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Review

Exploring the effectiveness of neuromodulation techniques in the diagnosis and management of vestibular disorders and migraine and its relevance to vestibular migraine

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Abstract: Vestibular Migraine (VM) is a complex neurological disorder characterized by episodic vertigo and migraine-like symptoms and is often misdiagnosed due to overlapping features with other vestibular and neurological conditions. In this review, we systematically explored the efficacy of exogenous (e.g., repetitive transcranial magnetic stimulation (rTMS) and transient DC Stimulation (tDCS)) and endogenous (e.g., EEG and infra-low frequency neurofeedback) neuromodulation techniques in diagnosing and managing vestibular disorders and migraines, with its relevance to VM. Analysis of 30 selected studies demonstrated promising outcomes in symptom reduction, with notable effectiveness in refractory and chronic cases. Studies involving both neuromodulation techniques improve various symptoms of vestibular disorders and migraine, positioning neuromodulation as a valuable adjunct to the available standard care being employed with patients. Given the pathophysiological overlap between migraine and vestibular dysfunction, particularly involving cortical excitability, GABAergic inhibition, and hypothalamic-trigeminal dysregulation, neuromodulation offers a non-invasive, safe, and targeted approach for long-term VM management. Further high-quality clinical trials are warranted to establish standardized protocols and confirm the long-term efficacy of these neuromodulation modalities.

Keywords: vestibular migraine; repetitive transcranial magnetic stimulation (r-TMS); Transcranial Direct Current Stimulation (t-DCS); neuromodulation; migraine episode; inhibition; exogenous;

endogenous

Abbreviations: ABEP: Auditory Brainstem Evoked Potential; AICA: Anterior Inferior Cerebellar Artery; CMCT: Central motor conduction time; CSF: Cerebrospinal Fluid; CSSP: Cortical Stimulation Silent Period; CSD: Cortical Spreading Depression; DBS: Deep brain stimulation; DHI: Dizziness Handicap Index; DLFPC: Dorsolateral Prefrontal Cortex; EMG: Electromyography; ICHD: International Classification of Headache Disorders; MEP: Motor-evoked potentials; MdDS: Mal de debarquement syndrome; MIDAS: Migraine Disability Assessment Scale; MVS: Magnetic Vestibular Stimulation; SOC: Superior Olivary Complex; rTMS: Repetitive Transcranial Magnetic Stimulation; rMT: Resting motor threshold; PCS: Persistent post-concussion syndrome; Oz: Just above the occipital point; RCT: Randomized Controlled Trials; sTMS: Single-Pulse Transcranial Magnetic Stimulation; tDCS: Transcranial Direct Current Stimulation; TVS: Trigeminovascular system; TBI: Traumatic Brain Injury; TES: Transcranial Electromagnetic Stimulation ; TVS: Trigeminovascular system; VM: Vestibular Migraine; VRT: Vestibular Rehabilitation Therapy; VPN: Ventral Posteriomedial Nucleus; VNG: Videonystagmography; ILF: Infra-Low frequency

1. Introduction

The inner ear's otolith organ senses linear motion, while the semicircular canal detects angular motion. Together, these organs comprise the vestibular system, which is a sensory system based on the principle of fusion of bilateral sensors. The vestibular system aids in maintaining body equilibrium by providing information on head acceleration and linear and angular motions to the individual. Dysfunction in the vestibular system, whether peripheral or central, can lead to clinical manifestations such as vertigo or dizziness, with varying onset times and episode durations, often accompanied by additional symptoms [1]. One prominent symptom associated with vestibular disorders is a headache linked to vertigo. This relationship was first explained by Dietrich and Brandt in 1999 [2]. Vestibular Migraine (VM) is conceptualized as a diverse constellation of neurological impairments characterized by episodic vertigo and associated headaches. This condition stems from asymmetrical activation and deactivation of vestibular neuronal pathways during an episode [2]. To rule out the possibility that the symptoms are not due to other factors, VM is diagnosed based on a migraine history, the severity, frequency, and duration of the vestibular episodes, as well as the temporal correlation of migraine symptoms with vestibular episodes in at least 50% of cases [3]. Based on pathophysiological and epidemiological observations, migraines are involved in the vestibular systems and were previously sub-categorized under Migraine, as Basilar Migraine [4]. However, increasing recognition of coexisting vestibular manifestations such as dizziness, vertigo, unsteadiness, and sensitivity to motion alongside classical migraine symptoms like photophobia, phonophobia, headache, and visual aura has led to the reclassification of these presentations of VM. This change is grounded in criteria co-developed by the Barany Society and the International Headache Society-3 in 2018 [5]. According to the ICHD classification for VM, there are five episodes of moderate to severe vestibular symptoms, three of which last five minutes to seventy-two hours, and at least 50% of these episodes are linked to at least one of the three migraine features with headache. The nature of the headache may be characterized by unilateral location, pulsating quality, moderate to severe intensity, and aggravated by routine physical activities. The other symptoms included phonophobia and photophobia [5]. Even after

proper diagnostic criteria given by the ICDH and Barany Society, the pathophysiology of VM needs to be reviewed based on the variety of symptoms, thus requiring an upgraded diagnostic and treatment option [6]. The ambiguity of VM leads to different kinds of confusion among the professionals to correctly diagnose the disorder and leads to preferring the limited management options like Prophylactic treatments, Vestibular Rehabilitation Therapy (VRT), and modification of lifestyles, but the result remains inconclusive [7]. Based on the literature review, it is observed that migraine and VM symptoms can prevail in pediatric and younger adult demographics. One study indicates that 35% to 60% of children and adolescents experience dizziness with accompanying headaches [8]. Due to the ambiguous nature of VM and its clinical pathophysiology, it is quite challenging and remains either misdiagnosed or undiagnosed. 8−10% of individuals with vestibular symptoms had an anxiety or depression condition as the major cause of their illness, according to retrospective, cross-sectional, and prospective studies done over three decades [9]. Functional and mental illnesses may be primary, secondary, or concomitant concerns in many individuals presenting for examination of vestibular symptoms. Stated differently, vestibular symptoms are frequently caused, impacted, and complicated by psychiatric disorders. Psychiatric disorders are frequently to blame for the majority of morbidity and impairment, particularly in individuals who have long-term illnesses [9].

1.1. Neuromodulation techniques

Rapid technological advancements have established neuromodulation techniques as a groundbreaking solution for assessing and managing neurological disorders. These innovative approaches show tremendous promise for prosthetics and therapeutic applications and advance research in any medical field [10]. Neuromodulation operates as a non-invasive method utilizing temperature-regulating elements or magnets to modulate brain activity and has shown efficacy in mitigating various vestibular disorders, migraine attacks, and cluster headaches. Researchers have further expanded the scope of neuromodulation devices, highlighting their potential in treating VMs, a subtype that manifests symptoms such as vertigo, dizziness, and balance difficulties. The neuromodulation techniques can be divided into two types, i.e., Exogenous Neuromodulation Techniques and Endogenous Neuromodulation Techniques. Exogenous neuromodulation involves external stimulation techniques to influence neural activity, whereas endogenous neuromodulation refers to the brain's natural ability to regulate neural activity through biological and physiological mechanisms. We focus on both exogenous and endogenous neuromodulation techniques to explore the effectiveness of the same in diagnosing and managing vestibular disorders and migraine. Exogenous neuromodulation methods include repetitive transcranial magnetic stimulation (rTMS), transcranial direct current stimulation (tDCS), vagus nerve stimulation (VNS), and deep brain stimulation (DBS). The term "transcranial" in rTMS is pertinent and willful here, as it aligns with the terminology used for tDCS later in the article, emphasizing that both are noninvasive techniques involving stimulation across the skull. Endogenous neuromodulation methods, by contrast, include EEG feedback and Infra Low-Frequency Neurofeedback (ILF).

1.1.1. Endogenous neuromodulation techniques

Endogenous neuromodulation entails therapeutic methodologies that amplify the brain's intrinsic competence for self-regulation by harnessing real-time data indicative of its current functional state.

This paradigm is operationalized in modalities such as real-time fMRI and EEG neurofeedback. From a systems neuroscience perspective, the brain is conceptualized as a hierarchically structured, dynamically integrated, unitary, and hemodynamic entity. Consequently, any perturbation—whether informational or otherwise—regarding its regulatory efficacy exerts a pervasive influence across the system. By delivering temporally precise, state-specific feedback, this approach mitigates informational uncertainty and expedites neuroadaptive processes. Moreover, strategically focused modulation enables intervention preferentially directed toward neural circuits or functional domains exhibiting suboptimal performance. This intervention acknowledges and engages the brain's ontogenetically defined regulatory hierarchy, wherein foundational neural substrates must be stabilized and fortified to scaffold higher-order regulatory capacities. This ontological recapitulation facilitates functional restoration via a bottom-up, developmentally informed progression through successive regulatory strata [11].

Infra-Low-Frequency Neurofeedback: The principal aim of ILF neurofeedback is to bolster self-regulatory capabilities. Secondary advantages encompass symptom alleviation and functional recuperation. Investigations have demonstrated that systematically diminishing the target frequencies produces superior outcomes for complex ailments such as bipolar mood oscillations, migraines, seizures, and episodes of suicidality. This methodology culminated in the identification of Optimal Response Frequencies (ORFs), which signify the frequencies at which training attains maximum efficacy for each individual. While these frequencies may fluctuate based on their locus, two consistent correlations persist: one that operates across the entire ILF spectrum and another that pertains to the EEG spectrum. During training within the ILF domain, the glial-neuronal networks tasked with regulating tonic and resting state modulation are stimulated [12].

1.1.2. *Exogenous neuromodulation techniques*

a. Transcranial magnetic stimulation (TMS)

Transcranial Magnetic Stimulation (TMS) is a non-invasive treatment that stimulates nerve cells using electromagnetic pulses. It may help reduce the symptoms of various neurological and mental health conditions. TMS can be categorized into three main types: Single Transcranial Magnetic Stimulation (s-TMS), Paired Pulsed Transcranial Magnetic Stimulation (pp-TMS), and Repetitive Transcranial Magnetic Stimulation (r-TMS). Each type has different applications based on the pulses delivered to targeted areas of the brain. The s-TMS uses monophasic pulses to diagnose various neurological and psychiatric disorders. It measures the cortical and sub-cortical functions of the brain through parameters such as Resting Motor Potential (r-MT), Active Motor Potential (a-MT), Motor Evoked Potential (MEP), Cortical Silent Period (CSP), and Central Motor Conduction Time(CMCT).r-TMS in contrast, engages repetitive pulses with various stimulation parameters such as frequency, intensity, stimulation site, number of stimuli, and duration of treatment and is used to either inhibit or excite the targeted brain areas. It may also involve a heterogeneous sample of participants with differing characteristics such as age, type of depression (unipolar vs. bipolar), and level of treatment resistance. The r-TMS has been classified into two types, i.e., High-Frequency r-TMS (> 5 Hz) and Low-Frequency r-TMS (< 5 Hz). The High-frequency r-TMS excites the motor neurons, whereas the Low-Frequency r-TMS inhibits the motor neurons. Repeated low-frequency stimulation of a single neuron has been shown to cause long-term depression (LTD), a persistent inhibition of cell-cell communication; in contrast, repeated high-frequency stimulation can enhance cell-cell communication

through long-term potentiation (LTP) [13]. Approved by the FDA in 2008, TMS is primarily employed for depression treatment, particularly in cases resistant to standard interventions [14]. It is also used in neurological disorders, migraine, and the management of headaches [15].

The neurophysiological process involved in TMS: The human cerebral cortex harbors a densely packed array of neurons that preserve electrochemical gradients via an intricate network of ion channels and transporters, enabling the cortex to function as an effective bioelectrical conductor. When a pulsed magnetic field is applied transcranially using a precisely engineered coil, it induces electrical currents through the stratified architecture of the cortex. The coil design dictates the pulse characteristics, typically delivering a magnetic field intensity approaching 2 Tesla for a duration on the order of 10^{-5} seconds [16]. The degree of cortical activation is proportionally correlated with the intensity of the pulse. Computational simulations indicate that a 2-Tesla pulse activates a cylindrical volume of cortex approximately 1 cm in radius and 2 cm in height, with activation intensity exhibiting a steep decline from the central axis [17,18]. Low-intensity magnetic stimulation predominantly depolarizes neuronal axons, which exhibit a high concentration of voltage-gated ion channels. This depolarization precipitates action potentials that propagate along axonal pathways until they culminate at presynaptic terminals, where the release of neurotransmitters occurs. Most cortical neurons are excitatory and primarily utilize glutamate as their neurotransmitter of choice. A minority consists of inhibitory interneurons that secrete gamma-aminobutyric acid (GABA), which is critical in modulating excitatory activity and regulating circuit dynamics. Furthermore, projection neurons emanating from subcortical nuclei extend their axons to cortical targets, modulating neural activity by releasing neuromodulators such as acetylcholine, dopamine, norepinephrine, and serotonin. Consequently, even at relatively low stimulation intensities, transcranial magnetic stimulation (TMS) engages a heterogeneous array of excitatory and inhibitory neuronal populations, activating diffuse neuromodulatory systems. Given the extensive interconnectivity within cortical circuits, a solitary TMS pulse has the potential to incite a cascade of neural activity through both feedforward and feedback mechanisms, thereby amplifying its impact at the network level [19]. TMS shares methodological affinities with other brain mapping modalities, such as direct electrical stimulation, positron emission tomography (PET), and functional magnetic resonance imaging (fMRI), facilitating the exploration of specific sensory and motor cortical domains. Within this framework, TMS emerges as an invaluable instrument for investigating the cortical substrates implicated in VM symptomatology. Nonetheless, TMS is inherently constrained by limited spatial resolution, which hampers its capacity for fine-grained cortical mapping. Research has demonstrated that repetitive TMS (rTMS) not only engages neuronal pathways through axonal activation but also involves non-neuronal mechanisms that may elucidate the extensive range of physiological and behavioral effects observed [20,21]. At its core, rTMS capitalizes on neuroplastic mechanisms that promote synaptic reorganization within cortical networks, thereby contributing to its enduring effects on cerebral function.

b. Transcranial direct current stimulation (tDCS)

Transcranial direct current stimulation (tDCS) is a powerful technique for brain stimulation that effectively enhances or inhibits cognitive functions by modifying cortical excitability. By placing two electrodes on a patient's scalp, tDCS delivers a tiny electrical current that modulates activity in targeted brain regions in a reversible manner. In a standard uni-hemispheric tDCS arrangement, one electrode serves as the target electrode while the other acts as a reference electrode. The region of interest is stimulated by the target electrode, whose location is dictated by the task and hypothesis. Here, the target location should be on the cortical surface because scalp electrodes cannot reach deep brain

regions. The reference electrode is placed extra-cephalically in some montages. The effects of stimulation on cortical excitability can be examined using tDCS in conjunction with techniques such as TMS, fMRI, and EEG. It is important to briefly underline that integrating these techniques may lead to a better understanding of the links between the brain and behavior [22]. Recognized for its effectiveness, tDCS aids with anxiety, depression, and symptoms associated with neurological illnesses like Parkinson's disease, multiple sclerosis, stroke, and movement disorders. Major depression and schizophrenia are among the psychiatric symptoms that may be affected, according to new research [23]. It was initially developed to treat brain injuries and neuropsychiatric illnesses.

The neurophysiological mechanisms underpinning tDCS elucidate its capacity as a neuromodulatory intervention with therapeutic potential in managing VM. This non-invasive technique exerts its effects by delivering a subthreshold, unidirectional electrical current that perturbs transmembrane potentials, thereby altering the excitability landscape of cortical networks. At the anodal site, the induced shift in extracellular potential facilitates neuronal depolarization, effectively lowering the activation threshold and potentiating excitatory synaptic transmission. In contrast, the cathodal site promotes neuronal hyperpolarization, exerting a net inhibitory influence on underlying neuronal populations. Anodal stimulation, by elevating cortical excitability, induces neurovascular coupling responses, culminating in augmented regional cerebral perfusion to meet the escalated metabolic demands of heightened neuronal firing. This phenomenon has been empirically validated using functional near-infrared spectroscopy (fNIRS), which reveals significantly increased concentrations of oxygenated hemoglobin in response to anodal stimulation over the prefrontal cortex, relative to cathodal input [24]. Merzagora et al. (2010) further corroborated these findings, demonstrating that such stimulation elicits discernible metabolic upregulation within the engaged neural substrates. Beyond electrophysiological excitation, tDCS exerts neurochemical modulatory effects across multiple neurotransmitter systems. Evidence suggests that dopaminergic transmission is susceptible to modulation by tDCS and that its efficacy is contingent upon the neurochemical milieu. For instance, co-administration of citalopram, a selective serotonin reuptake inhibitor (SSRI), has been shown to amplify the neuroplastic effects of anodal tDCS [25], while rivastigmine, a cholinesterase inhibitor, attenuates its neuromodulatory efficacy, likely by disrupting acetylcholine-mediated synaptic potentiation [26]. Given its influence on both cortical excitability and neurotransmitter dynamics, tDCS presents as a compelling candidate for the therapeutic modulation of multimodal integration hubs implicated in VM. Specifically, regions such as the temporoparietal junction (TPJ) and dorsolateral prefrontal cortex (DLPFC), both integral to the processing of vestibular, spatial, and attentional information, are well-positioned as targets for neuromodulatory intervention. Notably, a study employing anodal stimulation over the right DLPFC reported significant enhancements in visual sustained attention, spatial working memory, and visual memory accuracy, indicating a facilitative effect on cognitive components of vestibular processing [27].

2. Aim of the study

This article presents a systematic review of existing research on vestibular disorders and migraine, with a focus on evaluating the potential application of neuromodulation techniques in the management of VM. We aim to assess the effectiveness of these techniques in alleviating clinical symptoms associated with both vestibular dysfunction and migraine, drawing upon findings from previously published studies. By critically examining the outcomes reported in the literature, this review seeks to

bridge existing knowledge gaps and provide meaningful insights into the broader therapeutic potential of neuromodulation in regulating brain activity related to vestibular and migraine conditions. Additionally, this work forms part of an ongoing research initiative aimed to identify the most suitable neuromodulation strategies for the effective treatment and long-term management of VM.

3. Methodology

A comprehensive search was conducted to gather relevant literature on the application of neuromodulation techniques for the treatment of vestibular disorders and migraines, as well as for assessing brain activity during migraine episodes. Databases such as PubMed, Google Scholar, Medscape, Embase, and Z-Library were systematically explored. Specific search phrases like "Neuromodulation in assessing Migraine" and "Neuromodulation in assessing and managing vestibular disorders" were used to identify studies focusing on both the diagnostic and therapeutic roles of neuromodulation in these conditions.

To better understand the pathophysiology of VM, initial searches included the phrase "pathophysiology of VM". However, the limited results prompted an expansion of the search criteria to include broader terms like "migraine", which helped capture a wider and more relevant pool of literature. This adaptive strategy enabled the collection of diverse and valuable studies that contribute to both the clinical management and theoretical understanding of migraine and vestibular disorders through neuromodulation.

The literature search covered publications from the inception of each database up to September 2023, with a focused review period from July 2022 to December 2023. To ensure the inclusion of the most recent developments, the review process was extended through December 2024, monitoring for any significant advancements beyond the initial study period.

The resulting body of literature forms the foundation of a detailed review, presented in Tables 1, 2, and 3, offering insights into the complex neurophysiological mechanisms underlying various vestibular disorders and migraine subtypes. This review underscores the growing relevance of neuromodulation techniques in advancing both research and clinical practice in this domain.

3.1. Selection process of studies

A total of 209 articles were initially identified for review, including 190 obtained through database searches and 19 accessed via Sci-Hub. After a preliminary screening based on abstract review, 10 articles were excluded for not meeting the relevance criteria of this study. The remaining 199 articles were then subjected to full-text screening by predefined inclusion criteria, resulting in the selection of 129 studies. Following a more detailed evaluation, 99 studies were excluded, primarily those focusing on the use of repetitive Transcranial Magnetic Stimulation (r-TMS) and tDCS for assessing various cortical and subcortical functions or for therapeutic purposes unrelated to vestibular disorders and migraine. Ultimately, 34 studies were deemed suitable for quantitative analysis. However, 4 of these were excluded after applying specific inclusion and exclusion criteria, as detailed in subsequent sections. From the final set of 30 studies, the literature was categorized based on the area of investigation and type of neuromodulation techniques. Six studies focused on motor cortex activation through neuromodulation; four examined phosphene threshold values in the visual cortex; and three explored cortical silent periods in migraine. The remaining studies investigated the therapeutic role of

neuromodulation in migraine management. Specifically, three studies evaluated neuromodulation as a prophylactic treatment, two focused on pain reduction, and one explored visual cortex activation and inhibition in migraineurs. Additionally, seven studies addressed the application of neuromodulation in vestibular disorders. Furthermore, three studies involving endogenous neuromodulation techniques in migraine management were included, along with a single study related to the management of vestibular disorders using endogenous methods. A detailed flowchart illustrating the entire study selection process, including the applied inclusion and exclusion criteria, is presented in Figure 1.

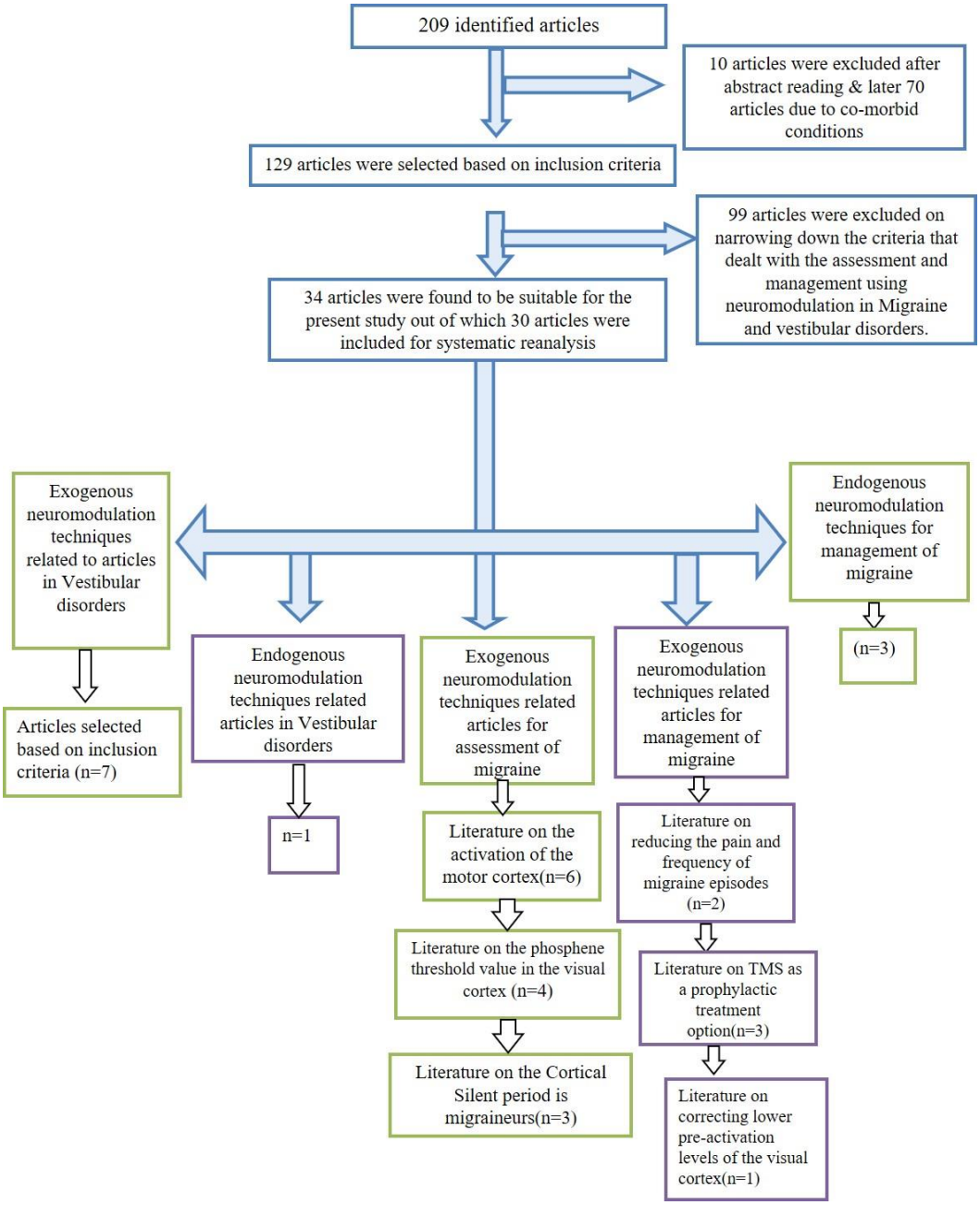

Figure 1. Flowchart depicting the various stages of selection of articles based on the inclusion and exclusion criteria.

3.2. Inclusion criteria

The inclusion criteria for this study involved a comprehensive review of clinical trials, case reports, and review articles that utilized neuromodulation techniques such as repetitive Transcranial Magnetic Stimulation (r-TMS), single-pulse Transcranial Magnetic Stimulation (s-TMS), and tDCS, and endogenous neuromodulation techniques such as ILF neurofeedback. These methods were applied to evaluate and modulate activity in cortical and subcortical brain regions in the context of vestibular disorders and migraines. The review encompassed various types of migraines, including menstrual migraines as well as chronic and acute migraine episodes, irrespective of the presence or absence of aura. Vestibular disorders presenting primarily with vertigo and dizziness were specifically included to assess the clinical effectiveness of neuromodulation interventions in alleviating these symptoms. Furthermore, studies that entailed neuromodulation techniques with vestibular rehabilitation therapy were also considered for inclusion to explore integrative treatment approaches.

3.3. Exclusion criteria

In this review, we intentionally delineated its scope by excluding studies about depression and other neurological pathologies, in order to retain a concentrated focus on vestibular disorders, with migraine, particularly VM, serving as the core clinical entity under investigation. This methodological decision was driven by the imperative to distil disorder-specific evidence and synthesize mechanistic and therapeutic insights that are uniquely applicable to migraine-related pathophysiology. Furthermore, to ensure translational relevance and maintain consistency in clinical applicability, preclinical (animal) studies were systematically excluded from the analysis.

4. Neuromodulation techniques in vestibular disorders

Besides traditional management options, recent research suggests that neuromodulation techniques can help reduce vestibular symptoms in vestibular disorders. A recent review study concluded that Neuromodulation has a promising future as a potential treatment for vestibular dysfunction. Techniques such as Magnetic Vestibular Stimulation (MVS), DBS, and Transcranial Magnetic Stimulation (TMS) represent sophisticated and customizable treatment modalities that could offer targeted relief for vestibular symptoms in individuals [28]. A notable study conducted by Cha et al. involved ten subjects (eight women) diagnosed with persistent Mal de Débarquement Syndrome (MdDS), with symptoms lasting between 10 to 91 months. Each participant received one session of rTMS across four counterbalanced protocols: Left 10 Hz (high frequency), left 1 Hz (low frequency), right 10 Hz, and right 1 Hz, directed at the dorsolateral prefrontal cortex (DLPFC). The results demonstrated that rTMS was well-tolerated among participants with MdDS, showing promising short-term symptom alleviation [29]. Furthermore, Tarnutzer et al. reported three distinct cases of vestibular decompensation stemming from vestibular neuronitis. Notably, the application of Low-frequency TMS (LFrTMS) over the contralateral vestibular cerebellum for five consecutive days led to significant improvement in postural stability among these patients [30]. In another investigation by Koganemaru et al., the efficacy of transcranial Direct Current Stimulation (t-DCS), in conjunction with vestibular rehabilitation, was assessed in a cohort of 30 patients experiencing chronic dizziness due to vestibular dysfunction. Participants underwent rehabilitation concurrently with either 20 minutes of t-DCS or

sham stimulation. Findings revealed that vestibular rehabilitation augmented by t-DCS yielded superior outcomes than rehabilitation alone [31]. Additionally, a case study by Paxman et al. focused on a 61-year-old male patient who experienced chronic dizziness following mild Traumatic Brain Injury (TBI). To evaluate the impact of rTMS on chronic dizziness, the patient underwent 10 sessions of 10 Hz rTMS stimulation. Post-treatment assessments indicated a noteworthy reduction in the Dizziness Handicap Index (DHI) scores from 41 to 20 points. This case concluded that rTMS is a safe and economically viable treatment option for chronic dizziness attributable to TBI [32].

A pilot, randomized, double-blinded study conducted by Moussavi et al. (2019) involved 22 participants to explore the efficacy of repetitive Transcranial Magnetic Stimulation (r-TMS) on persistent post-concussion syndrome (PCS). The findings indicated that r-TMS is a viable treatment option for individuals who have recently sustained concussions [33]. In another case study by Buard et al. (2020), low-frequency (1 Hz) r-TMS was administered unilaterally over two consecutive weeks to a 41-year-old male suffering from Mal de Débarquement Syndrome (MdDS). Post-treatment assessments revealed significant improvements in the Hospital Anxiety and Depression Scale (HADS) scores as well as balance metrics in the patient [34]. A double-blinded randomized controlled trial by Saki et al. (2022) involved 36 elderly individuals with chronic vestibular dysfunction who received vestibular rehabilitation combined with transcranial Direct Current Stimulation (t-DCS) targeted at the Dorsolateral Prefrontal Cortex (DLPFC) for 20 minutes. The bi-frontal t-DCS approach showed promise in alleviating vestibular symptoms in this demographic alongside vestibular rehabilitation [35]. An outline of various studies about distinct vestibular disorders and their treatments utilizing diverse neuromodulation techniques is comprehensively presented in Table 1.

Table 1. Overview of studies related to vestibular disorders using different neuromodulation techniques and the outcomes.

Sl no.	Authors	Vestibular disorders	Neuromodulation Techniques used & site of stimulation	No. of subjects	Results	Outcomes
1.	Cha YH et.al (2014) [29]	Mal de Debarquement Syndrome (MdDS)	rTMS Right 10Hz, And Right 1Hz over DLFPC	10 subjects with MdDS	rTMS well-tolerated in subjects with MdDS	Promising short-term improvement of symptoms
2.	TarnutzerM, et al. (2017) [30]	Vestibular Decompensation	Low-frequency rTMS (LFrTMS) over the vestibular cerebellar network	3 subjects with vestibular decompensation	Improvement in postural instability	Improvement in motor performance during rehabilitation
3.	Koganemaru et al. (2017) [31]	Chronic dizziness	t-DCS	30 patients with chronic dizziness	Improvement with vestibular rehabilitation	Improvement, along with vestibular rehabilitation and t-DCS, was more effective than with vestibular rehabilitation alone.

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Sl no.	Authors	Vestibular disorders	Neuromodulation Techniques used & site of stimulation	No. of subjects	Results	Outcomes
4.	Paxman et Al. (2018) [32]	Chronic dizziness followed by MILD TBI	Repetitive Transcranial Magnetic Stimulation (r-TMS)	1 subject (case study	DHI scores improved post-treatment with r-TMS	For individuals with mild traumatic brain damage who experience persistent post-traumatic dizziness, r-TMS is a safe and economical treatment option.
5.	Moussavi, Z., et al. (2019) [33]	Persistent Post-Concussion Syndrome (PCS)	Repetitive Transcranial Magnetic Stimulation(r-TMS)	22 subjects with PCS	-Improvement in and with depression with depression, with improvement in postural instability	Reduced mTBI headaches, -Non-invasive technique for mild traumatic brain injuries

Continued on next page

Sl no.	Authors	Vestibular disorders	Neuromodulation Techniques used & site of stimulation	No. of subjects	Results	Outcomes
6.	Buard et Al. (2022) [34]	Mal de Debarquement Syndrome (MdDS)	Repetitive Transcranial Magnetic Stimulation (r-TMS)	1 subject (case study)	-Suppression of chronic rocking dizziness improvement in the Dizziness Handicap Inventory (DHI) impact on anxiety and depression	Reduction in rocking dizziness Improved DHI impact on anxiety and depression Short-term efficacy demonstrated
7.	Saki, N., et al. (2022) [35]	Chronic vestibular dysfunction in the elderly	Transcranial Direct Current Stimulation (t-DCS) on DLFPC	36 subjects with chronic vestibular dysfunction	-Double-blind randomized controlled trial -Improvement in balance function Non-invasive approach	Positive outcomes in balance function. Non-invasive approach Evidence from a double-blind randomized trial

5. Effectiveness of neuromodulation techniques on migraine

5.1. Neuromodulation techniques to assess the activation of the motor cortex in migraine

The complexities surrounding the pathophysiology of migraines remain somewhat obscure; yet, neurophysiological research over the past few decades has revealed that individuals afflicted by migraines display interictal anomalies in their cortical information processing frameworks. These functional brain irregularities are dynamically variable, oscillating cyclically until a migraine episode occurs, at which point the cortical responsiveness appears to revert to a normative state. This was evidenced by evaluations of cortical evoked potentials (EPs). The migraineur's cerebral activity is frequently marked by atypical amplitude habituation of EPs in response to various sensory stimuli. Furthermore, the excitability of the cortex can be assessed non-invasively by applying transcranial magnetic stimulation (TMS) pulses to distinct cortical regions, followed by the documentation of evoked potential activity in these areas of the brain. In a pilot study, Maertens de Noordhout et al. (1992) used transcranial magnetic stimulation of the motor cortex in 10 patients with common migraine and 12 patients with unilateral classic migraine who experienced sensorimotor auras. In the case of classic migraine, they discovered that the side where auras occurred had a higher activation threshold by cortical stimulation than the unaffected side. Patients with common migraine, on the other hand, displayed typical reactions on both sides. This implies that patients with classic migraine who also experience sensorimotor auras have a clinical malfunction of the motor cortex [36]. Bettucci et al. (1992) evaluated the excitability threshold and the central motor conduction time (CMCT) in 254 female patients diagnosed with menstrual migraine, along with 10 healthy female subjects. They observed a significant increase in cortical excitability values and postulated that this increase may be a neurophysiological correlate for migraine without aura [37]. To assess the thresholds, latencies, and amplitudes of motor-evoked potentials (MEPs), Kamp et al. (1996) examined ten patients with migraine with aura, ten patients with migraine without aura, and ten control participants. Later, it was concluded that both hemispheres are equally involved in the migraine process, as evidenced by the fact that these characteristics were unrelated to the side of the headache [38]. The effectiveness in treating chronic migraine was demonstrated by Brighina et al. (2004), who investigated whether 12 sessions of high-frequency r-TMS over the left dorsolateral prefrontal cortex could improve chronic migraine in 11 patients. The conclusion concluded that high-frequency r-TMS could reduce chronic migraine symptoms [39]. To investigate "the metaplasticity of the primary motor cortex in migraineurs and healthy controls", Brighina et al. (2009) alternately administered t-DCS and r-TMS, which counteracted the mean MEP in both groups. They showed that between episodes, migraineurs' short-term homeostatic plasticity was altered, normalizing migraine habituation and establishing cortical inhibition and habituation [40]. In a study by Cosentino et al. (2014), 20 healthy controls, 14 chronic migraineurs, 48 patients with aura, and 66 patients with migraines without auras were included. Motor cortical responses were assessed during the interictal, preictal, ictal, and postictal stages of the migraine cycle. Different responses were seen depending on the frequency of attacks during the interictal phase, indicating that the excitability and fluctuations of the cortical area in the threshold for inhibitory metaplasticity may be essential to the process of migraine transformation and influence the recurrence of migraine attacks [41].

5.2. Neuromodulation technique to assess phosphene threshold levels during migraine

Neuromodulation techniques, particularly transcranial magnetic stimulation (TMS), are instrumental in assessing cortical excitability within migraine research. A widely utilized neurophysiological marker in this field is the phosphene threshold (PT)—the minimal stimulation intensity required to induce phosphenes, or visual phenomena resembling flashes of light in the absence of external stimuli. As a non-invasive measure of visual cortical excitability, PT is crucial in migraine pathology, where a dysregulated excitatory-inhibitory balance is often observed. Reduced PT values indicate heightened cortical excitability, typically evident during the interictal phase in migraine sufferers. The application of PT as a quantifiable metric has facilitated significant advancements in understanding regional variations in cortical responsiveness and the mechanisms underlying sensory processing abnormalities in individuals with migraine. Afra (2000) conducted an integrative study investigating cortical excitability in migraine through multiple modalities, including biochemical markers, psychophysical assessments, electrophysiological recordings, and transcranial magnetic stimulation (TMS) [42]. Biochemical findings, such as hypomagnesemia and elevated excitatory amino acids, suggest a movement toward cortical hyperexcitability, whereas electrophysiological data often reflect functional hyperexcitability, particularly in the form of attenuated preactivation and deficient sensory habituation. These conflicting patterns are likely attributable to methodological variability, heterogeneous patient profiles, and the differential timing of assessments concerning the migraine cycle. Moreover, the presence of genetic heterogeneity, including mutations in genes encoding ion channels, further complicates the neurophysiological phenotype of migraine. TMS data reinforce the diverse cortical functional profiles seen across migraine subtypes, emphasizing the necessity for methodological standardization, precise patient stratification, and temporal specificity in experimental design. Gerwig et al. (2003) assessed visual cortical excitability in migraine patients using both single-pulse and paired-pulse TMS, focusing on the comparison between phosphene thresholds (PT) and motor thresholds (MT) [43]. The absence of correlation between these thresholds suggests that MT does not reliably index visual cortical excitability, indicating a region-specific regulation of excitability that may involve distinct neurophysiological mechanisms. In a study by Young et al. (2004), the phasic evolution of TMS-induced PT was examined across repeated stimulations in both migraineurs and healthy individuals [44]. Migraine patients exhibited progressively lower PT values, suggesting either facilitatory cortical summation or impaired inhibitory modulation, consistent with an underlying excitability imbalance. Chadaide et al. (2007) extended this research by employing tDCS to probe interictal visual cortical excitability, again using PT as the principal measure [45]. Their findings revealed significantly reduced PT in migraineurs compared to controls, implicating a deficiency in cortical inhibitory control and further supporting the hypothesis of a maladaptive excitatory-inhibitory balance in the migraine brain.

5.3. Neuromodulation to assess the cortical silent period in migraineurs

The Cortical Silent Period (CSP), a direct indicator of motor inhibition, is obtained by electromyography (EMG) recording on a target muscle during transcranial magnetic stimulation (TMS). The CSP reflects the EMG quiet that follows TMS treatment. Although its origin remains a topic of debate, it is believed to arise from anatomical and physiological dysfunctions in the basal ganglia [46]. The CSP serves as a measure of spinal and cortical inhibition, primarily depending on

the activity of GABA B circuits [47]. In a 1999 study, Aurora et al. used TMS to determine the Cortical Stimulation Silent Period (CSSP) in nine migraine sufferers with aura and nine control subjects. They discovered that migraineurs with aura had a shorter CSSP duration than the controls, which may indicate that cortical neurons are more excitable and have less central inhibition [48]. Bohotini et al. (2002) studied changes in visual cortex excitability using low- and high-frequency repetitive TMS (r-TMS). The study involved 30 migraineurs and 20 healthy volunteers, focusing on the occipital cortex. Their findings indicated reduced habituation in migraineurs, attributed to a lower excitability level in the visual cortex [49]. Yuksel et al. (2021) conducted a study involving female subjects, 20 migraineurs with aura, 20 migraineurs without aura, and 30 healthy controls, during the pre-ovulatory phase of the menstrual cycle. They measured motor-evoked potentials (MEP) and resting motor thresholds (rMT) induced by r-TMS to evaluate cortical excitability. Their results revealed a shorter CSP in both migraineur groups, indicating the presence of motor hyperexcitability due to a reduction in GABAergic neuronal inhibition in migraineurs [50].

5.4. Neuromodulation technique to reduce pain and frequency of migraine episodes

A meta-analysis conducted by Lan et al. (2017) evaluated the efficacy of transcranial magnetic stimulation (TMS) as a treatment for migraines. This thorough review incorporated five Randomized Controlled Trials (RCTs) with a total of 313 participants, comparing the TMS cohort to a control group. The results highlighted that TMS was significantly effective in reducing migraine symptoms. Notably, the stimulation dosages and frequencies varied across the studies, with findings suggesting that higher-frequency TMS applied with a figure-of-8 coil over the left motor cortex provided optimal results, particularly in terms of stimulation parameters [51]. In a separate study, Narmashiri (2023) investigated the effects of tDCS in a cohort of 150 individuals suffering from chronic migraines. This extensive 11-week intervention comprised 25 sessions, each featuring two consecutive montages lasting 20 minutes, with an intensity set at 2000 μA. The researchers concluded that tDCS is a promising modality for both the prophylactic and therapeutic management of chronic migraines, underscoring its potential for long-term migraine relief [52].

5.5. Neuromodulation as a prophylactic treatment option

Teepker et al. (2010) examined the effects of r-TMS on 27 migraineurs over five days. Two groups of subjects were assigned: One received a placebo, and the other received true r-TMS. The placebo group used a sham coil in the shape of a figure eight, while the verum group received two trains of 500 pulses at a frequency of 1 kHz using a round coil. The study concluded that the verum group experienced a noteworthy reduction in the frequency of migraine attacks compared to the placebo group [53]. In a related study, Misra et al. (2013) examined a total of 25 patients, including eight with episodic migraines and 17 with chronic migraines, all diagnosed according to the standards set forth by the International Headache Society (IHS). In this study, r-TMS was administered on alternate days for three days, with each session consisting of 600 pulses given at a frequency of 10 Hz, while β-endorphin levels in serum and cerebrospinal fluid (CSF) were measured. The results demonstrated significant post-treatment decreases in headache frequency and severity, improved functional capacity, reduced reliance on analgesics, and elevated β-endorphin levels [54]. Additionally, Hammad et al. (2021) investigated the role of low-frequency r-TMS as a preventive measure for migraine, applied

interictally over five consecutive days. The researchers assessed biomarkers, specifically Neurokinin A, and utilized the Migraine Disability Assessment Scale (MIDAS) to evaluate the biomarker before and after the treatment. Their findings supported the effectiveness of low-frequency r-TMS as a prophylactic strategy for individuals suffering from migraines, regardless of aura presence [55].

5.6. To correct the lower pre-activation level and the inhibition of the visual cortex

Brighina et al. (2005) conducted a seminal study that examined the impact of 1 Hz r-TMS on the facilitatory and inhibitory processes of the motor cortex in migraineurs who experienced aura. The study aimed to determine whether the abnormal excitability patterns seen in these individuals extend beyond the sensory cortex into the motor areas. Remarkably, when compared to control participants, the findings suggest that those with migraines demonstrate significantly lower levels of intracortical inhibition in their baseline states [56]. For further insights into neuromodulation techniques designed to alleviate migraines, refer to Table 3.

Table 2. Exogenous neuromodulation studies on migraine exploring the assessment and management aspects.

Serial No.	Author	Exogenous Neuromodulation Modality & Targeted Neuroanatomical Site	Migraine Phenotype / Cohort Characteristics	Principal Outcomes	Distinctive Contributions
1	Maertens de Noordhout et al. (1992) [36]	TMS over the motor cortex	10 typical, 12 classical with aura	Higher activation threshold in aura migraine; motor cortex dysfunction.	The first study showed motor cortex hyperexcitability in migraine with aura.
2	Bettuci et al. (1992) [37]	TES over vertex	254 menstrual migraine, 10 controls	Increased cortical excitability in menstrual migraine.	Identifies cortical excitability as a potential biomarker for hormonal migraine

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Serial No.	Author	Exogenous Neuromodulation Modality & Targeted Neuroanatomical Site	Migraine Phenotype / Cohort Characteristics	Principal Outcomes	Distinctive Contributions
3	Kamp et al. (1996) [38]	TMS over the vertex	10 controls, 10 with aura, 10 without aura	No difference in MEP parameters between hemispheres.	Contradicts theories of unilateral cortical involvement in migraine.
4	Brighina et al. (2004) [39]	High-frequency rTMS over left DLPFC	11 chronic migraines	Significant symptom relief with rTMS.	An early study suggested non-invasive neuromodulation as a migraine treatment.
5	Bringina et al. (2009) [40]	rTMS over the motor cortex	9 with aura, 8 controls	Reduced cortical inhibition and abnormal habituation.	First evidence linking impaired neuroplasticity to migraine pathophysiology.
6	Cosentino et al. (2014) [41]	rTMS over the primary motor cortex	66 without aura, 48 with aura, 14 chronic, 20 controls	Motor cortical excitability fluctuates across migraine phases.	First study mapping cortical excitability changes throughout migraine cycles.
7	Afra et al. (2000) [42]	TMS over the motor cortex	Review study	Reduced excitability is linked to lower magnesium levels.	Supports the role of magnesium deficiency in migraine development.

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Serial No.	Author	Exogenous Neuromodulation Modality & Targeted Neuroanatomical Site	Migraine Phenotype / Cohort Characteristics	Principal Outcomes	Distinctive Contributions
8	Gerwig et al. (2003) [43]	Biphasic rTMS over the primary motor cortex	32 controls	No correlation between MT and visual cortex excitability.	Challenges the assumption that motor threshold reflects visual cortex changes.
9	Young et al. (2004) [44]	rTMS over occipital lobe	11 with aura, 10 without, 9 menstrual, 15 controls	Lower phosphene thresholds in migraineurs.	Reinforces the cortical spreading depression (CSD) hypothesis.
10	Chadaideet al. (2007) [45]	Biphasic TMS over occipital lobe (Oz) & tDCS	16 migraineurs, 9 controls	Migraineurs have lower phosphene thresholds, indicating reduced inhibition.	First study using tDCS to alter cortical excitability in migraine.
11	Aurora et al. (1999) [48]	TMS over the motor cortex	9 with aura, 9 controls	Shortened Cortical Silent Period (CSSP), increased cortical excitability.	Direct evidence of reduced inhibition in migraine with aura.
12	Bohotini et al. (2002) [49]	Low & high-frequency rTMS over the occipital lobe	30 migraineurs, 20 controls	Reduced habituation in the visual cortex.	Suggests migraine results from impaired sensory processing and cortical dysregulation.

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Serial No.	Author	Exogenous Neuromodulation Modality & Targeted Neuroanatomical Site	Migraine Phenotype / Cohort Characteristics	Principal Outcomes	Distinctive Contributions
13	Yuksel et al. (2021) [50]	rTMS over vertex (Cz)	20 with aura, 20 without, 30 controls	Motor hyperexcitability and reduced GABAergic inhibition.	Strong evidence linking GABA dysfunction to migraine pathogenesis.
14	Lan et al. (2017) [51]	Single-pulse TMS (various sites)	5 studies, 313 migraineurs	TMS significantly reduces migraine symptoms.	Large-scale meta-analysis confirming TMS efficacy in diverse migraine subtypes.
15	Narmashiri et al. (2023) [52]	Anodal/Cathodal tDCS	150 chronic migraineurs	tDCS effective for prevention and treatment.	Largest clinical trial supporting tDCS for chronic migraine management.
16	Teepker et al. (2010) [53]	Low-frequency rTMS over the vertex	27 migraineurs	Significant reduction in migraine attacks in the verum group.	Sham-controlled study proving rTMS reduces migraine frequency.

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Serial No.	Author	Exogenous Neuromodulation Modality & Targeted Neuroanatomical Site	Migraine Phenotype / Cohort Characteristics	Principal Outcomes	Distinctive Contributions
17	Misra et al. (2013) [54]	rTMS over the left frontal cortex	93 without aura, 7 with aura	Reduced headache frequency, severity, disability, and analgesic use; increased β-endorphin.	First study that has linked rTMS-induced pain relief to β-endorphin increase.
18	Hammad et al. (2021) [55]	Low-frequency rTMS over the vertex	30 without aura, 10 with aura	Low-frequency rTMS is effective as a prophylactic migraine treatment.	Demonstrates preventive benefits of rTMS beyond symptom relief.
19	Brighina et al. (2005) [56])	rTMS over the left-hand motor cortex	9 with aura, 8 controls	Migraineurs showed lower intracortical inhibition.	Suggests altered motor cortex excitability as a migraine biomarker.

6. Effectiveness of endogenous neuromodulation techniques on migraine

There is a well-established reciprocal relationship between migraine and mental health conditions. Major depression and migraine have a strong reciprocal association, with depression predicting first-onset migraine and migraine predicting first-onset depression [57]. The discovery that migraine is more frequently associated with poor sleep, anxiety, and catastrophizing thoughts raises questions about the idea that migraine is a sensitive brain state that can be impacted by everyday behavioral and psychosocial stressors [58]. One explanation for this could be the existence of particular psychological characteristics that, even in the absence of serious mental illnesses, fuel a vicious cycle in which migraine and maladaptive behavior reinforce one another [59]. According to recent research, while monoclonal antibodies that target the calcitonin gene-related peptide (CGRP) pathway are typically effective in treating patients who are difficult to treat, having an "anxious-fearful" personality combined with anxiety and current stressors is a poor predictor of treatment outcome [60]. By directing clinicians to integrate behavioral interventions, medication treatments, and stress management techniques to lessen migraine-related disability, a biopsychosocial model of migraine may open the door for an alternate therapeutic strategy. According to this concept, non-pharmacological therapies should be viewed as an extra therapy option for all patients rather than as a replacement for conventional headache management. In particular, a polymorphism in the 5-HT transporter gene and a particular genotype of the dopamine D2 receptor, an imbalance of serotonin neurotransmitters, and a disproportion between pro-inflammatory and anti-inflammatory cytokines in the hypothalamic-pituitary-adrenal axis may be the pathophysiological pathways that cause anxiety in conjunction with sleep-related disturbances to be a driver for migraine development and transformation [61]. The hypothalamus is part of the network of vestibular, visceral sensory, and nociceptive signals in Furman's VM pathophysiology model [62]. The suprachiasmatic nucleus (SCN) of the anterior hypothalamus contains a master precursor that is part of a complex molecular regulation mechanism that governs the circadian rhythm. Early circadian attack onset and induction of sleep quality were associated with a higher severity of VM attacks, indicating that VM patients might have a distinct endogenous pacemaker setup in the suprachiasmatic nucleus [63]. The SCN's circadian clock is a complicated network of diverse glial and neuronal cells. The time of sleep and wakefulness is the most evident example of circadian-regulated production [64,65]. The hypothalamus also plays a crucial regulatory function in sleep control, and it's interesting to note that several sleep-related nerve nuclei, including the raphe nucleus, locus coeruleus, and parabrachial nucleus, may be involved in the potential central pathophysiology of VM [66,67]. The hypothalamus sends signals to the locus coeruleus, which regulates the central and vestibular conduction pathways in VM during an episode.

In a 2010 study, Stokes and colleagues treated 37 individuals with migraines using an average of 40 sessions of combined neurofeedback and thermal biofeedback in an outpatient setting. All the patients were on some form of migraine medicine, whether it was rescue, preventive, or abortive. For at least two weeks before and during therapy, patients kept daily headache diaries that documented the frequency, intensity, duration, and the medications taken. Over an average of six months, treatments were administered three times per week on average. Following therapy, a formal interview was held, and headache diaries were reviewed. To determine the longevity of therapy effects, a formal interview was conducted 14.5 months after treatment on average. The study involving three types of biofeedback for migraine had a more robust effect size than combined studies on thermal biofeedback alone for migraine. All combined neuro and biofeedback interventions were effective in reducing the frequency

of migraines with clients using the medication, yielding a more favorable outcome (70% experiencing at least a 50% reduction in headaches) than just medications alone (50% experiencing a 50% reduction) [68]. Legarda et al. (2022) explored the use of ILF neurofeedback as a nonpharmacological treatment for patients with refractory primary headache disorders, including chronic migraines. The authors hypothesized that ILF brain training influences the re-regulation of hypothalamic (and limbic) networks and that refractory primary headache syndromes represent a dysregulated state or chronic instability of hypothalamic-trigeminal connections (top-down dysmodulation). In the integrative treatment of refractory migraine, trigeminal autonomic cephalgia, and other primary headache diseases, their neurology practice views ILF Neurotherapy as a crucial tool. The study highlights the benefits of early ILF neurotherapy, including reduced emergency room visits, avoidance of medication overuse, and improved patient resilience to anesthetic procedures when surgery is necessary. This approach presents a promising alternative for individuals unresponsive to conventional pharmacological treatments [69].

Sasu (2022) conducted a case study on an unmedicated individual experiencing persistent symptoms of Persistent Postural-Perceptual Dizziness (PPPD), which had continued for three years following diagnosis. The individual underwent 32 sessions of Infra-Low Frequency Neurofeedback (ILF NF)**,** resulting in substantial symptom abatement, not only of PPPD-related symptoms but also of comorbid issues such as anxiety, intrusive violent thoughts, and suicidal ideation**.** Improvements were documented through both pre- and post-treatment Continuous Performance Test (CPT) data and consistent session-by-session symptom tracking. ILF NF emerged as a powerful adjunct to the patient's treatment plan, enabling both symptom relief and a deeper resolution of core dysregulations**,** particularly those linked to impaired arousal and excitability regulation. The study suggests this is possible due to the restoration of intrinsic functional connectivity within the default mode and salience networks—a mechanism also relevant to chronic migraine**,** which shares underlying neuroregulatory dysfunction. Although the researchers focused on PPPD, their findings strongly support ILF NF's broader applicability to migraine and other chronic neurophysiological conditions, especially where conventional treatments fall short [70]. Another randomized, crossover sham-controlled study by Arina et. al (2022) evaluated the effectiveness of ILF neurofeedback in 30 patients with tension-type headaches (TTH). Each participant underwent ten sessions of ILF neurofeedback and ten sessions of sham neurofeedback. Results showed a significant decrease in headache frequency during the ILF neurofeedback sessions compared to the sham condition. The authors concluded that ILF neurofeedback holds promise as a preventive treatment for TTH [71].

Table 3. The Endogenous neuromodulation technique used for migraine and vestibular disorders.

Authors	Endogenous Neuromodulation techniques used	Migraine subtypes /headache type	Key findings
Stokes et al (2010) [68]	Thirty-seven individuals with migraines received an average of 40 sessions of combined EEG, hemoencephalography (HEG), and thermal biofeedback in an outpatient clinical setting.	Not mentioned	All combined neuro and biofeedback interventions were effective in reducing the frequency of migraines with clients using medication, yielding a more favorable outcome (70% experiencing at least a 50% reduction in headaches) than just medications alone (50% experiencing a 50% reduction)
Legarda et. al (2022) [69]	3 clinical cases involving individuals with primary headache disorders were treated using infralow frequency (ILF) neurofeedback	Headache with psychogenic origin	In the integrative treatment of refractory migraine, trigeminal autonomic cephalgia, and other primary headache diseases, neurology practice views ILF neurotherapy as a crucial tool.
Sasu et al. (2022) [70]	An individual with PPPD without any medication	PPPD with psychogenic aspects involved	ILF NFB significantly reduced those symptoms while also improving other concomitant symptoms, such as anxiety, intrusive violent thoughts, and suicidal thoughts.
Arina et. Al (2022) [71]	30 patients with tension-type headaches (TTH)	tension-type headaches (TTH)	a significant decrease in headache frequency during the ILF neurofeedback sessions compared to the sham condition.

7. Discussion

The vestibular system represents a rudimentary yet highly intricate neural network, characterized by complex interconnections between vestibular neurons within both cortical and subcortical pathways of the brain [72]. This study was primarily conducted to assess the utility of neuromodulation techniques, such as repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS), in addressing vestibular disorders and migraines, with a particular focus on their potential applicability to VM. The vestibular system is tightly integrated with the vestibulo-cerebellum, particularly the flocculonodular lobe, which plays a pivotal role in maintaining balance and regulating eye movements. This system operates through ascending pathways involving the peripheral labyrinths, the eighth cranial nerves, and central pathways originating from the vestibular nuclei. During basilar migraine attacks, transient brainstem dysfunctions can emerge, leading to significant changes in the pontomesencephalic brainstem. These changes often result in prolonged interwave III-V latencies as observed in Auditory Brainstem Evoked Potentials (ABEP), a critical diagnostic tool [73]. Additionally, vascular compromise to the inner ear is a noted concern in VM, given that the anterior inferior cerebellar artery (AICA), which supplies blood to critical structures such as the anterolateral pons, middle cerebellar peduncle, and cerebellar flocculus, is intricately linked to the basilar artery, which ensures perfusion to the brainstem and cerebellar regions [74]. The phenomenon of cortical spreading depression (CSD) is particularly relevant, as it signifies a slow wave depolarization that propagates across brain networks, leading to diminished blood and oxygen perfusion, changes in vascular tone, and impaired energy metabolism [75]. Importantly, these waves can extend to the vestibular cortex or the vestibular nuclei in the brainstem, potentially precipitating vestibular symptoms characteristic of VM. Further research has suggested a vasoactive connection between the cochlea and the vertebrobasilar system, mediated through trigeminal sensory neurons, which further elucidates the complex relationship between vestibular and vascular dysfunction in migraine pathophysiology [76]. These insights underscore the profound overlap between migraine and VM, particularly in terms of the shared neural pathways that mediate the clinical manifestations, which extend to the peripheral vestibular system. The interconnectedness of the thalamocortical network, vestibular systems, vascular systems, brainstem nociceptive pathways, and VM pathophysiology is visually represented in Figure 2, offering a comprehensive view of the complex dynamics underlying VM.

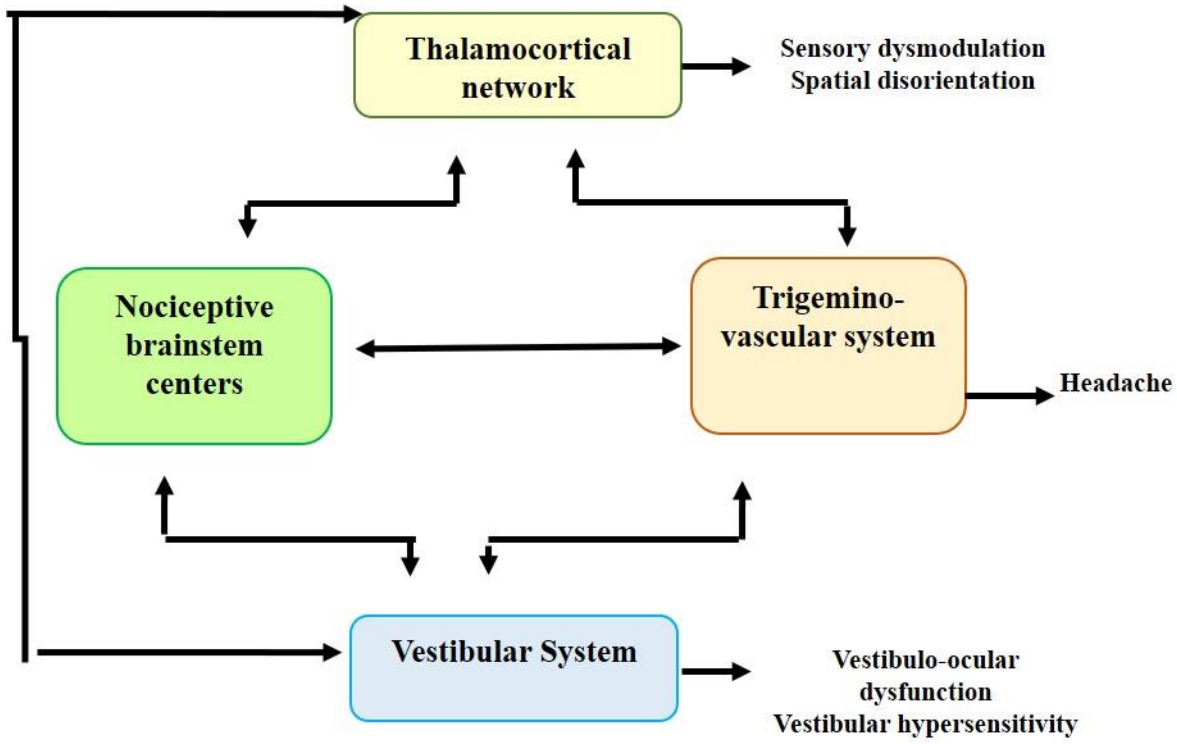

Figure 2. Mechanism of pathogenesis in VM concerning different networks and systems (VM).

The different centers and systems within the thalamocortical network can give rise to different types of clinical manifestations of VM.

7.1. Factors to consider for implementing neuromodulation techniques on VM

Neuromodulation techniques have facilitated the resolution of neuropsychiatric disorders and neuromotor conditions [77]. These methods have significantly contributed to the alleviation of migraines, with limited evidence suggesting their role as an adjunctive therapy in migraine management [78]. When focusing solely on the outcomes of various neuromodulation techniques, it is evident from the studies mentioned that these approaches have shown promising and positive results in resolving both vestibular disorders and migraines. Brain-derived neurotrophic Factor (BDNF) is broadly disseminated throughout the central nervous system, encompassing the hippocampus, amygdala, and hypothalamus. It is associated with the pathophysiology of migraines and can influence brain development, differentiation, neurogenesis, and synaptic plasticity [79]. BDNF levels are notably elevated in individuals experiencing migraines and are particularly heightened during migraine attacks, underscoring the role of neurotrophic factors in nociceptive pathways [80]. Neuronal LTD and LTP are induced as a result of exposure to Transcranial Magnetic Stimulation (TMS), leading to alterations in synaptic strength. A study highlighted that BDNF levels can be diminished through modified BDNF binding affinity via LTP, demonstrating that repetitive TMS fosters cortical plastic changes by enhancing BDNF–TrkB signaling [81]. Glutamate serves as the primary excitatory neurotransmitter within the CNS, and various paroxysmal neurological disorders are influenced by alterations in brain

excitability resulting from disruptions in glutamate homeostasis. Specifically, glutamate acts as a potent inducer of CSD, and an imbalance in glutamate release and clearance contributes to the onset of migraines [82]. Both glutamate and N-methyl-D-aspartate Receptors (NMDAR) play a pivotal role in the initiation of migraine aura and pain [83]. The molecular mechanisms underlying the changes induced by TMS are likely associated with NMDA receptors on the postsynaptic membrane. In its resting state, magnesium ions obstruct a cationic channel within NMDA receptors [84]. Once the cell membrane depolarizes, this blockage is lifted, permitting calcium ions to enter the postsynaptic neuron, ultimately leading to the induction of LTP [85]. Consequently, it can be inferred that rTMS may assist in alleviating the clinical manifestations of migraines linked to glutamate and NMDA activity. Additional research revealed that migraineurs exhibit diminished GABA levels in the anterior cingulate gyrus (ACC) and medial prefrontal cortex (mPFC) [86]. GABA also influences GABAergic inhibitory interneurons in visual cortices due to its dysfunction [87]. Researchers demonstrated that a 20-minute session of inhibitory 1 Hz r-TMS increased GABA levels [88]. The resting motor threshold is a global indicator of excitability throughout the brain, acting as an essential parameter in single-pulse TMS (s-TMS). The rMT and PT exhibit a correlation. Although the strength of this linear relationship changes depending on the TMS settings, a single TMS measure, such as PT or rMT, can be used as a stand-in for cortical excitability across several brain areas [89].

Given the overlapping pathophysiological substrates between migraine and vestibular systems, particularly involving the hypothalamic-trigeminal-vestibular axis, ILF neurofeedback appears to address the core instability in VM. By restoring balance across cortical networks and autonomic pathways, ILF NF not only reduces migraine frequency but also mitigates vertigo and psychiatric comorbidities often seen in VM. These findings, though preliminary, suggest ILF neurofeedback holds promise as a non-invasive, enduring treatment strategy for VM, meriting further clinical investigation. Hence, neuromodulation techniques provide valuable insights into brain excitability through assessments. The studies discussed above suggest that various factors impacting migraineurs may also be present in VM. Therefore, it can be postulated that the application of neuromodulation techniques in VM patients may yield favorable outcomes. An examination of the present study's aim reveals that comparable positive outcomes have also been reported in cases of vestibular disorders. The results indicate that conditions such as chronic vertigo, mal de barquement syndrome, vestibular decomposition, and persistent post-concussion syndrome have been ameliorated through neuromodulation techniques. Furthermore, numerous factors linked to migraine pathogenesis have also been addressed through these methodologies. Upon evaluating VM, it is transparent that periodic diagnostic tests provide insight into the functional status of both peripheral and central vestibular dysfunction associated with this condition [90]. Figure 3 illustrates the interconnected pathophysiological mechanisms of migraine and vestibular dysfunction converging at shared central structures such as the hypothalamus, brainstem, and thalamocortical network. Increased cortical excitability, reduced GABAergic inhibition, and hypothalamic dysregulation are implicated in both migraine and vestibular symptoms, including vertigo and headache. Neuromodulation techniques such as rTMS, Transcranial Direct Current Stimulation (tDCS), and ILF Neurofeedback are shown to modulate these disrupted networks by restoring cortical balance, enhancing synaptic plasticity, and improving neurochemical regulation. These interventions result in the reduction of migraine attacks, improvement in vestibular function, and mitigation of associated psychiatric comorbidities, offering a promising, non-invasive, and targeted therapeutic strategy for long-term VM management.

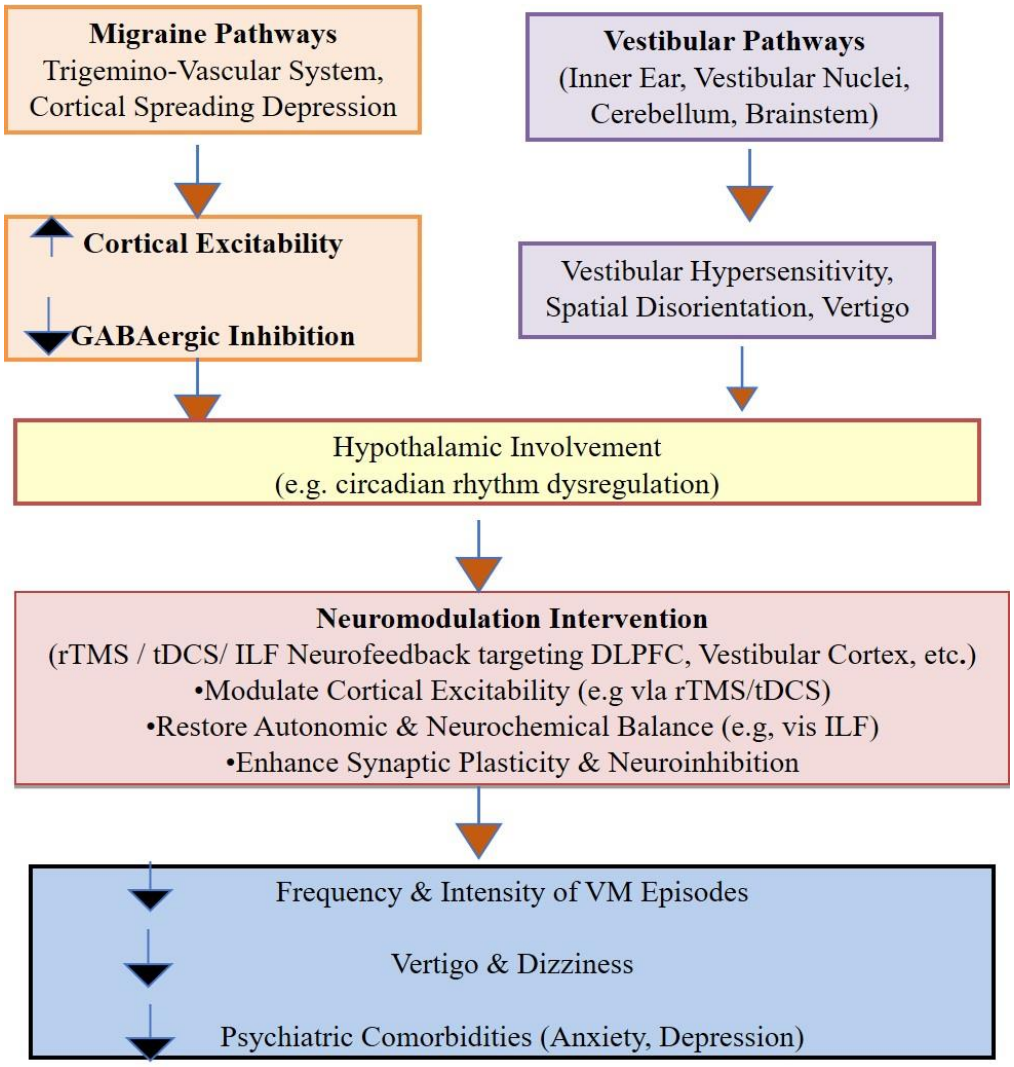

Figure 3. Flowchart illustrating how neuromodulation techniques may influence the anatomical and physiological pathways involved in Vestibular Migraine (VM) by addressing both migraine and vestibular systems through targeted neuromodulation.

7.2. Possible long-term outcomes of neuromodulation techniques in VM

The long-term efficacy of neuromodulation techniques, both exogenous and endogenous, has become an area of increasing interest, especially in managing chronic and refractory cases of VM. While evidence is predominantly short-term and focused on symptom relief, emerging studies have highlighted the potential of these techniques to bring about sustained neuroplastic changes and functional recovery over extended periods.

7.2.1. Exogenous neuromodulation (rTMS, tDCS)

Exogenous approaches such as rTMS and tDCS have demonstrated lasting effects by engaging mechanisms such as long LTP and LTD, which underlie synaptic remodeling. Repeated rTMS sessions have been associated with persistent reductions in headache frequency and vestibular symptoms up to

3–6 months post-intervention in certain cohorts. Similarly, tDCS-induced changes in cortical excitability have been shown to modulate pain pathways and sensory integration circuits with delayed but sustained improvements when used adjunctively with vestibular rehabilitation.

7.2.2. Endogenous neuromodulation (ILF neurofeedback)

ILF neurofeedback, a form of endogenous neuromodulation, works by enhancing the brain's self-regulatory capacity throughout sessions by way of adaptive and individualized protocols. Studies report continued symptom relief in migraine and related disorders even months after discontinuation of training. These benefits are hypothesized to stem from improved autonomic regulation, stabilization of hypothalamic-limbic activity, and recalibration of dysfunctional default mode and salience networks. Moreover, ILF neurofeedback offers a non-pharmacological strategy for relapse prevention, especially in patients with psychiatric comorbidities or poor medication tolerance.

7.3. Limitations

a. The limitations of this study can be articulated, including the absence of sweeping literature examining the usefulness of neuromodulation techniques in the treatment of VM. Furthermore, numerous studies present conflicting conclusions regarding the beneficial outcomes of neuromodulation methods in chronic migraine management, as well as the requisite protocols for repetitive transcranial magnetic stimulation (r-TMS) in this context. Besides, the assessment of bias quality and the validity of blinding in the included trials was inadequately discussed. To sufficiently comprehend the possible blow of various cortical and subcortical regions of the brain and their contributions to the embodiment of symptoms in VM, it is compulsory to establish a standardized procedural protocol in a large sample size. The longer follow-up time is required for neuromodulation techniques to observe the relapse, ensure safety monitoring, and side effects. The acceptance of neuromodulation techniques as a validated treatment for VM would represent a significant advancement in the field of vestibular sciences. This exceeds the recommended safety levels for the auditory system (OSHA). Although seemingly innocuous, repeated exposure to this intense sound can lead to acoustic trauma. To meet this demand, a study was done where quiet TMS (qTMS) device was introduced that combines two essential ideas: The TMS pulse sound's primary frequency components, which are normally between 2 and 5 kHz, are first moved to higher frequencies that are over the upper threshold of human hearing, which is around 20 kHz. Moreover, the TMS coil's mechanical and electrical design minimizes the amount of sound produced at audible frequencies (< 20 kHz) while producing suprathreshold electric field pulses. A new, multilayer coil design is used to achieve the improved acoustic qualities of the coil. The authors also summarized a proof-of-concept qTMS prototype that uses ultra-brief pulses at conventional amplitudes to reduce noise loudness by 19 dB(A) [91].

b. Seizures: While the risk of seizure from TMS was described by Rossi et al. (2009) as "very low", it has never been quantified, and common assumptions, such as that single-pulse or low-frequency stimulation is less risky than rTMS within the recommended limits, have not been tested [92].

c. Even with sham tDCS, the following side effects were noted: Mild tingling (70.6%), moderate weariness (35.3%), and light itching under the stimulus electrode (30.4%). Furthermore, skin issues were the most frequent side effects; however, they went away following tDCS. Insomnia (0.98%),

headache (11.8%), and nausea (2.9%) were recorded following tDCS [93]. Compared to repetitive transcranial magnetic stimulation (rTMS), the incidence of notable adverse effects, including headache, was much lower following tDCS (11.8% in tDCS and 23% in rTMS) [94,95].

8. Conclusion and future scope

The study posits that neuromodulation techniques, owing to their promising outcomes in preaching vestibular disorders and migraines, represent a powerful path to the management of VM. When combined with prophylactic treatments, lifestyle modifications, and VRT, these techniques may prove to be a valuable adjunctive therapy in the comprehensive management of vestibular conditions. Neuromodulation could be particularly beneficial for patients with refractory VM or those who are contraindicated for pharmacological therapies. However, it is essential to note that the data available on migraines and vestibular disorders cannot be universally generalized, as most studies are RCTs. Despite this, the findings are promising, indicating a potential for significant relief from symptoms associated with these disorders. In addition, identifying the optimal candidates for non-invasive brain stimulation in the treatment of VM requires a deeper understanding of its pathophysiology, including the potential involvement of both cortical and subcortical structures within the brain. Integrating neuromodulation with neuroimaging-guided targeting and personalized stimulation protocols could substantially enhance the precision of therapeutic interventions in VM. Future clinical trials should incorporate neurophysiological biomarkers, such as rMT, phosphene thresholds, and GABA levels measured via magnetic resonance spectroscopy (MRS), to objectively monitor treatment effects and utilize these as potential diagnostic biomarkers for VM. Moreover, a comprehensive investigation into how non-invasive neuromodulation might synergize with contemporary pharmacological treatments for both the acute management and prevention of VM attacks is warranted. This integration could potentially offer a more holistic treatment strategy. Rigorous, well-controlled trials will be essential to establish the efficacy of neuromodulation techniques, not only as adjuncts to pharmacotherapy but possibly as a primary intervention for VM. Therefore, we advocate for the painstaking integration of neuromodulation into the assessment and management strategies for VM to optimize patient outcomes and augment the breadth of effective treatments.

Use of generative-AI tools declaration

The authors declare that they have not used any Artificial Intelligence (AI) tools in the creation of this article.

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Conflict of interest

The authors report no conflicts of interest in the preparation of this manuscript.

Author contributions

The authors made substantial contributions to the conception or design of the work, as well as the acquisition, analysis, or interpretation of data. These contributions are as follows:

Conceptualization: Dinesh Bhatia and Koyel Das; Methodology: Koyel Das and Henry Benson Nongrum; Validation: Dinesh Bhatia, Koyel Das, and Tania Acharjee; Formal Analysis: Dinesh Bhatia and Koyel Das; Investigation: Dinesh Bhatia and Koyel Das; Resources: Dinesh Bhatia and Koyel Das; Data Curation: Dinesh Bhatia and Koyel Das; Visualization: Dinesh Bhatia, Tania Acharjee, Koyel Das; Writing Contributions: Original Draft Preparation: Koyel Das and Henry Benson Nongrum; Review and Editing: Dinesh Bhatia and Tania Acharjee.

References

1. Strupp M, Dlugaiczyk J, Ertl-Wagner BB, et al. (2020) Vestibular disorders. *Deutsch Ärztebl Int* 117: 300−310. https://doi.org/10.3238/arztebl.2020.0300
2. Dieterich M, Obermann M, Celebisoy N, et al. (2016) VM: the most frequent entity of episodic vertigo. *J Neurol* 263: 82–89. https://doi.org/10.1007/s00415-015-7905-2
3. Shen Y, Qi X (2022) Update on diagnosis and differential diagnosis of VM. *Neurol Sci* 43: 1659–1666. https://doi.org/10.1007/s10072-022-05872-9
4. Lempert T, Neuhauser H (2009) Epidemiology of vertigo, migraine, and VM. *J Neurol* 256: 333–338. https://doi.org/10.1007/s00415-009-0149-2
5. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition (beta version). Cephalalgia, 2013. 33: 629–808. Available from: https://doi.org/10.1177/0333102413485658
6. Alghadir AH, Anwer S (2018) Effects of vestibular rehabilitation in the management of a VM: a review. *Front Neurol* 9: 440. https://doi.org/10.3389/fneur.2018.00440
7. Lempert T, Olesen J, Furman J, et al. (2021) Vestibular migraine: diagnostic criteria (Update)[1]. *J Vestibul Res* 32: 1–6. https://doi.org/10.3233/ves-201644
8. Langhagen T, Lehrer N, Borggraefe I, et al. (2015) VM in children and adolescents: clinical findings and laboratory tests. *Front Neurol* 5: 292. https://doi.org/10.3389/fneur.2014.00292
9. Dieterich M, Staab JP, Brandt T (2016) Functional (psychogenic) dizziness, *Handbook of Clinical Neurology*, 447−468, https://doi.org/10.1016/B978-0-12-801772-2.00037-0
10. Luan S, Williams I, Nikolic K et al. (2014) Neuromodulation: present and emerging methods. *Front Neuroeng* 7: 27. https://doi.org/10.3389/fneng.2014.00027
11. Staab JP, Rohe DE, Eggers SD, et al. (2014) Anxious, introverted personality traits in patients with chronic subjective dizziness. *J Psychosom Res* 76: 80−83. https://doi.org/10.1016/j.jpsychores.2013.11.008
12. Othmer S, Othmer SF (2024) Endogenous neuromodulation at infra-low frequency: method and theory. Preprints. https://doi.org/10.20944/preprints202310.1085.v2

13. Noda T, Nishikawa M, Matsuda Y, et al. (2025) Efficacy and safety of low-frequency repetitive transcranial magnetic stimulation for bipolar depression: a study protocol for a multicenter, double-blind, randomized, sham-controlled trial. *Front Psychiatry* 16: 1393605. https://doi.org/10.3389/fpsyt.2025.1393605
14. Hallet M (2007) Transcranial magnetic stimulation: a primer. *Neuron* 55: 187199. https://doi.org/10.1016/j.neuron.2007.06.026
15. Wassermann E, Epstein C, Ziemann U, et al. (2008) *Oxford Handbook of Transcranial Stimulation*. Oxford: Oxford University Press. https://doi.org/10.1093/oxfordhb/9780198568926.001.0001
16. Cowey A (2004) The Ferrier Lecture 2004 What can transcranial magnetic stimulation tell us about how the brain works? *Philosophical Transactions of the Royal Society B: Biological Sciences* 360: 1185−1205. https://doi.org/10.1098/rstb.2005.1658
17. Huerta PT, Volpe BT (2009) Transcranial magnetic stimulation, synaptic plasticity, and network oscillations. *J Neuroeng Rehabil* 6: 7. https://doi.org/10.1186/1743-0003-6-7
18. Walsh V, Pascual-Leone A (2003) *Transcranial Magnetic Stimulation: A Neurochronometrics of Mind*. Cambridge: The MIT Press. https://doi.org/10.7551/mitpress/6896.001.0001
19. Allen EA, Pasley BN, Duong T, et al. (2007) Transcranial magnetic stimulation elicits coupled neural and hemodynamic consequences. *Science* 317: 1918−1921. https://doi.org/10.1126/science.1146426
20. Nitsche MA, Paulus W (2011) Transcranial direct current stimulation–update 2011. *Restor Neurol Neurosci* 29: 463492. https://doi.org/10.3233/rnn-2011-0618
21. Thair H, Holloway AL, Newport R, et al. (2017) Transcranial direct current stimulation (tDCS): a beginner's guide for design and implementation. *Front Neurosci* 11: 641. https://doi: 10.3389/fnins.2017.00641
22. Fertonani A, Pirulli C, Miniussi C (2011) Random noise stimulation improves neuroplasticity in perceptual learning. *J Neurosci* 31: 15416−15423. https://doi.org/10.1523/jneurosci.2002-11.2011
23. Berthelot N, Lemieux R, Garon Bissonnette J, et al. (2020) Uptrend in distress and psychiatric symptomatology in pregnant women during the coronavirus disease 2019 pandemic. *Acta Obstet Gyn Scan* 99: 848–855. https://doi.org/10.1111/aogs.13925
24. Cui X, Bray S, Reiss AL (2009) Functional near-infrared spectroscopy (NIRS) signal improvement based on negative correlation between oxygenated and deoxygenated hemoglobin dynamics. *NeuroImage* 49: 3039–3046. https://doi.org/10.1016/j.neuroimage.2009.11.050
25. Merzagora AC, Foffani G, Panyavin I, et al. (2010) Prefrontal hemodynamic changes produced by anodal direct current stimulation. *NeuroImage* 49: 2304−2310. https://doi.org/10.1016/j.neuroimage.2009.10.044
26. Emre M, Aarsland D, Albanese A, et al. (2004) Rivastigmine for dementia associated with Parkinson's disease. *New Engl J Med* 351: 2509–2518. https://doi.org/10.1056/nejmoa041470
27. Stonsaovapak C, Hemrungroj S, Terachinda P, et al. (2020) Effect of anodal transcranial direct current stimulation at the right dorsolateral prefrontal cortex on the cognitive function in patients with mild cognitive impairment: a randomized double-blind controlled trial. *Arch Phys Med Rehab* 101: 1279–1287. https://doi.org/10.1016/j.apmr.2020.03.023
28. Han BI, Song HS, Kim JS (2011) Vestibular rehabilitation therapy: review of indications, mechanisms, and key exercises. *J Clin Neurol* 7: 184. https://doi.org/10.3988/jcn.2011.7.4.184

29. Cha YH, Cui Y, Baloh R, et al. (2013) Repetitive transcranial magnetic stimulation for mal de debarquement syndrome. *Otol Neurotol* 34: 175–179. https://doi.org/10.1097/mao.0b013e318278bf7c
30. Tarnutzer AA, Ward BK, Shaikh AG, et al. (2023) Novel ways to modulate the vestibular system: Magnetic vestibular stimulation, deep brain stimulation, and transcranial magnetic stimulation / transcranial direct current stimulation. *J Neurol Sci* 445: 120544. https://doi.org/10.1016/j.jns.2023.120544
31. Koganemaru S, Goto F, Arai M et al. (2017) Effects of vestibular rehabilitation combined with transcranial cerebellar direct current stimulation in patients with chronic dizziness: an exploratory study. *Brain Stimul* 10: 576–578. https://doi.org/10.1016/j.brs.2017.02.005
32. Paxman E, Stilling J, Mercier L, et al. (2018) Repetitive transcranial magnetic stimulation (rTMS) as a treatment for chronic dizziness following mild traumatic brain injury. *BMJ Case Rep* 2018: 226698. https://doi.org/10.1136/bcr-2018-226698
33. Moussavi Z, Suleiman A, Rutherford G, et al. (2019) A pilot randomised double-blind study of the tolerability and efficacy of repetitive transcranial magnetic stimulation on persistent post-concussion syndrome. *Sci Rep* 9: 5498. https://doi.org/10.1038/s41598-019-41923-6
34. Buard I, Lopez-Esquibel N, Schoeneberger S, et al. (2020) Transcranial magnetic stimulation as treatment for mal de debarquement syndrome: case report and literature review. *Cogn Behav Neurol* 33: 145–153. https://doi.org/10.1097/wnn.0000000000000224
35. Saki N, Bayat A, Nikakhlagh S, et al. (2022) Vestibular rehabilitation therapy in combination with transcranial direct current stimulation (tDCS) for treatment of chronic vestibular dysfunction in the elderly: a double-blind randomized controlled trial. *Braz J Otorhinolar* 88: 758–766. https://doi.org/10.1016/j.bjorl.2020.11.004
36. Maertens de Noordhout A, Pepin JL, Schoenen J, et al. (1992) Percutaneous magnetic stimulation of the motor cortex in migraine. *Electroencephalography and Clinical Neurophysiology/Evoked Potentials Section* 85: 110–115. https://doi.org/10.1016/0168-5597(92)90076-n
37. Bettucci D, Cantello R, Gianelli M, et al. (1922) Menstrual migraine without aura: cortical excitability to magnetic stimulation. *J Head Face Pain* 32: 345–347. https://doi.org/10.1111/j.1526-4610.1992.hed3207345.x
38. Van Der Kamp W, Van Den Brink AM (1996) Interictal cortical hyperexcitability in migraine patients demonstrated with transcranial magnetic stimulation. *J Neurol Sci* 139: 106–110. https://doi.org/10.1016/s0022-510x(96)00044-5
39. Brighina F, Piazza A, Vitello G, et al. (2004) rTMS of the prefrontal cortex in the treatment of chronic migraine: a pilot study. *J Neurol Sci* 227: 67–71. https://doi.org/10.1016/j.jns.2004.08.008
40. Brighina F, Palermo A, Fierro B (2009) Cortical inhibition and habituation to evoked potentials: relevance for pathophysiology of migraine. *J Headache Pain* 10: 77–84. https://doi.org/10.1007/s10194-008-0095-x
41. Cosentino G, Fierro B, Vigneri S, et al. (2014) Cyclical changes of cortical excitability and metaplasticity in migraine: evidence from a repetitive transcranial magnetic stimulation study. *Pain* 155: 1070–1078. https://doi.org/10.1016/j.pain.2014.02.024
42. Afra J, Proietti Cecchini A, Sándor PS, et al. (2000) Comparison of visual and auditory evoked cortical potentials in migraine patients between attacks. *Clin Neurophysiol* 111: 1124–1129. https://doi.org/10.1016/s1388-2457(00)00271-6

43. Gerwig M, Kastrup O, Meyer BU, et. al. (2003) Evaluation of cortical excitability by motor and phosphene thresholds in transcranial magnetic stimulation. *J Neurol Sci* 215: 75–78. https://doi.org/10.1016/s0022-510x(03)00228-4
44. Young WB, Oshinsky ML, Shechter, et. al. (2004) Consecutive transcranial magnetic stimulation: phosphene thresholds in migraineurs and controls. *J Head Face Pain* 44: 131–135. https://doi.org/10.1111/j.1526-4610.2004.04028.x
45. Chadaide Z, Arlt S, Antal A, et al. (2007) Transcranial direct current stimulation reveals inhibitory deficiency in migraine. *Cephalalgia* 27: 833–839. https://doi.org/10.1111/j.1468-2982.2007.01337.x
46. Zeugin D, Ionta S (2021). Anatomo-functional origins of the cortical silent period: spotlight on the basal ganglia. *Brain Sci* 11: 705. https://doi.org/10.3390/brainsci11060705
47. Paci M, Di Cosmo G, Perrucci MG, et al (2021) Cortical silent period reflects individual differences in action-stopping performance. *Sci Rep* 11: 15158. https://doi.org/10.1038/s41598-021-94494-w
48. Aurora SK, al-Sayeed F, Welch KM, et al. (1999) The cortical silent period is shortened in migraine with aura. *Cephalalgia* 19: 708–712. https://doi.org/10.1046/j.1468-2982.1999.019008708.x
49. Bohotin V, Fumal A, Vandenheede M, et al (2002) Effects of repetitive transcranial magnetic stimulation on visual evoked potentials in migraine. *Brain* 125: 912–922. https://doi.org/10.1093/brain/awf081
50. Yuksel H, Topalkara KK (2021) Increased cortical excitability in female migraineurs: a transcranial magnetic stimulation study conducted in the preovulatory phase. *J Clin Neurol* 17: 236. https://doi.org/10.3988/jcn.2021.17.2.236
51. Lan L, Zhang X, Li X, et al. (2017) The efficacy of transcranial magnetic stimulation on migraine: a meta-analysis of randomized controlled trials. *J Headache Pain* 18: 86. https://doi.org/10.1186/s10194-017-0792-4
52. Narmashiri A, Akbari F (2023) The effects of transcranial direct current stimulation (TDCS) on the cognitive functions: a systematic review and meta-analysis. *Neuropsychol Rev* 35: 126−152. https://doi.org/10.1007/s11065-023-09627-x
53. Teepker M, Hötzel J, Timmesfeld N, et al. (2010) Low-frequency rTMS of the vertex in the prophylactic treatment of migraine. *Cephalalgia* 30: 137–144. https://doi.org/10.1111/j.1468-2982.2009.01911.x
54. Misra UK, Kalita J, Bhoi SK, et al. (2013) High-rate repetitive transcranial magnetic stimulation in migraine prophylaxis: a randomized, placebo-controlled study. *J Neurol* 260: 2793–2801. https://doi.org/10.1007/s00415-013-7072-2
55. Hammad AB, Elsharkawy RE, Abdel Azim GS, et al. (2021) Repetitive transcranial magnetic stimulation as a prophylactic treatment in migraine. *Egypt J Neurol Psychiatry Neurosurg* 57: 5. https://doi.org/10.1186/s41983-020-00254-4
56. Brighina F, Giglia G, Scalia S, et al. (2005) Facilitatory effects of 1 Hz rTMS in the motor cortex of patients affected by migraine with aura. *Exp Brain Res* 161: 34–38. https://doi.org/10.1007/s00221-004-2042-7
57. Molgat CV, Patten SB (2005) Comorbidity of major depression and migraine—A Canadian population-based study. *Can J Psychiat* 50: 832–837. https://doi.org/10.1177/070674370505001305

58. Dussor G (2019) Discoveries in migraine mechanisms and therapeutic targets. *Curr Opin Physiol* 11: 116–124. https://doi.org/10.1016/j.cophys.2019.10.013
59. Borsook D, Maleki N, Becerra L, et al. (2012) Understanding migraine through the lens of maladaptive stress responses: a model disease of allostatic load. *Neuron* 73: 219–234. https://doi.org/10.1016/j.neuron.2012.01.001
60. Carboni L, Khoury AE, Beiderbeck D (2022) Neuropeptide Y, calcitonin gene-related peptide, and neurokinin a in brain regions of HAB rats correlate with anxiety-like behaviours. *Eur Neuropsychopharm* 57: 1–14. https://doi.org/10.1016/j.euroneuro.2021.12.011
61. Kauppila E, Vanninen E, Kaurijoki S, et al. (2013) Influence of serotonin transporter gene polymorphism (5-HTTLPR Polymorphism) on the relation between brain 5-HT transporter binding and heart rate-corrected cardiac repolarization interval. *Plos One* 8: e50303. https://doi.org/10.1371/journal.pone.0050303
62. Furman JM, Marcus DA, Balaban CD (2013) VM: clinical aspects and pathophysiology. *Lancet Neurol* 12: 706–715. https://doi.org/10.1016/s1474-4422(13)70107-8
63. Pistoia F, Salfi F, Saporito G, et al. (2022) Behavioral and psychological factors in individuals with migraine without psychiatric comorbidities. *J Headache Pain* 23: 110. https://doi.org/10.1186/s10194-022-01485-x
64. Powers SW, Kashikar-Zuck SM, et al. (2013) Cognitive behavioral therapy plus amitriptyline for chronic migraine in children and adolescents. *JAMA* 310: 2622. https://doi.org/10.1001/jama.2013.282533
65. Bottiroli S, De Icco R, Vaghi G, et al. (2021) Psychological predictors of negative treatment outcome with Erenumab in chronic migraine: data from an open-label long-term prospective study. *J Headache Pain* 22: 114. https://doi.org/10.1186/s10194-021-01333-4
66. Schwartz WJ, Klerman EB (2019) Circadian neurobiology and the physiologic regulation of sleep and wakefulness. *Neurol Clin* 37: 475–486. https://doi.org/10.1016/j.ncl.2019.03.001
67. Hastings MH, Maywood ES, Brancaccio M, et al. (2018) Generation of circadian rhythms in the suprachiasmatic nucleus. *Nat Rev Neurosci* 19: 453. https://doi.org/10.1038/s41583-018-0026-z
68. Stokes DA, Lappin MS (2010) Neurofeedback and biofeedback with 37 migraineurs: a clinical outcome study. *Behav Brain Funct* 6: 9. https://doi.org/10.1186/1744-9081-6-9
69. Legarda SB, Michas-Martin PA, McDermott D (2022) Remediating intractable headache: an effective nonpharmacological approach employing infralow frequency neuromodulation. *Front Hum Neurosci* 16: 894856. https://doi.org/10.3389/fnhum.2022.894856
70. Sasu R (2022) Infra-low frequency neurofeedback in persistent postural-perceptual dizziness—Case report. *Front Hum Neurosci* 16: 959579. https://doi.org/10.3389/fnhum.2022.959579
71. Arina M, Zhao H, Rasgado-Toledo J (2022) Infralow neurofeedback for tension-type headache: a randomized, crossover sham-controlled study. *Front Human Neurosci* 16: 891323. https://doi.org/10.3389/fnhum.2022.891323
72. Kirsch V, Keeser D, Hergenroeder T, et al. (2016) Structural and functional connectivity mapping of the vestibular circuitry from human brainstem to cortex. *Brain Struct Funct* 221: 1291–1308. https://doi.org/10.1007/s00429-014-0971-x
73. Young A, Cornejo J, Spinner A (2023) Auditory brainstem response.
74. Yamada T, Dickins QS, Arensdorf K, et al. (1986) Basilar migraine: polarity-dependent alteration of brainstem auditory evoked potential. *Neurology* 36: 1256−1260. https://doi.org/10.1212/wnl.36.9.1256

75. Yoo H, Mihaila DM (2022) Neuroanatomy, vestibular pathways.
76. Ricci A, Rubino E, Pietro Serra G, et al. (2024) Concerning neuromodulation as treatment of neurological and neuropsychiatric disorders: insights gained from selective targeting of the subthalamic nucleus, para-subthalamic nucleus, and zona incerta in rodents. *Neuropharmacology* 256: 110003. https://doi.org/10.1016/j.neuropharm.2024.110003
77. Walsh GS (2021) Dynamics of modular neuromotor control of walking and running during single and dual task conditions. *Neuroscience* 465: 1–10. https://doi.org/10.1016/j.neuroscience.2021.04.004
78. Taslim S, Shadmani S, Saleem A, et al. (2024) Neuropsychiatric disorders: bridging the gap between neurology and psychiatry. *Cureus* 16: e51655. https://doi.org/10.7759/cureus.51655
79. Fletcher JL, Murray SS, Xiao J (2018) Brain-derived neurotrophic factor in central nervous system myelination: a new mechanism to promote myelin plasticity and repair. *Int J Mol Sci* 19: 4131. https://doi.org/10.3390/ijms19124131
80. Fischer M, Wille G, Klien S, et al. (2012) Brain-derived neurotrophic factor in primary headaches. *J Headache Pain* 13: 469–475. https://doi.org/10.1007/s10194-012-0454-5
81. Bliss TV, Cooke SF (2011) Long-term potentiation and long-term depression: a clinical perspective. *Clinics* 66: 3–17. https://doi.org/10.1590/s1807-59322011001300002
82. Meldrum BS (2000) Glutamate as a neurotransmitter in the brain: review of physiology and pathology. *J Nutr* 130: 1007S−1015S. https://doi.org/10.1093/jn/130.4.1007s
83. Jewett BE, Thapa B (2022) Physiology, NMDA receptor.
84. Blanke ML, VanDongen AM (2009) Activation mechanisms of the NMDA receptor.
85. Chervyakov AV, Chernyavsky AY, Sinitsyn DO, et. al. (2015) Possible mechanisms underlying the therapeutic effects of transcranial magnetic stimulation. *Front Human Neurosci* 9: 303. https://doi.org/10.3389/fnhum.2015.00303
86. Wu X, Han S, Yang Y, et al. (2022) Decreased brain GABA levels in patients with migraine without aura: an exploratory proton magnetic resonance spectroscopy study. *Neuroscience* 488: 10–19. https://doi.org/10.1016/j.neuroscience.2022.02.010
87. Tremblay R., Lee S, Rudy B (2016) GABAergic interneurons in the neocortex: from cellular properties to circuits. *Neuron* 91: 260–292. https://doi.org/10.1016/j.neuron.2016.06.033
88. Caparelli E, Backus W, Telang F, et al. (2012). Is 1 Hz RTMS always inhibitory in healthy individuals?. *Open Neuroimag J* 6: 69–74. https://doi.org/10.2174/1874440001206010069
89. Phylactou P, Pham T, Narskhani N, et al. (2024) Phosphene and motor transcranial magnetic stimulation thresholds are correlated: a meta-analytic investigation. *Prog Neuro-Psychoph* 133: 111020. https://doi.org/10.1016/j.pnpbp.2024.111020
90. Zuniga SA, Adams ME (2021) Efficient use of vestibular testing. *Otolaryng Clin N Am* 54: 875–891. https://doi.org/10.1016/j.otc.2021.05.011
91. Peterchev AV, Murphy DL, Goetz SM (2015) Quiet transcranial magnetic stimulation: status and future directions. *Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE Engineering in Medicine and Biology Society*, 226–229. https://doi.org/10.1109/EMBC.2015.7318341
92. Rossi S, Antal A, Bestmann S, et al. (2021) Safety and recommendations for TMS use in healthy subjects and patient populations, with updates on training, ethical and regulatory issues: expert guidelines. *Clin Neurophysiol* 132: 269–306. https://doi.org/10.1016/j.clinph.2020.10.003

93. Matsumoto H, Ugawa Y (2016) Adverse events of tDCS and tACS: a review. *Clin Neurophys Pract* 2: 19–25. https://doi.org/10.1016/j.cnp.2016.12.003
94. Magnezi R, Aminov E (2016) Comparison between neurostimulation techniques, repetitive transcranial magnetic stimulation vs electroconvulsive therapy for the treatment of resistant depression: patient preference and cost-effectiveness. *Patient Prefer Adher* 10: 1481–1487. https://doi.org/10.2147/PPA.S105654
95. Xia Y, Xu Y, Li Y, et al. (2022) Comparative efficacy of different repetitive transcranial magnetic stimulation protocols for stroke: a network meta-analysis. *Front Neurol* 13: 918786. https://doi.org/10.3389/fneur.2022.918786

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