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Next-generation neuromodulation in tinnitus: multimodal approaches and deep targets

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Tinnitus affects an estimated 14% of adults worldwide, and when accompanied by cognitive strain or emotional distress, it is classified as tinnitus disorder. Despite decades of investigation, no widely applicable therapy reliably reduces the percept itself, as current clinical mainstays mostly attenuate distress. This perspective article synthesizes recent advances in neuromodulation and argues for a strategic pivot from unimodal, open-loop cortical stimulation to multimodal, circuit-informed, and depth-capable interventions. We summarize mechanistic frameworks that implicate three partially overlapping pathways: lateral auditory generators, medial salience-attention evaluators, and descending inhibitory "noise-canceling" pathways whose imbalance is thought to sustain the percept and its affective load. Evidence across repetitive transcranial magnetic stimulation and transcranial electrical stimulation indicates reproducible but modest, short-lived improvements in standard outcomes, with high heterogeneity and unclear dose verification. Peripheral approaches such as transcutaneous electrical nerve stimulation show signals of efficacy in selected phenotypes but are vulnerable to expectancy effects. By contrast, bimodal auditory-somatosensory protocols demonstrate larger and more durable benefits in recent trials, consistent with timing-sensitive plasticity and engagement of neuromodulatory systems. We further highlight emerging depth-capable methods, including low-intensity transcranial focused ultrasound and transcranial photobiomodulation, which can non-invasively modulate corticothalamic hubs implicated in tinnitus. Building on these, we propose multimodal sequencing with direct engagement of deeper network nodes across the lateral, medial, and descending pathways. Durable relief rarely comes from a single open-loop intervention. An integrated programme that combines multimodal stimulation, deeper and cleaner targeting, and personalization offers the most credible route to clinically meaningful, generalizable benefit in defined tinnitus subgroups.

KEYWORDS

tinnitus, neuromodulation, repetitive transcranial magnetic stimulation, transcranial electrical stimulation, bimodal stimulation, transcranial focused ultrasound, photobiomodulation

1 Introduction

Tinnitus, "the conscious awareness of a tonal or composite noise for which there is no identifiable corresponding external acoustic source," is a common auditory phenomenon with a complex, multifactorial basis (De Ridder et al., 2021). It is broadly classified as objective or subjective: objective tinnitus, or *somatosound*, arises from internal bodily sources such as vascular flow (Baguley et al., 2013), whereas this article focuses on chronic subjective tinnitus, the perception of sound without any identifiable internal or external source, which has been present for at least 3 months (Han et al., 2009; Mazurek et al., 2022). Current estimates suggest that more than 740 million adults globally are affected, approximately 14% of the population (Chen et al., 2024). Tinnitus frequently co-occurs with hearing loss and a range of other health problems, and patients vary widely in both symptom severity and hearing profiles (Mazurek et al., 2022). When tinnitus is associated with significant cognitive strain, emotional distress, or disruption of daily functioning, it is classified as tinnitus disorder (De Ridder et al., 2021). In large US samples, roughly one in four individuals with tinnitus report anxiety or depression, and prevalence increases with age, underscoring its particular relevance in aging populations (Tunkel et al., 2014; Bhatt et al., 2017). Evidence from European population studies highlights the central role of comorbidities in shaping tinnitus. For example, non-auditory comorbidities (e.g., metabolic, cardiovascular, and psychiatric disorders) have been linked to tinnitus-related hearing loss and symptom profiles, and these relationships vary systematically with age (Tziridis et al., 2025a). In addition, a UK cross-sectional study identified insomnia, hearing-related distress, and anxiety as the strongest predictors of tinnitus severity, with the highest severity observed in subgroups with the greatest overall comorbidity burden (Beukes et al., 2021). Risk factors associated with tinnitus further include noise exposure, Ménière's disease, modifiable lifestyle factors (e.g., diet), adverse reactions to pharmacological interventions, and head injury or other forms of trauma (Biswas et al., 2023).

The impact of tinnitus extends beyond the individual, imposing substantial burdens on healthcare systems and the economy. For example, a study from the Netherlands estimated nationwide societal costs of €6.8 billion, including €1.9 billion in healthcare expenditure (Maes et al., 2013). A more recent German study estimated annual tinnitus-related socioeconomic costs at approximately €22 billion, a magnitude approaching half of the estimated annual healthcare and productivity costs attributed to diabetes in Germany (approximately €42 billion), highlighting tinnitus as a substantial public health concern (Tziridis et al., 2022).

At present, no treatment has demonstrated consistent, long-term efficacy in reducing the perception of tinnitus. In standard clinical practice, approaches such as cognitive behavioral therapy and conventional sound therapy are mainly designed to improve coping and reduce tinnitus-related distress, with limited emphasis on directly modulating tinnitus-related circuits or inducing targeted neuroplastic change (Han et al., 2021; Mazurek et al., 2022). However, recent advances in mechanistically informed sound-based approaches for selected tinnitus subgroups have begun to show promising benefits (Sendesen and Turkyilmaz, 2024; Yukhnovich et al., 2025; Tziridis et al., 2025b). Overall, the most notable exception remains cochlear implantation, which has been shown to produce sustained reductions in tinnitus loudness, the outcome most sought by patients, but only in individuals with unilateral deafness; given this restricted indication, it lies outside the scope of the present article (Mertens et al., 2016; Husain et al., 2018). To evaluate treatment effects, standardized questionnaires capture different dimensions of tinnitus, including the Tinnitus Handicap Inventory (THI), the Tinnitus Functional Index (TFI), and loudness measured with a Visual Analog Scale (VAS) (Hall et al., 2016; Raj-Koziak et al., 2018). Clinically meaningful improvement is commonly defined as a reduction of at least 13 points on the TFI and at least 7 points on the THI (Zeman et al., 2011; Meikle et al., 2012). Nonetheless, progress in clinical research remains constrained by the absence of established biomarkers and objective outcome measures (Kleinjung et al., 2024).

Reflecting the now widely held view of tinnitus as a disorder of neuroplasticity, recent efforts have therefore shifted toward interventions designed to modulate the underlying neural activity. Neuromodulation applies targeted electrical, magnetic, or mechanical stimuli to shift neuronal excitability, retune aberrant network rhythms, and engage synaptic plasticity that can produce lasting changes in large-scale circuits (Davidson et al., 2024). Among the most widely studied are non-invasive stimulation techniques, such as repetitive transcranial magnetic stimulation (rTMS), various transcranial electrical stimulation (tES) techniques, transcutaneous electrical nerve stimulation (TENS), and neurofeedback approaches. Bimodal protocols that combine sound with vagus nerve stimulation (VNS) or auditory-somatosensory stimulation have also attracted increasing interest. In addition, the emergence of novel technologies in the broader field of neuroscience such as transcranial focused ultrasound (tFUS), transcranial pulse stimulation (TPS), and transcranial photobiomodulation (tPBM) have opened new avenues for tinnitus research that warrant evaluation.

In this article, we review state-of-the-art neuromodulation approaches for tinnitus, outlining mechanisms, clinical evidence, and practical next steps. We then discuss innovative technologies and protocols that expand targets and optimize therapeutic options, with particular attention to multimodal integration and depth-capable targeting.

2 Neural mechanisms and therapeutic targets in tinnitus

Tinnitus typically arises from auditory deafferentation following damage to the auditory pathway, most often due to sensorineural hearing loss (Liberman and Kujawa, 2017; Park et al., 2023). It subsequently persists as a systems-level problem and is thought to be driven by an imbalance among three partially overlapping pathways: (i) a lateral auditory pathway that generates and stabilizes the phantom percept's acoustic features; (ii) a medial salience/valuation-attention pathway that determines awareness, priority, and affective load; and (iii) a descending inhibitory pathway that normally gates irrelevant activity before it reaches conscious perception (Elgoyhen et al.,

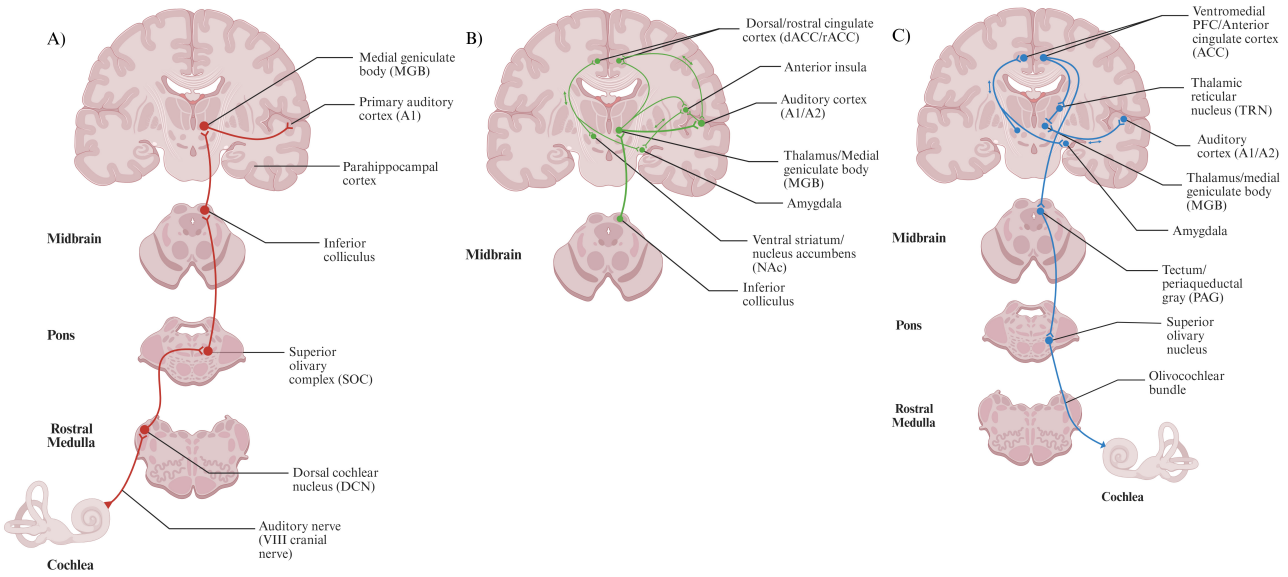

FIGURE 1
Schematic illustration of three partially overlapping pathways implicated in chronic tinnitus. **(A)** The lateral auditory pathway (red) depicts the canonical ascending auditory stream from the cochlea via the auditory nerve (VIII cranial nerve) to the dorsal cochlear nucleus (DCN), superior olivary complex (SOC), inferior colliculus, medial geniculate body (MGB), and primary auditory cortex (A1), with projections to parahippocampal cortex. This pathway is thought to generate and stabilize the acoustic features of the phantom percept. **(B)** The medial salience/valuation-attention pathway (green) highlights nodes that ascribe relevance and affective load to the tinnitus signal, including the inferior colliculus, MGB, auditory cortex (A1/A2), anterior insula, dorsal/rostral anterior cingulate cortex (dACC/rACC), amygdala, and ventral striatum/nucleus accumbens (NAc). **(C)** The descending inhibitory pathway (blue) illustrates proposed gating and gain-control mechanisms, extending from ventromedial prefrontal cortex (vmPFC) and anterior cingulate cortex (ACC) through the thalamic reticular nucleus (TRN), MGB, and auditory cortex (A1/A2), as well as midbrain tectum/periaqueductal gray (PAG), superior olivary nucleus, and the olivocochlear bundle projecting back to the cochlea. Together, these lateral, medial, and descending modules contribute to a systems-level framework in which tinnitus emerges when aberrant auditory activity and salience attribution exceed top-down inhibitory control. Figure created with BioRender.com.

2015; Rauschecker et al., 2010, 2015; Leaver et al., 2016; Krauss et al., 2016; De Ridder and Vanneste, 2021; De Ridder et al., 2022; Knipper et al., 2021; Schilling et al., 2023; see Figures 1A–C). When lateral and medial drive exceed inhibitory control, the tinnitus percept is thought to persist (De Ridder et al., 2022). Moreover, resting-state neuroimaging studies consistently demonstrate aberrant coupling between the auditory cortex and default mode, salience-attention, and executive control networks, supporting a multi-network model of sustained tinnitus perception (Schlee et al., 2008; Carpenter-Thompson et al., 2015; Roberts, 2018; De Ridder et al., 2022; Graetz et al., 2025).

Following deafferentation, neurons in the dorsal cochlear nucleus (DCN) show increased spontaneous firing, enhanced synchrony, and hyperexcitability, changes that propagate rostrally through the inferior colliculus and medial geniculate body (MGB) to the auditory cortex (Shore et al., 2016; Marks et al., 2018; Eggermont and Tass, 2015; De Ridder et al., 2015; see Figure 1A). These alterations have also been interpreted in terms of stochastic resonance, whereby intrinsic neural noise is boosted to compensate for reduced input but can be misread as sound and perceived as tinnitus (Krauss et al., 2016; Schilling et al., 2023). At the auditory cortex, tinnitus is further associated with increased spontaneous activity and abnormal synchrony, while sensorineural hearing loss, often accompanied by tinnitus, induces reorganization of tonotopic maps (van der Loo et al., 2009; Noreña and Eggermont, 2006). At the systems level, resting-state EEG/MEG often shows reduced alpha alongside increased delta-theta and focal gamma over auditory cortices, consistent with thalamocortical dysrhythmia (TCD) models (Llinás et al., 1999; De Ridder et al., 2015; Vanneste et al., 2018). In TCD, reduced sensory input to thalamocortical columns allows alpha activity to slow into theta, while reduced GABA-A mediated lateral inhibition at the border between deafferented and intact frequency maps produces an "edge effect": low-frequency activity in the deprived zone surrounded by increased gamma, with theta-gamma coupling thought to encode the positive phantom percept (Vanneste et al., 2018). With greater peripheral loss, processing can shift toward parahippocampal areas (auditory memory/context) and thus consolidation (De Ridder and Vanneste, 2021).

Whether the generated auditory pattern becomes consciously intrusive depends on the salience network primarily centered on the anterior insula and dorsal anterior cingulate cortex (dACC) (De Ridder et al., 2011, 2014; De Ridder and Vanneste, 2021; see Figure 1B). This causal involvement is supported by neurosurgical evidence. Early frontal leucotomy studies in tinnitus showed that surgery could markedly reduce tinnitus-related distress without reliably abolishing the tinnitus percept itself (Beard, 1965). More recent work in patients with treatment-resistant depression

demonstrates that anterior cingulotomy lesions within the anterior mid-cingulate cortex causally disrupt negative affect processing and cognitive control (Tolomeo et al., 2016). Additionally, conscious auditory perception can be demonstrated only when abnormal activity in the auditory cortex is coupled with engagement of the fronto-parietal attention network (Roberts, 2018; Mazurek et al., 2022). Indeed, tinnitus taxes limited attentional resources and has been associated with reduced selective auditory attention (Roberts et al., 2013; Sedley, 2019; Jensen et al., 2021). Neuroimaging work shows that tinnitus onset is associated with increased theta activity in the pregenual anterior cingulate cortex (pgACC) and reduced theta connectivity between pgACC and auditory cortex, while increased alpha activity in the dACC correlates with tinnitus-related distress (Vanneste et al., 2019, 2024; Chen et al., 2018). A recent machine learning analysis showed that alpha and gamma power together with auditory-limbic connectivity predict susceptibility to brief acoustic suppression, with alpha-band features among the strongest predictors (Shabestari et al., 2025).

Within a descending gating framework, reduced efficacy of pregenual and subgenual medial prefrontal regions (pgACC/sgACC/vmPFC) may fail to recruit the thalamic reticular nucleus to inhibit the medial geniculate relay ("thalamic gating"), permitting aberrant activity to reach and persist in the auditory cortex (Rauschecker et al., 2010, 2015; Leaver et al., 2016; De Ridder and Vanneste, 2021; see Figure 1C). In parallel, the insufficient engagement of brainstem efferent gain control, via midbrain projections (e.g., tectal/periaqueductal regions) that influence the superior olivary complex (SOC), potentially fails to regulate cochlear activity (De Ridder et al., 2012; Terreros and Delano, 2015). Additionally, a paradoxical reward process is thought to contribute to persistence, in which activity within the nucleus accumbens (NAc) coupled with pgACC/vmPFC reinforces tinnitus and biases gating in favor of the ongoing percept (Hullfish et al., 2018; De Ridder and Vanneste, 2021). Preclinical evidence suggests that activating the auditory thalamic reticular nucleus attenuates salicylate-induced hyperactivity in the auditory cortex (Dai et al., 2024). Meanwhile, resting-state fMRI Granger causality showed an association between tinnitus distress and altered bidirectional connectivity between the NAc and the PFC in chronic tinnitus (Xu et al., 2019).

The ascending lateral, medial, and descending pathways form separable yet functionally coupled modules. Bottom-up auditory dysrhythmia in the lateral stream primarily supplies the phantom signal, the medial salience system determines access to awareness, attention capture, and affective load and, in case of failure to inhibit aberrant signals along the descending pathway, the tinnitus persists. Clinically, this three-pathway, systems-level framing motivates circuit-specific, multimodal, and deep-reaching interventions: targeting auditory relays such as the auditory cortex, and the DCN/MGB; recalibrating salience and affective hubs including dACC and pgACC, anterior insula, and parahippocampus; and strengthening the descending gate from vmPFC to the thalamic reticular nucleus and downstream efferents. With this in mind, we shift from "what is disordered" to "what can be rewired," beginning with a review of established non-invasive neuromodulation approaches.

3 Established unimodal non-invasive stimulation

3.1 Repetitive transcranial magnetic stimulation

Repetitive transcranial magnetic stimulation applies electromagnetic fields to non-invasively modulate cortical excitability and network dynamics from outside the skull. Repeated magnetic pulses are thought to induce lasting neuroplastic changes in targeted cortical regions and their associated networks, thereby altering dysfunctional patterns of activity (Huerta and Volpe, 2009; Davidson et al., 2024). While no universal protocol has been established for tinnitus, rTMS typically involves placement of a magnetic coil over the auditory cortex, (left) temporoparietal junction (TPJ), or multiple cortical sites, with stimulation often delivered as up to 2,000 pulses at low frequency ($\leq$1 Hz) and at 100%−110% of the resting motor threshold per daily session for 1–2 weeks ($\approx$10 sessions) (Schoisswohl et al., 2022; Park et al., 2023; see Figure 2A). Low frequency stimulation is usually associated with a decrease in cortical excitability, while high frequency stimulation ($\geq$5 Hz) is associated with an increase in excitability (Rossi and Mandalà, 2024).

While rTMS is widely used in neuropsychiatry to treat disorders such as depression and obsessive-compulsive disorder, the effectiveness of rTMS in chronic tinnitus remains a matter of debate (Park et al., 2023; He et al., 2025). A systematic review that pooled 74 verum study arms found that active rTMS, overall, was more likely than sham to yield significant pre-post improvement, reinforcing a genuine (albeit modest) treatment signal (Schoisswohl et al., 2019; Lefebvre-Demers et al., 2021). More recently, a meta-analysis by He et al. (2025) found that rTMS reduced THI vs. sham both immediately after treatment (mean difference −11.54) and at one month (−10.98), but no consistent benefit on the loudness match and no sustained THI effect at 6 months. These findings suggest that while rTMS can achieve statistically significant symptom reduction in the short-term, the effect sizes remain moderate and of uncertain clinical relevance. Additionally, lower stimulation intensity has been linked to greater tinnitus improvement, whereas higher doses add no benefit, may even invert effects and potentially reflect individual anatomical differences (Schoisswohl et al., 2019; Denton et al., 2021). Moreover, adding the (dorsolateral) prefrontal cortex (DLPFC) to temporal stimulation has not shown efficacy over temporal only, arguing against routine dual site protocols in unselected patients (Kreuzer et al., 2015; Lehner et al., 2016). To date, neuronavigation has not consistently outperformed standard coil positioning in tinnitus rTMS trials (Langguth et al., 2010; Schoisswohl et al., 2019), and broader attempts at personalization have likewise failed to produce robust clinical benefits (Kreuzer et al., 2017; Schoisswohl et al., 2022). This suggests that, at present, the choice of target region and technical parameters (e.g., pulse number, intensity) may be more important for treatment outcome than further gains in spatial precision.

Further rTMS work should prioritize careful clarification of dose-response relationships at the auditory cortex rather than dose escalation or routine DLPFC add-ons, and should adopt consistent

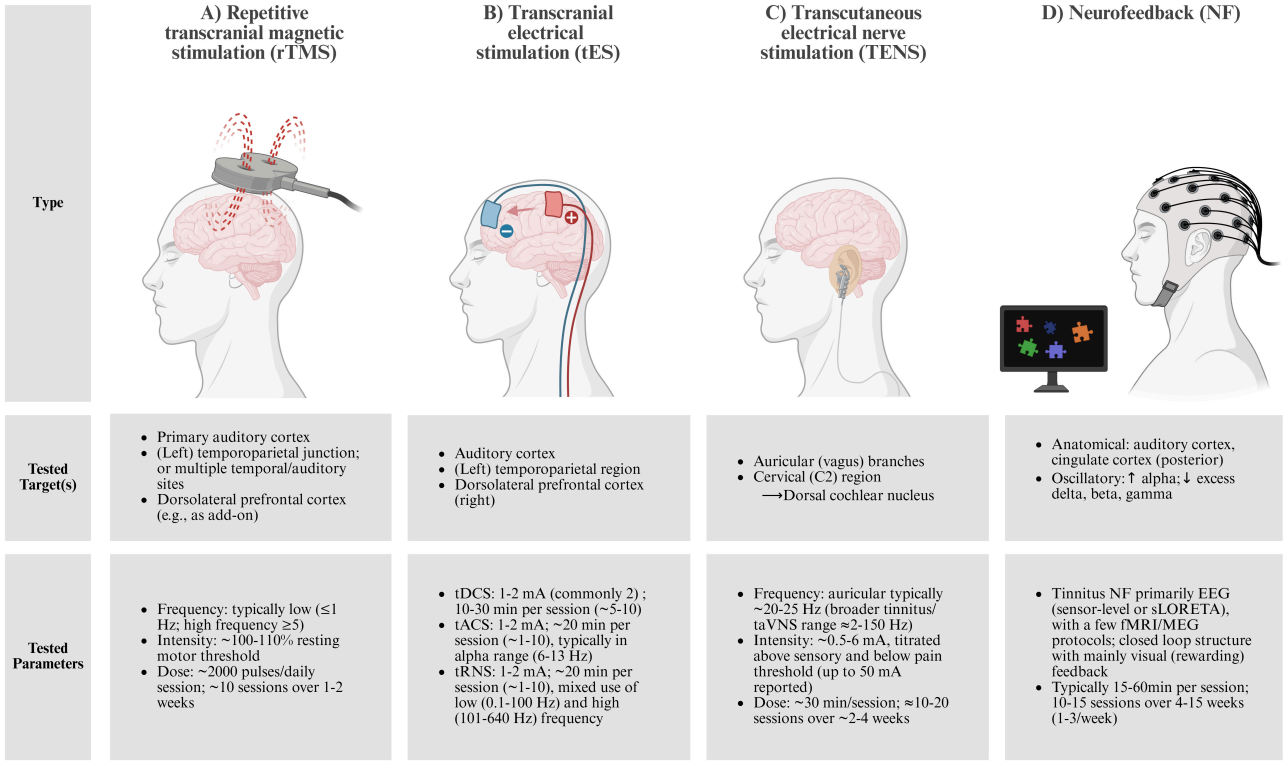

FIGURE 2
Schematic overview of commonly studied non-invasive neuromodulation techniques for chronic tinnitus. From left to right, panels depict **(A)** repetitive transcranial magnetic stimulation (rTMS), **(B)** transcranial electrical stimulation (tES), **(C)** transcutaneous electrical nerve stimulation (TENS), and **(D)** neurofeedback (NF). For each modality, the figure summarizes typical stimulation targets and parameters reported in tinnitus trials. rTMS protocols most commonly target the auditory cortex/temporoparietal region, with additional frontal targets (e.g., DLPFC) in some studies, using low-frequency (≤1 Hz) or high-frequency (≥5 Hz) stimulation over multiple sessions. tES includes transcranial direct current stimulation (tDCS) and transcranial alternating current stimulation (tACS), typically targeting the left temporoparietal/auditory region and/or DLPFC with repeated sessions; tACS frequency is selected to modulate oscillatory activity (e.g., alpha/theta). TENS protocols commonly stimulate auricular (vagus) branches or cervical (C1-C2) regions, with some approaches aiming to engage dorsal cochlear nucleus-related pathways. NF protocols use EEG-based feedback (including sLORETA or sensor-level EEG) to train modulation of oscillatory activity (e.g., alpha, theta, delta, beta, gamma) over multiple sessions. Parameter ranges shown reflect representative values across published tinnitus studies and are not intended to define standardized clinical protocols. Abbreviations: rTMS, repetitive transcranial magnetic stimulation; tES, transcranial electrical stimulation; TENS, transcutaneous electrical nerve stimulation; NF, neurofeedback; tDCS, transcranial direct current stimulation; tACS, transcranial alternating current stimulation; DLPFC, dorsolateral prefrontal cortex; EEG, electroencephalography; sLORETA, standardized low-resolution brain electromagnetic tomography; Hz, hertz; mA, milliampere; mV, millivolt; C1-C2, upper cervical spinal nerves; DCN, dorsal cochlear nucleus. Figure created with BioRender.com.

reporting of technical parameters to enable comparability. At the same time, novel cortical targets and state-dependent hubs that have been linked to tinnitus perception deserve exploration (e.g., pgACC and connected salience regions) (Vanneste et al., 2024). Given differences in target depth, this could possibly require deep-reach coil designs (e.g., deep TMS) or functional-connectivity-informed strategies. Indeed, advances in broader neuropsychiatry research, such as FDA-cleared deep TMS protocols using H-coil systems (e.g., BrainsWay devices) and accelerated dosing schedules, illustrate how dosing schedules and coil geometry can be modernized without defaulting to higher intensities or non-specific dual-site stimulation (Zangen et al., 2023).

3.2 Transcranial electrical stimulation

Another family of non-invasive methods is tES (Figure 2B), which delivers low-intensity currents (typically 0.5 to 3 mA) to generate weak electric fields that modulate brain activity (Rossi and Mandalà, 2024). Different tES approaches vary depending on stimulation settings such as electrode placement, number of electrodes, waveform type, frequency, and duration. The current is administered through two or more scalp electrodes connected to a waveform generator (Woods et al., 2016; Rossi and Mandalà, 2024). Notably, recent evidence indicates that a substantial part of its effects may arise from secondary transcutaneous activation of peripheral nerves, particularly branches of the trigeminal, vagus, and occipital nerves, thereby blurring the line between "cortical" and "peripheral" stimulation (van Boekholdt et al., 2021; Luckey et al., 2023).

Some of the most widely used methods include transcranial direct current stimulation (tDCS), transcranial alternating current stimulation (tACS), and transcranial random noise stimulation (tRNS). In tinnitus studies, tDCS most commonly targets the (left) temporoparietal region, the auditory cortex, and the DLPFC (Chen et al., 2023). tDCS modulates cortical excitability

by shifting neuronal membrane potentials toward sustained depolarisation or hyperpolarisation, effectively biasing neurons to fire more or less readily (Nitsche and Paulus, 2000). tDCS is further associated with induced neuroplasticity and downstream neuromodulator release (Davidson et al., 2024). Meanwhile, tACS delivers sinusoidal alternating currents that rhythmically modulate membrane potentials at a specific external frequency, thereby entraining and aligning the timing and synchrony of ongoing neural oscillations (Antal and Herrmann, 2016; Vossen et al., 2015; Kasten et al., 2019). Finally, tRNS applies randomly varying currents across a broad frequency range, utilizing stochastic resonance, where the addition of noise increases the sensitivity of neurons to weak inputs, thereby enhancing excitability and facilitating plasticity in neural circuits (Vanneste et al., 2013b; Antal and Herrmann, 2016).

The evidence for clinical effectiveness of tES in tinnitus remains limited. For tDCS, including high-definition tDCS, the literature converges on the finding that repeated-session protocols (≈1–2 mA, typically 2 mA, for about 20 min; 5–10 sessions) can yield significant but small and short-term reductions in tinnitus symptom severity compared with sham or waitlist controls (Shekhawat et al., 2015; Labree et al., 2022). Hoare et al. (2024) performed a meta-analysis demonstrating a significant overall difference between tDCS and the control. However, heterogeneity across studies was high, and following a sensitivity analysis, which excluded a high-risk-of-bias study, the overall effect was rendered non-significant. Moreover, the few trials with follow-up assessments found that benefits were not sustained beyond the immediate post-treatment period (Pal et al., 2015; Mares et al., 2022). Notably, across stimulation sites, the (right) DLPFC appears to be the most promising target (Chen et al., 2023), possibly due to stimulation of functionally connected regions (e.g., ACC) or indirectly via peripheral afferents and downstream neuromodulator releases as mentioned earlier (Luckey et al., 2023).

Compared to the relatively extensive tDCS literature, evidence for tACS is far more preliminary, with only a handful of small trials typically using low-intensity sinusoidal currents of about 1.5–2 mA for ∼20 min over 1–8 sessions (6–13 Hz), targeting auditory or prefrontal regions (Vanneste et al., 2013a,b; Claes et al., 2014; Chen et al., 2023). To date, most tACS studies have not shown consistent clinical benefit, irrespective of whether the auditory cortex or DLPFC were stimulated, even though the approach remains conceptually attractive given its potential to entrain relevant oscillatory activity (Vossen et al., 2015; Chen et al., 2023). For instance, alpha-frequency tACS has been shown to increase alpha power and modulate large-scale oscillatory activity in healthy participants (Vossen et al., 2015; Cabral-Calderin et al., 2016).

The clinical evidence for tRNS in tinnitus also remains mixed. Studies suggest that tRNS (0.1–640 Hz; 1–2 mA for ∼20 min/session) may produce stronger acute reductions in tinnitus loudness than tDCS or tACS (Vanneste et al., 2013a; Claes et al., 2014; Chen et al., 2023; Alashram, 2024), and can effectively reduce tinnitus symptoms, particularly when placed over the auditory cortex and DLPFC (Vanneste et al., 2013a; Joos et al., 2015). Indeed, Mohsen et al. (2019) reported clinically significant average THI score reductions (−16.66 points) and also showed that multiple-session tRNS regimens produced greater suppression of tinnitus compared with single-session protocols. Meanwhile, Kreuzer et al. (2019) and Shin et al. (2023) found no treatment benefit over sham.

Hence, for tES, the largest evidence base concerns tDCS, where a pooled benefit was found in a recent meta-analysis but became non-significant when a high-risk-of-bias study was removed (Hoare et al., 2024). Across heterogeneous protocols, larger effects tended to occur with higher doses or when compared with waitlist rather than sham, and only one trial reported neurophysiological change (Souza et al., 2020), underscoring the need to replicate objective EEG endpoints (Yadollahpour et al., 2017; To et al., 2017). Future optimization should prioritize dose and delivered electric field rather than montage fine-tuning: meta-analytic evidence points to 5–10 sessions of about 20 min, and spatial specificity in conventional tDCS appears less critical than achieving a sufficient, well-distributed E-field at the cortical target (Labree et al., 2022; Hoare et al., 2024). Because individual anatomy strongly shapes current delivery, upcoming trials should consider integrating MRI-based current flow modeling to estimate and standardize field intensity, extent, and direction, reducing variance and enabling genuinely target- and dose-verified protocols (Ciechanski et al., 2018; Lee et al., 2021; Hoare et al., 2024). However, given the resource intensity of such approaches, relatively small effect sizes, and the recent emergence of more efficient stimulation protocols, the cost-benefit balance raises the question of whether pursuing tDCS as a standalone tinnitus therapy remains worthwhile. tACS remains relatively understudied yet conceptually promising, warranting further investigation. Evidence from other neuropsychiatric conditions suggests that individualized, repeated tACS combined with behavioral training may induce durable neural and clinical benefits (Agboada et al., 2025). Meanwhile, tRNS findings are encouraging, though long-term evidence is limited, study quality varies, and cortical targets explored to date remain narrow (Alashram, 2024). Future work should broaden target sites, employ standardized protocols, assess sustained outcomes, and examine combined treatment strategies.

3.3 Transcutaneous electrical nerve stimulation

In addition to approaches designed to target the cortex, peripheral stimulation techniques have also been explored. Transcutaneous electrical nerve stimulation (TENS; Figure 2C) is a non-invasive electrotherapy that stimulates muscles and nerves through surface electrodes and is widely used in pain management due to reflex activation of sympathetic inhibitory neurons and reflex inhibition of parasympathetic excitatory neurons (Aydogan et al., 2022). In tinnitus, TENS is applied not only to the auricle, mastoid, or external auditory canal but also frequently to the upper cervical region (particularly C2) to target the dorsal cochlear nucleus (DCN) (Soylemez et al., 2025). The DCN integrates auditory inputs with direct and indirect inputs from the dorsal column, spinal trigeminal nuclei, dorsal raphe, and locus coeruleus (Zhang and Guan, 2007; Vanneste et al., 2010; Malfatti et al., 2022). By modulating DCN activity, TENS is proposed to block abnormal

sensory signals (Luo et al., 2012), engage major neuromodulator-releasing brainstem nuclei (e.g., for acetylcholine, norepinephrine, serotonin, and dopamine), and increase cochlear blood flow (Byun et al., 2020).

While evidence for TENS efficacy in tinnitus is promising, it is often confounded by placebo effects (Park et al., 2023). Two randomized controlled trials (RCTs) of TENS applied to auricular branches reported improvements in tinnitus severity and depressive symptoms compared to baseline, but substantial gains were also reported in sham groups (Kapkin et al., 2008; Tutar et al., 2020). Auricular-style protocols typically use stimulation of the left concha or nearby auricular sites at low-to-mid frequencies (≈20–25 Hz), short pulse widths (≈0.05–1.0 ms) and intensities titrated above sensory but below pain threshold (often ≤~6 mA, within a broader 0.5–50 mA range), yet with heterogeneous schedules across studies (Gerges et al., 2024). A meta-analysis of five studies (three RCTs) using transcutaneous vagus nerve stimulation found an overall small effect, with post-treatment reductions in THI but no improvements in tinnitus loudness ratings, and no differences between unilateral and bilateral stimulation at 4 weeks (Fernández-Hernando et al., 2023). More recently, a controlled pilot study of cervical (C2) TENS reported statistically significant reductions in tinnitus severity measures in both idiopathic and somatic tinnitus patients, although the authors note that the small sample size and short follow-up limit the generalizability of the findings (Soylemez et al., 2025). Notably, the long-term efficacy of TENS remains largely unknown (Chen et al., 2023). Given that TENS's most established role is symptomatic pain relief (e.g., via gate-control mechanisms) and efficacy may wane with prolonged use (Jastreboff, 2007; Maeda et al., 2017), its pragmatic value in tinnitus may be as an adjunct for patients with neck-pain/somatic modulation to support habituation and quality of life rather than as a stand-alone, targeted tinnitus therapy (Soylemez et al., 2025). Next steps in research may include the launch of sham-controlled trials using standard THI/TFI/VAS primaries with ≥3–6-month follow-up, stratified by tinnitus subtype to determine whether any tinnitus reductions persist beyond acute sessions.

3.4 Neurofeedback

Neurofeedback is an endogenous neuromodulation approach that uses real-time brain activity in a closed-loop to condition targeted neural functions via reinforcement learning, typically with visual feedback (Sulzer et al., 2024; see Figure 2D). Originating with EEG in the 1950s, it now spans additional modalities (e.g., MEG, fMRI, fNIRS, and more) to modulate circumscribed circuits rather than control external devices (Sulzer et al., 2024). Applied to tinnitus, EEG, and source-localized protocols (e.g., sLORETA) commonly aim to reinforce higher alpha and reduce excess delta, theta, and gamma over auditory and related hubs such as the cingulate, aiming to rebalance oscillations and lower the salience of the phantom sound (Güntensperger et al., 2019; Jensen et al., 2023). A systematic review of five smaller studies (2010–2020) reported consistent reductions in tinnitus distress and, variably, loudness alongside shifts toward increased alpha and decreased delta and gamma, typically using ~10–15 NF sessions of about 15–60 min, while noting heterogeneity, small samples, and mixed durability across follow-up (Varela Barrenechea, 2023). Since then, in a three-arm randomized trial ($n = 94$), researchers compared ten sessions of alpha to delta ratio EEG neurofeedback with beta to theta ratio neurofeedback and a minimal intervention control (Jensen et al., 2023). The alpha-delta arm showed the largest numerical reduction in tinnitus distress on the THI (≈10 points pre-post), although group differences in THI did not reach significance, while for tinnitus intensity a significant time-by-group interaction indicated that both neurofeedback arms improved more than the minimal-intervention control up to 3-month follow-up. More recently, a randomized trial found that 15 weekly sessions of real-time fMRI neurofeedback targeting bilateral auditory cortex produced larger and more sustained improvements in THI than 10 weeks of CBT at 6 months and at a smaller twelve-month follow-up (THI for fMRI −28 at 6 months and −30 at 12 months; CBT −12 at six, and −4 at 12 months), with additional gains in sleep and functioning, and with successful downregulation of auditory cortex activity during training (Gninenko et al., 2024). However, interpretation is tempered by the small sample ($n = 21$ for fMRI-NF), lack of a sham control, and the cost/technical complexity of MRI-based neurofeedback limiting scalability.

Looking forward, reviews and expert commentaries emphasize the importance of personalized, network-targeted protocols that reflect tinnitus heterogeneity, with credible sham controls, standardized outcomes, and long-term follow-ups (Varela Barrenechea, 2023; Kleinjung et al., 2023). Since systems already exist for remote brainwave recording, it may be feasible to deliver EEG neurofeedback at home under telehealth guidance, increasing dose and access while laying the groundwork for larger multicentre trials and combined treatment approaches (Kleinjung et al., 2023).

4 Multimodal and device-specific approaches

The shortcomings of prominent unimodal brain stimulation techniques arguably highlight a need to engage broader networks, more diverse and deeper targets along the auditory and frontostriatal pathways, and exploit the mechanisms of neuromodulation-induced neuroplasticity to promote consolidated auditory perceptual learning, sustainably counteracting the tinnitus-related maladaptive changes. Hence, we now turn to approaches designed to engage multiple inputs and deeper nodes of the tinnitus network.

While the exact mechanism underlying bimodal stimulation is still debated, the current consensus suggests a multilevel, timing-sensitive plasticity mechanism: pairing sound with either somatosensory input (e.g., trigeminal/tongue stimulation) or vagal afferent activation drives synaptic plasticity and desynchronization in hyperactive auditory circuits while also engaging diffuse neuromodulatory systems that regulate plastic change (Marks et al., 2018). Thus, bimodal stimulation potentially retunes central gain and synchrony along the auditory pathway, reducing the salience and persistence of the tinnitus percept (Jones et al., 2023).

Foundational preclinical work showed that pairing nucleus basalis stimulation with tones in adult rats can drive pronounced, frequency-specific reorganization of primary auditory cortex maps

(Kilgard and Merzenich, 1998). Subsequent work pairing vagus nerve stimulation (VNS) with tones demonstrated similarly targeted plasticity in A1, expanding representation around the paired tone and abolishing behavioral tinnitus proxies, with effects persisting for weeks (Engineer et al., 2011). A prospective randomized, double-blind pilot in implanted patients found greater improvement on the THI with paired VNS than control at 6 weeks (between-group difference not statistically significant) (Tyler et al., 2017). Mechanistically, paired VNS in patients was associated with reduced gamma and increased alpha synchronization in the left auditory cortex, plus decreased theta-band connectivity with dorsal and subgenual ACC and the parahippocampus, with theta-alpha connectivity changes associated with loudness suppression (Vanneste et al., 2017). Meanwhile, pairing transcutaneous VNS with sound has yielded positive, though still preliminary results (Shim et al., 2015; Ylikoski et al., 2020). Clinical outcomes remain variable and require confirmation in larger, sham-controlled trials.

Bimodal auditory-somatosensory stimulation, on the other hand, has gained notable traction over recent years. Pilot work has combined auditory therapy with microcurrent stimulation around the ear (Lee et al., 2024). In a 3-month trial, 60% of patients receiving combined therapy achieved clinically meaningful loudness reductions on VAS compared with 27% in the sound-only group, and two patients in the combined arm reported complete disappearance of tinnitus. Moreover, in a randomized, double-blind trial of 99 patients with somatic tinnitus, bisensory auditory-somatosensory stimulation was delivered via charge-balanced biphasic pulse trains to the skin over the trigeminal ganglion or upper cervical nerves (C1-C2) (Jones et al., 2023). This protocol, designed to induce spike-timing dependent plasticity [long-term depression (LTD)] in cochlear nucleus circuits, produced clinically meaningful improvements in 53%–65% of participants, with significant TFI reductions (−12.0 intent-to-treat; −13.2 per protocol at 6 weeks) and tinnitus loudness that persisted for up to 36 weeks. In contrast, auditory-only stimulation produced no clinically significant effects.

Some of the largest clinical investigations of bimodal auditory-somatosensory stimulation come from the TENT A1, TENT A2, and TENT A3 trials evaluating Neuromod's Lenire device (Boedts et al., 2024). Using charge-balanced biphasic pulse trains delivered to the tongue and time-locked to sound, the TENT A1 trial (n = 326) tested three timing schedules differing in the precision of pairing and the use of background wideband noise (Conlon et al., 2020). All produced significant 12-week improvements (pooled THI −14.2; TFI −13.6), with most gains in the first 6 weeks and a later plateau, suggesting strict millisecond pairing and wideband noise may not be essential. Indeed, TENT A2, a randomized double-blind optimisation study (n = 191), confirmed that pure tones without noise are sufficient, with two bimodal arms showing similar six-week improvements (Arm 1: THI −12.9, TFI −11.6; Arm 2: THI −11.5, TFI −11.7), and showed that resetting parameters at week 6 yielded further benefit by week 12 (pooled THI −18.5; TFI −15.3) that persisted at 12 months (THI −20.2; TFI −17.3); the sound-only arm improved mainly after tongue stimulation was added, supporting a specific somatosensory contribution (Conlon et al., 2022). TENT A3, a multisite trial that ultimately led to Lenire's FDA *De Novo* approval in 2023 (n = 112), used an active control and found that in moderate to severe tinnitus (THI ≥38) bimodal treatment outperformed sound therapy alone at 6 weeks for THI responders (58.6% vs. 43.2%), while sound alone may suffice initially for milder cases (Boedts et al., 2024). Real-world data from a U.S. cohort (n = 220) reported a 91.5% clinically meaningful improvement at about 12 weeks with a mean THI change of −27.8 and high adherence, though effect size differences likely reflect duration, heterogeneity, and confounds, underscoring the need for cautious interpretation and patient subtyping (McMahan and Lim, 2025). Together, the TENT A1-A3 trials support tongue-sound bimodal stimulation as a clinically useful option for at least a subset of patients (see Figure 3A for an overview).

There is an ongoing debate as to whether precise spike-timing is essential for therapeutic effects in tinnitus. Evidence from Jones et al. (2023) suggests that millisecond-level timing-dependent bisensory stimulation, derived from animal models of LTD in the DCN, produces significant and durable symptom reduction, whereas Conlon et al. (2022) and other studies, including from the broader literature, demonstrate clinical benefits without strict millisecond-level timing (Tyler et al., 2017; Dawson et al., 2021). This suggests that while precise timing may optimize efficacy, co-activations and diffuse neuromodulatory systems possibly also drive clinically meaningful change. Future work should implement adaptive mid-course optimization, stratify and power by baseline severity, pre-specify responder groups, and consider personalized timing and somatosensory targeting to maximize engagement and outcomes. It may also be worth testing additional, broader state-modulating designs that pair transcutaneous stimulation with auditory training to activate neuromodulatory systems and network plasticity beyond strict spike timing rules.

5 Depth-capable methods with tinnitus potential

5.1 Focused ultrasound and transcranial pulse stimulation

Transcranial focused ultrasound (tFUS) delivers mechanical acoustic energy concentrated at millimeter-scale foci using concave lenses or phased arrays, enabling non-invasive access to deep targets with high spatial precision (Davidson et al., 2024; Attali et al., 2025). In other words, it achieves spatial precision comparable to traditional, invasive deep brain stimulation (DBS), though non-invasively, with lower temporal resolution, while exceeding the spatial accuracy of rTMS and tES (Vanneste et al., 2025).

At the biophysical level, focused ultrasound interacts with brain tissue through a combination of mechanical and thermal effects. The oscillating pressure field generates acoustic radiation force and microscopic tissue displacements, and, over repeated pulses, can raise local temperature (Baek et al., 2022). The biologically relevant dose is shaped by intensity metrics such as the spatial-peak temporal-average intensity (ISPTA), which reflects average power over time and is closely related to cumulative thermal load, and the spatial-peak pulse-average intensity (ISPPA), which reflects peak intensity during the active pulse and is relevant

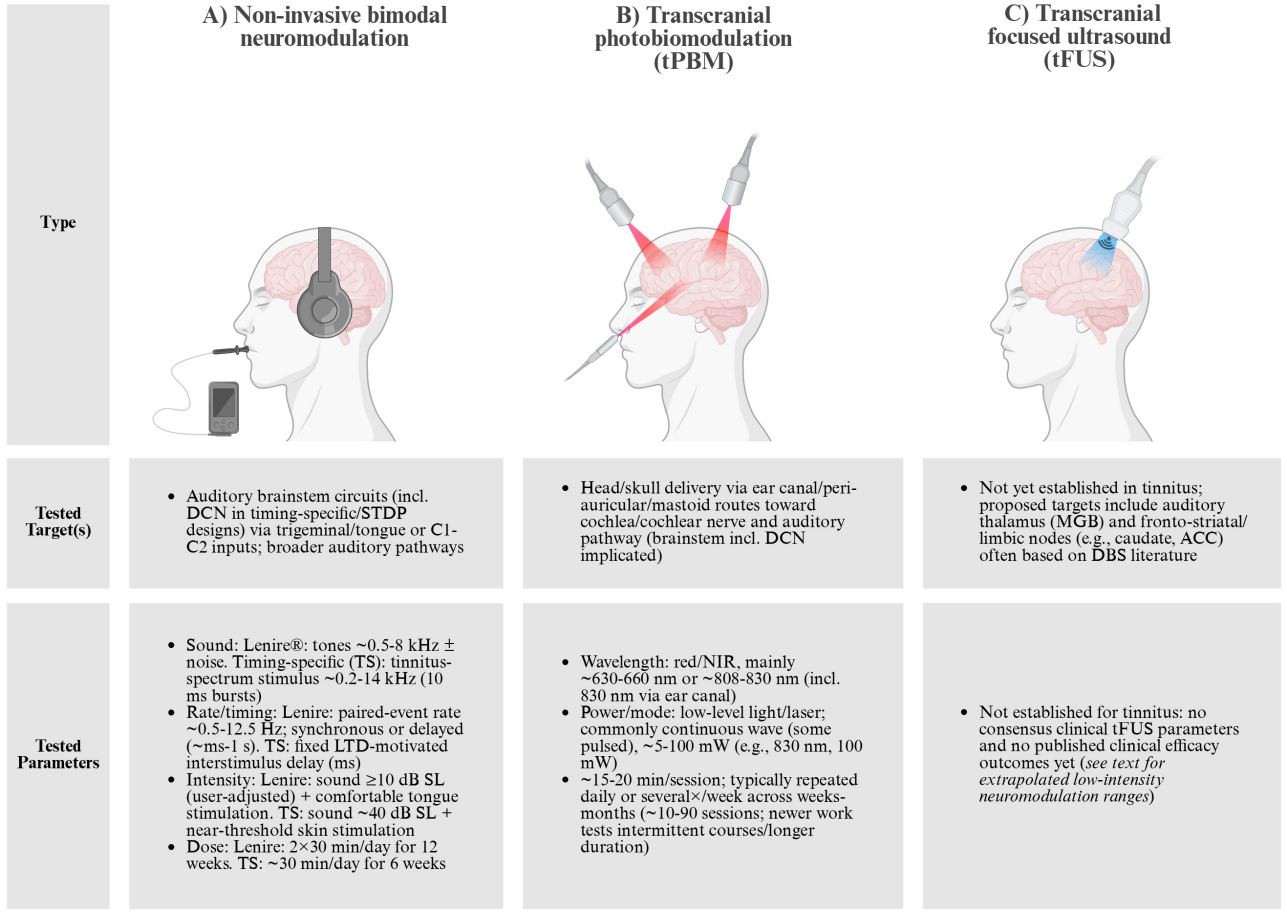

FIGURE 3
Emerging and depth-capable neuromodulation approaches for tinnitus. From left to right, panels depict **(A)** non-invasive bimodal neuromodulation combining auditory and somatosensory input, **(B)** transcranial photobiomodulation (tPBM), and **(C)** transcranial focused ultrasound (tFUS). Bimodal neuromodulation (Panel A) pairs sound with brief somatosensory pulse trains delivered to the tongue or upper cervical region (C1-C2) and, in some paradigms, vagal afferents; parameters are protocol-dependent and the ranges shown are derived primarily from Lenire® tongue-sound clinical trials and from timing-specific auditory-somatosensory protocols targeting trigeminal/C1-C2 inputs (e.g., Jones et al., 2023) and are not exhaustive given substantial inter-protocol variability. Overall, timing can follow spike-timing-dependent plasticity (STDP)-inspired principles or more loosely paired schedules. The Lenire® approach (Neuromod Devices Ltd., Dublin, Ireland) is shown as an illustrative commercial example of auditory-somatosensory bimodal stimulation. Transcranial photobiomodulation (tPBM; including transmeatal [ear-canal] and peri-auricular delivery) uses red/near-infrared (NIR) light to target cochlear and auditory pathway structures. For tFUS, potential deep targets (e.g., auditory thalamus [MGB] and fronto-striatal/limbic nodes such as caudate and ACC) are often proposed based on the broader neuromodulation/DBS literature, but there are no published controlled clinical efficacy outcomes available yet. Overall parameter ranges are derived from existing tinnitus studies and remain non-standardized. dB SL, decibels sensation level; DCN, dorsal cochlear nucleus; C1-C2, upper cervical spinal nerves; TS, timing-specific; STDP, spike-timing-dependent plasticity; tPBM, transcranial photobiomodulation; NIR, near-infrared; tFUS, transcranial focused ultrasound; MGB, medial geniculate body; ACC, anterior cingulate cortex; DBS, deep brain stimulation; Hz, hertz; nm, nanometer; mW, milliwatt. Figure created with BioRender.com.

for mechanical and instantaneous thermal effects, together with mechanical index (MI), duty cycle, pulse structure, and patient-specific skull transmission (Aubry et al., 2025; Keihani et al., 2024; Vanneste et al., 2025).

Overall, tFUS can be grouped into three therapeutic regimes: (i) high-intensity thermal ablation, where focal temperatures above ~55–60 °C create coagulative lesions and underpin MRI-guided functional neurosurgery, using continuous or high duty-cycle sonication to produce permanent tissue destruction; (ii) microbubble-assisted, pulsed FUS for transient blood-brain barrier (BBB) opening, which increases local permeability for drug delivery and typically reverses within 24–48 h, as intravenously injected microbubbles undergo stable cavitation in the ultrasound field and transiently loosen endothelial tight junctions; and (iii) low-intensity tFUS neuromodulation, where subthermal, pulsed mechanical forces produce micron-scale tissue displacements and associated deformations of the neuronal membrane, engaging mechanosensitive ion channels and modulating excitability and network dynamics (Kamimura et al., 2020; Prieto et al., 2020; Sorum et al., 2021; Baek et al., 2022; Vanneste et al., 2025; Barksdale et al., 2025).

While not yet systematically tested in tinnitus, two of these applications offer potential treatment avenues. First, low-intensity sonication can precisely modulate deep neuronal excitability, allowing image-guided, non-invasive engagement of limbic salience/distress hubs (Mahoney et al., 2023; Peng et al., 2024).

Recent studies have demonstrated causal thalamic engagement: MRI-guided low-intensity tFUS to the anterior thalamus increased heat-pain thresholds vs. sham in healthy adults (Badran et al., 2020), and individualized real time fMRI-guided ultrasound selectively modulated the human lateral geniculate nucleus (Martin et al., 2025). Such findings indicate precise control of sensory thalamic relays and potentially provide a methodological analog for the MGB and other deep brain structures (e.g., caudate nucleus), changes that may lead to a reduction in tinnitus. Indeed, a recent review of traditional DBS in tinnitus has illustrated how targeted stimulation of the MGB or caudate nucleus led to large reductions in tinnitus severity in case studies (Basner et al., 2024; Devos et al., 2023; Cheung et al., 2020). Hence, the ability of low-intensity focused ultrasound to safely and non-invasively modulate deep nuclei supports its translational potential in tinnitus.

Second, transient BBB opening could theoretically be utilized to enhance central exposure to interventions that dampen hyperexcitability in auditory relays. Proof-of-concept comes from broader preclinical work showing that focused ultrasound can assist in the delivery of systemic GABA into a targeted cortical site, producing focal suppression of neural activity verified with fMRI (Todd et al., 2019). However, this is based on theoretical and preliminary evidence, requires more research, and should be interpreted with caution, given the range of side effects associated with such interventions.

Meanwhile, transcranial pulse stimulation (TPS) is a related ultrashort pulse modality (lasting 3 μs), which delivers single-cycle shockwave-like pulses at low repetition (e.g., 1–5 Hz). In contrast, transcranial focused ultrasound uses high-frequency sinusoidal waves in long sonication trains lasting several 100 milliseconds (Davidson et al., 2024). One noted advantage of TPS over tFUS includes a lower thermal load due to very low time-averaged energy, which can reduce unwanted heating (Matt et al., 2022). Clinically, TPS has been shown to act as an oscillation regulator by damping abnormal network coupling and synchrony even when the carrier frequency stays unchanged (Manganotti et al., 2025). Hence, while still speculative, TPS could potentially be used to reduce pathological theta-gamma coupling in tinnitus. Together, current research demonstrates practical, human-level feasibility for deep-node neuromodulation, the same ingredients needed to further test focused ultrasound for both the perceptual and affective dimensions of tinnitus.

5.2 Transcranial photobiomodulation

Transcranial photobiomodulation applies low-irradiance (0.01 to 10 W/cm^2) red or near-infrared light within the optical window of roughly 600–1,300 nm to the scalp (and, in some protocols, intranasal, intraoral, or transauricular routes) to modulate brain metabolism and networks (Lin et al., 2024; see Figure 3B). Photons are absorbed primarily by cytochrome-c-oxidase, leading to nitric-oxide dissociation, enhanced electron transport, increased mitochondrial membrane potential, ATP production, and brief redox and calcium signaling; downstream effects may include improved cerebrovascular dynamics, anti-inflammatory cytokine shifts, and longer-horizon gene expression programmes supporting neuroprotection and adaptive neuroplasticity/genesis (De Freitas and Hamblin, 2016; Hamblin, 2017; Choi et al., 2024; Montazeri et al., 2024). Efficacy is strongly dose-dependent with a biphasic response, so reporting wavelength, irradiance, fluence, pulse structure, site, and session number is essential; pulsed delivery is common and can shape oscillatory activity (for example, 810 nm at 40 Hz increased oscillatory power, connectivity, and synchrony) (Huang et al., 2009; Zomorrodi et al., 2019). Early human work spans depression, cognitive impairment, and neurodegeneration with safety signals and emerging controlled trials, while device papers emphasize careful wavelength and dosing choices for reliable cortical and mesial engagement (Lin et al., 2024; Fernandes et al., 2024). Some additional benefits of tPBM are its safety, affordability, and convenient application both in clinical environments and potentially at home (Lin et al., 2024).

Recently, the use of tPBM in tinnitus management has increasingly been explored (Talluri et al., 2022; Choi et al., 2024). RCT-focused reviews up to 2022 were largely null relative to sham but highlighted pervasive heterogeneity and poor parameter reporting that limited firm conclusions (Talluri et al., 2022). More recent systematic reviews that include broader comparators conclude that tPBM is generally superior to no treatment for short-term symptom reduction, while still considering evidence quality mixed (Nikookam et al., 2023, 2024). Since then, emerging studies yielded more encouraging results: an 830 nm device (to the ear canal) combining preclinical and human work reported signals of clinical improvement in chronic high-frequency tinnitus with acceptable safety, and a follow-up randomized trial suggests intermittent schedules with longer overall treatment duration may be advantageous (significant reductions in loudness and on the THI emotional subscale) (Choi et al., 2024, 2025). Complementary preclinical data show symptomatic improvement alongside objective auditory measures, indicating tPBM's ability to increase markers of neuroplasticity and neurogenesis such as doublecortin (DCX) in the DCN, where plastic changes may be of advantage in tinnitus (Montazeri et al., 2024).

Although intermittent tPBM may yield short-term reductions in tinnitus loudness and distress, its clinical utility remains investigational and requires confirmatory, adequately powered trials. From an exploratory angle, tPBM could further be tested as a metabolic primer that is paired with pharmacology or neuromodulation to improve engagement of tinnitus circuits. Studies may attempt "pre-treating" with near-infrared tPBM before administering agents that dampen regional hyperexcitability or neuroinflammation (e.g., in the auditory cortex), and sequencing protocols such as tPBM over the auditory cortex or DCN followed by phase-two bimodal or electrical stimulation, repeated in alternating blocks. Parameter choices can follow the broader literature, where 808–810 (or 1,064) nm and pulsed delivery are common, and 20–30 min sessions are frequently reported across device surveys and meta-analyses (Lin et al., 2024; Ji et al., 2023; Fernandes et al., 2024). Regarding oscillations, a recent preprint observed that 40 Hz pulsing at near-infrared wavelengths yielded stronger alpha power increases than expected, contrary to initial hypotheses that 10 Hz would best enhance alpha, suggesting testable protocols to balance alpha or gamma in tinnitus (Mathew et al., 2025). Moreover, emerging data suggest that longer overall treatment duration may matter more than shortening inter-session

intervals, which supports pragmatic intermittent schedules (Choi et al., 2025). Finally, as the delivery technologies mature and allow more precise dosing at depth (e.g., modern lasers, 1,267 nm), deeper nodes can be considered for cleaner, target-specific tPBM interventions (Lin et al., 2024).

6 Discussion, future directions and concluding remarks

A comparative reading of current neuromodulation modalities suggests a promising future for next-phase tinnitus therapeutics. Open-loop, unimodal cortical stimulation (rTMS and the tES family) has produced reproducible but modest and often short-lived benefits, with outcomes especially sensitive to dose, site, and individual anatomy. Peripheral approaches such as TENS and auricular vagal stimulation are mechanistically plausible and appear helpful in selected phenotypes, yet effects are frequently confounded by expectancy and remain unconsolidated. By contrast, target-aware multimodal strategies, most notably auditory-somatosensory pairing, produce larger and more durable improvements in multiple recent trials, presumably because they induce a "window" of heightened plasticity, which is concurrently leveraged to promote a neural rewiring of auditory circuitry. Moreover, depth-capable methods occupy a complementary niche: traditional options like DBS have yielded large but early-stage effects in refractory cases, while non-invasive ultrasound-based methods (tFUS, TPS) are emerging as practical tools to non-invasively access the MGB, DCN, or frontostriatal hubs with millimeter-scale precision. In parallel, photobiomodulation offers a safe, scalable metabolic and anti-inflammatory intervention that may potentiate paired treatments. Collectively, these early signals justify shifting research from isolated nudges to hypothesis-driven, multimodal, circuit-informed programmes tested in rigorous, placebo-aware trials.

Progress will depend on confronting several persistent challenges head-on. First, heterogeneity remains a major obstacle. Tinnitus is not one disorder, but a family of phenotypes defined by audiometric profile, tinnitus pitch, hyperacusis, somatic modulatability, affective comorbidity, and neurophysiological signatures (e.g., alpha deficits, theta-gamma coupling, and auditory-limbic dysconnectivity). One-size-fits-all protocols arguably dilute effects and obscure responders. Closely linked is the absence of validated biomarkers that stratify patients a priori, confirm target engagement *in vivo*, and predict durable responses. Additionally, trial design requires optimization. Expectancy and placebo responses are substantial, shams are often inadequate or insufficiently matched, follow-up is commonly short, and parameter reporting is inconsistent. Treatment outcomes need to be consistently reported in a standardized manner, including TFI/THI/VAS scores, and potentially need to be broadened to include neurophysiological endpoints. Finally, the true dose that eventually reaches its (sub)cortical target is rarely verified. Without individualized current flow/field modeling, dosimetry, skull-transmission estimates, or photonic parameter reporting, dose-response relationships will likely remain unclear.

Indeed, the most actionable opportunity to address tinnitus in the near future appears to be principled multimodal integration, an explicitly pragmatic "use all weapons available" stance (De Ridder et al., 2024). In practice, this means combining and sequencing interventions to address ascending lateral, medial, and descending pathways, and to consolidate durable plastic change. The near-term focus should be the optimization of multi/bimodal protocols in light of successful trials with auditory-somatosensory pairing. Protocols should prioritize pairing schedules that proved effective in practice, while also extending parameter settings beyond millisecond spike-timing precision to test alternative, network-level plasticity mechanisms. Promising peripheral targets deserve additional clinical testing, including the greater occipital nerve, which has extensive evidence in pain models and may modulate relevant brainstem nuclei (e.g., nucleus tractus solitarius and locus coeruleus) (Miller et al., 2016; De Ridder and Vanneste, 2017; To et al., 2017). Where home devices permit, it may be valuable to pair or sequence (bimodal) stimulation sessions with neurofeedback blocks that reinforce alpha restoration and reduce excessive theta-gamma coupling, with the aim of consolidating treatment effects. Recently updated safety guidelines on low-intensity electrical stimulation report no additional safety concerns for at-home use (Antal et al., 2025).

Another avenue worth exploring is instructing active rather than passive listening in auditory stimulation. Coupled auditory retraining that requires attention, discrimination, and adaptive difficulty may be more likely to consolidate plasticity than background listening (Hoare et al., 2012; Hemanth and Vipin Ghosh, 2022). Recent sound-based work further suggests that carefully tailored acoustic stimulation can yield measurable benefits in defined tinnitus subgroups. For example, individually matched sound enrichment shaped to the hearing-loss region and tinnitus pitch, and low-intensity noise centered on the tinnitus frequency delivered via hearing aids, have each produced substantial within-group reductions in tinnitus handicap over weeks to months, albeit in relatively narrowly characterized samples (Sendesen and Turkyilmaz, 2024; Tziridis et al., 2025b). Together, these findings indicate that optimizing auditory input (e.g., spectrum, level, dosing, and engagement demands) can produce clinically relevant change in selected phenotypes and should remain a key consideration for the acoustic arm of future bimodal or multimodal neuromodulation protocols.

Given the substantial inter-individual variability, tinnitus trials should also consider exploring closed-loop, brain-state-triggered stimulation. While not yet tested for tinnitus, one study introduced alpha closed-loop auditory stimulation to modulate human alpha power, frequency, and connectivity in a phase-dependent manner (Hebron et al., 2024). Meanwhile, Mulyana et al. (2022) demonstrated that real-time closed-loop tES within a functional MRI framework can optimize alternating-current stimulation frequency and phase between network nodes. Adapting these state-contingent paradigms to gate stimulation on alpha-dominant or reduced theta-gamma states in tinnitus circuits could further enhance target engagement (e.g., in multimodal stimulation contexts). Finally, metabolic priming could also be tested, for example short near-infrared photobiomodulation over A1 just before each session to enhance mitochondrial activity, anti-inflammatory dynamics, and the probability of adaptive plasticity. In parallel, exploring pilots of low-intensity, imaging-guided focused ultrasound to key relays across the lateral auditory

and medial salience networks, starting with the MGB and the DCN, and extending to anterior cingulate and ventral striatal hubs, might turn out beneficial. Additionally, such interventions could then be followed by structured bimodal and auditory retraining to consolidate gains.

Methodological upgrades are equally important. Trials should adopt adaptive, multi-arm platform designs that compare sound-based therapy, unimodal stimulation, and multimodal approaches, under a common framework with response-adaptive randomization and one, 6 and/or 12-month follow-ups. Where possible, shams must be sensation-matched and paired with formal blinding checks. Expectancy should be measured and modeled as a covariate rather than treated as negligible. Dose verification should become routine: for tES and rTMS, individual imaging-based current flow and field modeling and reporting of delivered electric field and pulse counts; for tFUS and TPS, ISPTA and ISPPA, duty cycle, focal size, skull correction, and navigation error; for tPBM, wavelength, irradiance, fluence, pulsing, site geometry, and session number/length. A core outcome set should be reported in every trial, including THI/TFI/VAS with minimal clinically important differences, loudness, patient global impression, anxiety, and depression measures, and adherence, potentially complemented by EEG and connectivity endpoints. Finally, an open science posture, including preregistration, harmonized data structures, and routine sharing of raw EEG and analysis code, will accelerate biomarker validation and enable credible meta science.

In sum, the field's recent lessons point in a coherent direction. Tinnitus most likely persists because complex network-level changes maintain a maladaptive percept and its affective load. Therefore, durable relief will seldom follow from a single, open-loop intervention. A strategy that integrates repeated multimodal stimulation, deeper and cleaner targeting, and (closed-loop) personalization, conducted within placebo-aware, dosage-verified, and outcome-rich trials, offers the clearest path to translating mechanistic insight into reliable, generalizable benefit for defined tinnitus subgroups.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

FB: Writing – original draft, Writing – review & editing. SV: Writing – original draft, Writing – review & editing.

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Conflict of interest

The author(s) declared that this work was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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The author(s) declared that generative AI was not used in the creation of this manuscript.

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