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Efficacy Of Theta Burst Stimulation Therapy For Depressive Disorder: A Systematic Review

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Abstract

Introduction- A comprehensive review of research on Theta burst stimulation is presented in this article. A type of transcranial magnetic stimulation called theta burst stimulation (TBS) modifies brain activity by delivering magnetic pulse bursts. It is used in two ways: Continuous (cTBS) to block neurones and Intermittent (iTBS) to activate them. It is frequently used to treat mental and neurological disorders including depression.

Method- The systematic review was conducted using Pub Med, Science Direct and Google Scholar electronic database.

Aim- The aims of the review were to provide a comprehensive overview of TBS as an innovative therapeutic approach, highlighting its mechanisms, clinical outcomes, and potential advantages over traditional treatments.

Conclusion- Theta Burst Stimulation (TBS) is a modern and time-efficient technique in Transcranial Magnetic Stimulation, aimed at adjusting brain activity. It has proven to be a valuable treatment for several neurological and psychiatric disorders, with depression being a key focus. Supported by clinical studies, TBS is recognized for its safety and effectiveness, making it a promising avenue for future therapeutic advancements.

Keywords: Theta burst stimulation, Intermittent TBS, Continuous TBS, Transcranial magnetic stimulation, depression

Introduction

Theta Burst Stimulation (TBS) therapy is a sophisticated type of Transcranial Magnetic Stimulation (TMS) that has gained recognition as an effective option for treating depression, particularly in cases where conventional therapies fail to deliver results. Depression, a widespread mental health condition, impacts millions worldwide and is marked by persistent sadness, diminished interest in activities, and compromised cognitive and physical abilities. Although pharmacological and therapeutic treatments exist, many individuals face challenges with treatment-resistant depression, necessitating innovative solutions like TBS.

TBS works by using precisely patterned magnetic pulses to influence brain activity. Its two main approaches—Intermittent Theta Burst Stimulation (iTBS) and Continuous Theta Burst Stimulation (cTBS)—are designed to either boost or reduce neural activity. For depression treatment, iTBS is often utilized, administering bursts of three pulses at 50 Hz, repeated at 5 Hz, within a session lasting around three minutes. This method targets the dorsolateral prefrontal cortex, a region essential for mood and cognitive regulation.

Research has shown TBS to be effective in relieving symptoms of depression. For example, a randomized trial published in JAMA Network Open revealed that

iTBS was as successful as high-frequency repetitive TMS (rTMS) in reducing depression severity while offering shorter treatment sessions. Additionally, findings from a study in BMC Psychiatry highlighted the potential of accelerated TBS (aTBS), involving multiple daily sessions, in amplifying antidepressant effects.

Objective

The main goal of this systematic review is to thoroughly analyze and consolidate existing research on the effectiveness of theta burst stimulation (TBS) therapy for major depressive disorder (MDD). It seeks to offer an in-depth exploration of TBS as a novel treatment method, emphasizing its underlying mechanisms, therapeutic results, and distinct benefits compared to conventional approaches.

Material and Method

Systematic review was tried to be conducted according to PRISMA (preferred reporting item for systematic and Meta analysis). The systematic review was conducted using Pub Med, Science direct and Google Scholar.

Inclusion Criteria:

1. Studies evaluating the use of theta burst stimulation (TBS) therapy, including intermittent TBS (iTBS) and continuous TBS (cTBS) protocols.
2. Articles published in English.

Exclusion Criteria:

1. Studies evaluating treatments other than theta burst stimulation (e.g., traditional rTMS, ECT, pharmacotherapy) unless TBS is a comparative intervention.
2. Studies evaluating the use of TBS for conditions other than depressive disorder.
3. Articles published in languages other than English.

Results

After searching database 4992 documents in total were locate, every detail of the paper was examined and duplicate records were eliminated. Additionally only 14 articles were selected for systematic review.

Mechanism Of Theta Burst Stimulation

TBS works by targeting specific areas of brain associated with mood regulation, particularly the dorsolateral prefrontal cortex

Stimulation of neural activity

Stimulated neurons in the BLP FC through magnetic pulses, As this area is under active in individual but depression

↓

Neuroplasticity

Stimulation promotes neuroplasticity, brain's ability to reorganise and form new neural connection

↓

Helps in re storing normal activity in the affected brain circuit

↓

Regulation of neurotransmitter

TBS influences the release of neurotransmitter like serotonin and dopamine, which play a crucial role in mood regulation

↓

Reduction of over activity another reason

by stimulating DLPFC, PBS helps to reduce overactivity in other brain reason, search as amygdala which is often hyperactive in depression

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Types Of Tbs

Theta Burst Stimulation (TBS) is a specialized form of Transcranial Magnetic Stimulation (TMS) aimed at addressing neurological and psychiatric disorders by modulating brain activity through magnetic pulses targeted at specific brain regions. It is divided into two distinct types:

1. Intermittent Theta Burst Stimulation (iTBS): Designed to stimulate underactive neurons, this excitatory method is commonly used to treat conditions such as depression. It involves bursts of magnetic pulses delivered in intervals, primarily targeting the left dorsolateral prefrontal cortex. The right dorsolateral prefrontal cortex is stimulated continuously for about 40 seconds during the process, with up to 600 pulses applied.
2. Continuous Theta Burst Stimulation (cTBS): This inhibitory approach focuses on reducing excessive neuronal activity, making it suitable for conditions like anxiety or PTSD. Magnetic pulses are delivered in a continuous sequence, typically targeting the right dorsolateral prefrontal cortex. In this method, the left dorsolateral prefrontal cortex receives stimulation for two seconds, followed by an eight-second pause between sessions. Over the course of 190 seconds, 600 pulses are administered.

Clinical Evidance Supporting Tbs

Theta Burst Stimulation (TBS) therapy has been extensively studied for its clinical applications, particularly in neurological and psychiatric conditions.

Tbs Vs Traditional Antidepressant Treatments

TBS offers several advantages and difference compared to traditional depression treatment like anti depression medication psychotherapy and even repetitive transcranial magnetic stimulation (rTMS).

Component	Theta burst stimulation	Traditional antidepressant treatment
Treatment duration	sessions are shorter last 3 to 10 minutes	where medications are long term therapy session last 45 to 60 minutes
Mechanism	uses electromagnetic pulses to target a specific brain areas	alters brain chemistry example antidepressant of focuses on thought pattern example therapy
Side effects	minimal mild headache or discomfort add a stimulation site	significant medication effect like weight gain nausea and drowsiness
Efficacy	effective for treatment resistant depression compareable to TMS	works well for many but may fail in severe or resistant cases
Availability	It is still emerging and may not be widely accessible yet	established and broadly available

Wischnewski Miles and Dennis JLG Schlutter (2015) conducted a review to evaluate the effectiveness and temporal effects of TBS in healthy individuals. Their findings indicated that continuous TBS applied for 40 seconds suppresses cortical activity, while TBS applied for 20 seconds excites the cortex for up to 20 minutes. These insights provide valuable normative data on the scale and duration of previously induced changes in cortical excitability.

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Daan Neuteboom et al.'s September 2023 review examined the efficacy, safety, and tolerability of accelerated intermittent theta burst stimulation (aiTBS) in patients with mild depressive disorder. The findings revealed that immediately following treatment, response rates ranged from 20% to 86.4%, and remission rates from 10% to 86.4%. After four weeks, response rates varied from 0% to 66.7%, and remission rates from 0% to 57.1%. The study also reported a significant reduction in suicidality scores, highlighting aiTBS as a safe and well-tolerated approach with no serious adverse events observed.

Outcomes of TBS

Over the past decade, theta burst stimulation (TBS) therapy has gained recognition as an effective treatment for depression, with a response rate of 42.1% and a remission rate of 16%. Older patients showed significantly higher response rates compared to younger individuals. Xiao Tao et al. (2025) reported that both rTMS and TBS effectively reduced depression and anxiety symptoms, with similar side effect profiles. However, TBS is more time-efficient, with sessions lasting only 192 seconds, making it a cost-effective option.

Studies indicate TBS success rates range between 70% and 80%, with symptoms sometimes fully resolving after one session. TMS has also shown efficacy in patients under 60 and those resistant to antidepressant medications. Blumberger et al. (2018) demonstrated that iTBS was equally effective as high-frequency rTMS for treatment-resistant depression but required significantly less time per session, enhancing efficiency.

The Scania Accelerated Intermittent Theta-burst Implementation Study (SATIS), published in PLOS ONE, highlighted the feasibility and effectiveness of accelerated iTBS, achieving faster antidepressant responses in some cases with results comparable to conventional iTBS. The EARLY-BURST Trial, a randomized sham-controlled study, confirmed the safety and effectiveness of iTBS for adolescents and young adults with depressive disorders, emphasizing its potential as an early intervention.

Benefits

Theta Burst Stimulation (TBS) therapy has emerged as a groundbreaking treatment for depression, particularly for those with treatment-resistant cases. This advanced form of Transcranial Magnetic Stimulation (TMS) utilizes magnetic pulses in specific patterns to regulate brain activity and offers a range of clinically supported benefits.

Key Advantages of TBS for Depression:

1. **Effective Symptom Relief:** Research shows that Intermittent Theta Burst Stimulation (iTBS) is as effective as high-frequency repetitive TMS (rTMS) in reducing depressive symptoms. A study in *JAMA Psychiatry* revealed that iTBS achieves similar results to rTMS but with significantly shorter treatment durations.
2. **Time Efficiency:** TBS sessions are notably shorter, lasting about 3 minutes compared to the 37-minute sessions for traditional rTMS, making it more practical for both patients and clinicians.
3. **Rapid Results:** Accelerated TBS (aTBS), which involves multiple sessions per day, has demonstrated the ability to deliver fast antidepressant effects, particularly for acute depressive episodes.
4. **Non-Invasive and Safe:** TBS is a non-invasive therapy with minimal, short-lived side effects such as mild headaches or scalp discomfort, making it suitable for a wide range of patients.
5. **Precise Targeting:** TBS focuses on the dorsolateral prefrontal cortex, a brain area involved in mood regulation, enhancing its effectiveness in treating depression.
6. **Versatile Applications:** Beyond depression, TBS is being studied for its potential to treat other conditions like anxiety and post-traumatic stress disorder, showcasing its adaptability.

Overall, TBS represents a major advance in neuromodulation, offering an effective, efficient, and well-tolerated treatment option. Its ability to provide rapid therapeutic benefits with minimal side effects makes it a promising first-line treatment for treatment-resistant depression. Ongoing research continues to optimize its protocols and explore its broader applications, solidifying its importance in mental health care.

Treatment Protocols

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Theta Burst Stimulation (TBS) protocols are designed to regulate brain activity through specific magnetic pulse patterns. The primary protocols include:

1. **Intermittent Theta Burst Stimulation (iTBS):**

Goal: Boosts brain activity.

Pulse Pattern: Bursts of three pulses at 50 Hz, repeated at 5 Hz intervals.

Duration: Roughly 3 minutes per session.

Uses: Primarily applied to treat depression.

2. **Continuous Theta Burst Stimulation (cTBS):**

Goal: Reduces brain activity.

Pulse Pattern: Similar to iTBS but delivered continuously without pauses.

Duration: Approximately 40 seconds per session.

Uses: Suitable for conditions requiring inhibitory effects.

Potential Challenges And Future Direction

While Theta Burst Stimulation (TBS) shows significant potential, it encounters certain hurdles that require attention for further advancement:

Individual Response Variability: The effectiveness of TBS differs among individuals, influenced by variations in brain structure, neuroplasticity, and specific conditions.

Optimizing Protocols: Establishing ideal stimulation parameters, including intensity, frequency, and duration, remains a challenge to maximize therapeutic benefits.

Limited Data on Long-Term Impact: Comprehensive studies are needed to better understand the long-term safety and efficacy of TBS.

Accessibility Barriers: The high costs associated with equipment, training, and therapy restrict its availability to a broader population.

These areas highlight the need for ongoing research and innovation in TBS therapy to enhance its application and accessibility.

Future Directions:

1. Personalized Medicine: Utilizing neuroimaging and machine learning to design tailored TBS protocols based on individual brain characteristics may improve treatment efficacy.
2. Combination Therapies: Combining TBS with interventions like cognitive-behavioral therapy or pharmacological treatments can potentially enhance patient outcomes.
3. Broader Applications: Investigating TBS for conditions such as post-traumatic stress disorder and chronic pain could extend its therapeutic use.
4. Technological Advancements: Developing affordable and portable TBS devices would increase accessibility and encourage widespread adoption.

These developments underline the importance of ongoing research and innovation to fully harness the potential of TBS therapy.

Innovation And Limitations

Innovations

1. Accelerated TBS Protocols: Studies have investigated the use of multiple daily sessions to expedite antidepressant effects, showing promise in improving treatment efficiency.
2. Neuroimaging Integration: Techniques like functional MRI are being utilized to refine brain region targeting, enhancing the precision and overall effectiveness of TBS.
3. Combination Therapies: TBS is being combined with pharmacological treatments and psychotherapy to optimize therapeutic outcomes and achieve better results.

Limitations

1. Variability in Patient Response: Individual factors such as age, depression severity, and comorbidities affect TBS outcomes, emphasizing the importance of customized treatment approaches.
2. Long-Term Efficacy: Although short-term benefits of TBS are established, further studies are needed to evaluate its durability and effectiveness in preventing relapses.
3. Accessibility Issues: Restricted access to TBS in certain regions and healthcare facilities hampers its widespread adoption, underscoring the need for improved availability.

Conclusion

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Theta Burst Stimulation (TBS) stands out as an innovative and efficient therapy for depression, showcasing notable clinical effectiveness. It serves as a viable alternative to traditional repetitive Transcranial Magnetic Stimulation (rTMS), offering shorter sessions without compromising therapeutic results. Intermittent TBS (iTBS) activates underactive neural pathways, addressing the neurobiological disruptions associated with depressive disorders. Backed by numerous studies, especially in cases of treatment-resistant depression, TBS has established itself as a valuable tool in contemporary psychiatry. Its safety, adaptability, and growing range of applications further enhance its clinical utility. As research continues to refine protocols and maximize outcomes, TBS is positioned as a significant advancement in depression treatment, instilling hope for those battling this condition.

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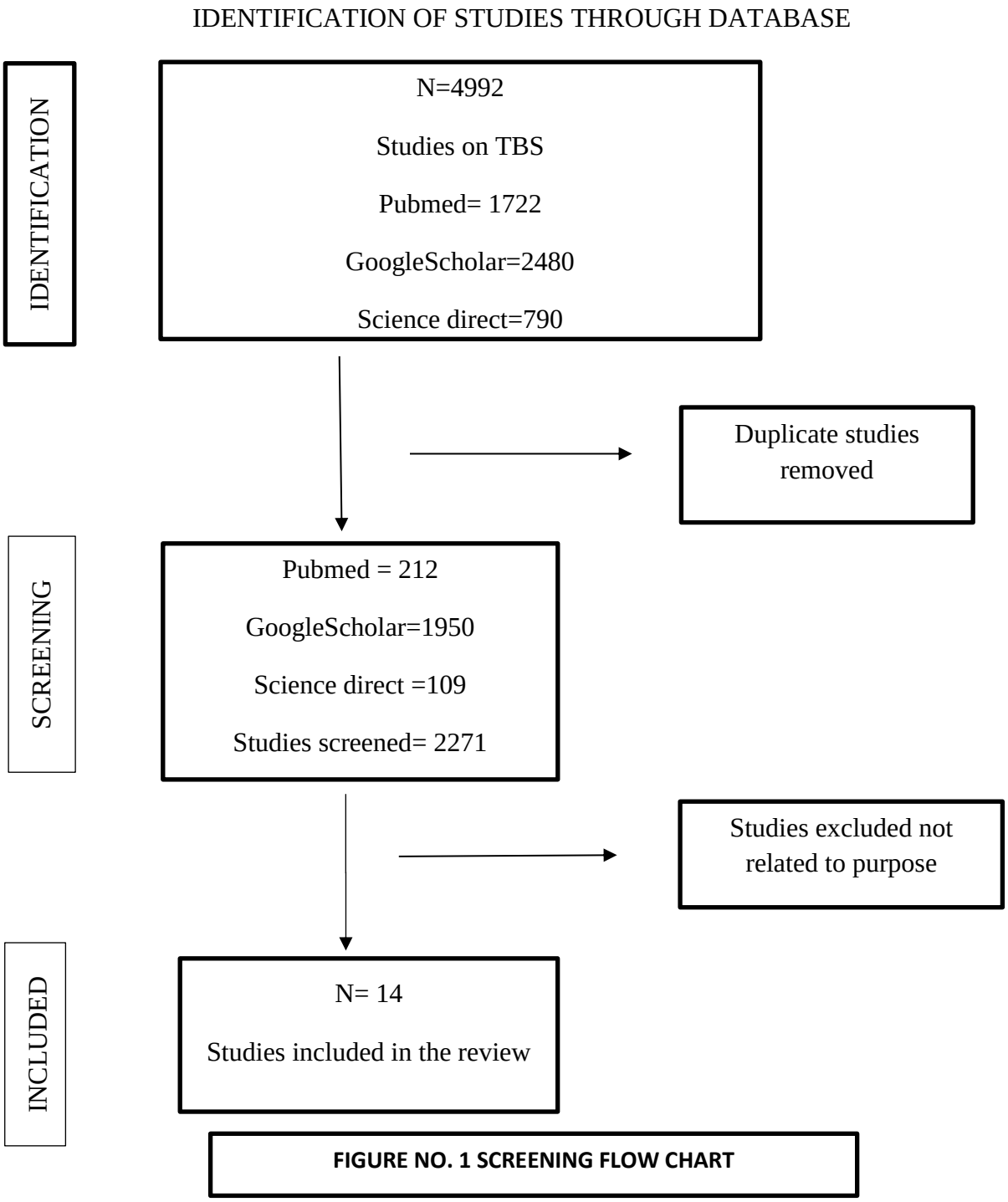

FIGURE NO. 1 SCREENING FLOW CHART

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AUTHOR /YEAR	TITLE OF THE STUDY	METHODS/MEASUREMENTS	RESULT
Xiao Tao et al, 2024	A meta-analysis comparing the effectiveness and safety of repetitive transcranial magnetic stimulation versus theta burst stimulation for treatment-resistant depression	A randomized controlled trial (RCT) was carried out to compare the effectiveness of rTMS and TBS in managing treatment-resistant depression (TRD). The study included data from PubMed, Embase, the Cochrane Library, and Web of Science, covering publications up to July 31, 2024. Five RCTs involving a total of 1,196 participants were analyzed, with 553 patients receiving rTMS and 663 undergoing TBS treatment.	The analysis revealed no significant differences between rTMS and TBS in alleviating depression (SMD = -0.07, 95% CI [-0.19, 0.04]) or anxiety (SMD = -0.02, 95% CI [-0.15, 0.11]). Similarly, there were no notable differences in side effects, such as headaches (OR = 1.00, 95% CI [0.72, 1.40]), nausea (OR = 1.42, 95% CI [0.79, 2.54]), or fatigue (OR = 0.87, 95% CI [0.46, 1.64]). Both rTMS and TBS demonstrate equal effectiveness in reducing symptoms of depression and anxiety while maintaining similar side effect profiles. However, TBS is notably more time-efficient, with sessions completed in just 192 seconds, making it a cost-effective treatment option. These findings highlight TBS as a viable and practical choice for addressing treatment-resistant depression (TRD).
Nathan Bakker et al, 2015	rTMS of the dorsomedial prefrontal cortex for major depression: safety, tolerability, effectiveness, and outcome predictors for 10 Hz versus intermittent theta-burst stimulation	A study aimed to compare the safety, effectiveness, and predictors of outcomes for DMPFC-rTMS using two protocols: a 10 Hz protocol (30 minutes) and an iTBS protocol (6 minutes). This large, naturalistic, retrospective case series involved a chart review of 185 patients experiencing medication-resistant major depressive episodes. These patients underwent 20–30 sessions of DMPFC-rTMS (10 Hz protocol: n = 98; iTBS protocol: n = 87) at a single clinic in Canada between 2011 and 2014.	Before treatment, patients in both 10 Hz and iTBS groups showed similar clinical characteristics, except for iTBS patients being older. A total of 7912 DMPFC-rTMS sessions were conducted (10 Hz: 4274; iTBS: 3638) without any seizures or serious adverse events, and no differences in early discontinuation rates. Response and remission rates, as well as pre- and post-treatment scores, were comparable between the two groups across measures like the Beck Depression Inventory-II and Hamilton Rating Scale for Depression. Mixed-effects modeling

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			also found no significant differences in treatment outcomes over time.
Chaomeng Liu PhD, et al , 2024	Efficacy and Safety of Theta Burst Versus Repetitive Transcranial Magnetic Stimulation for the Treatment of Depression: A Meta-Analysis of Randomized Controlled Trials	This meta-analysis aimed to evaluate and compare the safety and therapeutic efficacy of TBS therapy and standard rTMS in treating depression. It incorporated data from nine randomized controlled trials (RCTs), comprising ten comparable pairs. Using quality-effects (QE) and random-effects (RE) models, the odds ratios for response, remission rates, and adverse events were calculated. Antidepressant effects were assessed through changes in depression scores, expressed as standardized mean differences.	Out of 602 RCTs, nine studies involving 1124 patients (616 treated with TBS and 508 with standard rTMS) were analyzed. No significant difference was observed in response rates between the two methods. TBS demonstrated comparable efficacy and safety to standard rTMS, with the added benefit of shorter daily sessions. This meta-analysis supports further advancement of TBS as a treatment for depression.
Hsuan-Te Chu, 2021	Efficacy and tolerability of theta-burst stimulation for major depression: A systematic review and meta-analysis	This study adhered to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses. A comprehensive literature search was conducted from 1990 to May 24, 2020, and a random-effects meta-analysis was performed, focusing on response and remission rates for depression and dropout rates as key outcome measures.	The analysis included 10 studies—6 randomized controlled trials (RCTs; n = 294) and 4 uncontrolled clinical trials (n = 297). It found an overall response rate effect size of 0.38 (95% CI: 0.29–0.48) and a remission rate effect size of 0.20 (95% CI: 0.13–0.29). TBS demonstrated notable efficacy without major adverse events and was more time- and energy-efficient compared to standard rTMS. The findings confirm that applying TBS to the dorsolateral prefrontal cortex yields significant antidepressant effects with good tolerability.
Christian Plewnia et al, 2014	Treatment of major depression with bilateral theta burst stimulation: A randomized	In this randomized-controlled trial, 32 patients with major depression (MD) underwent six weeks of treatment, consisting of 30 sessions. The treatments included either sequential intermittent, excitatory TBS (iTBS) targeting the left dlPFC combined with continuous, inhibitory TBS (cTBS)	The study found more responders in the cTBS group (n=9) than in the sham-stimulation group (n=4), with an odds ratio of 3.86 (p=0.048). Secondary analysis using the BDI indicated a higher remission rate in the cTBS group (n=6) compared to the sham group (n=1), with an odds

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	controlled pilot trial	targeting the right dlPFC, or bilateral sham stimulation. The primary outcome measure was the treatment response, defined as a Montgomery–Åsberg Depression Rating Scale (MADRS) reduction of ≤50% compared to baseline. Secondary outcomes included response and remission rates assessed using the Hamilton Depression Rating Scale (HAMD) and the Beck Depression Inventory (BDI). .	ratio of 9 (p=0.061). These results provide initial evidence that six weeks of iTBS to the left and cTBS to the right dlPFC is a safe, effective, and superior treatment for MDD when combined with pharmacological and psychotherapeutic approaches.

TABLE NO. 1 CLINICAL EVIDANCES SUPPORTING TBS

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