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Potential Epigenetic Mechanisms of High-Frequency rTMS in the Treatment of Major Depression: A Brief Report of Current Evidence

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ABSTRACT

Introduction: Repetitive Transcranial Magnetic Stimulation (rTMS) is an FDA-approved, non-invasive neuromodulation technique with clinically supported efficacy in the management of treatment-resistant major depressive disorder (TRD). Although the clinical effectiveness of high-frequency rTMS applied to the left dorsolateral prefrontal cortex (DLPFC) is well established, the molecular mechanisms underlying its long-term therapeutic effects remain incompletely understood. The aim of this brief report is to examine the possible epigenetic modifications (DNA methylation, histone modifications, microRNA) associated with the antidepressant effects of rTMS in light of current literature, and to evaluate the dose-response relationship that may affect treatment response within the framework of homeostatic plasticity.

Methods: A summary of current literature from the PubMed, Web of Science, and Google Scholar databases is presented using the keywords "rTMS," "major depression," "epigenetics," "histone modifications," "DNA methylation," "miRNA," and "homeostatic plasticity." Clinical and preclinical studies specifically investigating the molecular effects of rTMS on synaptic plasticity were included.

Results: The reviewed studies suggest that rTMS may not merely provide transient electrical stimulation but may also operate through an "epigenetic regulatory" mechanism capable of permanently altering neuronal gene expression. In preclinical studies, changes in histone acetylation (e.g., regulation of CDK5 and PSD-95) and specific microRNAs (e.g., miR-146a-5p) have been observed to modulate synaptic plasticity. Furthermore, it has been proposed that the dose-response relationship of rTMS is non-linear; excessive stimulation may activate "homeostatic plasticity" mechanisms, thereby reducing synaptic sensitivity.

Discussion: Current findings indicate that rTMS may exert an antidepressant effect by reorganizing synaptic plasticity through epigenetic modifications. Enhancing treatment efficacy depends on optimizing the dosage by considering homeostatic balances and integrating epigenetic biomarkers capable of predicting treatment response into clinical practice. Future personalized treatment protocols should be designed based on these molecular and neurophysiological insights.

Keywords: DNA methylation, epigenetics, histone modifications, major depressive disorder, neuroplasticity, rTMS

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INTRODUCTION

Repetitive Transcranial Magnetic Stimulation (rTMS) is a non-invasive neuromodulation method that modulates neuronal activity by delivering repetitive magnetic pulses externally to the cerebral cortex. The application of high-frequency (≥5 Hz) rTMS specifically to the left dorsolateral prefrontal cortex (DLPFC) received FDA approval in 2008 due to its ability to provide significant clinical improvements in patients with treatment-resistant major depression (1). In standard clinical practice, the left DLPFC is typically targeted for 4 to 6 weeks with a frequency of 10 Hz, an intensity of 100–120% of the motor threshold, and approximately 3000 pulses per day. With this protocol, a response of more than 50% can be achieved in about half of the patients, and remission is achieved in one-third (2).

Highlights

- **rTMS modulates gene expression via DNA methylation and histone modifications.**
- **MicroRNA changes are associated with rTMS-related neuroplastic effects.**
- **Sex-based epigenetic differences should be considered in personalizing rTMS.**
- **BDNF promoter methylation may play a key role in rTMS.**
- **The proxy validity of peripheral biomarkers limits clinical interpretation.**

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The non-invasive nature of rTMS and its lower systemic side-effect profile compared to pharmacotherapy make it a significant alternative to electroconvulsive therapy (ECT) in resistant cases (3,4). However, the molecular basis of the long-term neurobiological effects of rTMS remains an active topic of research. While it has been suggested that acute effects may modulate synaptic plasticity via mechanisms akin to "Long-Term Potentiation" (LTP) and may increase the release of brain-derived neurotrophic factor (BDNF), the cellular mechanisms ensuring the persistence of these effects are complex. Current data suggest that epigenetic mechanisms (DNA methylation, histone modifications, and microRNAs), which regulate gene expression without altering the DNA sequence, may play a critical role in the brain's long-term adaptive response to rTMS treatment (1,5,6).

METHODS

Ethical Statement

This brief report summarizes preclinical and clinical studies examining the effects of high-frequency repetitive transcranial magnetic stimulation (rTMS) on epigenetic mechanisms in the treatment of major depression. Therefore, ethics committee approval is not required, and an ethics committee exemption certificate has been obtained (Decision no: 61351342/020-12. Date: 03.02.2026).

Literature Search

A literature search was conducted across the PubMed, Web of Science, and Google Scholar databases, focusing on studies published between January 2000 and January 2026, using the keywords "rTMS," "major depression," "epigenetics," "DNA methylation," "histone modification," "microRNA," and "neuroplasticity." Studies were evaluated based on their relevance to the topic, methodological adequacy, and publication quality, and included studies were selected based on these criteria. Due to the lack of a sufficient number of randomized controlled clinical trials and homogeneous data in the current literature, a systematic review or meta-analysis could not be performed; instead, existing preclinical and clinical findings were synthesized qualitatively.

To observe the hierarchy of evidence, the findings were classified into two main categories: "preclinical" and "clinical." Studies were examined according to the epigenetic mechanism involved; namely, DNA methylation, histone modifications, and microRNA regulation. Finally, the dose-response relationship in rTMS applications and the concepts of homeostatic plasticity were evaluated within the context of neurobiological mechanisms.

RESULTS

A summary of selected studies on the effects of rTMS on epigenetic mechanisms is presented in Table 1.

DNA Methylation

DNA methylation is a fundamental mechanism that generally represses gene expression by adding a methyl group to CpG (cytosine-phosphate-guanine) dinucleotides in gene promoter regions (7,8).

Preclinical studies

Animal models and *in vitro* cell lines provide important evidence regarding the potential of rTMS for epigenetic regulation and neuroplasticity, suggesting that rTMS may not only induce transient electrical activity but also act as a regulator of neuronal gene expression (9,10). Recent studies on human neuron-like cell lines have indicated that rTMS application can directly trigger synaptic plasticity mechanisms at the cellular level (9). In animal models involving rodents exposed to chronic stress, it has been shown that stress represses gene expression in association with increased DNA methylation in the promoter region of the BDNF gene and changes in chromatin structure in the hippocampus (10). It is proposed that interventions such as rTMS in these same models increase BDNF expression and markers of synaptic plasticity; this effect may be related to epigenetic mechanisms involving DNMT/HDAC enzyme activities and chromatin remodeling (10).

Epigenetic regulation of the BDNF gene, in particular, has become a critical focal point in understanding the response to pharmacological and stimulation therapies (11). Preclinical studies have shown that the BDNF promoter contains multiple exons and that stress and antidepressant interventions can preferentially alter the methylation profile in specific regions, most notably exon IV (10,11). However, these findings are largely derived from animal models, and whether similar exon-specific methylation changes are observed in human studies remains a subject of debate. Possible reasons for these discrepancies include species differences, tissue accessibility (using peripheral blood instead of brain tissue), and heterogeneity in rTMS protocols (12).

These findings suggest that the restructuring of the epigenetic order disrupted by stress may play a role in the antidepressant effect of rTMS; however, direct effects on BDNF promoter methylation require further studies.

Clinical studies

In human studies, methylation profiles in peripheral blood samples before and after rTMS have been examined. In an epigenetic study conducted on patients with treatment-resistant depression, genome-wide DNA methylation profiles were analyzed prior to 36 sessions of rTMS (7). The study identified differentially methylated regions (DMRs) in genes related to neurodevelopment (HOXA4, HOXA5), immune response (RUNX1), and synaptic function (EFNB1) between responders and non-responders to treatment. These findings suggest that pretreatment methylation profiles may hold biomarker potential in predicting the rTMS response (7).

Histone Modification

Another regulator of chromatin structure is the acetylation and methylation of histone proteins. These epigenetic mechanisms loosen or tighten the chromatin structure, allowing the activation or repression of gene expression at the transcriptional level (13).

Preclinical studies

Animal models clearly demonstrate the effects of rTMS on histone modifications. It has been shown that 15 Hz rTMS applied to the mouse frontal cortex increases gene expression by increasing histone H3 acetylation at the promoter of the CDK5 gene, which plays a role in synaptic plasticity; conversely, it suppresses the PSD-95 gene by decreasing H4 acetylation (1). Importantly, the observation that these effects of rTMS disappear when a histone deacetylase (HDAC) inhibitor is administered indicates that specific histone modifications may play a determining role in the efficacy of the treatment (1). Similarly, in a chronic stress model, it has been reported that 5 Hz rTMS increases histone H3K9 trimethylation (a repressive mark) and H2B acetylation in the frontal cortex and hippocampus, and these changes correlate with a reduction in depressive behaviors (6). These results demonstrate that rTMS modulates gene transcription in a multifaceted manner, in both the activation and repression directions (1).

Table 1. Summary of major preclinical and clinical studies examining the epigenetic effects of high-frequency rTMS in major depression

Author-year	Study type	Sample / model	rTMS protocol	Investigated epigenetic mechanism	Main findings	Significance for the study
Thomson et al. (2020)	Pre-clinical	In vitro (human neuron-like cell line)	General rTMS stimulation	DNA methylation / Synaptic Plasticity	rTMS directly triggers synaptic plasticity mechanisms at the cellular level.	Provides foundational mechanistic evidence that rTMS acts as a gene expression regulator at the cellular level, not merely electrically.
Tsankova et al. (2006)	Pre-clinical	Chronic stress rodent model	General antidepressant intervention	DNA methylation (BDNF promoter region)	Modulates stress-induced methylation in the hippocampus, enabling chromatin remodeling via DNMT/HDAC activities.	Explains the role of rTMS in reconstructing the epigenetic order disrupted by stress and its effect on BDNF.
Dahrendorff et al. (2025)	Clinical	TRD patients (peripheral blood)	36 sessions of rTMS	Genome-wide DNA methylation (DMR)	Differentially methylated regions were detected in HOXA4, HOXA5, RUNX1, and EFNB1 genes in treatment responders.	Demonstrates at the clinical level the potential of peripheral DNA methylation profiles to serve as an "epigenetic biomarker" predicting rTMS response.
Etiévant et al. (2015)	Pre-clinical	Mouse frontal cortex	15 Hz rTMS	Histone modification (H3 and H4 acetylation)	Increases H3 acetylation at the CDK5 gene while decreasing H4 acetylation at the PSD-95 gene. The effect disappears with an HDAC inhibitor.	Shows that rTMS can modulate gene transcription both towards activation and repression via chromatin remodeling processes.
Meneses-San Juan et al. (2023)	Pre-clinical	Chronic stress rodent model	5 Hz rTMS	Histone modification (H3K9 trimethylation, H2B acetylation)	Reduces depressive behaviors by increasing specific histone modifications in the hippocampus and frontal cortex.	Confirms that rTMS can restore neuro-epigenetic balance by reversing stress-induced maladaptive epigenetic signatures.
Hobara (2010) & Lopez (2013)	Clinical	Major depression patients (PBMC)	General antidepressant treatment	Histone modification (HDAC, H3K27me3)	Impaired HDAC expression observed in patients; clinical response correlated with decreased H3K27me3 and increased BDNF.	Establishes the clinical counterpart (translational bridge) in humans of pre-clinical rTMS-histone data.
Guo et al. (2014)	Pre-clinical	Focal cerebral ischemia rat model	10 Hz rTMS	miRNA modulation (miR-25)	Suppresses p57 protein by increasing miR-25 in ischemic tissue, promoting neural stem cell proliferation and neurogenesis.	Proves that magnetic stimulation supports neural stem cell proliferation and structural plasticity via the miR-25 pathway.
Valiuliene et al. (2023)	Clinical	TRD patients (peripheral blood)	rTMS treatment	miRNA modulation (miR-146a-5p, miR-16-5p, miR-93-5p)	Anti-inflammatory miR-146a-5p increased in responders; other miRNAs showed positive correlation with symptom reduction.	Indicates that the anti-inflammatory effects of rTMS are regulated at the translational level via miRNA modulation.

BDNF: brain-derived neurotrophic factor; CDK5: cyclin-dependent kinase 5; DNA: deoxyribonucleic acid; EFNB1: ephrin-B1 gene; H2Bac: histone H2B acetylation; H3: histone H3; H3K9me3: trimethylation at the 9th lysine residue of histone H3; H4: histone H4; HDAC: histone deacetylase; HOXA4/HOXA5: homeobox A4/A5 genes; Hz: hertz; LTP: long-term potentiation; miRNA: micro ribonucleic acid; PSD-95: postsynaptic density protein 95; rTMS: repetitive transcranial magnetic stimulation; RUNX1: runt-related transcription factor 1; TRD: treatment-resistant depression.

Clinical studies

In vivo clinical studies investigating the direct effects of rTMS application on histone modifications in humans are still in their infancy compared to the DNA methylation literature. Due to the methodological limitations of measuring chromatin dynamics in the living human brain, current data rely mostly on clinical depression studies conducted on peripheral blood mononuclear cells (PBMCs). Studies on human patients have shown that major depressive disorder is associated with impaired histone deacetylase (HDAC) expression profiles in PBMCs (14). Furthermore, it has been demonstrated that a positive clinical response to treatment is directly correlated with a decrease in histone H3 lysine 27 trimethylation (H3K27me3) and an increase in BDNF levels in peripheral blood (15).

When the HDAC modulation and specific histone acetylation/methylation findings observed in preclinical rTMS models are synthesized with these clinical data, it emerges as a strong hypothesis that rTMS may exert systemic antidepressant effects in humans through similar chromatin remodeling mechanisms. However, specific human studies are needed to directly validate these cellular epigenetic adaptations as peripheral biomarkers in patients receiving rTMS.

MicroRNAs (miRNA)

miRNAs, which are small non-coding RNA molecules, fine-tune gene expression at the post-transcriptional level by repressing mRNA translation or triggering mRNA degradation (16).

Preclinical studies

It has been shown in animal models that rTMS significantly alters miRNA expression profiles during neural recovery and neurogenesis processes. For example, in rat models of focal cerebral ischemia, 10 Hz rTMS has been found to significantly increase miR-25 expression in the ischemic brain tissue (17). It has been reported that this increase in miR-25 suppresses the p57 protein, which arrests the cell cycle, thereby promoting neural stem cell proliferation and neurogenesis (17). These findings support the notion that the neuroplastic effects of rTMS may occur partially through miRNA-mediated pathways. Although the stem cell proliferation data obtained in the ischemia model are thought to parallel mechanisms that reverse the "decreased hippocampal neurogenesis" picture seen in major depression, the direct equivalent of these miRNA pathways specifically in depression models remains an active topic of research.

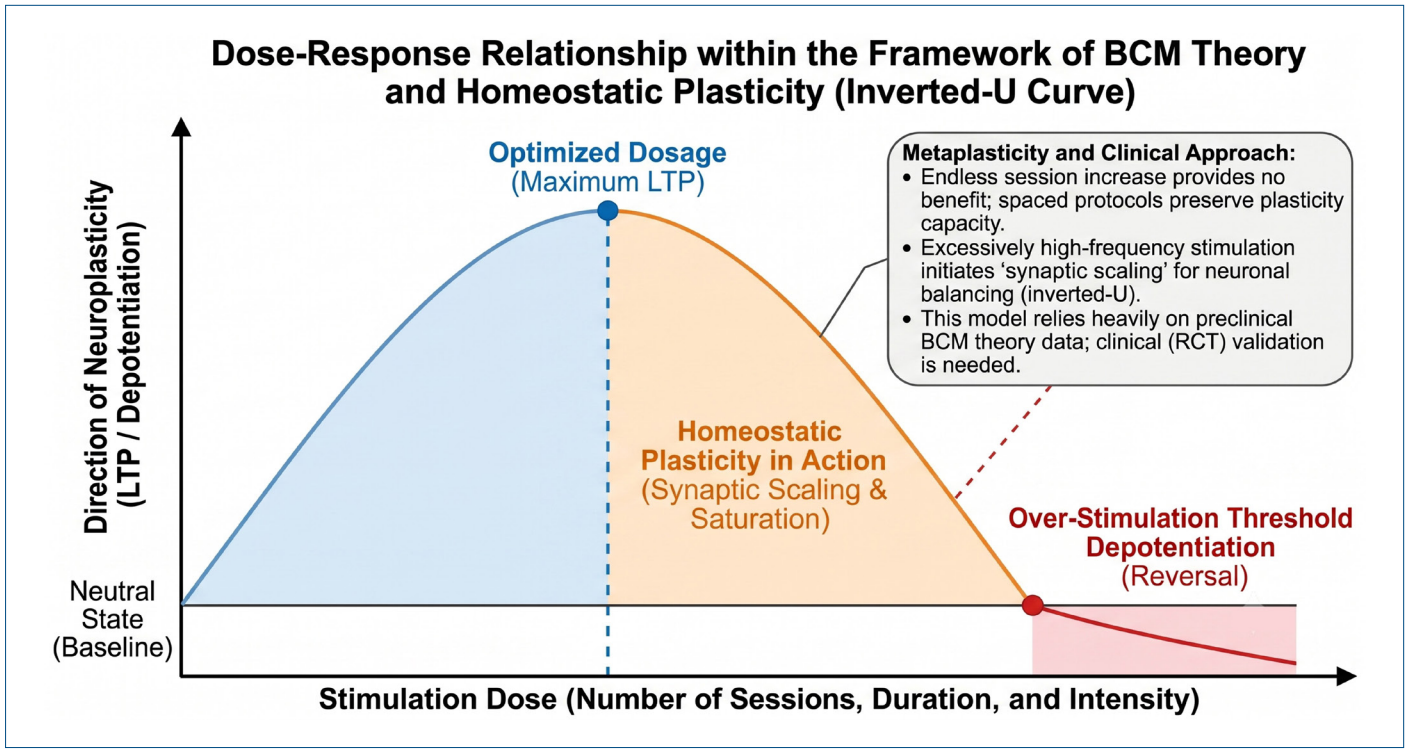

Figure 1. Inverted-U dose-response curve in neuromodulation [the effect of stimulation dose (sessions/intensity) on neuroplasticity, based on the BCM theory and homeostatic plasticity (synaptic scaling) mechanisms. An optimized dose yields maximum LTP, whereas overstimulation leads to saturation and ultimately depotentiation (synaptic weakening). To preserve metaplasticity, intermittent protocols are essential rather than limitless session increases (19)].

Clinical studies

In human studies, the effects of rTMS treatment on miRNA profiles are investigated specifically in patients with treatment-resistant depression (TRD). A recent study on TRD patients found that miR-146a-5p levels, known for their anti-inflammatory effects, significantly increased in the group showing clinical improvement (responders to treatment) following rTMS therapy (16). Furthermore, the same study reported that the levels of miR-16-5p and miR-93-5p measured in peripheral blood showed a positive correlation with the reduction in depressive symptoms (16). These data indicate that specific miRNAs (especially miR-146a-5p) carry significant biomarker potential in predicting the clinical success of rTMS treatment and explaining its therapeutic mechanism of action.

When evaluated broadly, findings obtained from preclinical animal models and clinical human studies, despite having different levels of evidence, present a consistent and mutually supportive neuroepigenetic pattern. The primary reason for this translational consistency is that epigenetic regulatory principles such as chromatin remodeling, DNA methylation, and histone modification are highly conserved evolutionarily and operate on the same molecular principles in both rodent and human neurobiology (13). Especially with epigenetics gaining critical importance in elucidating the etiopathogenesis and treatment mechanisms of psychiatric disorders in recent years, it is increasingly recognized that animal models—in which cellular mechanisms can be understood—and human studies targeting therapeutic biomarkers hold complementary clinical value (8).

Dose-Response Relationship and Long-Term Protocols

The efficacy of rTMS treatment is closely related to parameters such as frequency, intensity, and the number of sessions, but this relationship is not always linear (18).

Stimulation Intensity

Another animal study demonstrated that LTP formation in the rat hippocampus follows an "inverted-U" curve according to stimulation intensity (18). While maximum plasticity is achieved at moderate intensity (100% motor threshold), efficacy decreases at very low or very high intensities (above 120%) (Figure 1). This situation can be explained by homeostatic plasticity mechanisms in the brain limiting overstimulation (18).

Homeostatic Plasticity and Dose Optimization

Although increasing the number of sessions in clinical trials is generally associated with a better response, neurophysiological data suggest caution regarding the duration and intensity of stimulation. As stated in a consensus report, when the cerebral cortex is overstimulated, it tends to balance neuronal activity (synaptic scaling) by activating "homeostatic plasticity" mechanisms. In alignment with the Bienenstock-Cooper-Munro (BCM) theory, this situation suggests that continuous and excessively high-frequency stimulation can eventually saturate synaptic strengthening (LTP) or reverse it (depotentiation). For this reason, rather than an endless increase in sessions, intermittent protocols or optimized dosages that manage the brain's plasticity capacity (metaplasticity) may provide biologically more sustainable improvement (19). Nevertheless, the 'inverted-U' type dose-response relationship discussed within the framework of homeostatic plasticity is largely based on preclinical data and neurophysiological theories (such as the BCM theory); more randomized controlled trials are needed to ascertain the exact clinical counterpart of this situation.

DISCUSSION

According to studies, high-frequency rTMS may be considered not just an electrical stimulation, but also an "epigenetic intervention" in the treatment of major depression (5). Current literature indicates that

rTMS can alter the expression of neurotrophic factors like BDNF and synaptic proteins through epigenetic modifications (methylation, histone acetylation, miRNA). These mechanisms may form the biological basis of the clinical improvement (maintenance of remission) that continues even after the end of rTMS treatment (6).

When the obtained findings are evaluated from a holistic perspective, it is thought that rTMS stimulation exerts its effects through complementary epigenetic mechanisms rather than a single pathway in neuronal networks. According to one proposed model; while the rearrangement of chromatin structure via histone modifications may facilitate the expression of neurotrophic factors like BDNF, simultaneously altering miRNA profiles can stabilize synaptic plasticity by fine-tuning this process at the translational level (the conversion of mRNA copies into functional proteins in ribosomes) (1,6,7,16). It is suggested that DNA methylation changes may contribute to the long-term calibration of gene expression in this process (6). The dynamic structure of this multi-layered epigenetic interaction may partially explain why rTMS demonstrates a cumulative antidepressant effect as sessions progress, rather than an instantaneous one.

Clinical Implications and Personalized Treatment

The heterogeneity of the response to treatment is one of the greatest challenges for clinicians. It is thought that epigenetic biomarkers evaluated in peripheral blood before treatment (e.g., specific methylation signatures or miR-146a-5p levels) can be used as a potential tool to predict whether the patient will respond to rTMS (6,15). For example, patients with a high inflammatory burden and suppression of related miRNAs may show resistance to standard rTMS protocols, and rTMS protocols combined with anti-inflammatory strategies may be considered for these patients (20,21).

Furthermore, findings on homeostatic plasticity necessitate the optimization of treatment protocols. Instead of persistently continuing treatment in patients whose clinical response plateaus after 30 sessions, it may be more effective to switch to intermittent maintenance therapies or to develop new protocols based on "metaplasticity" principles (pre-stimulations that increase the brain's plasticity capacity).

Sex Differences

Evidence that major depression and epigenetic variables differ by sex is growing stronger (22,23). It is known that the prevalence of depression in women is approximately twice as high as in men; it has been proposed that this difference is partly shaped through epigenetic interactions with gonadal hormones (e.g., the regulatory role of estrogen on DNA methylation enzymes and histone modification profiles) (24). Although the majority of the reviewed rTMS studies did not adequately report on sex balance, it is observed that the proportion of female participants is higher in some clinical samples. How sex-based epigenetic differences might affect the rTMS response has not yet been systematically investigated; however, this knowledge constitutes an important dimension for the design of personalized treatment protocols. It is of great importance for future studies to consider the sex variable as both a biological and a methodological factor.

Proxy Validity of Peripheral Biomarkers

Most of the clinical studies reviewed in this paper measure epigenetic markers from peripheral blood (PBMC, serum). The extent to which peripheral epigenetic markers reflect changes in the central nervous system ("proxy marker validity") is a controversial methodological issue. While some studies suggest that certain DNA methylation and miRNA changes may correlate between the brain and peripheral tissues, this relationship varies significantly across genes and tissues (25). Therefore, interpreting findings obtained from peripheral blood biomarkers as a reflection of epigenetic changes in brain tissue requires a cautious epistemic stance. Postmortem brain tissue studies and emerging neuronal exosome analyses stand out as promising methods to bridge this gap; however, human data in this field are still limited.

Limitations and Future Directions

Current human studies mostly rely on peripheral markers; in vivo imaging of epigenetic changes in brain tissue is not yet possible. It is crucial for future studies to focus on long-term outcome tracking research that monitors how long the protective effect of rTMS lasts and how the epigenetic profile changes in cases of relapse (19,26). Furthermore, systematically investigating the sex variable and exon-specific methylation profiles of the BDNF promoter in human samples stands out as a primary methodological necessity for future personalized protocol studies.

As a result, classical high-frequency rTMS is known to be a reliable and effective tool in the treatment of major depression. However, based on the preclinical and clinical studies examined in this work, it has been concluded that the mechanism of action of rTMS may be closely related to epigenetic changes (DNA methylation, histone modifications, and miRNA regulation) that regulate synaptic plasticity. It is evaluated that enhancing treatment efficacy may depend on optimizing dosage by considering homeostatic balances and integrating epigenetic biomarkers capable of predicting treatment response into clinical practice. Sex-specific epigenetic differences and methodological limitations regarding the proxy validity of peripheral biomarkers constitute priority agenda items for future research. It is hoped that these developments at the intersection of neuroscience and genetics may contribute to the development of more targeted and personalized rTMS protocols for treatment-resistant depression in the future.

Ethics Committee Approval: Ethics committee approval is not required, and an ethics committee exemption certificate has been obtained (Decision no: 61351342/020-12. Date: 03.02.2026).

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REFERENCES

1. Etiévant A, Manta S, Latapy C, Magno LAV, Fecteau S, Beaulieu JM. Repetitive transcranial magnetic stimulation induces long-lasting changes in protein expression and histone acetylation. Sci Rep. 2015;5:16873. [Crossref]
2. Sackeim HA, Aaronson ST, Carpenter LL, Hutton TM, Mina M, Pages K, et al. Clinical outcomes in a large registry of patients with major depressive disorder treated with transcranial magnetic stimulation. J Affect Disord. 2020;277:65–74. [Crossref]
3. Noda Y, Daskalakis ZJ, Ramos C, Blumberger DM. Repetitive transcranial magnetic stimulation to maintain treatment response to electroconvulsive therapy in depression: a case series. Front Psychiatry. 2013;4:73. [Crossref]
4. Ontario Health (Quality). Repetitive transcranial magnetic stimulation for people with treatment-resistant depression: a health technology assessment. Ont Health Technol Assess Ser. 2021;21:1–232.
5. Cirillo G, Di Pino G, Capone F, Ranieri F, Florio L, Todisco V, et al. Neurobiological after-effects of non-invasive brain stimulation. Brain Stimul. 2017;10:1–18. [Crossref]

6. Meneses-San Juan D, Lamas M, Ramírez-Rodríguez GB. Repetitive transcranial magnetic stimulation reduces depressive-like behaviors, modifies dendritic plasticity, and generates global epigenetic changes in the frontal cortex and hippocampus in a rodent model of chronic stress. Cells. 2023;12:2062. [Crossref]
7. Dahrendorff J, Pages K, Currier G, Sarker MH, Graham Z, Louis-Jacques AF, et al. Epigenetic profiles of response to transcranial magnetic stimulation in treatment resistant depression. BMC Med Genomics. 2025;18:181. [Crossref]
8. Schiele MA, Gottschalk MG, Domschke K. The applied implications of epigenetics in anxiety, affective and stress-related disorders -a review and synthesis on psychosocial stress, psychotherapy and prevention. Clin Psychol Rev. 2020;77:101830. [Crossref]
9. Thomson AC, Kenis G, Tielens S, De Graaf TA, Schuhmann T, Rutten BPF, et al. Transcranial magnetic stimulation-induced plasticity mechanisms: TMS-related gene expression and morphology changes in a human neuron-like cell model. Front Mol Neurosci. 2020;13:528396. [Crossref]
10. Tsankova NM, Berton O, Renthal W, Kumar A, Neve RL, Nestler EJ. Sustained hippocampal chromatin regulation in a mouse model of depression and antidepressant action. Nat Neurosci. 2006;9:519–525. [Crossref]
11. Boulle F, van den Hove DLA, Jakob SB, Rutten BP, Hamon M, van Os J, et al. Epigenetic regulation of the BDNF gene: implications for psychiatric disorders. Mol Psychiatry. 2012;17:584–596. [Crossref]
12. Ikegame T, Bundo M, Murata Y, Kasai K, Kato T, Iwamoto K. DNA methylation of the BDNF gene and its relevance to psychiatric disorders. J Hum Genet. 2013;58:434–438. [Crossref]
13. Schiele MA, Domschke K. Epigenetics at the crossroads between genes, environment and resilience in anxiety disorders. Genes Brain Behav. 2018;17:e12423. [Crossref]
14. Hobara T, Uchida S, Otsuki K, Matsubara T, Funato H, Matsuo K, et al. Altered gene expression of histone deacetylases in mood disorder patients. J Psychiatr Res. 2010;44:263–270. [Crossref]
15. Lopez JP, Mamdani F, Labonte B, Beaulieu MM, Yang JP, Berlim MT, et al. Epigenetic regulation of BDNF expression according to antidepressant response. Mol Psychiatry. 2013;18:398–399. [Crossref]
16. Valiuliene G, Valiulis V, Zentelyte A, Dapsys K, Germanavicius A, Navakauskiene R. Anti-neuroinflammatory microRNA-146a-5p as a potential biomarker for neuronavigation-guided rTMS therapy success in medication resistant depression disorder. Biomed Pharmacother. 2023;166:115313. [Crossref]
17. Guo F, Han X, Zhang J, Zhao X, Lou J, Chen H, et al. Repetitive transcranial magnetic stimulation promotes neural stem cell proliferation via the regulation of MiR-25 in a rat model of focal cerebral ischemia. PLoS One. 2014;9:e109267. [Crossref]
18. Chen S, He X, Wei X, Huang J, Zhang J. After-effects of repetitive transcranial magnetic stimulation with parameter dependence on long-term potentiation-like plasticity and object recognition memory in rats. Front Neurosci. 2023;17:1144480. [Crossref]
19. Karabanov A, Ziemann U, Hamada M, George MS, Quartarone A, Classen J, et al. Consensus paper: probing homeostatic plasticity of human cortex with non-invasive transcranial brain stimulation. Brain Stimul. 2015;8:442–454. [Crossref]
20. Rajkumar RP. Immune-inflammatory markers of response to repetitive transcranial magnetic stimulation in depression: a scoping review. Asian J Psychiatr. 2024;91:103852. [Crossref]
21. Pedraz-Petrozzi B, Insan S, Spangemacher M, Reinwald J, Lamadé EK, Gilles M, et al. Association between rTMS-induced changes in inflammatory markers and improvement in psychiatric diseases: a systematic review. Ann Gen Psychiatry. 2024;23:31. [Crossref]
22. Bangasser DA, Valentino RJ. Sex differences in stress-related psychiatric disorders: neurobiological perspectives. Front Neuroendocrinol. 2014;35:303–319. [Crossref]
23. Labonté B, Engmann O, Purushothaman I, Menard C, Wang J, Tan C, et al. Sex-specific transcriptional signatures in human depression. Nat Med. 2017;23:1102–1111. [Crossref]
24. McCarthy MM, Auger AP, Bale TL, De Vries GJ, Dunn GA, Forger NG, et al. The epigenetics of sex differences in the brain. J Neurosci. 2009;29:12815–12823. [Crossref]
25. Nikolova YS, Hariri AR. Can we observe epigenetic effects on human brain function? Trends Cogn Sci. 2015;19:366–373. [Crossref]
26. Rachid F. Maintenance repetitive transcranial magnetic stimulation (rTMS) for relapse prevention in with depression: a review. Psychiatry Res 2018;262:363–372. [Crossref]