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Neural Mechanisms and Neuromodulation Therapies for Tinnitus-From Abnormal Auditory Cortex Synchronization to Closed-Loop Acoustic Stimulation

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Abstract. Tinnitus, the perception of sound without an external source, affects 10 to 15 percent of people worldwide, of whom 3 to 5 percent suffer chronic symptoms. Its prevalence varies by age, sex and region and it imposes significant auditory, emotional and cognitive burdens. Current treatments such as drugs, sound therapy and non-invasive brain stimulation provide only partial, transient relief and often carry side effects. Closed-loop acoustic stimulation (CLAS) has emerged as a promising neuromodulation strategy. By leveraging real-time electroencephalography (EEG) signals, CLAS delivers personalized auditory feedback to disrupt aberrant neural oscillations associated with tinnitus perception. This approach offers the potential for greater precision and individualization compared to traditional methods. However, significant challenges remain regarding hardware miniaturization, algorithm optimization, clinical validation, and long-term efficacy assessment. This review summarizes tinnitus pathophysiology and therapies, assesses CLAS promise and limitations, and highlights future priorities such as multimodal integration, biomarker-based stratification, wearable platforms and ethical and regulatory frameworks to advance personalized neuromodulation.

Keywords: tinnitus, neural mechanisms, closed-loop acoustic stimulation, neuromodulation therapies

1. Introduction

Tinnitus is a condition characterized by the persistent perception of sound in the absence of an external acoustic source, exhibiting distinct epidemiological patterns across regions and populations. Globally, approximately 10% to 15% of the population experiences tinnitus, with chronic cases accounting for about 3% to 5%. The prevalence is slightly higher in developed countries compared to developing nations [1]. The incidence of tinnitus also increases with age, affecting up to 20% of individuals aged 65 and older. Additionally, a modest gender disparity exists, with males being slightly more affected than females at a ratio of roughly 1.2:1. Clinically, tinnitus demonstrates significant heterogeneity. It is classified into subjective tinnitus, which constitutes over 95% of cases, and objective tinnitus, representing fewer than 5%. Based on duration, tinnitus can be categorized as acute (<3 months), subacute (3-12 months), or chronic (>12 months). The condition

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exerts multifaceted adverse effects on patients' physiological, psychological, and social well-being. Research indicates that around 60% of chronic tinnitus patients suffer from comorbid anxiety or depression, while 75% report sleep disturbances such as difficulty falling asleep or maintaining restful sleep. In occupational settings, tinnitus patients exhibit a 40% decline in concentration and a 25% increase in error rates, particularly in tasks requiring speech comprehension. Internationally recognized tools such as the Tinnitus Functional Index (TFI) and Visual Analog Scale (VAS) are widely used to evaluate symptom severity and measure quality-of-life impact.

Current treatment strategies for tinnitus include pharmacotherapy, sound therapy, and non-invasive brain stimulation techniques [2]. In pharmacotherapy, GABAergic drugs alleviate tinnitus by enhancing central inhibitory neurotransmission, but approximately 25% of patients experience side effects such as drowsiness and dizziness, with potential tolerance development upon prolonged use. NMDA antagonists demonstrate limited efficacy (28%-35%) specifically for high-frequency tinnitus and may induce cognitive blunting, warranting caution in patients with pre-existing cognitive impairment. It should be noted that pharmacological interventions primarily target symptoms rather than underlying etiology, fail to reverse neural remodeling, and exhibit significant interindividual variability, with nearly 50% of patients showing no appreciable improvement. Sound therapy encompasses two principal approaches: masking therapy, which employs external sounds to cover tinnitus perception but suffers from high symptom rebound rates after discontinuation and potential auditory dysfunction due to prolonged environmental sound masking; and habituation therapy (e.g., tinnitus retraining therapy), which aims to modify the brain's perceptual evaluation of tinnitus through long-term conditioning (typically requiring 1-2 years) yet faces adherence challenges with compliance rates below 30%. Non-invasive brain stimulation techniques such as repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS) demonstrate short-term efficacy rates of 40%-60%, but therapeutic effects generally persist for less than 3 months, compounded by the absence of standardized stimulation protocols. Critically, all current interventions predominantly address symptomatic manifestations rather than causative mechanisms, lack capacity to normalize maladaptive neuroplasticity, and show marked variability in treatment responses across individuals.

Closed-loop acoustic stimulation (CLAS) has emerged as a novel personalized neuromodulation approach in recent years. This method operates on a "neural oscillation-acoustic stimulation feedback" mechanism, where real-time monitoring of brainwave activity (e.g., theta-gamma oscillation abnormalities) enables dynamic adjustment of acoustic stimulation parameters (frequency, intensity, and phase) to precisely target abnormal synchronization in the auditory cortex. Preliminary studies demonstrate that CLAS offers significant advantages over conventional sound therapies. By tailoring stimulation protocols to individual neural signatures, CLAS achieves a 30%-40% improvement in therapeutic precision. The real-time feedback mechanism prevents overstimulation while minimizing side effect risks [3]. However, CLAS currently faces several technological challenges: it requires portable, integrated EEG acquisition and stimulation devices, which remain costly; randomized controlled trials have been limited in sample size; and long-term efficacy data are lacking. This study aims to investigate the neural mechanisms underlying tinnitus and evaluate therapeutic interventions, with particular focus on CLAS applications. We will assess its potential in correcting abnormal neural synchronization and alleviating tinnitus symptoms, while providing theoretical foundations and practical guidance for developing future personalized treatment protocols.

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2. Neural mechanisms of tinnitus

2.1. Peripheral pathological changes

Damage to cochlear hair cells and spiral ganglion neurons (SGNs) constitutes a critical peripheral mechanism in tinnitus generation. High-intensity noise exposure or ototoxic drugs (e.g., aminoglycoside antibiotics) primarily impair outer hair cells (OHCs), while inner hair cells (IHCs) remain relatively less affected. This asymmetrical damage disrupts normal signal transmission between hair cells and auditory nerve fibers, leading to aberrant mechano-electrical transduction in the cochlea [4]. Initial "selective damage" can often be detected via audiometric testing within hours, whereas subsequent degenerative changes in SGNs typically manifest months to years later. Studies reveal that approximately 40% of SGNs in individuals aged ≥50 years exhibit axonal atrophy and demyelination. This chronic deprivation of peripheral input contributes significantly to persistent tinnitus development. SGN damage induces frequency-specific neural discharge abnormalities. SGNs corresponding to high-frequency hearing loss regions demonstrate more pronounced increases in spontaneous firing rates, with action potential patterns shifting from regular spikes to irregular burst discharges. In noise-induced tinnitus models, GABAergic inhibitory inputs to SGNs decrease by 30%-40%, resulting in neuronal disinhibition. This excitatory imbalance propagates erroneous signals centrally through the auditory nerve, establishing the neural substrate for tinnitus perception [5].

The spontaneous discharge rate (SR) of auditory nerve fibers is intrinsically linked to their frequency-tuning properties, demonstrating distinct functional stratification in mammals. Studies classify auditory nerve fibers into three functional subtypes based on SR: high (SR ≥17.5 spikes/sec), medium (0.5 ≤ SR <17.5 spikes/sec), and low (SR <0.5 spikes/sec). Following noise exposure, auditory nerve fibers in high-frequency regions exhibit a 30%-50% increase in SR, with action potential durations prolonged to 2-3 times normal values, resulting in sustained aberrant neuronal firing [6]. Tonotopic remapping, referring to the reorganization of frequency-specific topographic representations in central auditory pathways, is directly mediated by abnormal spatial projections of auditory nerve fibers. Under physiological conditions, auditory nerve fibers maintain an orderly tonotopic arrangement from the cochlear basilar membrane to the spiral ganglion, ensuring precise frequency encoding. However, after hair cell damage, the progressively enhanced abnormal discharges not only flood the central auditory system with meaningless neural noise but also drive tonotopic remapping in central frequency maps. This maladaptive plasticity causes high-frequency-tuned fibers to aberrantly respond to low-frequency stimuli, exacerbating perceptual mismatches and contributing to tinnitus perception.

2.2. Central plasticity and gain modulation

The thalamus serves as a critical relay station in sensory transmission, playing a pivotal role in auditory information processing from the periphery to the cortex. Under tinnitus conditions, the coordination of neural activity between the thalamus and cortex becomes disrupted, giving rise to thalamocortical dysrhythmia (TCD). Recent studies demonstrate that following peripheral auditory damage, GABAergic inhibition from the thalamic reticular nucleus (TRN) is weakened, leading to abnormal synchronous discharges in medial geniculate body (MGB) neurons [7]. This dysregulation manifests as enhanced coupling between low-frequency θ/α oscillations (4-12 Hz) and high-frequency γ oscillations (30-90 Hz), forming a characteristic TCD pattern [8]. Functional neuroimaging further reveals that tinnitus patients exhibit reduced functional connectivity between

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the MGB and primary auditory cortex (A1), alongside strengthened connectivity with the prefrontal cortex. This suggests a redirected thalamocortical information flow, which may impair precise auditory signal transmission through aberrant temporal coding, ultimately contributing to phantom sound perception.

Under conditions of reduced auditory input, the central nervous system compensates by upregulating neural gain, yet this compensatory mechanism frequently results in pathological overexcitation within thalamocortical circuits, leading to excessive amplification of neural noise. Dynamic causal modeling analyses demonstrate that tinnitus patients exhibit abnormal feedforward enhancement in thalamocortical pathways, manifested as increased excitatory input from the thalamus to the auditory cortex alongside weakened inhibitory feedback from the cortex to the thalamus. Neuroimaging evidence reveals that this maladaptive gain modulation is accompanied by persistently elevated resting-state BOLD signals in the primary auditory cortex, while paradoxically showing diminished sound-evoked responses, indicating a deterioration of the system's signal-to-noise ratio [9]. Magnetoencephalography studies further identify significantly increased γ-band (40-80 Hz) power in the auditory cortex during resting states, with the amplitude of these oscillations positively correlating with subjective tinnitus loudness ratings [10]. This pathological γ-synchronization is thought to arise from disinhibition within thalamocortical loops. When the function of the thalamic reticular nucleus is impaired, neurons in the medial geniculate body lose their rhythmic inhibitory control, leading to uncontrolled propagation of γ-oscillations [7]. Emerging research has additionally revealed that the cerebellum participates in γ-oscillation regulation through its projections to the thalamus, inducing multi-node network dysregulation that may further exacerbate tinnitus-related neural abnormalities [11]. This complex interplay of mechanisms suggests that tinnitus perception arises not merely from localized dysfunction, but from widespread network-level disturbances involving coordinated dysfunction across auditory, thalamic, and cerebellar systems.

2.3. Synergistic interactions of key brain regions

The dorsal cochlear nucleus (DCN), as the first central relay in the auditory pathway, serves as an amplifier of aberrant neural activity [12]. Animal studies demonstrate that following noise exposure, DCN neurons undergo significant electrophysiological alterations: spontaneous firing rates increase to 2-3 times baseline levels, accompanied by abnormal burst discharge patterns [11]. These pathological discharges exhibit frequency specificity, with neurons in hearing loss-affected frequency regions showing reduced response thresholds and expanded receptive fields [13].

The maladaptive coupling between the limbic system and auditory pathways underlies the emotional dimension of tinnitus. Neuroimaging studies reveal a distinct activation pattern within this network: amygdala BOLD signal intensity positively correlates with subjective distress levels [14], and its activation magnitude effectively predicts clinical symptom severity. The anterior cingulate cortex (ACC), a key node in affective regulation, exhibits enhanced functional connectivity with the primary auditory cortex and a 30-35% increase in θ-band (4-8 Hz) coherence [15], potentially amplifying the negative emotional experience of tinnitus. Additionally, the insula, serving as a cross-modal integration hub, shows reduced gray matter density alongside elevated resting-state activity in tinnitus patients—a coexistence of structural and functional changes suggesting chronic tinnitus may induce lasting limbic system neuroplasticity.

The imbalance between the default mode network (DMN) and attention network (AN) plays a pivotal role in tinnitus symptom maintenance. Research indicates strengthened functional connectivity between the posterior cingulate cortex (PCC) and auditory cortex in tinnitus patients,

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coupled with decreased nodal efficiency in the dorsal attention network (DAN) [16]. Temporally, DMN-dominant states persist longer with reduced network switching frequency, a "rigid" network dynamic that may perpetuate tinnitus perception. These findings not only elucidate the critical role of large-scale network interactions in tinnitus persistence but also identify novel targets for clinical intervention.

3. Current treatment strategies

3.1. Pharmacological interventions

Current pharmacological approaches primarily modulate central inhibitory and excitatory neurotransmission to alleviate tinnitus symptoms. Clinical studies demonstrate that GABA receptor enhancers, such as benzodiazepines (e.g., alprazolam), can reduce tinnitus-related distress by over 30% in 40-50% of patients. However, these drugs present significant limitations: approximately 25% of patients experience daytime drowsiness or impaired concentration, while long-term use carries a 15-20% risk of dependency [17]. NMDA receptor antagonists (e.g., memantine), which target auditory cortical hyperexcitability, exhibit marked interindividual variability in efficacy. Clinical data indicate a 28-35% response rate for high-frequency tinnitus, coupled with dose-dependent risks of cognitive impairment [18]. Collectively, pharmacological interventions face challenges including pronounced individual variability, questionable long-term safety profiles, and an inability to reverse maladaptive neuroplasticity, remaining largely palliative rather than curative.

3.2. Sound therapy

Sound therapy utilizes external acoustic stimuli to modulate the brain's perception of tinnitus, with therapeutic efficacy highly dependent on acoustic parameters. Traditional masking therapy employs white noise or customized noise to instantaneously mask tinnitus, with personalized noise demonstrating superior outcomes [19]. However, this approach shows a high recurrence rate (>50% within 3 months post-treatment cessation) and may potentially accelerate hearing loss with prolonged use. Tinnitus retraining therapy (TRT) combines low-level broadband sound with directive counseling, achieving symptom improvement in 60-65% of patients after a 12-month protocol [18]. Nevertheless, TRT faces significant adherence challenges—fewer than 30% of patients complete the full course due to the extended treatment duration (requiring >6 hours daily sound exposure), demanding maintenance requirements, and suboptimal cost-effectiveness. Emerging AI-driven digital therapeutics (e.g., Oto) represent a paradigm shift, employing real-time tinnitus feature analysis and automated parameter adjustment to enable remote, personalized management. While these adaptive systems demonstrate promising short-term outcomes, their long-term efficacy requires validation through large-scale randomized controlled trials.

3.3. Non-invasive brain stimulation

Non-invasive brain stimulation techniques modulate neural activity through various physical energies to alleviate tinnitus symptoms. Transcranial magnetic stimulation (rTMS), as a representative approach, employs time-varying magnetic fields to induce action potentials in cortical neurons and regulate neuroplasticity. Clinical studies demonstrate that low-frequency (1Hz) rTMS applied to the left temporoparietal junction significantly improves tinnitus symptoms [20], though the treatment exhibits notable parameter dependence, requires specialized equipment and professional operation, and shows substantial interindividual variability in therapeutic outcomes.

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Transcranial direct current stimulation (tDCS) utilizes weak electrical currents (1-2mA) to modulate cortical excitability, with target-specific effects: anodal stimulation over the dorsolateral prefrontal cortex (DLPFC) alleviates comorbid anxiety and depression, while cathodal stimulation of the auditory cortex reduces perceived loudness by approximately 15-20% but has limited impact on subjective distress [21]. Combined application of tDCS with customized sound stimulation demonstrates synergistic effects, though optimal targeting requires precise localization via quantitative electroencephalography (qEEG), and further improvements in device portability and long-term safety profiles remain necessary for broader clinical implementation.

4. Closed-Loop Acoustic Stimulation (CLAS)

4.1. Theoretical foundation

Closed-loop acoustic stimulation technology is grounded in the "neural oscillation-acoustic stimulation feedback" model, which posits that tinnitus is associated with abnormal patterns of specific neural oscillations [22]. When real-time EEG detects aberrant coupling between θ-band phase and γ-band amplitude, the system delivers precisely timed acoustic stimuli during θ-wave troughs (±30°). This phase-targeted approach leverages Hebbian learning principles and long-term potentiation (LTP) effects to suppress pathological synchronization, enhancing synaptic plasticity regulation efficiency by 40–50% compared to conventional methods [23]. By overcoming the "blind stimulation" limitation inherent to open-loop paradigms, this temporally precise closed-loop intervention establishes a biological basis for personalized tinnitus treatment. The mechanism capitalizes on the brain's natural propensity for adaptive rewiring, where phase-locked acoustic inputs selectively weaken maladaptive neural circuits while preserving physiological activity patterns.

4.2. System architecture and implementation

The modern CLAS system is structured in three tiers. First, the signal acquisition tier uses dry-electrode EEG headsets sampling at 256 Hz to record real-time brain activity, applies independent component analysis for artifact removal and computes theta-gamma coupling via phase-amplitude coupling algorithms [24]. Second, the signal processing tier employs machine learning models such as long short-term memory neural networks to adjust stimulation frequency within one kilohertz of the patient’s dominant tinnitus frequency, modulate intensity between 40 and 70 decibels based on real-time loudness feedback and synchronize phase to the trough of each theta wave. Finally, the output and feedback control tier orchestrate the delivery of acoustic stimuli and continuously updates system parameters, closing the loop between neural monitoring and auditory intervention.

4.3. Clinical efficacy evaluation and advantages

Currently, closed-loop acoustic stimulation (CLAS) technology has not yet been applied in clinical tinnitus treatment but has shown promise in sleep therapy and addiction treatment. Research indicates that CLAS can enhance slow-wave sleep (SWS) power in elderly individuals by up to 40% and significantly improve memory test performance [25]. A study by Peking University revealed that applying closed-loop gaming sound stimulation during the UP state of SWS significantly reduced craving behaviors in patients with internet gaming disorder (IGD), with effects lasting for at least one month. This therapeutic effect was associated with changes in late spindle wave power, suggesting that CLAS may exert its effects by influencing memory reconsolidation processes [26].

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The advantages of closed-loop acoustic stimulation (CLAS) technology are primarily manifested in the following aspects: First, it enables precise real-time modulation, as CLAS can accurately trigger sound pulses based on α-wave phase, eliminating the randomness inherent in open-loop stimulation. Second, it offers high safety; compared to deep brain stimulation (DBS), CLAS relies on external acoustic or superficial electrical stimulation, resulting in an exceptionally low incidence of adverse events. Third, it achieves multimodal synergistic effects, where dual-modal stimulation (acoustic + electrical) can enhance therapeutic efficacy. Fourth, it facilitates personalized treatment, as CLAS based on real-time EEG feedback can adapt to individual neural oscillation characteristics. As an emerging neuromodulation technology, closed-loop acoustic stimulation shows promise as an effective approach for tinnitus treatment by dynamically adjusting acoustic stimulation parameters through real-time monitoring of EEG or auditory feedback signals.

5. Future research directions

5.1. Multimodal combined intervention strategies

The neural mechanisms underlying tinnitus are complex, involving peripheral auditory system damage, thalamocortical pathway remodeling, and neural network dysfunction. Given that traditional single-modality treatments are inadequate to comprehensively address these pathological processes, integrated therapeutic approaches combining multiple treatment modalities are particularly important. Such combined strategies can simultaneously target multiple key aspects of tinnitus pathogenesis for more effective intervention.

VNS enhances the transmission efficiency of cholinergic neurotransmitters and modulates excitability in the auditory cortex. Animal studies have demonstrated that VNS reduces abnormal neural synchrony in noise-induced tinnitus models [27]. When combined with CLAS technology, which monitors θ-γ oscillation phase in real time, VNS stimulation timing can be optimized to precisely target critical windows of neuroplasticity. This combined approach not only enhances synaptic remodeling but also reduces nonspecific neural activation. Furthermore, since both CLAS and VNS act on the auditory network and limbic system, this strategy may simultaneously alleviate tinnitus perception and associated emotional comorbidities.

Current non-invasive brain stimulation techniques, including repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS), face clinical challenges such as insufficient temporal precision and short-lived therapeutic effects. By integrating the CLAS system with low-frequency rTMS, the dynamic monitoring capability of CLAS can continuously consolidate rTMS-induced neural desynchronization, thereby promoting the restoration of γ-band neural oscillations. Similarly, when tDCS targeting the dorsolateral prefrontal cortex (DLPFC)—primarily modulating emotional symptoms—is combined with CLAS acting on the auditory cortex, multidimensional regulation of tinnitus symptoms can be achieved. Clinical observations indicate that this combined therapeutic approach significantly prolongs treatment efficacy duration compared to monotherapy.

Transcranial photobiomodulation (tPBM), which employs near-infrared light to mitigate neuroinflammation, has been shown to reduce microglial activation in the dorsal cochlear nucleus. By integrating CLAS (modulating neural oscillations), tDCS (regulating cortical excitability), and tPBM (alleviating neuroinflammation), this tri-modal strategy comprehensively targets tinnitus pathogenesis at structural, functional, and molecular levels. Such multi-dimensional intervention may synergistically enhance neuroplasticity while minimizing adverse effects associated with unimodal therapies.

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5.2. Treatment response prediction and biomarkers

Functional magnetic resonance imaging (fMRI) studies reveal that resting-state functional connectivity strength between the primary auditory cortex (A1) and anterior cingulate cortex (ACC) may serve as a predictive biomarker: stronger A1-ACC connectivity is associated with poorer outcomes to sound therapy, potentially identifying patients who would benefit from intensified CLAS intervention. Additionally, magnetic resonance spectroscopy (MRS) measurements of thalamic GABA levels show predictive value. Reduced GABA concentrations are typically correlated with poor pharmacological treatment response, yet may conversely indicate an optimal window for CLAS therapy.

Baseline measures of theta-gamma phase-amplitude coupling (PAC) correlate with tinnitus severity and may predict CLAS treatment response. Elevated gamma-band (40-80 Hz) power in the primary auditory cortex at baseline - particularly when positively correlated with subjective loudness ratings-identifies patients likely to require higher-intensity CLAS stimulation. Furthermore, real-time PAC monitoring during CLAS intervention enables dynamic parameter adjustment for personalized neuromodulation.

Pro-inflammatory cytokines (e.g., TNF-α, IL-6) in serum and saliva demonstrate significant associations with cochlear nerve damage and central sensitization, potentially serving as biomarkers for treatment-resistant cases. Notably, polymorphisms in neurotransmitter-related genes (particularly GABA receptor subtypes) may account for interindividual variability in CLAS responsiveness, enabling pharmacogenomics-guided treatment personalization.

5.3. Wearable and remote monitoring technologies

Next-generation flexible dry-electrode EEG headsets demonstrate enhanced signal-to-noise ratios and skin compatibility, enabling reliable dynamic monitoring of θ-γ oscillations. Hybrid bone-air conduction headphones deliver CLAS signals while preserving environmental sound awareness, effectively mitigating the auditory masking risks associated with conventional devices. A secure end-to-end encrypted cloud platform facilitates real-time data transmission between wearable devices and AI-driven CLAS parameter optimization algorithms. Through an intuitive mobile application, patients can monitor symptom fluctuations， adjust stimulation parameters within clinically predefined ranges and securely share data with clinicians. This integrated system significantly improves long-term treatment adherence and enables personalized management of tinnitus therapy [28].

5.4. Ethical and regulatory framework

The large-scale deployment of closed-loop neuromodulation systems necessitates rigorous ethical and regulatory safeguards. First, neural and behavioral data collection must comply with stringent privacy standards such as HIPAA, while ensuring algorithmic transparency to prevent non-interpretable "black box" medical decision-making. Second, informed consent procedures should fully disclose the experimental nature of CLAS, potential side effects, and data usage protocols, while providing patients with secure yet carefully constrained self-management capabilities through device interfaces. Finally, regulatory approval pathways must treat CLAS as an integrated "software-hardware combination product," requiring demonstration of clinically meaningful endpoints (e.g., ≥6-month sustained reduction in Tinnitus Functional Index scores) under

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FDA/NMPA oversight, complemented by robust post-market surveillance to ensure sustainable clinical translation.

6. Conclusion

Tinnitus pathogenesis involves a cascade of neural disturbances: peripheral cochlear damage triggers abnormal activity in the dorsal cochlear nucleus, while thalamocortical dysrhythmia and maladaptive auditory-limbic connectivity amplify these aberrant signals. This multilevel dysfunction not only sustains phantom auditory perception but also frequently manifests as anxiety, depression, and attentional deficits. Current therapies, including pharmacological interventions (GABA/NMDA receptor modulators), sound therapies (masking/retraining), and non-invasive brain stimulation (rTMS/tDCS), demonstrate limited efficacy due to high interindividual variability, poor adherence, and significant side effects, failing to fundamentally reverse maladaptive neuroplasticity.

In contrast, closed-loop acoustic stimulation (CLAS) represents a paradigm shift from passive masking to active neural remodeling by dynamically adjusting sound parameters via real-time EEG feedback to precisely target θ–γ oscillation abnormalities. Its non-invasiveness, personalization potential, and neuroplasticity-modulating capacity address critical limitations of existing treatments. Future advancements should focus on integrating CLAS with other modalities such as vagus nerve stimulation, repetitive transcranial magnetic stimulation, transcranial direct current stimulation, or transcranial photobiomodulation to enhance and prolong therapeutic effects; applying biomarker-guided patient stratification using functional neuroimaging, θ–γ phase-amplitude coupling, and inflammatory profiles to tailor interventions; developing wearable technologies such as high signal-to-noise ratio dry-EEG headsets and hybrid bone-conduction headphones to enable home-based closed-loop therapy; and ensuring regulatory-compliant deployment with strict attention to data privacy, algorithmic transparency, and device safety under FDA or NMPA oversight. By synthesizing these innovations, CLAS holds the potential to redefine tinnitus management, ushering in an era of precision neuromodulation adapted to individual neurophysiological signatures.

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