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Case Report

rTMS for Recurrent Major Depressive Disorder and Generalized Anxiety Disorder Comorbid with Thalamic Pain Syndrome: A Case Report

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Abstract

This paper examines the utilization of repetitive transcranial magnetic stimulation (rTMS) to treat recurrent Major Depressive Disorder (MDD) and Generalized Anxiety Disorder (GAD) in a patient comorbid with Thalamic Pain Syndrome (TPS), a type of central post-stroke pain. TPS is a consequence of thalamic injury and is characterized by chronic neuropathic pain that is insufficiently responsive to pharmacological treatment. Symptoms of TPS can increase the risk of MDD and GAD, negatively impacting quality of life. Repetitive Transcranial Magnetic Stimulation (rTMS) is an FDA-approved modality for treatment-resistant major depressive disorder (MDD) and has shown promise for off-label treatment of anxiety disorders. Quantitative psychometric questionnaires were administered weekly via PHQ-9 (Patient Health Questionnaire-9) and GAD-7 (Generalized Anxiety Disorder-7), revealing symptom reductions of 95.5% and 88.2%, respectively. An improvement was noted in neuropathic pain symptoms, as indicated by a 10.2% reduction in Neuropathic Pain Scale (NPS) scores. The patient reported improved quality of life, as demonstrated by an increased ability to cope with TPS symptoms. Furthermore, the patient was no longer suicidal after completing 36 rTMS treatments. Further large-scale, randomized, and blinded trials are recommended to validate the efficacy of rTMS as a modality for complex neuropsychiatric and pain-related comorbidities.

Keywords: *Repetitive Transcranial Magnetic Stimulation (rTMS); Dorsolateral Prefrontal Cortex (DLPFC); Neuromodulation; MDD (Major Depressive Disorder); PHQ-9 (Patient Health Questionnaire-9); GAD-7 (Generalized Anxiety Disorder-7 Item Scale); Motor Threshold (MT); Thalamic Pain Syndrome (TPS); Neuropathic Pain Scale (NPS)*

Introduction

Thalamic Pain Syndrome (TPS), a type of Central Post Stroke Pain (CPSP), is a chronic and fatiguing pain disorder that typically arises following a stroke, otherwise known as a cerebrovascular incident. The condition usually manifests as damage to the ventral posterior nuclei of the thalamus, which are responsible for transmitting pain, temperature, and touch-related sensations to the brain. Injury to the sensory relay nuclei results in the brain's inability to suppress pain impulses, leading to abnormal pain signals characterized by spontaneous burning sensations and increased generalized pain sensitivity. Chronic and acute pain are exacerbated by increased activation of microglia and NLRP3 inflammasomes. This increased activation leads to damage to GABAergic inhibitory circuits in the thalamus, which are responsible for dampening pain [1,2].

Apart from sensory symptoms, TPS can significantly influence a person's emotional and psychological well-being. The thalamus and areas of the limbic and prefrontal systems are interconnected, playing a crucial role in mood regulation. If any of these systems are lesioned, individuals may experience difficulties regulating mood, leading to signs of depression [3,4]. Long-term pain, compounded with restricted activity and reduced well-being, can increase the risk of depression. Among patients, common symptoms of depression seen in TPS are fatigue, lack of motivation, insomnia, and a decrease in social behavior. Because TPS has a delayed onset after the initial cerebrovascular incident, pharmacological interventions have been relatively unsuccessful. In the majority of TPS patients, these treatments are only temporarily effective or provide partial relief [5]. Therefore, alternative strategies, such as non-invasive lesion-based neuromodulation methods, including Repetitive Transcranial Magnetic Stimulation (rTMS), have been explored in recent years.

rTMS is a non-invasive treatment approved as a neuromodulation intervention for Major Depressive Disorder (MDD) [6]. Compared to invasive treatments such as deep brain stimulation and electroconvulsive therapy, which carry inherent risks and have adverse side effects, rTMS is a globally safe neuromodulation intervention [6,7]. rTMS is applied to the scalp at the left dorsolateral prefrontal cortex (DLPFC) during which an electrical current is passed through magnetic coils to create an electromagnetic field that permeates the scalp, skull, and cerebrospinal fluid, depolarizing axons and modulating neurons associated with depressive symptoms [7,8]. Based on the position of neurons, the depolarization of axons leads to anterograde propagation of action potentials, thereby enhancing brain connectivity and engaging underactive cortical regions [9]. Additionally, evidence suggests that alternative neuron positioning initiates backward-propagating action potentials (bAP), allowing the induction of associative synaptic plasticity and dendritic depolarization. Improved synaptic plasticity, promoted by bAP and dendritic depolarization, is essential for enhanced neural network reorganization, resulting in a lasting effect on cortical excitability [6,10]. rTMS influences cortical excitability, modulating disrupted neural circuits, leading to improved clinical symptoms in neuropsychiatric disorders [11].

Because depression is typically linked to a hyperactive right hemisphere (RH) and a hypoactive left hemisphere (LH), rTMS has advantages in being administered at various frequencies [12]. The low-frequency application of rTMS, administered to the right side of the brain at frequencies below 5 Hz, has shown inhibitory responses on cortical excitability and synaptic depression. High-frequency rTMS, administered at frequencies over 5 Hz, has been shown to increase cortical excitability [11]. Repetitive, rapid succession pulses at various frequencies administered through rTMS have been shown to induce longer-lasting changes in brain activity and long-term potentiation [8,13].

The most common side effect of rTMS is varying levels of pain and discomfort, with patients often experiencing mild scalp tenderness. Pain may also occur due to patient susceptibility, improper coil placement, as well as magnetic pulse intensity and frequency [14]. Other common side effects include transient dizziness and headaches, which are found to occur in up to 1/3 of patients [15,16]. Lastly, rTMS can potentially induce seizures as a serious side effect, but the risk is very low, estimated to be < 0.003%, or 1 in every 30,000 treatments [17,18]. In addition, rTMS has been administered in patients with a history of seizure disorders and brain lesions, despite increased seizure risk [19,20]. Screening these patients and adhering to safety guidelines minimizes the risk of seizures from rTMS.

This study proposes that rTMS will be effective in improving depressive symptoms and anxiety in a patient with TPS. Furthermore, we evaluate the efficacy of treating the DLPFC for reducing neuropathic pain symptoms.

Case History

We report the case of a 40-year-old female patient who has a history of a brain hemorrhage, two strokes affecting the thalamus, and a subsequent medically induced coma (lasting 48 hours) in April 2022, resulting from a procedural complication during the embolization of a dural arteriovenous fistula located behind her left ear. Since her surgery, the patient had struggled to recover from the physical and emotional impacts of her thalamic pain syndrome. Despite intensive physical therapy, the patient continued to suffer from recurrent anatomically right-dominant neuropathic pain resulting from the thalamic injury. The fluctuating pain manifested all day in various forms, including a burning cold sensation, a prickly sensation, and a stinging sensation similar to a sunburn injury. Her depressive symptoms also emanated from significant tinnitus and vertigo stemming from the dural arteriovenous fistula located behind her left ear.

The patient reported symptoms consistent with MDD, such as feelings of hopelessness, loss of interest in pleasurable activities, fatigue, and intermittent suicidal ideation without a plan. In addition, the patient endorsed having symptoms consistent with General Anxiety Disorder (GAD), such as feeling constantly worried, having difficulty relaxing, and being easily agitated. The patient had unsuccessfully tried multiple medications, including pregabalin, duloxetine, and amitriptyline, to manage her thalamic pain. Furthermore, she failed antidepressant trials with duloxetine, bupropion, and fluoxetine, finding them to be ineffective.

Materials and Methods

Subject

The participant was recruited based on a clinical diagnosis of MDD refractory to 2 antidepressants of different classes, as well as comorbid anxiety, thalamic pain, vertigo, and chronic tinnitus. The participant did not have any contraindications that would prevent TMS treatment, including ferromagnetic implants within 12 inches of the head, a cardiac pacemaker, an implantable cardioverter defibrillator, or a history of epilepsy or brain lesions. The patient's stroke history was reported as a singular incident and non-chronic, caused by failed surgery for a dural arteriovenous fistula (AVF). Informed consent was obtained regarding TMS, possible side effects, and the treatment protocol, including the Motor Threshold determination procedure. Additionally, the subject was informed of the option to discontinue treatment at any time. The subject consented to a treatment plan of 36 rTMS treatments over 8 weeks, along with weekly psychometric questionnaires.

Repetitive transcranial magnetic stimulation (rTMS) treatment

rTMS was administered by trained neurotechnologists using the Stimware software, which is installed in the Apollo TMS Therapy System. Using the 10 - 20 system, the F3 location (Left Dorsolateral Prefrontal Cortex) corresponding to Brodmann areas (BA) 8 and 9 was approximated on the scalp. From the 9th treatment onwards, the patient additionally administered low-frequency rTMS to the F4 location to target anxiety symptoms (Right Dorsolateral Prefrontal Cortex). For motor threshold (MT) determination, the DLPFC was approximated 5.5 cm anterior to the location on the primary motor cortex that elicited a contralateral thumb twitch at the lowest intensity. Treatment parameters for left DLPFC stimulation constituted a frequency of 10 Hz, 3000 pulses, 40 pulses per train, and an intertrain interval of 11 seconds. For the right DLPFC treatment, a continuous train of 700 pulses at 1 Hz was administered per session. Motor Evoked Potential (MEP) was 42%. Treatments were administered for 18 minutes and 34 seconds on F3 and 11 minutes and 40 seconds on F4. Treatment intensity was capped at 100% of the MT, which the patient tolerated throughout treatment without scalp discomfort, headache, or seizures.

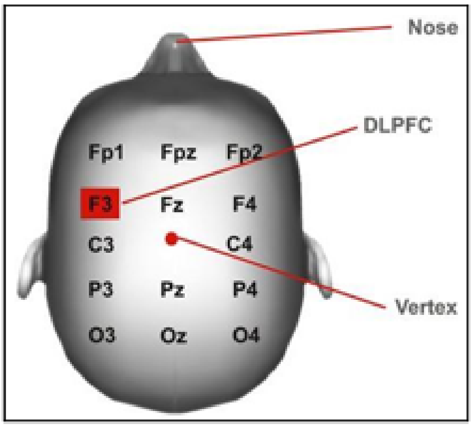

Figure 1: *rTMS treatment locations.*

Psychometric questionnaire administration

The rTMS treatment response was systematically monitored using standardized psychometric questionnaires. The Patient Health Questionnaire-9 (PHQ-9) and Generalized Anxiety Disorder-7 (GAD-7) were administered weekly throughout treatment.

Neuropathic pain scale (NPS)

The NPS was administered weekly to monitor central neuropathic pain response to rTMS. The NPS is currently the only tool validated for central neuropathic pain [21]. The questionnaire assessed 10 pain domains by using a 0 to 10 scale. The scale includes eight items that assess eight specific qualities of neuropathic pain: "sharp", "hot", "dull", "cold", "sensitive", "itchy", "deep", and "surface" pain [22]. Furthermore, it includes two items that assess the global aspects of pain intensity and pain unpleasantness.

Results

Test Scores	03/31/2025	04/14/2025	04/23/2025	04/30/2025	05/07/2025	05/14/2025	05/21/2025	05/29/2025	06/04/2025
PHQ-9	22	21	18	16	16	11	7	8	1
GAD-7	17	19	15	13	12	8	4	7	2

Table 1

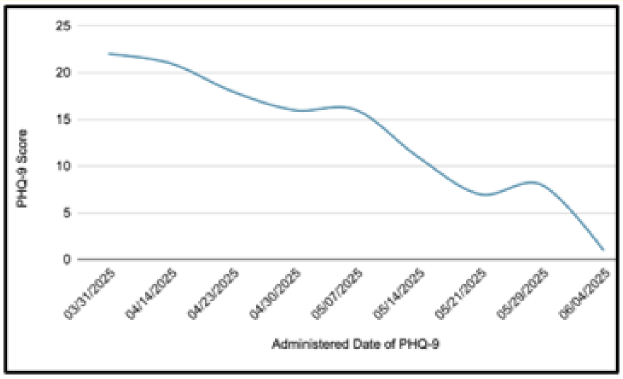

Figure 2: *PHQ-9 scores.*

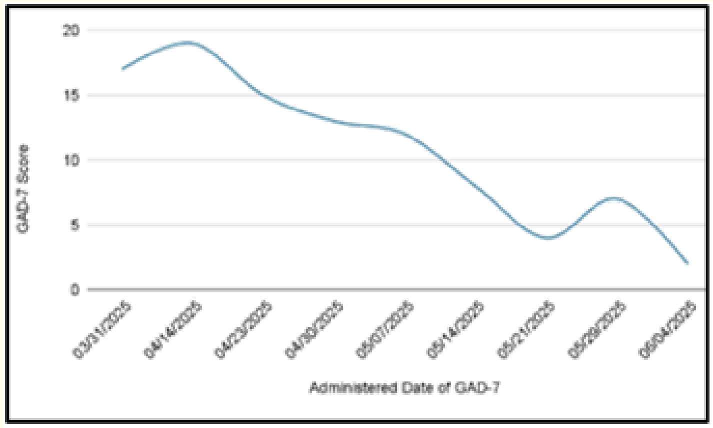

Figure 3: *GAD-7 scores.*

NPS scores

Item	1st Week of Treatment (4/15/2025)	Midpoint (5/14/2025)	1 Week After Final Treatment (6/12/2025)
Intensity	7	7	7
Sharpness	4	5	6
Hotness	2	4	2
Dullness	3	4	4
Cold	9	8	8
Sensitivity	0	2	2
Itchiness	3	3	0
Pleasantness	8	8	8
Deep Pain	5	5	3
Surface Pain	8	4	4
Total Pain Score	49	50	44

Table 2

Discussion

Our study demonstrates that rTMS was effective in treating symptoms of MDD and GAD in the patient, as evident by reductions of 95.5% and 88.2% in PHQ-9 and GAD-7 scores, respectively. However, the patient showed a modest improvement in neuropathic pain symptoms as her total NPS score decreased by 10.2%. Despite a modest reduction in pain, the patient progressively reported elevation in her mood, increased motivation and interest, and a renewed sense of optimism for her life. The patient endorsed increased motivation to participate in daily exercise, including walking, attending the gym, and practicing Pilates. Furthermore, the patient reported a renewed interest in reading and writing her own novel that was absent prior to initiating treatment. Improved neuroplasticity following rTMS was also evidenced in her efforts to alleviate pain by trying alternate treatments such as acupuncture and transcutaneous electrical nerve stimulation (TENS) therapy. Patient confirmed that her ability to cope with her chronic diagnosis and pain had improved significantly, leading to improved resilience over a short span of rTMS. The patient was no longer suicidal after completing 36 rTMS treatments.

A possible explanation for the effectiveness of rTMS in treating our patients' MDD and GAD symptoms is its impact on brain-derived neurotrophic factor (BDNF). BDNF is the most abundant and widely distributed neurotrophin in the central nervous system. It is essential due to its role in neuronal development, synaptic plasticity, neurogenesis, neuroprotection, learning, memory, and mood regulation [23]. In a study conducted by Mojtbavi., *et al*. they found that serum BDNF levels in patients with post-stroke depression (PSD) were lower than those without depression. Moreover, they found low serum levels of BDNF during the chronic stage of a stroke. They also found that BDNF levels were improved by post-stroke physical training and rehabilitation [24]. Moreover, multiple open-label and sham-controlled studies using high-frequency rTMS targeting the DLPFC have demonstrated an increase in serum BDNF induced by rTMS [25]. Additionally, rTMS has been shown to increase BDNF levels in patients with GAD [26].

To our knowledge, some studies have shown rTMS to be effective in treating post-stroke depression. A meta-analysis done in 2017 by Shen., *et al.* on 22 RCTs (n = 1764 patients) showed a mean decrease in Hamilton Depression Rating Scale (HAMD) score of 6.09. However, limited studies have specifically studied the efficacy of rTMS in treating depression in patients with a stroke of thalamic origin. This distinction is vital because 20% to 33% of centralized post-stroke pain results in thalamic pain [27]. Therefore, our findings add to the limited available literature for treating patients with depression and TPS.

Finally, in the United States, approximately 1 in 5 children experience comorbidities with mental illness, including depression and anxiety, which lead to poor general health outcomes. Adolescents with substance use disorders exhibit high rates of co-occurring mental illness, with over 60% meeting diagnostic criteria for another psychiatric condition in community-based treatment programs. Comorbidities are influenced by both genetic (DNA antecedents) and environmental (epigenetic) factors. Given the significant impact of psychiatric comorbidities on individuals' lives, our laboratory performed a study to uncover common mechanisms through a Genome-Wide Association Study (GWAS) meta-meta-analysis [28]. GWAS datasets were obtained for each comorbid phenotype, followed by a GWAS meta-meta-analysis using a significance threshold of $p < 5E\text{-}8$ to validate the rationale behind combining all GWAS phenotypes. The combined and refined dataset was subjected to bioinformatic analyses, including Protein-Protein Interactions and Systems Biology. Pharmacogenomics (PGx) annotations for all potential genes with at least one PGx were tested, and the genes identified were combined with the Genetic Addiction Risk Severity (GARS) test, which included 10 genes and eleven Single Nucleotide Polymorphisms (SNPs).

In addition, the STRING-MODEL was employed to discover novel networks and Protein-Drug interactions. Results: Autism Spectrum Disorder (ASD) was identified as the top manifestation derived from the known comorbid interaction of anxiety, depression, and attention deficit hyperactivity disorder (ADHD). The STRING-MODEL and Protein-Drug interaction analysis revealed a novel network associated with these psychiatric comorbidities.

The findings of [28] suggest that these interactions are linked to "dopamine homeostasis" as a therapeutic outcome. The GWAS analysis study [28] provides a reliable genetic and epigenetic map that could assist healthcare professionals in the therapeutic care of patients presenting with multiple psychiatric manifestations, including anxiety, depression, and ADHD. The results highlight the importance of targeting dopamine homeostasis in managing ASD linked to these comorbidities. These insights may guide future pharmacogenomic interventions to improve clinical outcomes in affected individuals and may represent a potential mechanism for the clinical results of rTMS for Recurrent Major Depressive Disorder and Generalized Anxiety Disorder Comorbid with Thalamic Pain Syndrome.

Limitations of the Study

The use of rTMS in treating recurrent MDD and GAD comorbid with Thalamic Pain Syndrome was limited to a single case study. The efficacy and safety of rTMS in this population must be studied using large-scale, randomized, and blinded trials to validate the findings. Another limitation is potential response bias due to the use of self-reported psychometric assessments.

Conclusion

We report successful use of rTMS in treating MDD and GAD to successful remission in our patient comorbid with Thalamic Pain Syndrome. In addition, our study suggests that rTMS is a safe and viable option for patients with TPS, with no adverse side effects experienced by our patient. The efficacy and safety of rTMS in this population must be studied using large-scale, randomized, and blinded trials.

Author Contributions

KS conceptualized the study. The original draft of this manuscript was written by VR, HM, AK, HB, MO, and KS. Review and additional editing of the manuscript were conducted by SS, KM, CV, KB, DB, RB.

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Conflict of Interest Statement

The authors report no potential conflicts of interest regarding the publication of this paper. This manuscript has been read and approved by all authors.

Declaration of Patient Consent

Written informed consent was obtained from the patient to publish this paper. Participation in the study adhered strictly to patient privacy and HIPAA guidelines. The participant understood the potential risks and benefits of the interventions. rTMS was administered by certified neurotechnologists under the supervision of a board-certified psychiatrist.

Bibliography

1. Kadono Y., *et al*. "Repetitive transcranial magnetic stimulation restores altered functional connectivity of central poststroke pain model monkeys". *Scientific Reports* 11.1 (2021): 6126.

2. Wang G and Thompson SM. "Maladaptive homeostatic plasticity in a rodent model of central pain syndrome: thalamic hyperexcitability after spinothalamic tract lesions". *The Journal of Neuroscience* 28.46 (2008): 11959-11969.

3. Robinson P., *et al*. "Neurophysical modeling of brain dynamics". *Neuropharmacology* 28.1 (2003): S74-S79.

4. Hong W., *et al*. "Heterogeneous alterations in thalamic subfields in major depression disorder". *Journal of Affective Disorders* 295 (2021): 1079-1086.

5. Kim N., *et al*. "Network effects of brain lesions causing central post-stroke pain". *Annals of Neurology* 92.5 (2023): 834-845.

6. Somaa FA., *et al*. "Transcranial magnetic stimulation in the treatment of neurological diseases". *Frontiers in Neurology* 13 (2022): 793253.

7. Fox MD., *et al*. "Resting-state networks link invasive and noninvasive brain stimulation across diverse psychiatric and neurological diseases". *Proceedings of the National Academy of Sciences* 111.41 (2014): E4367-E4375.

8. Sharbafshaaer M., *et al*. "Repetitive transcranial magnetic stimulation (rTMS) in mild cognitive impairment: effects on cognitive functions-a systematic review". *Journal of Clinical Medicine* 12.19 (2023): 6190.

9. Müller-Dahlhaus F and Vlachos A. "Unraveling the cellular and molecular mechanisms of repetitive magnetic stimulation". *Frontiers in Molecular Neuroscience* 6 (2013): 50.

10. Griveau J., *et al*. "Interest of pentoxifylline in ICSI with frozen-thawed testicular spermatozoa from patients with non-obstructive azoospermia". *Reproductive BioMedicine Online* 12.1 (2006): 14-18.

11. Sharbafshaaer M., *et al*. "Harnessing brain plasticity: the therapeutic power of repetitive transcranial magnetic stimulation (rTMS) and theta burst stimulation (TBS) in neurotransmitter modulation, receptor dynamics, and neuroimaging for neurological innovations". *Biomedicines* 12.11 (2024): 2506.

12. Hecht D. "Depression and the hyperactive right-hemisphere". *Neuroscience Research* 68.2 (2010): 77-87.

13. Klomjai W., *et al*. "Basic principles of transcranial magnetic stimulation (TMS) and repetitive TMS (rTMS)". *Annals of Physical and Rehabilitation Medicine* 58.4 (2015): 208-213.

14. Rossi S., *et al*. "Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research". *Clinical Neurophysiology* 120.12 (2009): 2008-2039.

15. Lefaucheur JP., *et al*. "Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS): An update (2014-2018)". *Clinical Neurophysiology: Official Journal of the International Federation of Clinical Neurophysiology* 131.2 (2020): 474-528.

16. Loo CK., *et al*. "A review of the safety of repetitive transcranial magnetic stimulation as a clinical treatment for depression". *International Journal of Neuropsychopharmacology* 11.1 (2008): 131-147.

17. Stultz DJ., *et al*. "Transcranial Magnetic Stimulation (TMS) safety with respect to seizures: A literature review". *Neuropsychiatric Disease and Treatment* 16 (2020): 2989-3000.

18. Taylor JJ., *et al*. "Seizure risk with repetitive TMS: Survey results from over a half-million treatment sessions". *Brain Stimulation* 14.4 (2021): 965-973.

19. Lerner AJ., *et al*. "Seizures from transcranial magnetic stimulation 2012-2016: Results of a survey of active laboratories and clinics". *Clinical Neurophysiology* 130.8 (2019): 1409-1416.

20. Rossi S., *et al*. "Safety and recommendations for TMS use in healthy subjects and patient populations, with updates on training, ethical and regulatory issues: Expert Guidelines". *Clinical Neurophysiology* 132.1 (2021): 269-306.

21. May S and Serpell M. "Diagnosis and assessment of neuropathic pain". *F1000 Medicine Reports* 1 (2009): 76.

22. Galer B and Jensen M. "Development and preliminary validation of a pain measure specific to neuropathic pain: The Neuropathic Pain Scale". *Neurology* 48.2 (1997): 332-338.

23. Correia Ana Salomé., *et al*. "BDNF Unveiled: Exploring its role in major depression disorder serotonergic imbalance and associated stress conditions". *Pharmaceutics* 15.8 (2023): 2081.

24. Mojtabavi H., *et al*. "Circulating brain-derived neurotrophic factor as a potential biomarker in stroke: a systematic review and meta-analysis". *Journal of Translational Medicine* 20.1 (2022): 126.

25. Sophie MDD., *et al*. "Repetitive transcranial magnetic stimulation-induced neuroplasticity and the treatment of psychiatric disorders: state of the evidence and future opportunities". *Biological Psychiatry* 95.6 (2024): 592-600.

26. Lu R., *et al*. "The effect of bilateral low-frequency rTMS over dorsolateral prefrontal cortex on serum brain-derived neurotropic factor and serotonin in patients with generalized anxiety disorder". *Neuroscience Letters* 684 (2018): 67-71.

27. Dydyk A and Munakom S. "Thalamic pain syndrome". StatPearls (2023).

28. Lewandrowski KU., *et al*. "Genetic and regulatory mechanisms of comorbidity of anxiety, depression and ADHD: A GWAS meta-meta-analysis through the lens of a system biological and pharmacogenomic perspective in 18.5 M subjects". *Journal of Personalized Medicine* 15.3 (2025): 103.

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