Auditory and Vestibular Research

Eyes Closed vs. Eyes Open: Investigating Brain Activity Differences in Tinnitus Patients Using Multi-Channel Electroencephalography-A Preliminary Study

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Highlights

EEG shows distinct tinnitus-related power changes in eyes-closed vs. eyes-open states

Source analysis shows distinct tinnitus-specific neural patterns in two eye states

Tinnitus patients exhibit increased functional connectivity in eyes-closed state

Abstract

Background and Aim: Tinnitus, the perception of sound without an external source, significantly affects the quality of life for millions worldwide. Although many studies have explored its pathophysiology and neural underpinnings using various methods during resting states, the influence of eye state on neural activity remains poorly understood. This study examined brain activity differences between eyes-closed and eyes-open resting states in individuals with chronic tinnitus.

Methods: In this cross-sectional study, twenty patients with chronic tinnitus underwent Electroencephalography (EEG) during both eyes-closed and eyes-open resting states. EEG power spectra, source localization, and functional connectivity were analyzed across eight frequency bands. Paired-sample t-test and Statistical Non-Parametric Mapping (SnPM) test compared activity between these conditions.

Results: Eyes-closed recordings showed decreased delta, theta, and gamma power, increased alpha 1 and alpha 2 power, and a complex beta pattern (increased beta 1, decreased beta 2 and beta 3) compared to eyes-open. Source localization analysis revealed greater activity in regions associated with memory, attention, and emotional processing during eyes-closed compared to eyes-open. Functional connectivity analysis indicated stronger connections between auditory and memory-related regions in eyes-closed compared to eyes-open.

Conclusions: This preliminary study demonstrated distinct EEG power spectra, source localization, and functional connectivity between eyes-closed and eyes-open states in chronic tinnitus patients, suggesting state-specific neural patterns. Findings highlight interactions of sensory, cognitive, and affective processes, potentially relevant to tinnitus. Further research with control groups and larger samples is needed to confirm tinnitus-specific effects and optimize EEG conditions for elucidating neural mechanisms and guiding targeted interventions.

Keywords: Tinnitus; electroencephalography; eyes-closed; eyes-open; source localization; functional connectivity

Introduction

Tinnitus is the conscious perception of sound without an external source [1]. When it persists for six months or longer, it is considered chronic[2]. Tinnitus is highly prevalent worldwide, with rates ranging from 8-20% in the general population, making it the most common subjective auditory symptom[2]. About 6-25% of affected individuals report severe interference with daily life, leading to reduced quality of life and impairments in cognitive, emotional, and social functioning[2, 3]. The unclear pathophysiology and absence of reliable treatments further exacerbate its impact[1].

Although many studies have examined the neural mechanisms of tinnitus, important questions remain in this field[1]. Neuroimaging has revealed abnormal cortical activity in tinnitus patients compared with controls[4]. Electroencephalography (EEG), a widely used tool for assessing neural oscillations in tinnitus, has consistently shown alterations in multiple frequency bands. Reduced alpha activity in the auditory and prefrontal cortices, combined with increased theta and gamma power, has been reported in tinnitus patients[5]. A more recent work also highlights abnormal theta power in the anterior cingulate cortex and parahippocampus[6]. With advanced source localization and functional connectivity approaches, such as standardized low-resolution brain electromagnetic tomography (sLORETA), studies have demonstrated both the emergence of aberrant activity sources and altered connectivity among key tinnitus-related regions, including the auditory cortex, prefrontal cortex, cingulate cortex, insula, hippocampus, and parahippocampus[7-9]. However, a critical gap remains regarding how methodological variations, particularly the state of the eyes during EEG recordings, influence these findings.

The brain displays spontaneous neural activity even in the absence of external stimulation, known as the resting state[7]. Resting-state data are typically collected under two conditions: eyes-closed and eyes-open[10]. These states exhibit distinct neurophysiological signatures[11]. The eyes-closed condition is marked by increased alpha power, especially over posterior regions, reflecting relaxed attention and reduced sensory input[11, 12]. Conversely, eyes-open recordings show reduced alpha and greater beta activity in frontal regions, associated with arousal and visual processing[11]. Neuroimaging studies corroborate these findings, with eyes-closed linked to sensory-dominant network (e.g., sensorimotor and visual) activity, while eyes-open engages default mode, fronto-parietal, and salience networks[13]. Functional connectivity also differs: eyes-closed enhances connections within visual, auditory, and sensorimotor networks, whereas eyes-open increases coupling between visual and attention/arousal systems[14]. These variations underline the importance of eye state in interpreting resting EEG, yet little is known about its role in tinnitus research.

Previous tinnitus EEG studies have used eyes-open, eyes-closed, or both without directly comparing conditions[15]. Consequently, reported differences between tinnitus patients and

controls—or among patients themselves—may partly reflect uncontrolled eye state effects[15]. To date, no study has systematically compared EEG power, source localization, and functional connectivity between resting-state conditions in tinnitus. A better understanding of these influences is essential for clarifying tinnitus mechanisms and developing effective treatments[16].

In this preliminary study, we hypothesize that chronic tinnitus patients show distinct neural dynamics under eyes-open versus eyes-closed resting states, consistent with the network theory of tinnitus. This theory proposes that tinnitus emerges from abnormal interactions among auditory, attention, memory, and emotional networks, involving the auditory cortex, prefrontal cortex, cingulate cortex, insula, hippocampus, and parahippocampus[7, 9]. The eyes-closed state, with reduced sensory input and greater internal focus, is expected to enhance tinnitus-related activity and connectivity in the default mode and auditory-memory networks, reflected in increased alpha power in regions like the posterior cingulate and parahippocampal gyrus linked to distress and memory integration[3, 17]. In contrast, the eyes-open state, characterized by heightened visual attention, may suppress these introspective networks while increasing beta and gamma activity in attention-related areas, potentially modulating tinnitus through sensory competition[18, 19]. To test these hypotheses, we employed multi-channel EEG with sLORETA-based source localization and functional connectivity analysis. By recording both eyes-closed and eyes-open resting states in the same participants, we controlled for confounding factors such as age, gender, hearing loss, and tinnitus duration. This comprehensive analysis across eight frequency bands provided novel insights into how eye state modulates neural activity in tinnitus, with implications for optimizing EEG protocols and developing personalized, state-specific interventions.

Methods

Participants and clinical evaluations

This preliminary cross-sectional study involved 20 participants (7 females) diagnosed with chronic non-pulsatile tinnitus. They were recruited from the Tinnitus Clinic of Tehran University of Medical Sciences between August 2023 and April 2024. The mean age was 42.3±8.83 years, and none of participants had a history of Meniere's disease, otosclerosis, middle ear disorders, head trauma, or neurological issues. Individuals taking medication for psychological disorders were excluded. To ensure consistent cognitive status, participants were screened using the Persian version of the Mini-Mental State Examination (MMSE), and only those scoring 24 or higher were included. Audiometry and psychoacoustic tinnitus measurements (pitch and loudness matching) were performed in the audiology clinic. Eligible participants had pure-tone thresholds below 25 dB HL at 250–2000 Hz and below 40 dB HL at 4000–8000 Hz. Tinnitus intensity and annoyance were assessed with Visual Analogue Scales (VAS), ranging from 0 (none) to 100 (maximum). All participants completed the Tinnitus Handicap Inventory (THI) and Tinnitus Functional Index (TFI). All subjective chronic tinnitus types were included, without restrictions on psychoacoustic characteristics, duration, or laterality. **Table 1** shows demographic and clinical data.

Ethics declarations

Before evaluations, participants received a full explanation of study procedures and gave written informed consent for participation and data publication. The Ethics Committee of Tehran University of Medical Sciences approved the study (IR.TUMS.FNM.REC.1401.071). Research followed the World Medical Association Declaration of Helsinki, and participants' privacy rights were respected throughout.

Electroencephalography data collection and processing

EEG recordings were obtained using a 64-channel EB Neuro BE PLUS (EB Neuro S.p.A., Florence, Italy) in a soundproof room shielded from electromagnetic signals. Each participant sat upright on a comfortable chair and used a pillow to minimize muscle contractions. The recording duration was 6 minutes, divided into two 3-minute segments with eyes-open and eyes-closed. The order of recording EEG responses (in eyes-open and eyes-closed states) was counterbalanced across participants. Recordings were sampled using 30 active electrodes positioned at FP1, FP2, F7, F3, Fz, F4, F8, FT7, FC3, FCz, FC4, FT8, T7(T3), C3, Cz, C4, T8(T4), TP7, CP3, CPz, CP4, TP8, P7(T5), P3, Pz, P4, P8(T6), O1, Oz, and O2, according to the international 10-20 system, referenced to the linked earlobes. The ground electrode was placed on the forehead. The electrooculogram (EOG) was recorded using four electrodes positioned above, below, and near the outer canthus of the eyes to monitor eye movements and blinks. Impedances were kept below 10 kΩ. Data were sampled at 512 Hz and filtered from 0.5 to 70 Hz. Participants refrained from caffeinated beverages for 12 hours before EEG.

During the eyes-open condition, participants fixated on a cross mark placed 1 meter in front of them to minimize blinking and eyeball movements, thereby reducing ocular artifacts in EEG recordings. In the eyes-closed condition, participants were asked to close their eyes and imagine a fixed point of light ahead to limit residual movements. To ensure wakefulness and prevent light sleep, EEG signals were inspected in real time by trained personnel. If drowsiness signs—such as increased theta power, slowed alpha rhythm, or sleep spindles—was detected[20], the recording was paused. Participants were given a brief rest, and alertness was confirmed verbally before resuming. EOG data further detected eye movement patterns linked to drowsiness, ensuring only fully awake data were analyzed.

EEG analysis was performed offline in the MATLAB software (The Mathworks, Natick, MA, USA) with the EEGLAB toolbox (Swartz Center for Computational Neuroscience, San Diego, CA, USA). Using the EEGLAB, data were plotted and inspected for manual artifact rejection; then, an independent component analysis (ICA) was conducted to exclude remaining artifacts resulting from eye blinks, eye movement, teeth clenching, and electrocardiography from the EEG stream. After that, average Fourier cross-spectral matrices were computed for the eight frequency bands: delta (2–3.5 Hz), theta (4–7.5 Hz), alpha1 (8–10 Hz), alpha2 (10.5–12 Hz), beta1 (12.5–18 Hz), beta2 (18.5–21 Hz), beta3 (21.5–30 Hz), and gamma (30.5–44 Hz). For every band, absolute and relative powers were computed across all electrodes. A total of eight regions of interest (ROIs) were identified: the left frontal region (FP1, F3, FC3, F7), the right frontal region (FP2, F4, FC4,

F8), the central region (Fz, FCz, Cz, CPz, Pz), the left temporal region (FT7, T7, C3, TP7), the right temporal region (FT8, T8, C4, TP8), the left parietal region (CP3, P7, P3), the right parietal region (CP4, P8, P4), and the occipital region (O1, Oz, O2). The EEG power in each region was considered the average power of all electrodes within that region.

Source localization

We utilized the sLORETA software (The KEY Institute for Brain-Mind Research, Zurich, Switzerland) to estimate intracerebral neural sources of scalp electrical activity. This method employs a standardized, three-dimensional (3D) distributed, linear, minimum norm inverse solution, enabling precise localization with zero error. The algorithm calculates electrical neural activity by measuring current density (A/m^2) without assuming a predetermined number of active sources. The solution space comprises 6239 voxels (5 × 5 × 5 mm), limited to cortical gray matter, hippocampus, and amygdala as defined by the digitized MNI-152 template[6, 8]. Electrode coordinates are based on a probabilistic brain volume from 3D MRI images of 152 healthy subjects with 5 mm resolution[6]. For source localization, artifact-free EEG data were exported in ASCII format from MATLAB to sLORETA. Using the software, we computed EEG cross-spectrum and the sLORETA transformation matrix across eight frequency bands: delta (2–3.5 Hz), theta (4–7.5 Hz), alpha1 (8–10 Hz), alpha2 (10.5–12 Hz), beta1 (12.5–18 Hz), beta2 (18.5–21 Hz), beta3 (21.5–30 Hz), and gamma (30.5–44 Hz). These enabled the generation of a 3D cortical distribution of neuronal generators per band.

Functional connectivity

Coherence (linear dependence) and phase synchronization (non-linear dependence) between time series from different spatial locations are commonly used as connectivity indices[6, 8]. However, these measures are susceptible to instantaneous, non-physiological effects due to volume conduction. To address this limitation, Pascual-Marqui introduced novel measures that focus exclusively on non-instantaneous (lagged) connectivity, effectively eliminating the confounding effect of volume conduction[6]. These lagged phase synchronization and coherence measures provide insights into the level of interaction between different regions contributing to source activity, offering a descriptive assessment of synchrony rather than inferring directional or causal relationships. They can also indicate the sharing of information through axonal transmission[6].

In this study, we used the sLORETA connectivity toolbox to apply coherence and phase synchronization measures across eight frequency bands to assess lagged linear and nonlinear dependencies between brain regions. When dependence is present, these measures yield positive values, whereas they become zero when no dependence exists[6]. We selected twenty-eight Regions of Interest (ROIs) based on prior tinnitus research that revealed their established roles in tinnitus-related neural networks, as informed by the network theory of tinnitus[3, 8, 9]. See **Table 2** for the list of ROIs used in the study. Each ROI was defined as a single voxel closest to the region's centroid, with a 5 mm radius, to represent key nodes of tinnitus networks. This selection

ensures that our connectivity analyses capture interactions within and between networks critical to tinnitus pathophysiology.

Statistical analysis

We utilized SPSS 17 (IBM, Armonk, NY, USA) to conduct statistical analyses of EEG data. Data normality was tested with the Shapiro-Wilk test. Subsequently, we performed a paired sample t-test or its non-parametric equivalent (Wilcoxon signed-rank test) to compare relative and absolute powers of eight frequency bands across eight predefined ROIs between two recording conditions. For paired t-tests, effect sizes were calculated with Cohen's d, while for Wilcoxon tests, effect sizes were calculated with Cliff's delta to assess practical significance. The significance level was set at $p < 0.05$.

The sLORETA Statistical Non-Parametric Mapping (SnPM) test using LORETA-KEY's voxel-wise randomization (5000 permutations) was employed for source localization and functional connectivity analysis. This method estimates the empirical probability distribution for the max-statistic under null hypothesis comparisons through randomization, ensuring validity without Gaussian assumptions[6]. This approach corrects for multiple comparisons across all voxels and frequency bands. When comparing eyes-open versus eyes-closed conditions, whole-brain sLORETA statistical and functional connectivity maps were used for voxel-by-voxel comparisons using paired t-tests. Significant differences were defined at $p < 0.05$.

Results

The patient recruitment process for this study is illustrated in **Figure 1**. Of the 34 individuals with tinnitus assessed for eligibility, 20 met the criteria and were included in the study. **Table 1** presents the demographic and clinical characteristics of each participant.

Electroencephalography spectral power analysis

Absolute power changes

For the delta band, absolute power was significantly reduced only in the central region during eyes-closed versus eyes-open ($p < 0.05$). In the theta band, eyes-closed power was significantly lower than eyes-open over the right temporal and central regions ($p < 0.05$). For alpha 1, eyes-closed showed significantly increased power in the average channels and the right frontal, left and right parietal, and occipital regions ($p < 0.05$) compared to eyes-open. Alpha 2 analysis revealed higher power during eyes-closed across the average channels, left and right frontal, left temporal, central, left and right parietal, and occipital regions ($p < 0.05$). In beta 1, eyes-closed showed significant power increases in the right parietal and occipital regions ($p < 0.05$). Beta 2 exhibited significant power reductions in eyes-closed across average channels, left frontal, left and right temporal, central, and left and right parietal regions ($p < 0.05$). Beta 3 showed significantly lower eyes-closed

power in the right temporal region ($p < 0.05$). Similarly, gamma power was significantly decreased in the right temporal region during eyes-closed compared to eyes-open ($p < 0.05$). **Table 3** summarizes all statistically significant absolute power differences between eyes-closed and eyes-open conditions.

Relative power changes

Relative power analysis for the delta band showed significantly lower power in all regions ($p < 0.05$) during eyes-closed compared to eyes-open. In the theta band, eyes-closed exhibited significantly decreased power across average channels, left frontal, central, right temporal, left and right parietal, and occipital regions ($p < 0.05$) versus eyes-open. The alpha 1 band showed significantly increased power at right frontal and right temporal regions ($p < 0.05$) during eyes-closed. For alpha 2, eyes-closed had significantly higher power across average channels, right frontal, left and right temporal, central, left and right parietal, and occipital regions ($p < 0.05$). Beta 1 showed no significant differences ($p > 0.05$) between the two resting-states. Beta 2 had significantly decreased power across all regions ($p < 0.05$) in eyes-closed. Beta 3 showed a significant reduction in the right frontal and right temporal regions ($p < 0.05$) during eyes-closed. Gamma exhibited no significant differences ($p > 0.05$) between the two conditions. **Table 4** presents all significant relative power differences between eyes-closed and eyes-open conditions.

Source localization and functional connectivity analysis

Source localization analysis

The sLORETA source localization analysis showed a significant decrease in delta activity in the left precentral gyrus (BA 4) during eyes-closed versus eyes-open ($t = -2.91$, $p < 0.05$) **(Figure 2A)**. For Alpha 1, eyes-closed recordings showed significantly increased activity in the right parahippocampal gyrus (BA 19,30) ($t = 3.45$, $p < 0.05$), posterior cingulate (BA 30) ($t = 3.41$, $p < 0.05$), and lingual gyrus (BA 18,19) ($t = 3.27$, $p < 0.05$) compared to eyes-open **(Figure 2B)**. In Alpha 2, the eyes-closed exhibited significantly increased activity in the left fusiform gyrus (BA 36,37) ($t = 3.98$, $p < 0.01$), parahippocampal gyrus (BA 19) ($t = 3.53$, $p < 0.05$), superior temporal gyrus (BA 41) ($t = 3.33$, $p < 0.05$), posterior cingulate (BA 30) ($t = 3.30$, $p < 0.05$), lingual gyrus (BA 18) ($t = 3.27$, $p < 0.05$), and transverse temporal gyrus (BA 41) ($t = 3.19$, $p < 0.05$) relative to eyes-open **(Figure 2C)**. For beta 1, eyes-closed recordings showed significantly increased activity in the right posterior cingulate gyrus (BA 31) ($t = 2.68$, $p < 0.05$) **(Figure 2D)**. Gamma activity significantly decreased in the left superior parietal lobe (BA 7) during eyes-closed versus eyes-open ($t = -3.35$, $p < 0.01$) **(Figure 2E)**. No statistically significant differences were observed between conditions for theta, beta 2, and beta 3 ($p > 0.05$).

Functional connectivity analysis

The functional connectivity analysis demonstrated a marginally significant increase in lagged linear functional connectivity (coherence) between the right and left superior temporal gyri (auditory cortex, BA 42) in the alpha 1 band during eyes-closed versus eyes-open ($t = 4.914$, $p < 0.1$) **(Figure 3A)**. Additionally, in the beta 2 band, the eyes-closed recording exhibited significantly increased lagged linear functional connectivity (coherence) between the left superior temporal gyrus (auditory cortex, BA 41) and the following regions: the left posterior cingulate cortex (BA 31) ($t = 5.904$, $p < 0.05$), the right posterior cingulate cortex (BA 31) ($t = 6.362$, $p < 0.01$), and the right parahippocampal gyrus (BA 27) ($t = 6.488$, $p < 0.01$) compared to the eyes-open **(Figure 3B)**. Furthermore, there was a marginally significant increase in lagged nonlinear functional connectivity (phase synchronization) between the left anterior cingulate cortex (BA 24) and the left orbitofrontal cortex (BA 11) ($t = 5.073$, $p < 0.1$) for the gamma band during the eyes-closed versus the eyes-open **(Figure 3C)**. No significant linear or nonlinear functional connectivity differences were observed for the delta, theta, alpha 2, beta 1, and beta 3 bands.

Discussion

The present study examined differences in brain electrical activity between eyes-closed and eyes-open resting-states in individuals with chronic tinnitus. We employed multi-channel EEG recordings, source localization, and functional connectivity analysis to investigate these differences. Our findings revealed significant variations in EEG power spectra, source localization, and functional connectivity between the two resting-state conditions.

Electroencephalography power spectra

The results demonstrated a decrease in the power of delta and theta bands across various cortical regions during the eyes-closed condition compared to the eyes-open condition, potentially reflecting increased attentional processes[21, 22]. This finding aligns with the Petro et al. study that demonstrates reduced low-frequency oscillation power in the eyes-closed condition[21]. However, other studies have reported conflicting results[11, 23]. For example, Barry et al. observed reductions in the mean absolute power of delta and theta bands from the eyes-closed to the eyes-open resting-state [11]. These contradictory results may arise from differences in the study populations, recording techniques, or data analysis methods. Conversely, alpha power (alpha 1 and alpha 2 bands) significantly increased across most regions during the eyes-closed recording. These observations are consistent with established evidence regarding the dominance of alpha activity in the posterior regions during the eyes-closed resting-state, reflecting a state of relaxed alertness with reduced sensory input[11, 12]. It is worth noting that tinnitus perception is often associated with abnormal brain activity patterns, including alterations in the power of alpha and theta oscillations[5]. While the present findings do not directly address tinnitus, they highlight the complex interplay among brain states, sensory input, and neural oscillations, which may provide insights into the underlying mechanisms of tinnitus perception.

Beta power analysis revealed a more complex pattern. Beta 1 power increased in the right parietal and occipital regions during the eyes-closed recording, potentially reflecting enhanced attentional engagement or visual imagery[24], which may be relevant to tinnitus perception because it involves a heightened focus on auditory sensations[25]. However, beta 2 power decreased across most regions, while beta 3 power exhibited a decrease specifically in the right temporal and frontal areas during the eyes-closed condition. This pattern may be attributed to diminished visual information processing associated with the eyes-closed state[21]. Nonetheless, the role of decreased beta 2 and beta 3 power during the eyes-closed state and its relationship to tinnitus perception requires further exploration. Gamma power exhibited a decrease in the right temporal region during the eyes-closed condition. Gamma activity has been implicated in various cognitive functions, including sensory processing, attention, and memory[26]. The precise role of this reduction in the eyes-closed state remains to be elucidated and warrants further investigation. It may reflect altered auditory processing in this condition, possibly suggesting abnormal sensory gating or impaired neural synchrony[27, 28].

Source localization

The sLORETA analysis revealed distinct patterns of neural activity alterations between eyes-closed and eyes-open conditions across various frequency bands. The eyes-closed state exhibited decreased activity in the left precentral gyrus for the delta band, potentially indicating reduced motor response preparation[29], consistent with the brain's tendency to disengage from external stimuli during this state[21]. Conversely, increased activity was observed in the right parahippocampal gyrus, posterior cingulate cortex, and lingual gyrus during the eyes-closed recording for the alpha 1 band. These regions are known to be involved in memory function, spatial processing, and the Default Mode Network (DMN)[30, 31]. Notably, the parahippocampal gyrus and posterior cingulate cortex are core components of the DMN, which becomes more active when attention is directed inward, as in the eyes-closed condition[32]. Enhanced activity in these regions could potentially reflect the increased salience of internal stimuli, such as tinnitus, in the absence of external sensory input[17]. Additionally, the increased alpha band activity in these areas, particularly in the parahippocampal area, is associated with heightened tinnitus distress[33]. These findings align with Vanneste et al., emphasizing the role of the parahippocampal gyrus in tinnitus distress[3].

Similar trends were observed for the alpha 2 band, with additional activation in the left fusiform gyrus, superior temporal gyrus, and transverse temporal gyrus during the eyes-closed condition. These regions are associated with visual processing and auditory function[4, 34]. Enhanced neural activity observed in these regions during the eyes-closed resting-state in tinnitus patients may indicate the engagement of attentional selection or internal imagery processes linked to the chronic auditory phantom perception[8, 35].

For the beta 1 band, the eyes-closed condition demonstrated a significant increase in activity within the right posterior cingulate gyrus, a region implicated in internally directed cognition and conscious awareness [36]. This result corroborates the findings of Zimmerman et al. and suggests

a potential link between posterior cingulate activity and tinnitus severity[37], particularly during the eyes-closed condition when individuals might be more introspective and focused on their internal state[38]. Furthermore, the eyes-closed condition exhibited decreased activity in the left superior parietal lobe in the gamma band compared to the eyes-open state. The superior parietal lobe is involved in spatial attention and multisensory integration[39]. Rosemann and Rauscheker suggested the superior parietal lobe together with the orbitofrontal cortex and the supramarginal gyrus, is involved in compensatory processes that attenuate tinnitus perception[19]. Therefore, decreased activity in the superior parietal lobe during the eyes-closed state may reduce the effectiveness of these compensatory mechanisms, potentially exacerbating tinnitus perception. However, further research is needed to elucidate the underlying mechanisms of decreased superior parietal lobe activity during the eyes-closed condition in tinnitus patients.

Functional connectivity

The functional connectivity analysis revealed intriguing findings. The eyes-closed condition showed a marginally significant increase in lagged linear functional connectivity (coherence) between the bilateral superior temporal gyri (auditory cortex) in the alpha 1 band. Alpha band activity is associated with attention and inhibitory functions[40]. Its increased coherence between the bilateral superior temporal gyri during the eyes-closed condition might reflect sensory suppression mechanisms or aberrant neural activity attempting to suppress the augmented phantom auditory perception following eye closure[18].

Moreover, the eyes-closed condition demonstrated a significant increase in lagged linear functional connectivity (coherence) between the left superior temporal gyrus and the following regions: the bilateral posterior cingulate cortex, and the right parahippocampal gyrus in the beta 2 band. This indicates a strengthened functional connection between the auditory cortex and brain regions implicated in the DMN and memory function during the eyes-closed state in tinnitus patients[41]. This connectivity pattern may reflect the integration of the tinnitus percept with previous emotional memories, potentially contributing to increased tinnitus-related distress[9, 42]. These findings are consistent with previous studies[7, 9]. Vanneste and De Ridder reported increased functional connectivity between the auditory cortex and several brain regions, including the right posterior cingulate, the right insula, and the bilateral parahippocampal areas for the beta 3 band in tinnitus patients[9].

Finally, a marginally significant increase in lagged nonlinear functional connectivity (phase synchronization) was observed between the left anterior cingulate cortex and the left orbitofrontal cortex in the gamma band during the eyes-closed condition. This finding suggests enhanced communication between brain regions implicated in attention, emotional regulation, and emotional-cognitive control during a state of reduced sensory input[43]. Gamma band oscillations are known to be involved in sensory processing and attention[44]. This pattern of increased connectivity might reflect dysfunction in inhibitory processes that normally direct attention away from phantom sound perception, leading to heightened tinnitus awareness[45].

The role of eyes-closed and eyes-open electroencephalography in tinnitus assessment

The choice between eyes-closed and eyes-open conditions for EEG recordings in tinnitus patients is a critical consideration, as each offers distinct advantages. Eyes-closed conditions often exhibit increased alpha and beta band activity, which are associated with internal mental processes. This state may be more sensitive for detecting subtle tinnitus-related neural patterns. Conversely, eyes-open conditions more closely reflect real-world experiences and might better capture how tinnitus affects daily life. Ultimately, the optimal condition depends on the specific research question. In this preliminary study, comparing both resting-state conditions provided initial insights into their differential effects, suggesting that a comprehensive understanding may require incorporating both recording conditions in future research.

Clinical implications and possible applications

This preliminary study found distinct EEG patterns between eyes-closed and eyes-open resting states in chronic tinnitus patients, suggesting potential clinical applications. Key findings include increased alpha power in memory-related regions and stronger connectivity between auditory and emotional areas during eyes-closed condition, which may serve as biomarkers to differentiate tinnitus subtypes or assess severity. Such EEG signatures could improve diagnosis and guide personalized treatments, such as neurofeedback, transcranial magnetic stimulation (TMS), or transcranial electrical stimulation (TES), tailored to patient-specific brain activity and eye-state conditions. However, the findings are speculative due to small sample size and no control group. Larger studies linking EEG patterns with clinical outcomes are needed. Despite limitations, this work provides a framework for using state-specific EEG markers to improve individualized tinnitus management.

Limitations and future directions

This preliminary study explored the relationship between eye states and brain activity in individuals with tinnitus. Limitations include a small sample size (n = 20), preventing strong statistical conclusions, a cross-sectional design that precludes causal inferences, and the absence of a non-tinnitus control group. EEG differences were not correlated with tinnitus severity or distress due to the exploratory nature of the study. Future research should use a longitudinal study design with larger samples, include control groups, and investigate correlations with tinnitus measures. Advanced methods (e.g., time-frequency analysis, causal connectivity analysis, and multimodal imaging) are recommended to better characterize neural mechanisms and guide potential clinical applications.

Conclusion

In conclusion, this study highlighted distinct neural signatures in tinnitus patients during eyes-closed and eyes-open resting-states, revealing the interplay of sensory, cognitive, and emotional

processes. These findings underscore the potential for state-specific EEG markers to inform personalized diagnostics and therapies, such as neurofeedback or neuromodulation. While promising, further research with larger cohorts is needed to validate and expand these insights for clinical application.

Conflict of interest statement

The authors have no conflict of interest to declare.

Author's contribution statement

SN: Study design, acquisition of data, statistical analysis, interpretation of results, drafting the manuscript, and critical revision of the manuscript; FF: Study design, project supervision, interpretation of results, and critical revision of the manuscript; ST: Study design, statistical analysis, technical and material support, and critical revision of the manuscript; NZ: Study design, and critical revision of the manuscript.

All authors reviewed and approved the final version of the manuscript.

Data availability statement

Data will be made available on request.

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Table 1. Demographic data and clinical characteristics of the study participants.

No.	Age (year)	Sex	Tinnitus					L-VAS	A-VAS	THI	TFI
			Quality	Laterality	Duration (month)	Pitch (KHz)	Loudness Intensity (dBHL)				
1	24	Male	Tonal	Left	18	6	32	50	60	46	27.6
2	51	Male	Noise-like	Both Sides	48	8[a]	43	75	70	58	42.0
3	35	Male	Tonal	Both Sides	36	6	38	85	85	62	56.4
4	44	Female	Noise-like	Left	9	4[a]	29	40	50	32	8.2
5	43	Male	Tonal	Left	30	6	42	80	70	54	42.6
6	32	Male	Tonal	Right	48	8	43	65	60	46	38.0
7	47	Female	Tonal	Left	60	6	49	60	75	56	33.6
8	42	Female	Noise-like	Both Sides	60	4[a]	44	90	95	64	44.2
9	34	Male	Tonal	Right	96	8	39	70	70	48	41.8
10	28	Male	Tonal	Left	24	4	35	55	65	40	22.2
11	55	Female	Noise-like	Right	120	6[a]	52	90	90	58	52.0
12	49	Male	Noise-like	Left	60	6[a]	47	60	55	44	28.4
13	54	Female	Tonal	Right	48	4	50	75	90	62	45.6
14	37	Male	Noise-like	Left	12	6[a]	38	60	80	56	36.4
15	45	Male	Tonal	Both Sides	96	8	51	95	100	76	58.8
16	48	Female	Tonal	Left	30	6	47	70	80	60	40.2
17	43	Male	Tonal	Right	12	4	33	60	55	42	33.8
18	35	Female	Tonal	Right	36	4	31	40	50	38	13.4
19	54	Male	Noise-like	Both Sides	84	8[a]	50	80	85	52	50.2
20	46	Male	Tonal	Right	24	6	44	50	70	48	30.8
Mean (SD)	42.30 (8.83)	-	-	-	47.55 (31.3)	-	41.85 (7.17)	67.50 (16.26)	72.75 (15.08)	52.10 (10.51)	37.31 (13.16)

Abbreviations: L-VAS, loudness visual analogue scale; A-VAS, annoyance visual analogue scale; THI, tinnitus handicap inventory; TFI, tinnitus functional index; SD, standard deviation.

[a] Evaluated with Narrow Band Noise (NBN) stimuli.

Table 2. The regions of interest and their MNI Coordinates.

Regions of Interest (ROIs)	Brodmann Area (BA)	Centroid Voxel		
		X	Y	Z
Auditory Cortex	41L	-46	-29	10
	41R	47	-29	10
	42L	-62	-23	12
	42R	63	-24	12
	21L	-57	-18	-15
	21R	58	-17	-15
	22L	-56	-25	5
	22R	56	-22	3
Insula	13L	-39	-8	9
	13R	40	-7	9
Dorsal anterior cingulate cortex	24L	-8	2	36
	24R	7	1	36
Pregenual anterior cingulate cortex	32L	-9	29	21
	32R	8	30	20
Subgenual anterior cingulate cortex	25L	-8	18	-17
	25R	5	14	-14
Posterior cingulate cortex	31L	-11	-50	32
	31R	9	-48	33
Parahippocampus	27L	-19	-33	-4
	27R	18	-33	-4
	29L	-7	-50	7
	29R	6	-50	8
Orbitofrontal cortex	10L	-22	54	9
	10R	22	54	9
	11L	-18	43	-17
	11R	19	43	-17
Precuneus	7L	-17	-63	50
	7R	15	-63	49

Table 3. Significant differences in mean absolute power between eyes-closed and eyes-open resting-state conditions across different frequency bands.

Frequency band	Region	Eyes-closed		Eyes-open		Statistics	p-value[a]	Effect Size[b]
		Mean	SD	Mean	SD			
Delta	Central	291.2	559.61	435.85	698.53	Z= -2.052	0.04	-0.27
Theta	Central	136.28	201.56	520.61	1521.26	Z= -2.052	0.04	-0.27
	Right Temporal	105.67	106.25	176.88	269.56	Z= -2.334	0.02	-0.26
Alpha 1	Total Channels	450.41	448.82	199.03	179.10	Z= -2.237	0.018	0.45
	Right Frontal	452.17	522.98	221.40	244.20	Z= -2.294	0.022	0.38
	Left Parietal	431.34	663.29	170.58	298.05	Z= -2.535	0.011	0.38
	Right Parietal	625.14	682.88	110.08	92.36	Z= -2.938	0.003	0.55
	Occipital	1032.66	1339.60	328.39	905.26	Z= -3.058	0.002	0.72
Alpha 2	Total Channels	495.87	694.34	101.24	67.80	Z= -3.179	0.001	0.65
	Left Frontal	437.68	651.18	126.20	124.59	Z= -2.374	0.018	0.42
	Right Frontal	343.40	413.63	107.9	111.11	Z= -2.938	0.003	0.56
	Left Temporal	250.86	281.09	87.50	51.93	Z= -2.294	0.022	0.33
	Central	335.27	438.95	96.09	140.86	Z= -2.415	0.016	0.35
	Left Parietal	410.86	408.34	85.12	78.11	Z= -3.582	< 0.001	0.65
	Right Parietal	987.15	1888.43	65.76	45.03	Z= -3.421	< 0.001	0.78
	Occipital	1216.97	2045.36	144.86	231.72	Z= -2.938	0.003	0.53
Beta 1	Right Parietal	72.51	77.00	29.68	20.70	Z= -3.139	0.002	0.62
	Occipital	150.30	202.19	59.66	70.49	Z= -2.294	0.022	0.45
Beta 2	Total Channels	17.41	17.91	44.69	35.18	Z= -2.777	0.005	-0.50
	Left Frontal	18.50	25.87	51.68	65.68	Z= -2.334	0.02	-0.42
	Left Temporal	13.36	10.00	50.59	44.56	Z= -3.501	< 0.001	-0.65
	Central	11.54	22.50	35.92	44.54	Z= -2.254	0.024	-0.38
	Right Temporal	10.93	12.23	45.42	36.04	Z= -3.662	< 0.001	-0.69
	Left Parietal	10.49	8.48	40.79	47.08	Z= -2.938	0.003	-0.54
	Right Parietal	11.41	9.03	23.81	20.37	Z= -2.415	0.016	-0.31
Beta 3	Right Temporal	11.64	19.62	23.21	20.96	Z= -2.938	0.003	-0.42
Gamma	Right Temporal	15.08	18.55	24.48	18.01	Z= -2.535	0.011	-0.29

SD, standard deviation.

[a] All comparisons were made using the Wilcoxon signed-rank test.

[b] All effect size values are in Cliff's delta

Table 4. Significant differences in mean relative power between eyes-closed and eyes-open resting-state conditions across different frequency bands.

Frequency band	Region	Eyes-closed		Eyes-open		Statistics	p-value	Effect Size
		Mean	SD	Mean	SD			
Delta	Total Channels	22.73	10.08	36.21	8.76	t= -5.691	< 0.001[a]	-1.27[c]
	Left Frontal	27.84	16.44	41.16	10.20	t= -3.445	0.003[a]	-0.77[c]
	Right Frontal	24.38	12.37	40.36	11.87	t= -4.581	< 0.001[a]	-1.02[c]
	Left Temporal	31.87	18.06	43.73	11.04	t= -3.063	0.006[a]	-0.68[c]
	Central	19.34	10.63	33.06	10.13	t= -5.844	< 0.001[a]	-1.30[c]
	Right Temporal	23.82	12.34	38.30	12.94	t= -4.754	< 0.001[a]	-1.06[c]
	Left Parietal	21.39	14.54	32.83	13.73	Z= -3.248	0.001[b]	-0.49[d]
	Right Parietal	16.05	10.09	27.83	12.27	Z= -2.949	0.003[b]	-0.51[d]
	Occipital	13.74	9.03	28.22	13.50	t= -4.368	< 0.001[a]	-0.97[c]
Theta	Total Channels	12.44	7.20	18.41	5.47	Z= -3.472	< 0.001[b]	-0.59[d]
	Left Frontal	13.14	8.19	17.20	5.94	Z= -2.091	0.037[b]	-0.35[d]
	Central	12.89	7.91	22.05	6.36	t= -6.708	< 0.001[a]	-1.50[c]
	Right Temporal	12.92	7.83	17.79	6.37	Z= -2.427	0.015[b]	-0.39[d]
	Left Parietal	10.97	7.57	17.81	6.13	Z= -3.099	0.002[b]	-0.54[d]
	Right Parietal	9.51	6.67	18.65	8.65	Z= -3.659	< 0.001[b]	-0.65[d]
	Occipital	10.52	9.38	18.26	9.31	Z= -2.651	0.008[b]	-0.44[d]
Alpha 1	Right Frontal	29.03	16.41	19.27	5.89	Z= -2.315	0.021[b]	0.40[d]
	Right Temporal	28.11	14.36	20.23	5.87	Z= -2.277	0.023[b]	0.37[d]
Alpha 2	Total Channels	26.40	16.66	13.1	5.00	t= 3.292	0.004[a]	0.73[c]
	Right Frontal	21.92	16.05	11.67	5.35	Z= -2.389	0.017[b]	0.39[d]
	Left Temporal	20.02	12.19	10.45	5.86	Z= -2.763	0.006[b]	0.45[d]
	Central	28.81	20.29	12.72	4.98	Z= -3.061	0.002[b]	0.53[d]
	Right Temporal	23.98	14.58	12.25	6.20	t= 3.169	0.005[a]	0.70[c]
	Left Parietal	31.07	17.73	14.82	7.64	t= 4.109	< 0.001[a]	0.91[c]
	Right Parietal	33.13	22.63	15.95	5.97	Z= -2.912	0.004[b]	0.50[d]
	Occipital	32.63	22.61	16.94	9.08	Z= -2.389	0.017[b]	0.35[d]
Beta 2	Total Channels	1.13	0.64	4.54	3.02	t= -4.828	< 0.001[a]	-1.05[c]
	Left Frontal	1.05	0.72	2.90	1.62	Z= -3.024	0.002[b]	-0.66[d]
	Right Frontal	1.17	0.79	4.16	2.97	Z= -3.099	0.002[b]	-0.65[d]
	Left Temporal	1.10	0.54	4.54	3.00	t= -5.082	< 0.001[a]	-1.13[c]
	Central	1.00	0.76	4.06	2.75	Z= -3.248	0.001[b]	-0.72[d]
	Right Temporal	1.37	0.96	4.68	3.53	Z= -3.061	0.002[b]	-0.60[d]
	Left Parietal	1.17	0.78	5.40	4.61	Z= -3.099	0.002[b]	-0.64[d]
	Right Parietal	1.10	0.87	5.55	4.40	Z= -3.211	0.001[b]	-0.68[d]
	Occipital	1.11	0.77	5.96	5.18	Z= -3.024	0.002[b]	-0.65[d]
Beta 3	Right Frontal	1.17	1.16	1.55	0.83	Z= -2.352	0.019[b]	-0.42[d]
	Right Temporal	1.17	1.04	1.48	0.66	Z= -2.016	0.044[b]	-0.33[d]

SD, standard deviation.

[a] Paired sample t-test.

[b] Wilcoxon signed-rank test.

[c] Cohen's d value

[d] Cliff's delta value

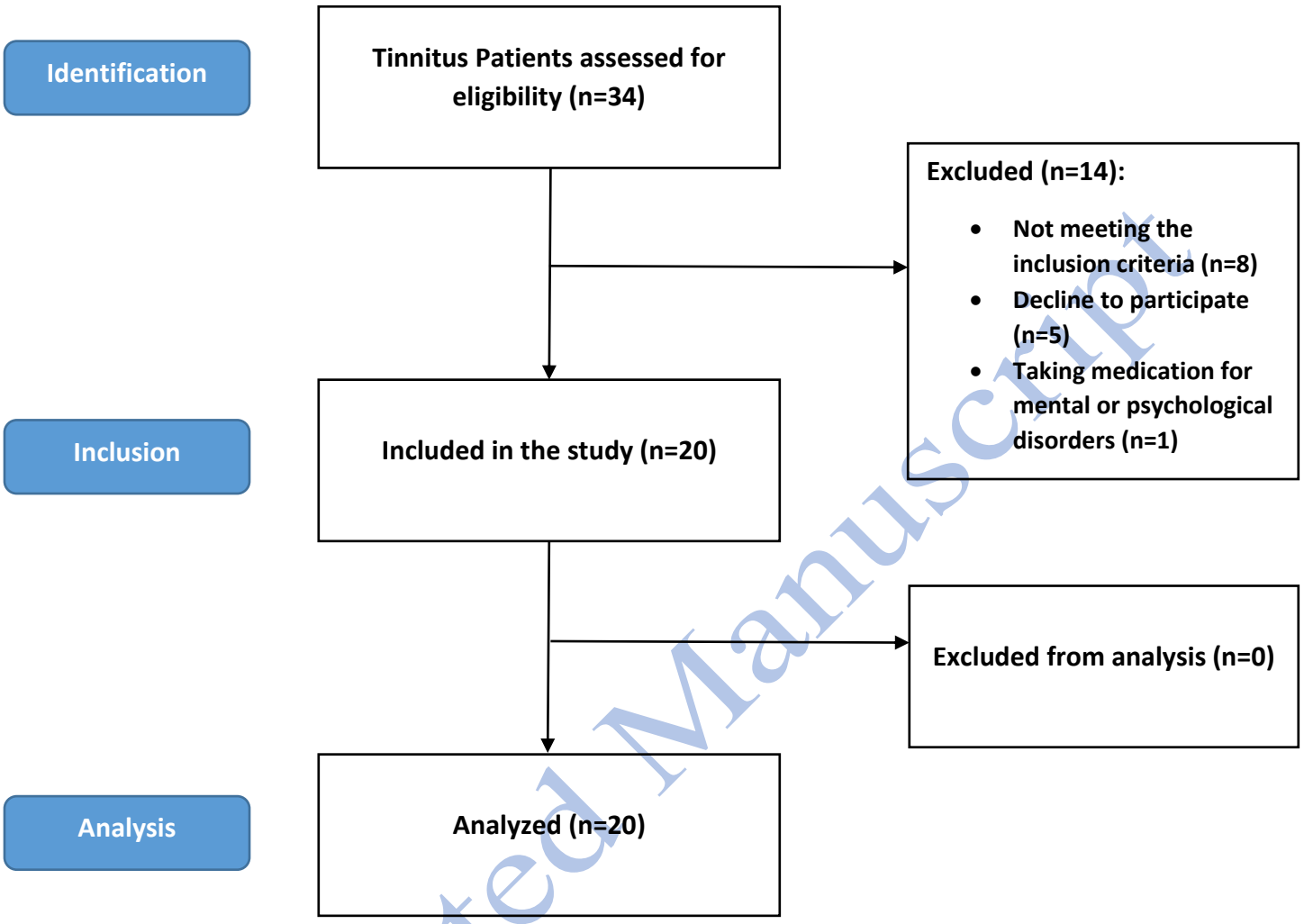
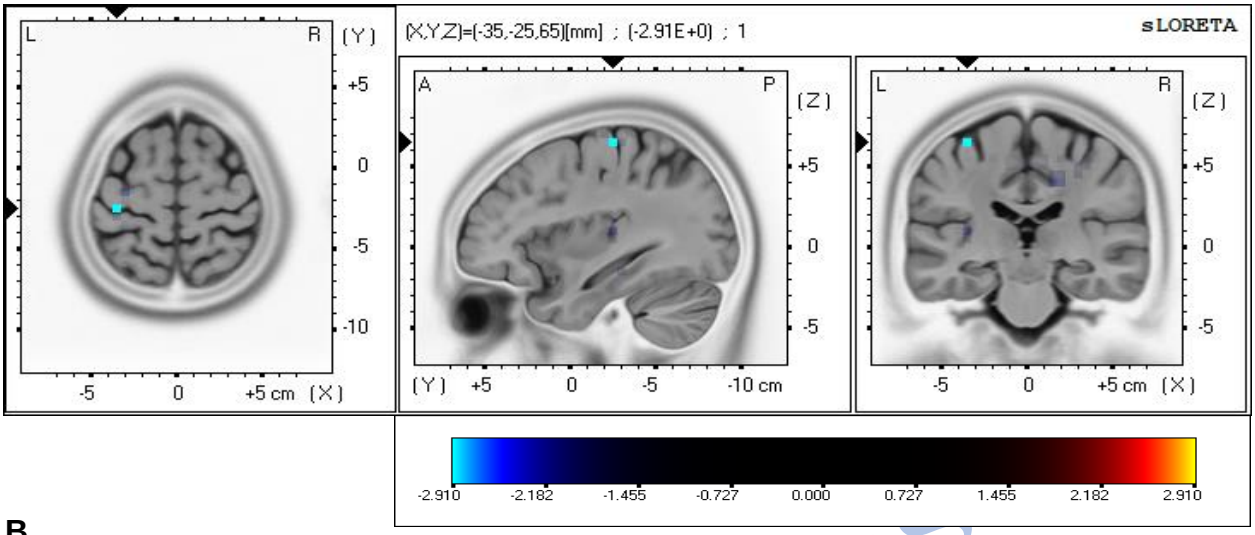


Figure 1. Study flow diagram.

A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-5
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(Y) +5 0 -5 -10 cm
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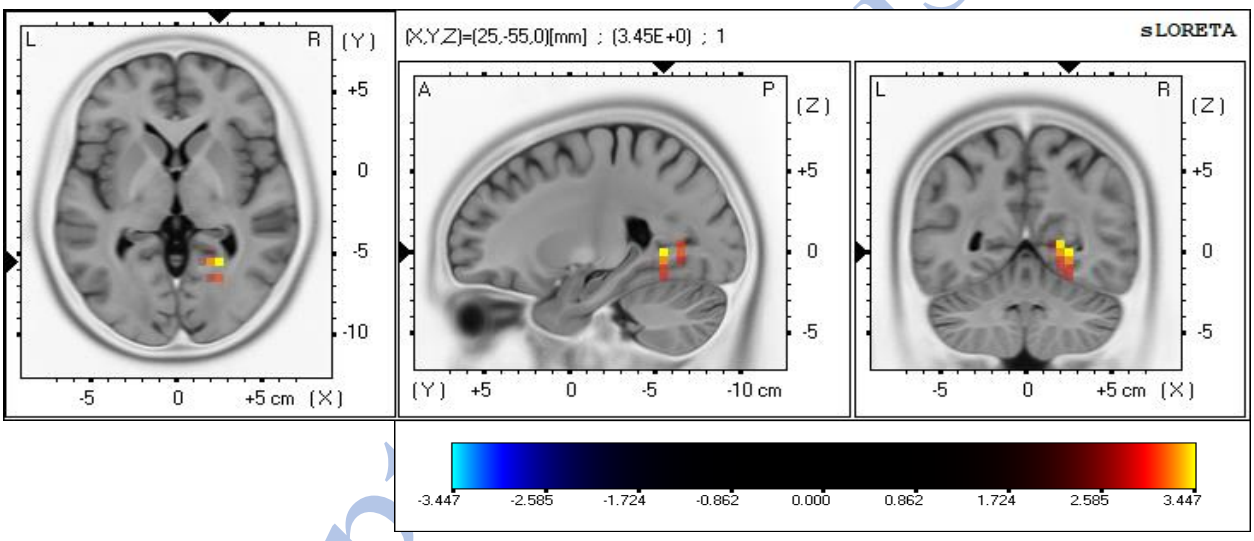
B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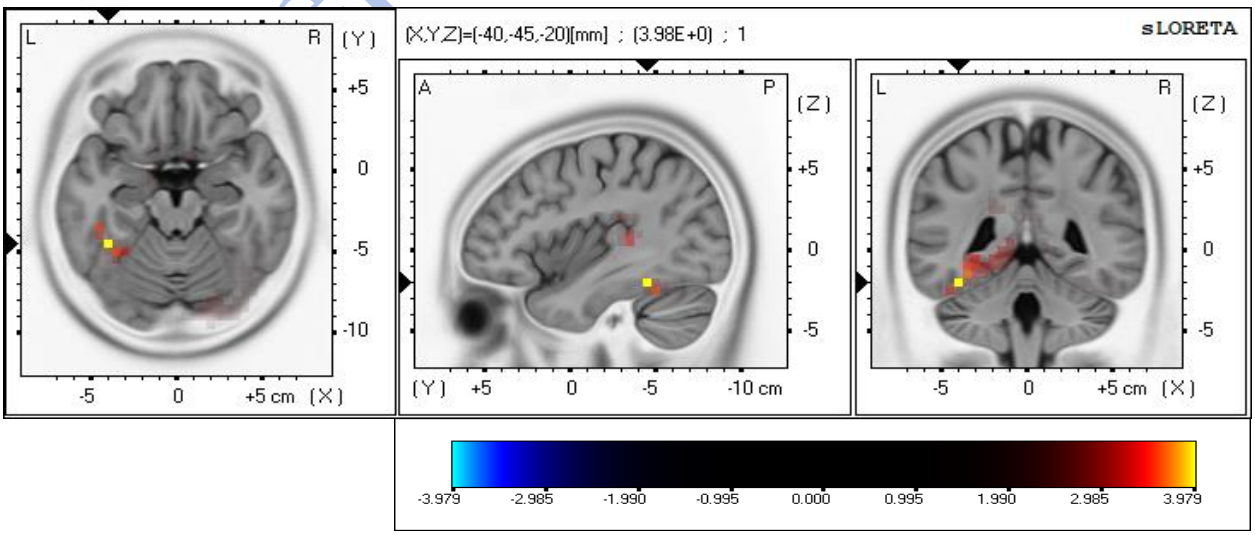
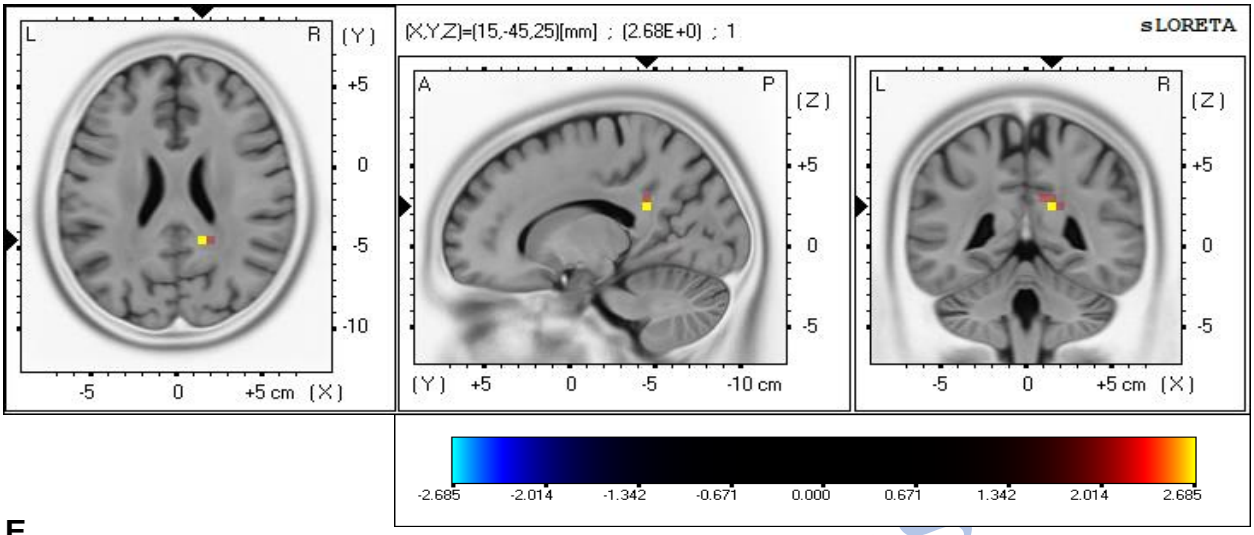
(Y) +5 0 -5 -10 cm
-3.447 -2.585 -1.724 -0.862 0.000 0.862 1.724 2.585 3.447

C


(X,Y,Z)=(-40,-45,-20)[mm] ; (3.98E+0) ; 1
sLORETA
L
R
(Y)
+5
0
-5
-10
-5 0 +5 cm (X)
A
P
(Z)
(Y) +5 0 -5 -10 cm
-3.979 -2.985 -1.990 -0.995 0.000 0.995 1.990 2.985 3.979

D



E

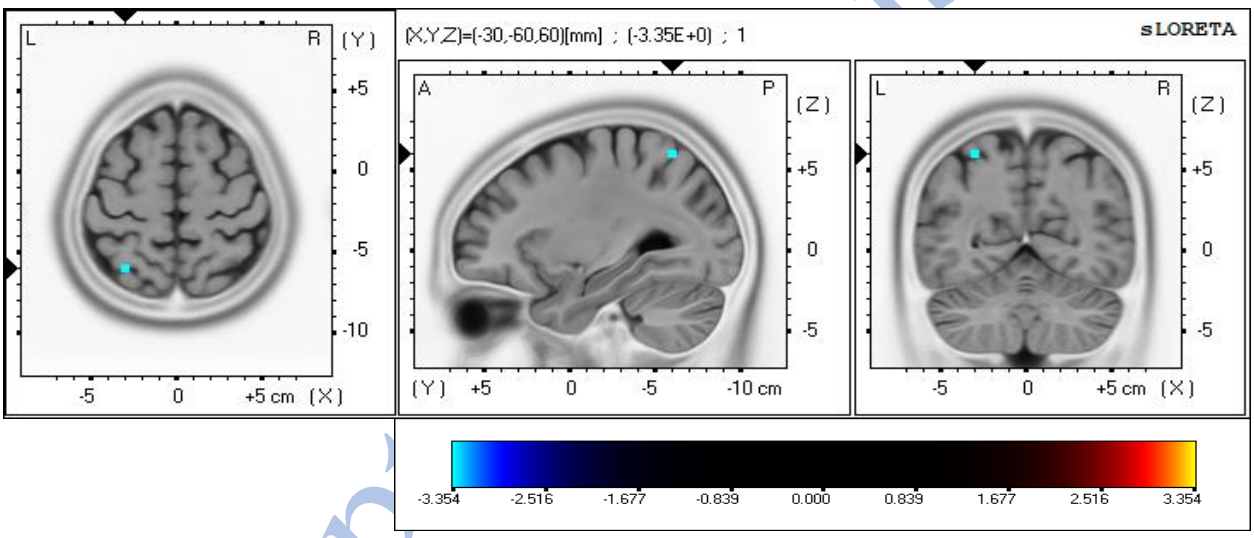
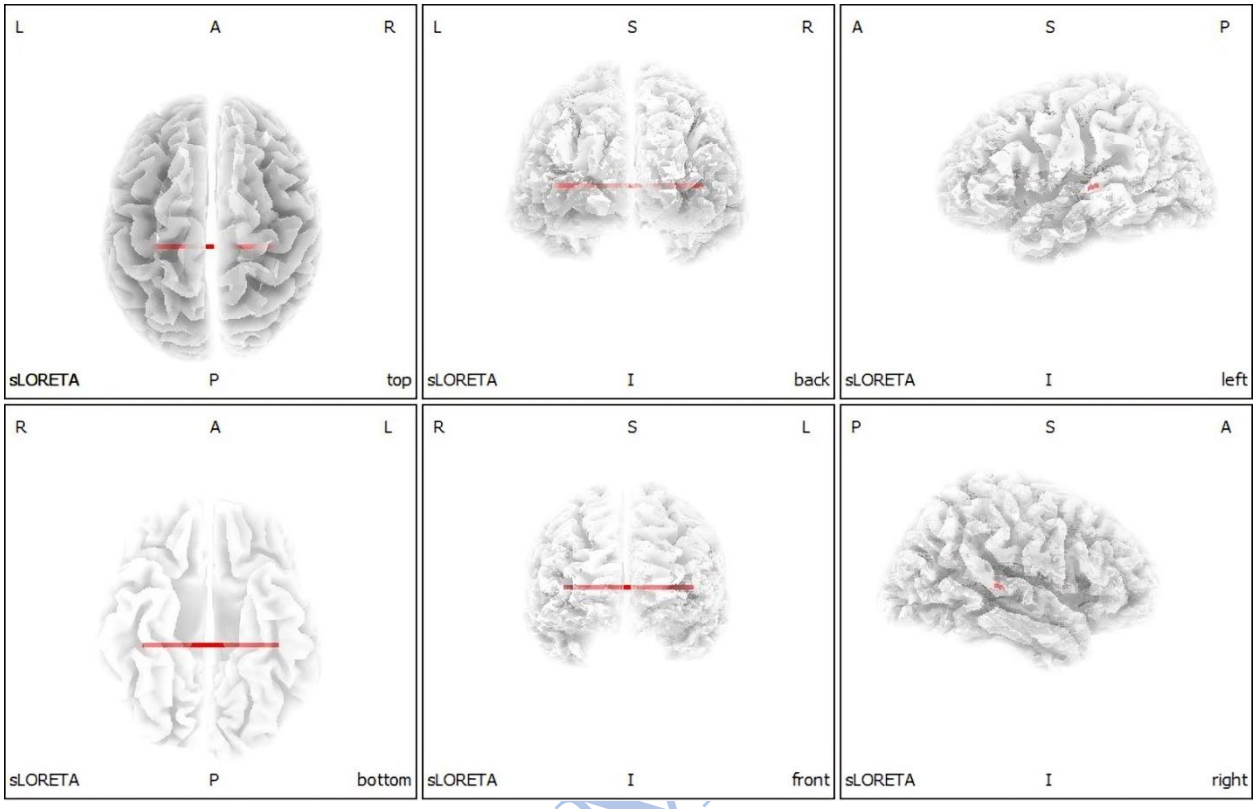
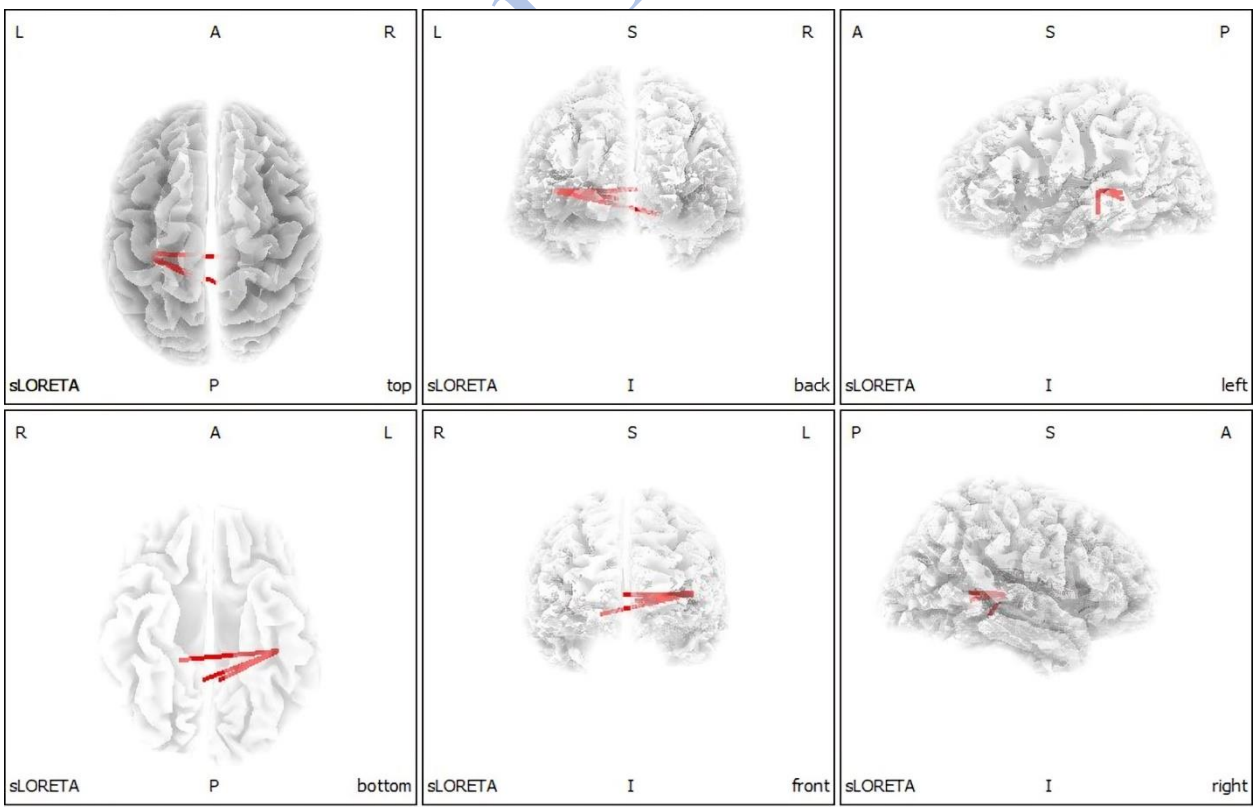


Figure 2. Whole-brain sLORETA contrast maps analysis between eyes-closed and eyes-open resting-states. Compared to the eyes-open state, the eyes-closed condition exhibited: (A) decreased delta band activity in the left precentral gyrus (BA 4); (B) increased alpha 1 band activity over the right parahippocampal gyrus (BA 19,30), posterior cingulate cortex (BA 30), and lingual gyrus (BA 18,19); (C) increased alpha 2 band activity in the left fusiform gyrus (BA 36,37), parahippocampal gyrus (BA 19), superior and transverse temporal gyri (BA 41), posterior cingulate cortex (BA 30), and lingual gyrus (BA 18); (D) increased beta 1 band activity over the right posterior cingulate cortex (BA 31); and (E) decreased gamma band activity in the left superior parietal lobe (BA 7). Yellow and blue colors in color bars represent the highest and lowest levels of activity, respectively. Abbreviation: BA, brodmann area.

A


L A R
sLORETA P top
L S R
sLORETA I back
A S P
sLORETA I left
R A L
sLORETA P bottom
R S L
sLORETA I front
P S A
sLORETA I right

B


L A R
sLORETA P top
L S R
sLORETA I back
A S P
sLORETA I left
R A L
sLORETA P bottom
R S L
sLORETA I front
P S A
sLORETA I right

C

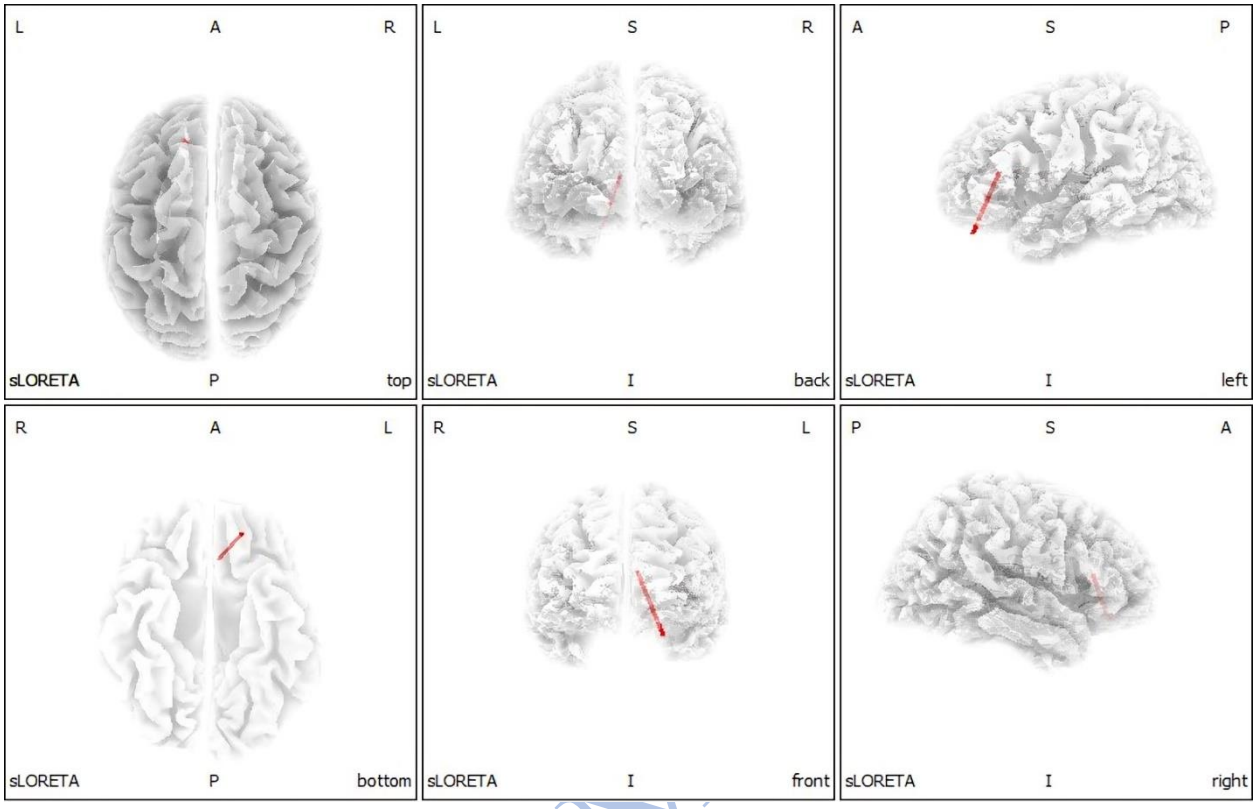


Figure 3. Functional connectivity contrast maps analysis between eyes-closed and eyes-open resting-states. Linear functional connectivity (coherence) analysis revealed (A) an increase in lagged linear functional connectivity between the right and left superior temporal gyrus (BA 42) in the alpha 1 band; and (B) increased lagged linear functional connectivity between the left superior temporal gyrus (BA 41) and both the left and right posterior cingulate cortex (BA 31), as well as the right parahippocampal gyrus (BA 27) in the beta 2 band during the eye-closed condition compared to the eyes-open condition. In addition, nonlinear functional connectivity (phase synchronization) analysis demonstrated (C) an increase in lagged nonlinear functional connectivity between the left anterior cingulate cortex (BA 24) and the left orbitofrontal cortex (BA 11) for the gamma band in the eyes-closed state compared to the eyes-open state. Abbreviations: BA, brodmann area; L, left; R, right; A, anterior; P, posterior; S, superior; I, inferior.