, developing standardized protocols for administration are some of the issues that still needs to be overcome in the Indian psychiatric field.

## Transcranial Magnetic Stimulation

The notion of Transcranial Magnetic Stimulation was first discovered by Micheal Faraday in 1831 who introduced the idea that the relationship between electrical energy and magnetic energy was reciprocal. However, it was Anthony Barker and his colleagues who began exploring the use of magnetic fields to alter electric signaling and the first stable TMS device was developed in 1985(Klomajai, 2015). The intent of the device initially was for diagnostic and research purposes. It was later developed and approved by the FDA in 2008 as a therapeutic device (Horvath,2011). TMS was first introduced in India around 1997.Over the years it has not only emerged as a potential nonpharmacological treatment modality for various neuropsychiatric disorders but also as an investigative tool to understand brain physiology as evidenced by various publications.

## Operational Mechanics

The TMS treatment, as stated earlier, is a non-invasive treatment option that involves the deliverance of magnetic pulses to the human brain using a hand-held stimulating coil that is applied to the patient's scalp, with the intention of electrically depolarizing neurons that cause depression.

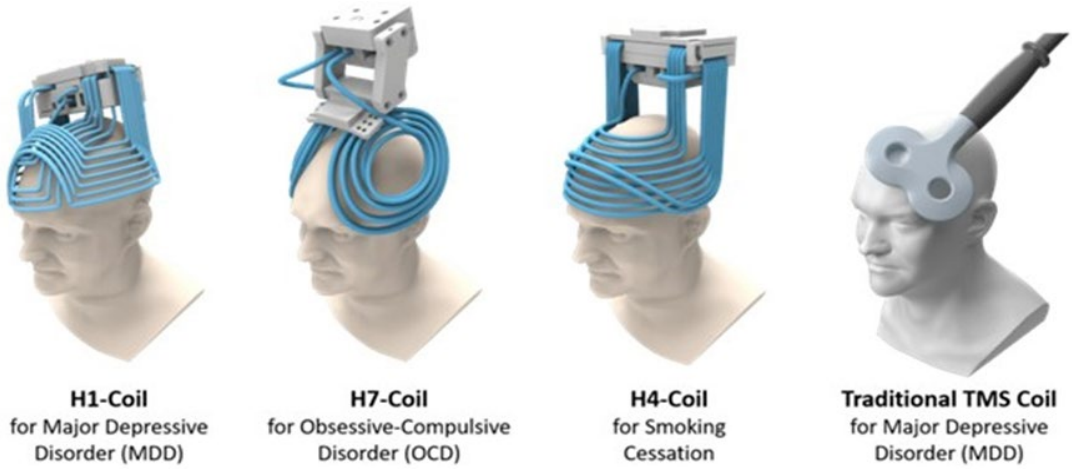


**Figure 1.** Types of TMS coils and tasks associated with each one (https://www.brainsway.com/how-does-it-work/build-deep-vs-traditional-tms/)

Two coils are situated around the scalp that produce multiple electrical currents with the help of a large capacitor that is charged by a transformer. For increased effectiveness, a high-tension cord is also attached to the scalp, connecting it with the coils. These coils can come in many different shapes, and each shape performs a different task (fig 1).

TMS utilizes a key law of physics, namely Faraday's Law of Electromagnetic Induction. This law states that “whenever there is a change in magnetic flux associated with a coil, Electromagnetic field is induced in that coil”. This relates to TMS, because when the capacitor is charged and magnetic pulses are sent out through the coils, a perpendicular magnetic field is released into the scalp, ultimately targeting white matter region of interest (The Clinical Brain Lab, 2019). Faraday's Law can also be applied to a secondary aspect of this treatment. Although two coils are present during treatment, in many cases, only one is used to emit an electrical current. In a study from 2016, researchers found that if one coil contained electricity and another was “devoid” of it, when the electrical current ran out in the latter, a small pulse would be shifted to the second coil

stimulating deeper areas of the brain (Noohi, 2016). Most coils used in transcranial magnetic stimulation (TMS) provide a shallow magnetic field that affects neurons mostly on the surface of the brain, delivered with coil shaped like the number eight. The H coil provided magnetic fields deeper in the brain, and devices using them provide what is called "deep TMS" (Bersani 2013). Single-pulse TMS (including paired-pulse TMS) is used to explore brain functioning, whereas repetitive TMS (rTMS) is used to induce changes in brain activity that can last beyond the stimulation period (Klomajai 2015). rTMS is delivered as either a single pulse with a frequency of <1 Hz, or as paired pulses through repetitive stimulation in many milliseconds at around 1-25 Hz. Patients are required to attend around 20-30 sessions at least with each session lasting an average of 20-30 minutes. Both TMS and rTMS treatments are meant to carry out different tasks, regular TMS treatment is meant to create cortical excitation among various regions, while rTMS is meant to exact neuronal excitation. When combined, both treatments are able to create substantial therapeutic improvements (Lingeswaran, 2011).

## Role of the DLPFC

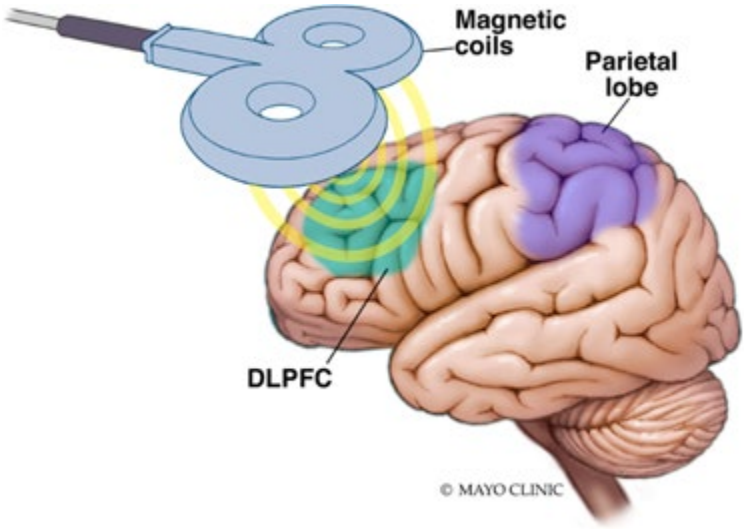


**Figure 2.** Operational procedure and key region of TMS therapy

Many regions of the brain are involved in major depressive disorders (MDD), namely the left dorsolateral prefrontal cortex (DLPFC), hippocampus and the subgenual anterior cingulate cortex (ACC). Due to the deep positioning of the ACC within the human brain, TMS treatment strives to target the DLPFC as it is easier to stimulate, shares a connection with the ACC, and controls mood regulation (Fox, 2012). The DLPFC and the ACC are connected through a network of cingulum bundles, which are tracts of white matter or nerves that play critical roles in facilitating communication between cortical and subcortical structures (Li, 2023). A study conducted in 2013 found that when the left DLPFC was stimulated using a type of TMS, patients who in the past showcased heavy amygdala recruitment and increased negative attention bias were able to enhance their respective attentional control capabilities. Put simply, when TMS was applied to the left DLPFC, patients were able to focus more on positive aspects compared to negative aspects, as well as improve deficient cognitive control commonly associated with MDD (Wolkenstein, 2013). It is believed that TMS therapy stimulates the cells within the DLPFC containing the neurotransmitters serotonin and norepinephrine, releasing them and creating a chemical balance within the brain, ultimately improving mood.

## Clinical Trials and Outcomes

Innumerable studies have been conducted to demonstrate the efficacy and effectiveness of the TMS therapy. We will focus on the studies evaluating TMS therapy for depression conducted in India. In a trial conducted by the Department of Psychiatry in New Delhi, researchers were able to study the efficacy of rTMS in a controlled environment. Patients who had exhibited intolerance to antidepressant medication within the first 6-8 weeks of taking it were given the rTMS treatment. This treatment was administered for five days a week for three weeks using the standard frequency of 15 Hz. All 22 participants received 3000 pulses per session or 10 pulses per second and their baseline ratings on the Hamilton Rating Scale for Depression (HAMD) or Mongomery-Asberg Depression Rating Scale(MADRS) were assessed. At the end of the treatment, the results were compared with the baseline ratings, and over 50% score change improvement was observed in 57% of the population in the HAMD scale where baseline ratings decreased from a mean of 21.79±5.36 to 10.64±4.25, and 37% of the population in the MADRS scale, where baseline ratings decreased from 38.25±8.53 to 25.50±10.79. This results in a composite score of a 50% response rate among all participants. These numbers shared relative similarity among many other Indian studies that had response rates of 40-60 percent (Verma, 2018).

In another study conducted by the Department of Psychiatry in Uttar Pradesh, 23 subjects recruited from the outpatient psychiatric department were screened to participate in the four-week session. 21 were chosen for treatment and attended a total of 20 sessions with five sessions a week. A standard frequency of 10 Hz was used for the duration of the trial and the stimulation was applied to the left DLPFC. Similar to the protocol followed by Verma and colleagues, baseline scores were recorded and compared to the HAMD scale, however this treatment also used Global Impressions-Severity and Global Impressions-Change scales to track responses to the aforementioned therapy. At the end of 4 weeks, 19 patients completed the study and were assessed. All of them had a reduction in total scores on HAM-D. Only 2 patients did not show significant change (Jhanwar, 2011)

An associate group in the department of psychiatry at NIMHNS conducted a randomized study that compared the effectiveness of sham rTMS to active rTMS. Sham stimulation refers to a type of therapy in which patients experience an environment similar to active stimulation, however little to no magnetic current is being applied to their scalp. A total of 23 patients, aged between 16 and 60 years of age, participated in this trial. The duration of the study lasted 2 weeks with patients receiving six sessions of rTMS per week. Similar to the protocols of the latter trials, a common 10 Hz frequency was used during stimulation with 10 trains of pulses per session that were applied to the left DLPFC. Nine patients participated in the active treatment, while 14 patients participated in the sham treatment, results showed negligible differences in outcomes between the two treatment groups, rTMS did not show an improvement at the end of two weeks (Lingeswaran, 2011). Contrasting results from this study could be attributed to a small sample size and limited duration of the study.

Finally, a systematic review analyzing the efficacy and safety of therapeutic TMS reviewed a total of 52 studies and concluded that rTMS was significantly effective in the treatment of depression, with respect to the safety and tolerability, rTMS was considered as a safe non-invasive brain stimulation technique with no serious adverse effects apart from known side effects of headache and local site discomfort as observed in most of the studies(Tikka, 2023). Overall, based on the evidence TMS seems to be a promising alternative in treating depression.

## Comparison to Electroconvulsive Therapy

An alternative treatment for depression is electroconvulsive therapy. Electroconvulsive therapy uses an electric current to induce a therapeutic seizure. Numerous studies have shown that ECT was more effective than rTMS in a controlled environment, however these same studies also showed that patients had a higher preference for

rTMS, and less adverse cognitive effects were associated with treatment (Reddy, 2017). The ECT treatment is a more invasive option for treating depression, hence the increased occurrence of adverse effects. A serious limitation of the ECT treatment is the inability to accurately target and control the amount of electrical current. This lack of control has led to manifestations of seizures during therapy (Lingeswaran, 2011). There have also been instances of ECT treatment causing deficits in delayed recall. Patients may suffer short term memory loss and frontal function impairment as well. Given all the significant drawbacks for ECT, patients prefer the less invasive TMS therapy over ECT. Additionally, TMS's lack of anesthesia makes it a preferable option (Lingeswaran, 2011).

## Conclusion

To conclude, Transcranial Magnetic stimulation as a treatment modality for depression is considered an effective therapeutic option as established from numerous studies and clinical trials. The non-invasive nature and negligible adverse effects of this treatment has generated a high patient preference, however more evidence is needed to establish standardized protocols, determine patient selection and increase efficacy. The future of TMS in India is dependent upon increasing awareness, availability and affordability of treatment across rural areas.

## Limitations

Although the prevalence of depression and depression related disorders is on the rise in India, seeking care for depression is not common. One major limitation to avail treatment for depression related disorders in India is a general lack of awareness. A qualitative screening study identified the main barrier to seeking treatment for depression symptoms, as lack of perceived need for treatment for these experiences. A primary reason for low perceived need was the conceptualization of depression-like experiences as an understandable response to adversity, including both social and economic difficulties and physical health problems. Participants considered tension-related problems to be distinct from mental illness, and outside the purview of health service (Roberts, 2020). A cultural bias also inhibits the Indian population in general to seek therapy for mental disorders. Myths and misconceptions regarding mental health are more prevalent in the rural areas both among people and medical professionals (Jugal, 2011). From a cultural perspective, there is a significant stigma associated with seeking help for mental disorders leading to neglect of mental health (Gururaj, 2016). Access to care is also considered a major limitation to seek therapy. A study conducted in rural India to evaluate patients seeking treatment for depression revealed 86% of the screened adults positive for depression did not seek treatment. Structural barriers to health care such as cost, distance to services were also reported as barriers to seek treatment (Roberts, 2020) (Gururaj, 2016).

The TMS treatment modality is still relatively new compared to other existing options in India, although it is gaining attention in the recent years, only major cities are currently equipped to provide TMS therapy, rural regions lack the accessibility to care. There is also lack of awareness both among patients and providers in rural India about TMS therapy, its applications and benefits. The therapy is also expensive making it unaffordable to a broader population.

Apart from the general limitations, the therapy itself is reported to have a few adverse effects namely, mild headaches, scalp muscle twitching, vasovagal syncope and very rare instances of mania or a seizure (Reddy, 2017). Also, a significant limitation can be long term results of the therapy. The effectiveness of the treatment was evaluated in a controlled environment, and researchers found that 62.5% of patients who underwent acute treatment, "achieved remission" and continued to stay in remission for the remaining time period, and 36.2% of patients only temporarily achieved remission and still required more session of rTMS and antidepressants. Although the percentage of patients who stayed in remission is greater than those who did not,

there is still the possibility that the antidepressant effects of rTMS may not last as long as expected (Kar, 2019). Patient related factors also contribute to the efficacy of TMS treatment. A study conducted in 2012 found that as the age of the patient increases, so does the antidepressant effectiveness of TMS and older patients responded significantly more to the treatment than younger patients (Pallanti, 2012). However, contradicting this data, another study found that the relationship between age and efficacy was inverse and younger patients responded to treatment better. This fluctuation in data is likely attributed to brain atrophy, in which the length between the scalp and pallium is increased as a patient's age also increases, ultimately decreasing the effectiveness of TMS (Somani, 2019). This condition is not present in all elderly patients; however, it limits our abilities to make a broader claim surrounding the relationship between treatment effectiveness and age.

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## References

Jaiswal A, Umesh S, Goyal N. Research on treatment-related aspects of depression from India in the preceding decade (2014-2023): An updated systematic review. Indian J Psychiatry. 2023 Nov;65(11):1112-1121. doi: 10.4103/indianjpsychiatry.indianjpsychiatry_810_23. Epub 2023 Nov 24. PMID: 38249143; PMCID: PMC10795667.

A Somani, SK Kar Efficacy of repetitive transcranial magnetic stimulation in treatment-resistant depression: thus far. General Psychiatry 2019 Aug 12;32(4):e100074.
doi: 10.1136/gpsych-2019-100074.

Klomjai W, Katz R, Lackmy-Vallée A. Basic principles of transcranial magnetic stimulation (TMS) and repetitive TMS (rTMS). Ann Phys Rehabil Med. 2015 Sep;58(4):208-213. doi: 10.1016/j.rehab.2015.05.005. Epub 2015 Aug 28. PMID: 26319963.

Horvath JC, Perez JM, Forrow L, Fregni F, Pascual-Leone A. Transcranial magnetic stimulation: a historical evaluation and future prognosis of therapeutically relevant ethical concerns. J Med Ethics. 2011 Mar;37(3):137-43. doi: 10.1136/jme.2010.039966. Epub 2010 Nov 24. PMID: 21106996.

Noohi S, Amirsalari S. History, Studies and Specific Uses of Repetitive Transcranial Magnetic Stimulation (rTMS) in Treating Epilepsy. Iran J Child Neurol. 2016 Winter;10(1):1-8. PMID: 27057180; PMCID: PMC4815479.

Fox MD, Buckner RL, White MP, Greicius MD, Pascual-Leone A. Efficacy of transcranial magnetic stimulation targets for depression is related to intrinsic functional connectivity with the subgenual cingulate. Biol Psychiatry. 2012 Oct 1;72(7):595-603. doi: 10.1016/j.biopsych.2012.04.028. Epub 2012 Jun 1. PMID: 22658708; PMCID: PMC4120275.

Li S, Chen J, Gao K, Xu F, Zhang D. Excitatory brain stimulation over the left dorsolateral prefrontal cortex enhances voluntary distraction in depressed patients. Psychol Med. 2023 Feb 28;53(14):1-10. doi: 10.1017/S0033291723000028. Epub ahead of print. PMID: 36852634; PMCID: PMC10600932.

Wolkenstein L, Plewnia C. Amelioration of cognitive control in depression by transcranial direct current stimulation. Biol Psychiatry. 2013 Apr 1;73(7):646-51. doi: 10.1016/j.biopsych.2012.10.010. Epub 2012 Dec 6. PMID: 23219367

Sangha Mitra Godi [1], Sai Krishna TikkaIndian research on transcranial magnetic stimulation: A bibliometric analysis Indian J Psychiatry. 2023 Apr;65(4):469-471.
doi: 10.4103/indianjpsychiatry.indianjpsychiatry_678_22. Epub 2023 Apr 11

Bersani FS, Minichino A, Enticott PG, et al. Deep Transcranial Magnetic Stimulation as a Treatment for Psychiatric Disorders: A Comprehensive Review. *European Psychiatry*. 2013;28(1):30-39. doi: 10.1016/j.eurpsy.2012.02.006

Verma, Rohit; Kumar, Nand; Kumar, Saurabh. Effectiveness of adjunctive repetitive transcranial magnetic stimulation in management of treatment-resistant depression: A retrospective analysis. Indian Journal of Psychiatry 60(3): p 329-333, Jul–Sep 2018. | DOI: 10.4103/psychiatry.IndianJPsychiatry_182_16

Jhanwar VG, Bishnoi RJ, Singh L, Jhanwar MR. Utility of repetitive transcranial magnetic stimulation as an augmenting treatment method in treatment-resistant depression.Indian J Psychiatry. 2011 Apr;53(2):145-8. doi: 10.4103/0019-5545.82543

Lingeswaran A. Repetitive Transcranial Magnetic Stimulation in the Treatment of depression: A Randomized, Double-blind, Placebo-controlled Trial. Indian Journal of Psychological Medicine. 2011;33(1):35-44. doi:10.4103/0253-7176.85393

Tikka SK, Godi SM, Siddiqui MA, Garg S. Evidence from Indian studies on safety and efficacy of therapeutic transcranial magnetic stimulation across neuropsychiatric disorders- A systematic review and meta-analysis. Indian J Psychiatry. 2023 Jan;65(1):18-35. doi: 10.4103/indianjpsychiatry.indianjpsychiatry_572_22. Epub 2023 Jan 13. PMID: 36874512; PMCID: PMC9983459.
Roberts, T., Shidhaye, R., Patel, V. *et al.* Health care use and treatment-seeking for depression symptoms in rural India: an exploratory cross-sectional analysis. *BMC Health Serv Res* **20**, 287 (2020). https://doi.org/10.1186/s12913-020-05162-0
Kishore, Jugal; Gupta, Avni; Jiloha, Ram Chander1; Bantman, Patrick2. Myths, beliefs and perceptions about mental disorders and health-seeking behavior in Delhi, India. Indian Journal of Psychiatry 53(4):p 324-329, Oct–Dec 2011. | DOI: 10.4103/0019-5545.91906
Gururaj G, Varghese M, Benegal V, Rao G, Pathak K, Singh L, et al. National Mental Health Survey of India, 2015-16: summary. Bengaluru: National Institute of Mental Health and Neurosciences, NIMHANS Publication. 2016(128):1–48.
Roberts T, Shidhaye R, Patel V, Rathod SD. Health care use and treatment-seeking for depression symptoms in rural India: an exploratory cross-sectional analysis. BMC Health Serv Res. 2020 Apr 6;20(1):287. doi: 10.1186/s12913-020-05162-0. PMID: 32252760; PMCID: PMC7137455.
Reddy MS, Vijay MS. Repetitive Transcranial Magnetic Stimulation for Depression: State of the Art. Indian J Psychol Med. 2017 Jan-Feb;39(1):1-3. doi: 10.4103/0253-7176.198951. PMID: 28250551; PMCID: PMC5329982.
Kar SK. Predictors of Response to Repetitive Transcranial Magnetic Stimulation in Depression: A Review of Recent Updates. Clin Psychopharmacol Neurosci. 2019 Feb 28;17(1):25-33. doi: 10.9758/cpn.2019.17.1.25. PMID: 30690937; PMCID: PMC6361049.

Pallanti S, Cantisani A, Grassi G, Antonini S, Cecchelli C, Burian J, Cauli G, Quercioli L. rTMS age-dependent response in treatment-resistant depressed subjects: a mini-review. CNS Spectr. 2012 Mar;17(1):24-30. doi: 10.1017/S1092852912000417. PMID: 22790115.