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Objective Neurophysiologic Characterization of Tinnitus and Post-COVID Auditory/Vestibular Sequelae Using BrainView EEG/ERP: A Translational Framework for Biomarker Discovery and Treatment Monitoring

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Abstract

Background: Tinnitus and related auditory/vestibular disorders remain limited by the absence of validated objective biomarkers. This contributes to heterogeneous diagnosis, inconsistent treatment selection, and reliance on subjective outcome reporting. Electroencephalography (EEG) and event-related potentials (ERPs) provide scalable neurophysiologic measures capable of quantifying oscillatory abnormalities, functional connectivity disruption, and cognitive-attentional processing changes implicated in tinnitus and post-infectious otologic sequelae.

Objective: To develop a translational framework for applying a clinically deployable EEG/ERP platform (BrainView) to tinnitus and ear-related manifestations, including post-COVID auditory and vestibular sequelae, for biomarker discovery, patient phenotyping, and treatment monitoring.

Methods (Conceptual Framework): We synthesize evidence from tinnitus EEG biomarker reviews, EEG-based classification research, and post-COVID otorhinolaryngologic literature, and map candidate neurophysiologic features onto BrainView platform capabilities, including resting-state EEG/QEEG, auditory/visual ERP paradigms, and normative comparisons.

Results: Current evidence supports candidate EEG biomarkers across alpha, theta, and gamma bands, with particular support for network/connectivity-derived measures and composite models. A large EEG classification study demonstrated the ability to discriminate tinnitus presence and distress severity using machine learning. Post-COVID studies demonstrate persistent auditory and vestibular symptoms, highlighting an unmet need for objective central nervous system assessment to distinguish peripheral versus central contributions.

Conclusion: BrainView provides a pragmatic EEG/ERP workflow with clinical-grade acquisition and automated reporting that may accelerate translation of EEG-based tinnitus biomarkers and help characterize post-COVID auditory/vestibular syndromes. Prospective validation is required to establish predictive utility, standardize protocols, and demonstrate clinical value in routine otologic care pathways.

Keywords

Tinnitus, EEG/ERP, Biomarkers, Functional Connectivity, Post-COVID Sequelae.

INTRODUCTION

Tinnitus is a prevalent condition characterized by phantom auditory perception without an external stimulus1. The noise may be constant or intermittent, perceived as ringing, buzzing, hissing, sizzling, roaring, chirping, or other sounds in the ear or ears or the head [1]. The impact of tinnitus extends beyond perceptual disturbance to include sleep disruption, cognitive impairment, anxiety, depression, and reduced quality of life [2]. Despite a well-defined presentation, tinnitus remains a highly prevalent yet mechanistically heterogeneous condition for which no validated objective biomarker is currently accepted for diagnosis, stratification, or treatment monitoring [3,4]. The neurophysiology of tinnitus creates major challenges for both routine clinical management and clinical trial endpoint selection. Contemporary electrophysiologic literature, including recent comprehensive reviews [1,5], indicates that tinnitus involves aberrant oscillatory activity (notably alterations across alpha, theta, and gamma bands), disrupted

auditory–non-auditory connectivity, and salience/attention network dysregulation, rather than a purely peripheral cochlear phenomenon [6]. Reviews emphasize that while candidate markers are promising, translation is limited by variability in acquisition paradigms, analytic approaches, and the absence of large prospective validation cohorts [6,7]. Importantly, the same central network mechanisms implicated in idiopathic tinnitus may also contribute to tinnitus and vestibulo-auditory symptoms observed after viral illness [8], raising the question of whether shared or distinct neurophysiologic signatures can be objectively identified.

Contemporaneously, SARS-CoV-2 infection has been associated with new or worsening auditory symptoms (including tinnitus and hearing loss) and vestibular symptoms (including dizziness and vertigo [9,10]. Vestibulo-auditory symptoms manifesting in acute infection but persisting through post-acute Covid sequalae (PASC) have been reported [11,12]. These clinical reports underscore the need for objective tools that may detect central functional alterations associated with symptoms and facilitate the estimate of the relative contribution of central versus peripheral mechanisms [13].

Resting-state electroencephalogram (EEG) studies implicate abnormalities in neural oscillations and functional connectivity across auditory pathways, attention networks, salience networks, and limbic circuits related to tinnitus and related auditory manifestations [14]. EEG is a noninvasive neurophysiologic technique that captures scalp-recorded electrical activity generated by neuronal ionic currents, enabling high temporal-resolution assessment of human brain dynamics [15]. Resting-state EEG has been widely applied to tinnitus research because it can directly quantify the timing, frequency content, and network-level characteristics of neural activity potentially underlying phantom auditory perception [16]. Multiple studies report that individuals with tinnitus demonstrate measurable differences in EEG parameters relative to healthy controls [7,17], including altered microstate temporal structure and syntax during rest [18,19]. Across the literature, tinnitus-associated effects have been described in several frequency bands, including delta, alpha, beta, and gamma rhythms, suggesting widespread oscillatory dysregulation rather than a single-band abnormality [20]. Although spontaneous activity has been more extensively examined in animal tinnitus models, human work using EEG and magnetoencephalography similarly reports band-specific changes, including increased delta and reduced alpha power [21,22] and regionally localized alterations across temporal, frontal, and frontotemporal areas [23,24]. Some investigations further implicate gamma-band activity, reporting elevated broadband spectral energy with correlations between tinnitus loudness and localized spectral power, consistent with central reorganization and heightened auditory network activation [25,26], while others report reductions in alpha/beta or gamma activity dependent on eyes-open versus eyes-closed conditions [17]. Notably, not all studies identify significant spectral differences between tinnitus and control groups [27], and findings across the power spectrum remain inconsistent, with reports of both increases and decreases in similar bands. Collectively, these mixed results underscore ongoing debate regarding the specific role of individual frequency bands in tinnitus pathophysiology and highlight the need for standardized protocols and multimodal or multivariate analytic approaches to improve reproducibility and clinical interpretability [28-30]. Given the heterogeneity of tinnitus etiologies and the non-specificity of many EEG measures to tinnitus versus distress, sleep disruption, and hearing loss, candidate EEG/ERP biomarkers should be framed as probabilistic stratification tools rather than diagnostic markers until validated in prospective multi-site cohorts.

The BrainView EEG/ERP platform is a clinically oriented system intended for acquisition and analysis of EEG and ERPs, including normative comparisons [31,32]. Its workflow characteristics, short duration, automated reporting, and portability, may enable scalable implementation of neurophysiologic phenotyping in outpatient tinnitus and post-COVID otology settings.

Multiple models propose that tinnitus is maintained by maladaptive central gain and aberrant network oscillations following peripheral deafferentation or cochlear injury. EEG signatures commonly discussed include altered alpha activity (e.g., reduced posterior alpha), increased slow-wave activity (theta/delta), and abnormal gamma-band activity, potentially reflecting altered thalamocortical circuitry and dysrhythmia. The variability across studies suggests that composite or network-level metrics may outperform single-band markers in clinical classification [33,34]. A growing proportion of tinnitus EEG studies emphasize functional connectivity measures (e.g., phase synchronization indices, coherence-like metrics) as candidate biomarkers. Connectivity-derived features have been shown to discriminate tinnitus characteristics such as laterality/location and may offer improved stability compared with isolated spectral features [35]. A notable EEG classification study acquired EEG from 129 tinnitus patients and 142 controls and developed classifiers that differentiated tinnitus patients from controls and further differentiated low- versus high-distress tinnitus [36]. This work provides proof-of-concept that multivariate EEG signatures can encode clinically meaningful tinnitus states [35,36].

In many patients, tinnitus severity is better explained by attentional capture and emotional salience than by perceived loudness alone. ERPs provide time-locked indices of sensory encoding and cognitive processing, making them particularly relevant to tinnitus phenotypes characterized by hypervigilance, reduced habituation, and cognitive intrusion. Phenotypes will be defined using a pre-specified framework integrating audiometry (degree/configuration of hearing loss), tinnitus laterality/duration, validated symptom burden (THI/TFI), and psychiatric/sleep covariates (PHQ-9, GAD-7, insomnia severity), enabling multivariable adjustment and subgroup stratification. The P300 ERP component, typically elicited through oddball paradigms, reflects processes related to attention allocation and context updating. ERP metrics (amplitude, latency, and behavioral response measures) may therefore serve as objective correlates of tinnitus intrusiveness and treatment response, particularly for interventions targeting habituation, attention control, and distress reduction [37]. Clinical follow-up studies and ear, nose, and throat (ENT) -focused reviews report tinnitus, hearing loss, dizziness, and balance disorders among patients recovering from COVID-19, including long-term follow-up in subsets [38]. PASC ENT literature emphasizes that self-reported symptoms are often not consistently confirmed by objective testing, highlighting the need to broaden objective assessment beyond peripheral measures alone [39].

Post-COVID auditory and vestibular manifestations may arise from multiple mechanisms, including peripheral injury (cochlear/vestibular), central auditory pathway changes, neuroinflammation, autonomic dysfunction, or indirect effects mediated by sleep and mood disturbances. EEG/event-related potential (ERP) is well suited to detect central network dysfunction contributing to symptom persistence and may provide additional discriminative value when combined with audiologic and vestibular testing. Within this context, clinically deployable EEG/ERP platforms such as BrainView may represent an important translational bridge and address the lack of validated objective biomarkers. The device enables standardized acquisition of resting-state EEG and ERPs with normative comparisons

and automated reporting, potentially allowing neurophysiologic profiling to be incorporated into outpatient tinnitus and post-infectious otology workflows.

Recent evidence also suggests that post-COVID sequelae frequently include tinnitus, hearing impairment, vertigo, and other balance-related complaints, increasing demand for objective central functional measures to distinguish peripheral otologic injury from central network dysfunction and related cognitive-emotional contributors. Spectral power, functional connectivity, microstate dynamics, and nonlinear complexity (entropy). The prevailing dogma suggests no single definitive EEG signature has achieved broad reproducibility, and clinical translation will likely require multivariate models that integrate spectral and connectivity measures and are validated across diverse populations [17]. This finding directly supports a phenotyping approach in which EEG/ERP data are used not as a unidimensional marker, but as a mechanistic stratification tool to separate tinnitus subtypes.

The BrainView system is described as an FDA 510(k)-cleared Class II medical device for acquisition, display, and storage of EEG and ERP activity using two or more electrodes.

Key platform elements relevant to tinnitus and ear-related manifestations include:

1. Clinical EEG/ERP acquisition suitable for resting-state EEG (QEEG feature extraction) and ERP paradigms.
2. Normative comparison capability, facilitating objective deviation scoring and standardized interpretation [32].
3. Workflow suitability for outpatient implementation, enabling potential registry-scale data capture in tinnitus clinics.

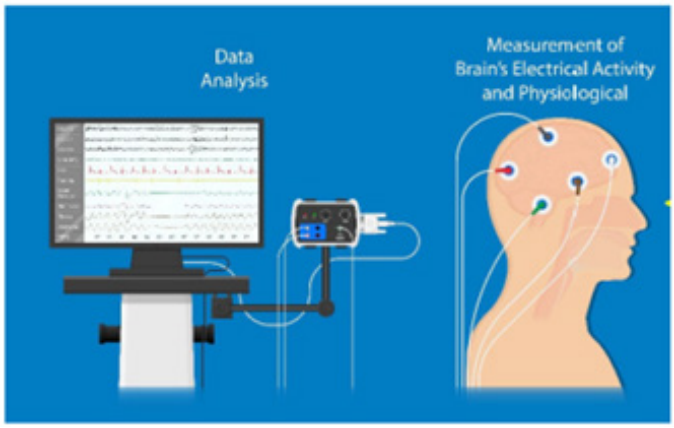

Figure 1: An illustration of a BrainView setup for an EEG test, where brain electrical activity is measured during a qEEG.

Participants are seated in a sound-attenuated, dimly lit room and instructed to minimize movement while passively viewing a randomized sequence of visual stimuli on a computer monitor (Figure 2).

From the current literature, three clinically relevant tinnitus phenotypes appear particularly well aligned with EEG and ERP measurement. First, deafferentation-driven tinnitus with compensatory central gain is supported by resting-state EEG findings showing altered oscillatory balance in tinnitus patients, including differences in alpha, theta, and gamma activity, consistent with maladaptive central gain mechanisms and disrupted thalamocortical signaling. Although results vary across cohorts, the convergence of evidence for oscillatory disruption suggests that QEEG-derived spectral and network features may help identify patients whose tinnitus is more strongly associated with hearing loss and sensory deafferentation. Second, distress-dominant tinnitus with salience/limbic dysregulation reflects the observation that tinnitus burden is highly variable and often driven more by distress and intrusiveness than loudness; neurophysiologic models increasingly implicate salience and affective networks in maintaining tinnitus-related impairment, and reviews report EEG alterations extending beyond auditory cortex into broader non-auditory networks, with effects often more pronounced in high-distress cases [7]. This supports the use of EEG signatures to differentiate patients in whom tinnitus distress may be primarily driven by heightened emotional salience, stress-response processes, and limbic involvement. Third, a cognitive/attention-dominant tinnitus phenotype is supported by studies using attention-demanding tasks and ERP paradigms, which suggest that tinnitus patients may exhibit differences in pre-stimulus alpha modulation and evoked theta activity during auditory cognitive processing, consistent with attentional capture, executive inefficiency, and impaired habituation [40]. These domains are well suited to ERP assessment, particularly through latency and amplitude metrics such as the P300 component and may complement resting EEG measures in characterizing tinnitus phenotypes relevant to clinical stratification and treatment planning.

Figure 2: An image of the BrainView Neural Scan System developed by Medeia Inc. The BrainView system is portable, easy-to-use, and non-invasive. The BrainView system is a 21-channel EEG/ERP amplifier with a dedicated laptop and testing supplies. The system utilizes high-quality circuit boards and components to allow for high-quality brain measurements, as well as essential heart rate variability data.

In practical terms, EEG/ERP-derived features can be combined with audiogram data and standardized symptom scales (e.g., THI/TFI) to build phenotype models, enabling a stratified approach to treatment selection and monitoring. A major clinical goal is to identify objective biomarkers that distinguish "high-burden" tinnitus, characterized by significant distress, functional impairment, and healthcare utilization, from low-burden tinnitus, where symptoms may be perceptually present but minimally disruptive. A large EEG classification study directly supports feasibility of this approach: EEG was recorded from 129 tinnitus patients and 142 controls, and machine-learning classifiers were able to differentiate tinnitus patients from controls and also distinguish low- versus high-distress tinnitus groups with strong performance. Critically, this study reported minimal overlap between features used for tinnitus detection and those used for

distress classification, implying that tinnitus distress may constitute a partially separable neurophysiologic state that can be independently quantified. This literature supports a clinical model in which BrainView EEG/ERP is used not solely for tinnitus "diagnosis," but as a biomarker adjunct that supports distress classification and risk stratification, potentially guiding more intensive behavioral interventions, psychiatric comorbidity evaluation, or neuromodulation approaches in high-burden subgroups.

Auditory and vestibular complaints are increasingly recognized in PASC, with symptoms including tinnitus, hearing loss, dizziness, vertigo, and balance dysfunction. A study reviewing COVID-era clinical charts identified patients with new or worsening auditory and vestibular symptoms and followed a subset longitudinally [41]. Additional ENT-focused reviews similarly emphasize tinnitus and vestibular symptoms as commonly reported, while also noting ongoing uncertainty about whether these symptoms reflect vestibular pathology, central dysfunction, or broader post-viral fatigue/autonomic syndromes. PASC auditory/vestibular symptoms can arise through multiple mechanisms: peripheral injury (cochlear or vestibular), central auditory pathway adaptation, neuroinflammation, autonomic dysregulation, and secondary effects of sleep and mood disturbance. Because many of these mechanisms implicate central network dysfunction, EEG/ERP provides a plausible physiological method for phenotyping PASC tinnitus and vestibular syndromes beyond standard peripheral testing. For PASC-related symptoms, a critical study design element as the field progresses is inclusion of comparator cohorts (post-COVID without tinnitus; idiopathic tinnitus without COVID history; matched controls), allowing assessment of whether post-COVID tinnitus represents a distinct neurophysiologic subtype or shares canonical tinnitus signatures [42].

Clinical outcomes remain heavily dependent on subjective rating scales that are vulnerable to expectancy effects, mood fluctuations, and non-specific improvement [43]. Recent reviews emphasize that a credible pathway toward objective endpoints will likely require integration of multiple EEG/ERP feature domains, including spectral power, connectivity/network measures, and task-based or ERP-derived metrics, with validation in longitudinal studies and machine-learning frameworks applied to large, heterogeneous datasets [44]. Within this context, repeated assessments using platforms such as BrainView could be operationalized as a clinical monitoring approach, enabling evaluation of whether symptom improvement following intervention corresponds to measurable changes in EEG/ERP markers, particularly connectivity and network-level measures that appear among the most consistently implicated domains in the tinnitus electrophysiology literature. A longitudinal biomarker strategy also addresses a persistent limitation of cross-sectional studies: even when group-level EEG signatures vary across cohorts, within-subject trajectories may prove more stable and clinically actionable as objective endpoints for monitoring response over time. Scoping and narrative reviews further suggest that cross-sectional case-control designs remain valuable for biomarker discovery but require greater standardization and careful inclusion of covariates, with recommended endpoints including classification accuracy for tinnitus presence and distress, correlations between EEG/ERP features and validated severity scales (THI/TFI), and subgroup differentiation such as post-COVID versus non-COVID phenotypes. At the same time, the literature increasingly supports prospective designs incorporating baseline and follow-up EEG/ERP to evaluate biomarker responsiveness and predictive utility, with endpoints focused on within-subject neurophysiologic change, associations with symptom improvement, and baseline predictors of treatment response in responder versus non-responder models. Given the consistent emphasis on the need for large validation cohorts, registry-based approaches may be particularly important; multi-site registries capturing BrainView outputs alongside standardized symptom measures, audiograms, and relevant covariates can support phenotype modeling, normative adjustment, replication, generalizability, and validation of EEG/ERP-derived objective endpoints. Notably, the EEG tinnitus literature also highlights that variability in patient selection (including hearing loss, tinnitus duration, laterality, and distress burden), EEG acquisition conditions, stimulation/task paradigms, preprocessing and artifact handling, and analytic feature definitions and statistical methods. To mitigate these limitations, reviews increasingly recommend multivariate models over single-band interpretations, systematic incorporation of audiologic and vestibular measures as key covariates, control for sleep disruption and psychiatric comorbidity (anxiety and depression) as well as medication effects, and prioritization of connectivity and network features where feasible, given their recurring identification as potentially stronger candidates for objective characterization. These analytic principles are consistent with scoping review conclusions that objective tinnitus measures are most likely to emerge from combined spectral and connectivity signatures validated at scale using machine-learning approaches. Despite this momentum, key barriers remain, including the non-specificity of many EEG changes to tinnitus (often reflecting stress, depression, or sleep deprivation), the substantial heterogeneity of tinnitus mechanisms that necessitates phenotype stratification, the susceptibility of EEG to artifacts requiring rigorous standardization, and challenges in translating electrophysiologic patterns into actionable clinical reports and decision pathways. Collectively, however, the literature supports EEG/ERP as a high-potential modality for objective characterization of tinnitus and related auditory/vestibular disorders, including post-COVID manifestations, while also underscoring that translation will depend on standardized protocols, multivariate approaches, and large validation cohorts integrating spectral and connectivity measures. Within this evidence landscape, BrainView may serve as a pragmatic translational platform by enabling clinical-grade EEG/ERP acquisition, normative comparisons, and workflow efficiency to support scalable patient phenotyping, distress stratification, and longitudinal monitoring in outpatient tinnitus and post-COVID otology care pathways [7,45], with prospective validation studies and registry-based real-world evidence generation representing critical next steps for establishing clinical utility, predictive value, and objective endpoints suitable for routine practice and clinical trials. However, EEG/ERP measures should be interpreted as complementary to audiologic and vestibular testing. To date, the strongest discriminative models are likely to emerge from multimodal integration rather than EEG alone.

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