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## Therapeutic applications and outcomes of transcranial magnetic stimulation: literature review

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### Abstract

**Background.** Transcranial magnetic stimulation (TMS) is a non-invasive brain stimulation method in which a magnetic field generated by alternating electric current induces electrical currents in the cerebral cortex. Therapeutic stimulation most commonly targets the dorsolateral prefrontal cortex (DLPFC), where reduced metabolic activity is associated with depressive symptom severity.

**Aim.** To analyze the therapeutic indications and clinical outcomes of TMS based on currently available literature.

**Materials and methods.** A literature search was performed in the PubMed database between 2025-05-01 and 2025-07-01 using predefined English keywords. A total of 78 articles were identified, of which 32 met the inclusion criteria. Publications from 2014 to 2025, including systematic reviews, randomized clinical trials, reviews, and retrospective studies in adult populations, were included.

**Results.** Available evidence shows that repetitive transcranial magnetic stimulation (rTMS) is a safe and effective treatment for treatment-resistant depression. Stimulation of the left DLPFC significantly reduces depressive symptoms, with clinical response commonly defined as a  $\geq 50\%$  symptom reduction. Approximately 60% of patients with suicidal ideation demonstrated improvement after treatment. In bipolar disorder, rTMS increased the probability of clinical response compared with placebo. In schizophrenia, low-frequency rTMS and continuous theta-burst stimulation (cTBS) reduced auditory hallucinations and improved negative symptoms.

**Conclusions.** TMS is an effective adjunctive treatment for treatment-resistant depression and shows promising benefits in bipolar disorder and schizophrenia, although further standardized studies are needed.

**Keywords:** transcranial magnetic stimulation, repetitive transcranial magnetic stimulation, theta burst stimulation, continuous theta burst stimulation, intermittent theta burst stimulation, dorsolateral prefrontal cortex, electroencephalogram, Hamilton Depression Rating Scale.

## 1. Introduction

TMS began to be applied for therapeutic purposes in 1985, when the first modern TMS device was invented [1]. It is a non-invasive method of brain stimulation in which specific cortical regions are stimulated by electrical impulses, thereby modulating neuronal activity. The mechanism of action of TMS is based on a magnetic field generated by alternating electric current, which induces the flow of electrical impulses. During electrical stimulation, current flows between two electrodes, while short, high-current pulses are generated in a magnetic coil, thereby creating a magnetic field. The magnetic impulse is of very high energy and typically lasts approximately 100  $\mu$ s. The magnetic coil plays an important role in generating and maintaining the effectiveness of the propagating impulse [2]. By selecting the appropriate position of the magnetic coil, impulses are directed toward the left dorsolateral prefrontal cortex (DLPFC). This region is associated with the pathogenesis of mood disorders [3]. Activated brain cells release neurotransmitters such as serotonin, norepinephrine, and dopamine. Thus, it is believed that during the TMS process, neurotransmitter imbalance is restored, the cerebral cortex is activated after the first stimulation procedure, and positive results become evident after several weeks [4].

The duration of the therapeutic procedure and the frequency of impulses are selected individually, taking into account the indication for TMS and the specific application algorithm. Several types of TMS are used in treatment, differing in impulse characteristics and frequency. Repetitive transcranial magnetic stimulation (rTMS) is a form of TMS in which the cerebral cortex is stimulated with repeated magnetic pulses to modulate neuronal activity. Low-frequency rTMS (1 Hz or less) is used to achieve cortical inhibition,

whereas high frequencies (5–20 Hz) exert an excitatory effect by increasing neuronal activity in the cortex [5]. In some cases, a shorter rTMS method known as theta-burst stimulation (TBS) is applied. During this procedure, impulses consist of three 50 Hz triplets repeated at a frequency of 5 Hz [6]. TBS may be continuous continuous theta-burst stimulation (cTBS) or intermittent theta-burst stimulation (iTBS). TBS is based on two main principles: repeated stimulation over a short period produces an effect no inferior to rTMS in controlling depressive symptoms, and intensively scheduled sessions have long-term efficacy [7]. The duration of a TMS treatment course may last several weeks, with sessions most commonly conducted 5 days per week, each lasting approximately 20–40 minutes [8].

During the TMS procedure, the patient's and the magnetic coil's positions are selected, and stimulation parameters are determined. During the procedure, the patient sits in a reclining chair with back and head support, aiming to achieve the most comfortable body position possible. Hearing protection is often used to protect against sounds generated by stimulation. To avoid unnecessary head movements that may reduce treatment accuracy, the patient's head is stabilized during stimulation. The device generating magnetic impulses is placed close to the patient's head, and the coil is positioned directly over the individually determined stimulation area on the scalp. Prior to stimulation, the individual intensity of magnetic impulses is determined by establishing the patient's individual "motor threshold" – the lowest level of magnetic stimulation that induces a slight contraction of the small muscles of the hand or fingers. During the course of treatment, the dose is usually increased from 80% to 120% of the patient's individual motor threshold. During stimulation, the patient may

experience mild tingling or vibration in the head area, as well as movements of the fingers, jaw, or eyebrows. After the procedure, the patient may return to daily activities, and no special precautionary measures are required [9]. The main advantages of TMS are that the procedure is non-invasive, does not require anesthesia, has no systemic side effects, and is safe and effective. In addition, TMS does not reduce alertness and does not require hospitalization.

## 2. Materials and methods

The search for articles was conducted in the PubMed database during the period from 2025-05-01 to 2025-07-01. The following English keywords were used for the search: transcranial magnetic stimulation, repetitive transcranial magnetic stimulation, theta-burst stimulation, intermittent theta-burst stimulation, continuous theta-burst stimulation, dorsolateral prefrontal cortex, treatment-resistant depression, beam F3 method, 5.5 cm rule, application of TMS in the treatment of schizophrenia, application of TMS in the treatment of bipolar disorder.

Using the keywords and their combinations, 78 articles were identified. A total of 32 scientific articles meeting the inclusion criteria were included in the review. Sources not older than 11 years, published between 2014 and 2025, were included in the review. Systematic reviews with or without meta-analysis, randomized clinical trials, reviews, and retrospective studies corresponding to the topic and examining the application of TMS in the adult population were selected for analysis. Sources older than 11 years, written in languages other than English, duplicated, or unavailable in full-text format were excluded from the review.

## 3. Results

### 3.1 TMS in the treatment of depression

First-line evidence-based methods for the treatment of depression are psychopharmacotherapy and psychotherapy; however, in cases of treatment-resistant depression, these methods alone are often insufficient. Approximately 30% of patients may be diagnosed with treatment-resistant depression – when no clinical improvement is observed despite the use of at least two antidepressants at adequate doses for a sufficient duration [9]. In cases of treatment-resistant depression, second-line treatment methods such as TMS become particularly important.

The use of rTMS in the left DLPFC region is an evidence-based method for the treatment of resistant depression. It is known that patients with depression exhibit lower metabolic activity of gray matter in the left DLPFC region [10]. From this, it is inferred that an imbalance between the left and right prefrontal cortex may be associated with the pathophysiology of depression. Most commonly, 10 Hz stimulation is applied in such patients [11]. To achieve clinical remission and a favorable long-term clinical response, at least 6–8 sessions are required. Moreover, neurophysiological evidence suggests that a greater effect of rTMS on cortical excitability is achieved if the second rTMS session is performed within 24 hours of the first session [12].

Precise selection of the cortical target for stimulation in the DLPFC region has not yet been standardized. Two methods for determining the exact stimulation site have become primary options – the 5.5 cm rule and the Beam F3 method. The 5.5 cm method is older and determines the stimulation site 5.5 cm anterior to the motor cortex (M1) region from the point that elicits movement of both of the patient's hand fingers. The Beam F3 method is anatomically based, with electrode

positioning determined using the international 10–10 electroencephalography (EEG) coordinate system. To maximize accurate localization of the stimulation target, neuronavigation based on individual neuroimaging data is increasingly applied, allowing more precise positioning of the magnetic coil and increasing treatment effectiveness compared to standard anatomical landmarks [13]. According to analyses, neuronavigation is the most accurate method; the Beam F3 method demonstrates greater accuracy compared to the 5.5 cm rule; however, no significant clinical difference in depression symptom relief has been observed between these methods [14,15].

In investigating the effect of rTMS in reducing the severity of depressive symptoms, a retrospective study assessed symptom reduction and remission depending on coil position during the procedure. The authors reported that dysphoric symptoms (depressed mood, reduced interest, suicidality) improved more when the stimulation target was directed toward the left DLPFC, whereas somatic symptoms (insomnia, decreased libido, irritability) were most effectively influenced by stimulation of the left dorsomedial prefrontal cortex (DMPFC) [16]. According to recent studies, overall improvement in depressive symptoms indicates that, despite highly precise focal cortical stimulation, rTMS stimulates broad neuronal networks in the brain and exerts a positive effect on most depressive symptoms [17].

Standard rTMS may also be beneficial for patients with depression who are at risk of suicide. A retrospective cohort study published in 2025 analyzed the application of bilateral rTMS in the DLPFC region in individuals with depression experiencing suicidal ideation and anxiety symptoms. During the study, patients received 30 rTMS sessions, and suicidal

ideation was assessed using the third item of the Hamilton Depression Rating Scale (HDRS). After treatment, suicidal symptomatology was reduced in approximately 60% of patients, and significant reductions in depressive and anxiety symptoms were observed [18].

A newer TBS methodology is increasingly applied in the treatment of depression. The literature frequently compares two main neuromodulation methods for treating antidepressant-resistant depression: high-frequency rTMS (10 Hz) and intermittent theta-burst stimulation (iTBS, 50 Hz). According to analyses, the effectiveness of both methods in reducing depressive symptoms and achieving remission is similar. However, iTBS has a greater practical advantage – a significantly shorter stimulation duration of only 192 seconds [19–21].

### 3.2 TMS in the treatment of bipolar disorder

Bipolar disorder is characterized by alternating episodes of mania and depression. Depressive symptoms occur in 70–80% of symptomatic bipolar disorder episodes and result in significant impairment in daily functioning. As in the treatment of depression, psychopharmacotherapy and psychotherapy are first-line treatment methods; however, in not all clinical cases are these methods effective in achieving regression of psychopathological symptoms [22]. TMS in the treatment of bipolar disorder may be an effective method, particularly during depressive episodes. In the literature, the response rate to rTMS in bipolar disorder treatment reaches approximately 40–50% [23].

During a depressive episode, functional, structural, and metabolic disturbances are observed in certain brain regions: hyperactivity of limbic regions (amygdala, hippocampus) and decreased functional

activity in prefrontal areas (DLPFC, anterior cingulate cortex) [24]. These regions are associated with emotion regulation, motivation, and self-control. According to neuroimaging data, TMS application is associated with increased activity in the anterior cingulate and prefrontal cortices responsible for mood regulation [25].

A systematic meta-analysis published in 2021 evaluated the efficacy of rTMS in treating depressive episodes of bipolar disorder. Clinical response was defined as a  $\geq 50\%$  reduction in depressive symptoms from baseline according to a depression rating scale. Analysis of 14 randomized controlled trials revealed that rTMS increased the likelihood of clinical response by 2.5 times compared with the placebo group. The study emphasized that the most significant clinical effect is achieved by stimulating the left DLPFC using high-frequency rTMS [26].

On the other hand, scientific literature indicates that the effect of TMS in the treatment of bipolar disorder remains limited due to the small number of studies, small sample sizes, and heterogeneity of control groups. More comprehensive and detailed studies are required to demonstrate the efficacy of rTMS in the treatment of this disorder [27].

### 3.3 TMS in the treatment of schizophrenia

In approximately one-third of patients with schizophrenia, symptom control with conventional antipsychotic medications is ineffective [28]. Treatment-resistant schizophrenia is defined as the failure to achieve symptom remission after the use of two antipsychotic medications for a sufficient duration (approximately 6–8 weeks) at optimal doses. In the literature, the benefit of TMS in the treatment of treatment-resistant schizophrenia is associated with

improved control of persistent auditory hallucinations and improvement of negative symptoms [29,30].

Auditory hallucinations are associated with increased activity in the left temporoparietal region, the activity of which is targeted for reduction during TMS treatment. According to studies, low-frequency rTMS (1 Hz) is most commonly used in treatment. It has been established that this frequency may help reduce neural activity and the intensity of hallucinations [31]. Continuous theta-burst stimulation (cTBS) may also be used, during which TBS is delivered continuously for approximately 20–40 seconds. When comparing the therapeutic effects of rTMS and cTBS in the treatment of auditory hallucinations, the literature emphasizes the superiority of the cTBS method [32]. In the literature, rTMS is considered a promising adjunctive treatment method for patients experiencing medication-resistant auditory (verbal) hallucinations. According to recent randomized clinical trials, this method may significantly reduce the intensity and frequency of hallucinations compared with placebo stimulation, and the effect may persist during the follow-up period [33].

Negative symptoms – such as low motivation and emotional withdrawal – are often insufficiently corrected with conventional antipsychotic medications. To address negative symptoms, the left DLPFC is most commonly stimulated, as its insufficient activity is associated with the pathophysiology of negative symptoms. High-frequency TMS stimulation (10 Hz or higher) is used to increase brain activity and alleviate negative symptoms. According to research data, patients undergoing TMS report greater motivation and improved cognitive and social functioning [33].

#### 4. Discussion

This literature review underscores the growing role of transcranial magnetic stimulation as a clinically relevant neuromodulation approach in major psychiatric disorders, particularly in patients who do not respond adequately to standard treatments. In treatment-resistant depression, stimulation of the left dorsolateral prefrontal cortex is the most consistently supported target, in line with neurobiological models emphasizing functional imbalance within prefrontal–limbic networks. Comparable efficacy between high-frequency rTMS and intermittent theta-burst stimulation suggests that shorter stimulation protocols may improve feasibility without compromising therapeutic outcomes. Emerging evidence also indicates a potential beneficial effect on suicidality, which is especially relevant for high-risk patient populations.

In bipolar disorder and schizophrenia, therapeutic effects of TMS appear to depend on symptom-specific targeting of dysfunctional neural circuits. Depressive episodes in bipolar disorder may benefit from excitatory prefrontal stimulation, although current evidence is limited by small sample sizes and methodological heterogeneity. In schizophrenia, inhibitory stimulation of temporoparietal regions is associated with reductions in auditory hallucinations, while excitatory prefrontal stimulation may alleviate negative symptoms. Despite promising findings, variability in study design, stimulation parameters, and outcome measures restricts the generalizability of results. Overall, TMS emerges as a safe and promising adjunctive treatment for treatment-resistant depression, with potential applications in bipolar disorder and schizophrenia that warrant further large-scale, standardized clinical trials.

#### 5. Conclusions

Transcranial magnetic stimulation is a safe and clinically effective adjunctive treatment, particularly for treatment-resistant depression. The strongest evidence supports stimulation of the left dorsolateral prefrontal cortex using repetitive transcranial magnetic stimulation or intermittent theta-burst stimulation, both of which significantly reduce depressive symptoms.

In bipolar disorder, TMS demonstrates beneficial effects mainly during depressive episodes, although current evidence remains limited by small and heterogeneous study samples. In schizophrenia, symptom-specific stimulation protocols may reduce auditory hallucinations and improve negative symptoms.

Overall, TMS represents a promising neuromodulation strategy in psychiatry; however, larger, methodologically standardized studies are required to optimize stimulation targets, treatment parameters, and long-term outcome assessment.

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