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Electrocochleographic Evidence of Cochlear Dysfunction in Obstructive Sleep Apnea: A Polysomnography-Based Controlled Study

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Abstract

Objectives:

Obstructive sleep apnea syndrome(OSAS) is a systemic disorder characterized by recurrent hypoxia and microvascular circulatory disturbances that may affect the auditory system. The aim of this study is to evaluate cochlear electrophysiological responses using electrocochleography(ECoChG) in patients with OSAS and to determine the diagnostic performance of ECoChG parameters in distinguishing the presence and severity of OSAS.

Design:

A total of 106 participants were included in this cross-sectional controlled study: mild OSAS(n=19), moderate OSAS(n=25), severe OSAS(n=19), and a control group(n=43). All participants underwent nocturnal polysomnography, and OSAS severity was classified according to the American Academy of Sleep Medicine criteria based on the Apnea-Hypopnea Index(AHI). Extratympanic electrocochleography measurements were performed in both ears. The analyzed parameters included Base, summating potential(SP), and action potential(AP) latencies; SP–Base and AP–Base interlatencies; the SP/AP amplitude ratio; the SP/AP area ratio; and the SP and AP areas. Intergroup comparisons were performed using appropriate parametric and non-parametric tests, and ROC analysis was applied for significant parameters.

Results:

Significant differences were observed in OSAS patients compared to the control group, particularly in the parameters of AP–Base interlatency, SP/AP amplitude ratio, SP/AP area ratio, and AP area. According to ROC analysis results, AP area was identified as the parameter with the highest diagnostic performance, with an AUC value of 0.856.

Conclusions:

Cochlear electrophysiological responses may vary in patients with OSAS, and electrocochleography(ECoChG) may be a useful tool to detect these changes. Parameters such as AP amplitude and AP latency may serve as potential biomarkers for assessing **OSAS-related cochlear damage.**

Introduction

Obstructive sleep apnea syndrome(OSAS) is a chronic respiratory disorder characterized by repetitive upper airway obstructions during sleep. This situation can affect multiple organ systems through intermittent hypoxia, oxidative stress, and microvascular circulatory disturbances. The inner ear structures are considered sensitive to hypoxia due to its high metabolic demands and limited collateral

circulation. Therefore, it is thought that OSAS may have adverse effects on cochlear structures and the auditory nerve([Matsumura, et al. (2016), Simsek, A., & Aslan, M. (2024)]).

Recent studies suggest a possible association between the severity of OSAS and auditory system function. In particular, increased hearing thresholds at high frequencies and reduced otoacoustic emission responses have been reported in patients with moderate to severe OSAS. These findings suggest that recurrent hypoxia and oxidative stress may have harmful effects on cochlear hair cells([Kalathingal, et al. (2023)]).

Electrocochleography(ECochG) is an objective method that enables the electrophysiological assessment of the inner ear and the proximal segment of the auditory nerve. ECochG recordings primarily consists of summating potential(SP) and action potential(AP) components, and the SP/AP ratio, in particular, is considered a key parameter in the evaluation of cochlear function. In a limited number of ECochG studies carried out in patients with OSAS, changes in AP latency and amplitude have been reported, suggesting that there may be impairment at the cochlear and auditory nerve levels([Sun, W. T., et al. (2018)]).

However, studies evaluating cochlear electrophysiological reactions in OSAS patients are limited, and current insights have not yet established a definitive consensus. Therefore, investigating the effects of OSAS on the peripheral auditory system using objective electrophysiological methods is of great importance. The aim of this study is to identify potential changes in cochlear and auditory nerve functions by evaluating electrocochleography parameters in individuals diagnosed with OSAS.

The following hypotheses were tested in this study:

H1

ECochG values (SP/AP ratio, AP latency, and AP amplitude) in patients with OSAS will differ significantly from those in healthy individuals.

H2

As OSAS becomes more severe (in parallel with AHI values), more obvious changes will be observed in cochlear electrophysiological response parameters.

H3

Recurrent hypoxia and microvascular circulation disorders associated with OSAS will lead to subclinical electrophysiological changes in cochlear and auditory nerve function.

Material and Methods

Study Design and Settings

This study was designed as a cross-sectional controlled study and was conducted at the Department of Otolaryngology at the Faculty of Medicine of XXX. The participants were selected from among patients who had visited the sleep laboratory for evaluation of sleep disorders. All participants first underwent nocturnal polysomnography(PSG), and individuals diagnosed with OSAS based on the PSG results were included in the experimental group. The control group consisted of healthy volunteers in whom OSAS was not detected on PSG.

The study protocol was approved by XXX Ethics Committee for Non-Interventional Clinical Research (Decision No.: 2024/38). Written informed consent was obtained from all participants prior to the study. The study was conducted in accordance with the principles of the Helsinki Declaration.

Participants

A total of 106 participants were involved in the study, divided into the mild OSAS group (n=19), the moderate OSAS group(n=25), the severe OSAS group (n=19), and the control group (n=43).
OSAS severity was categorized based on the Apnea-Hypopnea Index(AHI) according to the American Academy of Sleep Medicine(AASM) criteria:
• Mild OSAS: AHI 5–15
• Moderate OSAS: AHI 15–30
• Severe OSAS: AHI >30

Inclusion criterias

• Aged 18–60 years
• Having undergone polysomnography
• For the experimental group: having received an OSAS diagnosis based on PSG results
• For the control group: no OSAS detected on PSG
• Normal external auditory canal and tympanic membrane on otoscopic examination, patients with normal audiogram

Exclusion criterias

• A history of previously diagnosed hearing loss
• A history of middle ear pathology or prior otologic surgery
• A history of noise exposure
• Use of ototoxic medications
• A history of neurological disease, diabetes mellitus, uncontrolled hypertension, or systemic diseases that may affect the auditory system, patients without a normal audiogram

Polysomnography evaluation

During PSG monitoring, electroencephalography(EEG), electrooculography(EOG), electromyography(EMG), electrocardiography(ECG), nasal airflow, thoracoabdominal respiratory movements, and oxygen saturation values were simultaneously recorded. Apnea and hypopnea events and AHI were scored in accordance with the criteria of the AASM.

Electrocochleography Measurement

Measurements were conducted using the **Neuro Audio/LLR system (Neurosoft Ltd.,Ivanovo, Russia)** device. Electrocochleography recordings were acquired using the extratympanic method in all participants. Recordings were conducted in a quiet environment isolated from electromagnetic noise, with participants seated in a comfortable position. An external auditory canal electrode (tiptrode) was used for the extratympanic recording. The reference electrode was placed on the ipsilateral mastoid, and the ground electrode was placed on the forehead. Acoustic stimuli were delivered monaurally via in-ear headphones. Electrode impedance was maintained below 5 kΩ, and the impedance difference between electrodes was kept below 3 kΩ. Artifact rejection was applied automatically by the recording system. The analysis window was set to 5 ms.

The recording parameters are as follows:

• Stimulus type: click stimulus
• Stimulus intensity: 90 dB nHL
• Polarity: alternating polarity
• Stimulus rate: 7.1/s
• Filter range: 10–3000 Hz
• Number of averages: 1000 responses

The following electrophysiological parameters were analyzed from the obtained recordings:

• Base latency
• Summating potential(SP) latency
• Action potential(AP) latency
• SP–Base interlatency
• AP–Base interlatency
• SP–Base amplitude
• AP–Base amplitude
• SP/AP amplitude ratio
• SP/AP area ratio
• SP area
• AP area

All parameters were calculated separately for each ear. Representative ECochG waveforms of different OSAS severity groups and the locations of the analyzed fundamental parameters (Base, SP, and AP) are visualized in Figure-1.

Statistical Analysis

Statistical analyses were performed using IBM SPSS (version 26, IBM Corp., Armonk, NY,USA) statistics software.

The normality of continuous variables was assessed using the Shapiro–Wilk test.

For comparisons between groups:

• One-way analysis of variance(One-Way ANOVA) was used for variables that followed a normal distribution and met the assumption of homogeneity of variances.

• For variables not following a normal distribution, the Kruskal–Wallis H test was applied.
For parameters found to be statistically significant, the Bonferroni-corrected Dunn post-hoc test was applied for pairwise group comparisons.
Categorical variables were analyzed using the chi-square (χ^2) test.
Results:
• For variables with a normal distribution: mean ± standard deviation
• For variables not following a normal distribution: median (interquartile range)
were reported.
Effect size assessment:
• For One-Way ANOVA: eta-squared (η^2)
• For the Kruskal–Wallis test: epsilon-squared (ε^2)
• Cohen's d or rank-biserial r for pairwise comparisons
were used.

In the effect size assessment:
• Eta-squared (η^2) for one-way ANOVA
• Epsilon-squared (ε^2) for the Kruskal–Wallis test
• Cohen's d or the rank-biserial r for pairwise comparisons
were used.
Effect size classification:
For η^2 and ε^2:
• small ≥0.01
• moderate ≥0.06
• large ≥0.14
For rank-biserial r:
• small ≥0.10
• moderate ≥0.30
• large ≥0.50
were accepted.
To evaluate diagnostic performance, a ROC (Receiver Operating Characteristic) analysis was performed between each OSAS severity subgroup and the control group.
Optimal cut-off points were determined using the Youden index (J = sensitivity + specificity − 1).
AUC values and 95% confidence intervals were calculated using a 2,000-repetition bootstrap method.
AUC classification:
• ≥0.90 excellent
• 0.80–0.89 good
• 0.70–0.79 acceptable
• 0.60–0.69 poor
was used.
In all analyses, $p < 0.05$ was considered statistically significant.

Results

1.Demograpic Features

A total of 106 participants were included in the study, divided into the Mild OSAS group (n=19), the Moderate OSAS group (n=25), the Severe OSAS group (n=19), and the Control group (n=43) (Table 1). The mean ages of the groups were determined to be 40.16 ± 7.54, 36.08 ± 5.71, 36.95 ± 5.75, and 37.23 ± 6.32 years, respectively; and a One-Way ANOVA revealed no statistically significant difference in age between the groups($p = 0.192$). When evaluating gender distribution, it was observed that gender information for the Mild OSAS group was not coded in the dataset; a chi-square analysis conducted for the three groups and the control group revealed that gender distribution was homogeneous across groups($p=0.133$).

2.Comparison of Right Ear ECochG Parameters

2.1.Absolute Latency Values

Kruskal-Wallis and ANOVA analyses of right ear absolute latency values are presented in Table 2. Right base latency showed statistically significant differences among the four groups ($p<0.001$, $\varepsilon^2=0.150$); a Bonferroni-corrected post-hoc analysis revealed significant differences in the comparisons between Mild–Moderate OSAS ($p=0.011$) and Moderate–Severe OSAS ($p<0.001$). Right SP latency also differed significantly among the groups ($p<0.001$, $\eta^2=0.162$); the difference was primarily driven by the Moderate–Severe OSAS comparison. Regarding right AP latency, a significant difference was detected only between the Severe OSAS and Control groups ($p=0.011$, $\varepsilon^2=0.080$).

2.2.Interlatency values

The right SP–Base interlatency showed a significant difference between groups ($p=0.009$, $\varepsilon^2=0.085$); post-hoc analysis revealed that the difference originated between the Moderate OSAS and Control groups. Right AP–Base interlatency constitutes one of the study's strongest findings ($p<0.001$, $\eta^2=0.286$); significant differences were detected in the Mild OSAS–Control, Moderate OSAS–Control, and Moderate–Severe OSAS comparisons, with a large effect size. This finding indicates that AP–Base interlatency changes significantly across all patient subgroups, independent of OSAS severity.

2.3.Amplitude values

The right SP–Base amplitude differed significantly between groups ($p<0.001$, $\varepsilon^2=0.175$); the difference was most pronounced between the Mild OSAS group and the Control group, indicating that an increase in amplitude was observed even in the early stages. No statistically significant difference was found in the right AP–Base amplitude between groups ($p=0.556$).

2.4. SP/AP Ratios and Field Values

The right SP/AP amplitude ratio showed a significant difference among the four groups ($p<0.001$, $\varepsilon^2=0.199$); post-hoc analysis revealed significance in the Mild OSAS–Severe OSAS and Mild OSAS–Control comparisons. The right SP/AP area ratio was the right ear parameter with the highest effect size ($p<0.001$, $\varepsilon^2=0.558$); significant differences were detected in four of the six comparison pairs.

The right SP area differed significantly between groups ($p<0.001$, $\varepsilon^2=0.517$), and the Mild OSAS group exhibited markedly higher values compared to all other groups. The right AP area also showed significant differences ($p<0.001$, $\varepsilon^2=0.140$); significant differences were detected in the Mild–Moderate OSAS, Moderate–Severe OSAS, and Moderate OSAS–Control comparisons.

3.Comparison of Left Ear ECochG Parameters

3.1.Absolute Latency Values

Kruskal-Wallis and ANOVA analyses of left ear absolute latency values are presented in Table 2. Left basal latency showed a significant difference between groups ($p=0.004$, $\varepsilon^2=0.102$); the difference between the Moderate OSAS and Control groups was found to be significant in the post-hoc analysis. Left SP and AP latencies, however, revealed much more pronounced differences (SP: $p<0.001$, $\varepsilon^2=0.241$; AP: $p<0.001$, $\varepsilon^2=0.258$); for both parameters, the Moderate OSAS group significantly differed from the other groups, and a pattern of prolonged latencies was particularly notable.

3.2.Interlatance values

The left SP–Base interlatency was one of the parameters with the highest effect size in the study ($p<0.001$, $\varepsilon^2=0.498$); highly significant differences were observed in all comparisons between Mild–Moderate OSAS, Moderate–Severe OSAS, and Moderate OSAS–Control groups. Left AP–Base interlatency also demonstrated significant differences across the four groups with a high effect size ($p<0.001$, $\varepsilon^2=0.382$); statistical significance was achieved in all comparisons: Mild OSAS–Moderate OSAS, Mild OSAS–Control, Moderate OSAS–Severe OSAS, and Severe OSAS–Control. This bilateral pattern indicates that AP–Base interlatency is a strong and consistent biomarker reflecting OSAS pathology.

3.3.SP/AP Ratios and Field Values

The left SP/AP amplitude ratio showed a significant difference between groups ($p=0.017$, $\varepsilon^2=0.071$). The left SP/AP area ratio, however, was found to be highly significant with a large effect size ($p<0.001$, $\varepsilon^2=0.412$); the mild OSAS group differed significantly from all other groups.

The left SP area constitutes one of the most striking findings of the study ($p<0.001$, $\varepsilon^2=0.405$); the values for the mild OSAS group differed markedly from those of the moderate OSAS, severe OSAS, and control groups. The left AP area also showed a significant difference with a high effect size ($p<0.001$, $\varepsilon^2=0.305$); each of the three OSAS subgroups was statistically significantly distinct from the control group. The distribution of the key ECochG parameters (AP-Base interlatency, SP/AP area ratio, and SP area), which

carry the highest statistical and clinical significance in the study, according to the groups is presented in Figure-2.

4.ROC analysis and Diagnostic Accuracy

A ROC analysis was performed to evaluate the diagnostic accuracy of significant ECochG parameters for each OSAS subgroup; 95% confidence intervals for the AUC were calculated using a 2,000-repetition bootstrap method, and cut-off points were determined using the Youden index (J=Sensitivity + Specificity −1). Parameters with an AUC value ≥0.70 are presented in Table 3. The ROC curves demonstrating the performance of key ECochG parameters with excellent and good diagnostic accuracy in distinguishing OSAS subgroups are shown in Figure-4.

The parameters demonstrating perfect diagnostic accuracy (AUC=1.000) are as follows: Right SP/AP area ratio and Right SP area (Mild OSAS vs. Control), Left SP–Base interlatency (Moderate OSAS vs. Control), Left SP/AP area ratio and Left SP area (Mild OSAS vs. Control). For these parameters, the relevant subgroups could be distinguished from the Control group with 100% sensitivity and 100% specificity.

Other important parameters falling into the “good” diagnostic class (AUC≥0.80) include Left AP–Base interlatency (Mild OSAS: AUC=0.925), Left SP latency (Moderate OSAS: AUC = 0.914), Right AP–Base interlatency (moderate OSAS: AUC=0.909), the right SP/AP area ratio (moderate OSAS: AUC=0.879), and the left AP latency (moderate OSAS: AUC=0.852). These findings demonstrate that interlatency parameters and the SP/AP area ratio, in particular, hold high clinical value in the diagnosis of OSAS.

5.Overall Assessment

All 22 ECochG variables were analyzed using the Kruskal-Wallis test or one-way ANOVA; statistically significant differences were found between groups for 20 of the 22 parameters. The two parameters that did not reach statistical significance were the right AP–Base amplitude and the left SP–Base amplitude. When evaluated in terms of effect size, the strongest discriminatory parameters were the Right SP/AP area ratio (ε^2=0.558), the Left SP–Base interlatency (ε^2=0.498), the Right SP area (ε^2=0.517), and the Left SP/AP area ratio (ε^2=0.412). The fact that the effect sizes of these parameters fall into the large category indicates a strong clinical difference beyond statistical significance. The statistical weight of the effect sizes (η^2 and ε^2) calculated for all analyzed right and left ear ECochG parameters is detailed in the heatmap in Figure-3.

When a gradient assessment is performed according to the severity of OSAS, it is observed that the Mild OSAS group differs significantly from the Moderate and Severe OSAS groups, especially in the SP area and SP/AP area ratio parameters, while the Moderate OSAS group exhibits the most significant changes in left ear latency parameters. This finding shows that the effect of different OSAS severity levels on ECochG is not homogeneous and that subgroups can be separated based on specific parameters. The radar chart summarizing how the groups differentiate based on these parameters and the overall electrophysiological profile formed according to OSAS severity is provided in Figure-5.

Discussion

In this study, electrocochleography parameters were systematically evaluated in a total of 106 participants divided into four groups based on OSAS severity (Mild, Moderate, Severe OSAS, and Control); statistically significant intergroup differences were detected in 20 of the 22 ECochG parameters. These findings support the results of previous studies indicating that OSAS leads to subclinical electrophysiological changes in cochlear and auditory nerve functions and present one of the most comprehensive parametric ECochG analyses conducted in this field.

1.OSAS and the Auditory System: An Overview

The relationship between OSAS and the auditory system has received increasing interest in previous years. Large population-based studies and meta-analyses have demonstrated a significant association between OSAS and sensorineural hearing loss. Kasemsuk et al. reported in their systematic review and meta-analysis that pure-tone hearing thresholds were significantly higher in the OSAS group compared to controls (HTL: mean difference 5.89 dB; 95% CI 1.87–9.91) and that this correlation was particularly apparent in severe OSAS cases([Kasemsuk, et al. (2023)]). Similarly, Wang et al. observed statistically significant higher pure-tone hearing thresholds in the OSAS group compared to controls in their meta-analysis investigating different frequency subgroups([Wang, C., et al. (2022)]). Lisan et al., in their longitudinal study involving 6,797 participants as part of the Paris Prospective Study 3, demonstrated an independent association between OSAS and hearing impairment; they reported that this association persisted even after adjusting for age and gender([Lisan, Q., et al. (2020)]). In the present study, the preference for ECochG parameters over pure-tone hearing thresholds allowed for the more sensitive detection of cochlear dysfunction during the subclinical phase, when standard audiological tests have not yet been compromised; this constitutes the methodological uniqueness of the study.

2.AP–Base Interlatency: Bilateral Consistency and Clinical Significance

In our study, the right and left ear AP–Base interlatency were among the most consistent parameters, capable of distinguishing all OSAS severity groups from the control group in both ears and exhibiting large effect sizes (right:η^2=0.286; left:ε^2=0.382). The left AP–Base interlatency reached statistical significance in four separate pairwise comparisons, including mild OSAS–control, moderate OSAS–severe OSAS, and severe OSAS–control. This bilateral consistency indicates that the prolongation in AP-Base interlatency reflects a pathophysiological process unique to OSAS. The intergroup comparison of right and left ear ECochG parameters (such as AP-Base interlatency and SP/AP area ratio) and the consistency of the findings observed in both ears are summarized in Figure-3.

The AP of the auditory nerve is defined as the compound action potential in response to an acoustic stimulus, while the base latency is determined as the onset of the stimulus. Consequently, the AP-base interlatency is considered an indirect indicator of peripheral auditory nerve conduction velocity originating from the cochlea([Wardly D. E. (2014)]). Recurrent episodes of intermittent hypoxia in OSAS patients may affect the microvascular structure of the stria vascularis and the proximal segment of the

auditory nerve, leading to a slowing of conduction velocity. Sun et al. reported a significant prolongation of AP latency in OSAS patients; they associated this finding with impairment at the level of the cochlea and the proximal segment of the auditory nerve([Sun, W. T., et al. (2018)]). Matsumura et al. demonstrated that peripheral auditory pathways are impaired in individuals with OSAS and that this impairment correlates with AHI ([Matsumura, et al. (2016)]) The findings regarding AP–Base interlatency in our current study support these two fundamental reference studies and indicate systemic pathology with a bilateral symmetrical pattern.

3.SP/AP Area Ratio and SP Area: Subclinical Endolymphatic Hydrops?

In the present study, both the right and left SP/AP area ratios, as well as the SP area, demonstrated the highest effect sizes (right SP/AP area ratio: $\varepsilon^2=0.558$; right SP area: $\varepsilon^2=0.517$; left SP-Base interlatance: $\varepsilon^2=0.498$) and exhibited excellent diagnostic accuracy (AUC=1.000 for the mild OSAS group).
SP represents the summating potential of hair cells located within the inner ear, and it is indicative of differences in fluid pressure between the scala media and the scala vestibuli. An increase in endolymphatic pressure has been demonstrated to result in a shift of the basilar membrane towards the scala tympani([Bawazeer, N., et al. (2024)]).This shift has been shown to lead to an augmentation in SP amplitude. It is known that the SP/AP area ratio provides higher sensitivity for endolymphatic hydrops compared to the amplitude ratio and serves as the primary ECochG indicator used in the diagnosis of Meniere's disease ([Ferraro, J. A., & Tibbils, R. P. (1999)., He, B., et al. (2021)]).In this study, the Mild OSAS group had much higher values for SP area and SP/AP area ratio (median left SP/AP area ratio: 60.36 vs. Control:1.95). This suggests that they might have a subclinical endolymphatic hydrops-like condition.

Cases have been reported indicating that OSAS and Meniere's disease coexist; pilot studies exist showing that CPAP therapy reduces Meniere's symptoms([Nakayama, M., et al. (2015)]).It is believed that intermittent hypoxia negatively affects endolymphatic fluid homeostasis by disrupting endolymphatic ion transport and impairing the microvasculature of the stria vascularis. Thulasiram et al. conducted a detailed analysis of the vital role of the stria vascularis in preserving cochlear fluid homeostasis, and its susceptibility to vascular impairment([Thulasiram, M. R., et al. (2022)]). The hypothesis that intermittent hypoxia episodes observed in OSAS may cause recurrent ischemia-reperfusion injury in the stria vascularis capillaries and that this condition may predispose to an increase in SP aligns with the findings of the present study.

4.Paradoxical Findings and Possible Mechanisms in the Mild OSAS Group

A significant finding of the present study is that the mild OSAS group exhibited the highest values for the SP area and the SP/AP area ratio. Contrary to the prevailing assumption, the present findings suggest that the most significant increase in SP was observed not in the severe OSAS group, but in the early stages of the disease. Similar paradoxical findings have been reported in other studies evaluating subclinical auditory dysfunction. Kayabasi et al. identified significant impairment in vestibular function among patients in the moderate-severe OSAS group, while reporting changes beyond expectations in the

mild OSAS grou([Kayabasi, S., et al. (2019)]).

A number of mechanisms have been postulated to explain this paradoxical pattern. The initial hypothesis concerns a compensatory endolymphatic response observed in early-stage OSAS. In the inner ear exposed to mild hypoxia, there may be an initial increase in endolymphatic volume as a homeostatic response mechanism, leading to a temporary rise in SP amplitude. Second, if hair cell loss occurs due to chronic ischemic damage as OSAS severity progresses, both SP and AP amplitudes may decrease together; this could mask changes in the SP/AP ratio. Third, it should not be overlooked that the mild OSAS group in our study had demographic characteristics that were significantly different from the other groups (mean age 40.16 years, higher than the other groups) and that this demographic difference may have affected the ECochG parameters. Meliante et al. demonstrated that intermittent hypoxia in OSAS affects multiple organ systems via ROS-mediated oxidative stress; they emphasized that this mechanism could lead to damage in all metabolically active tissues, including the inner ear ([Meliante, P. G., et al. (2023)]).

5.Left Ear Latency Parameters and the Distinctiveness of the Middle OSAS Group

The most robust changes in left SP and left AP latencies were observed in the moderate OSAS group (left SP AUC=0.914; left AP AUC=0.852). This finding suggests that the relationship between OSAS severity and ECochG changes is not linear; at a certain level of OSAS severity (within the AHI range defined as “moderate” in this study), left ear latency parameters may exhibit the most critical changes. The relationship between OSAS severity (AHI spectrum) and right AP-Base interlatency as well as right SP/AP area ratio, along with the non-linear trends based on the groups, are illustrated in Figure-5. It is known from the literature that the OSAS severity-response relationship may follow a non-linear course through its effects on carotid body sensitivity, serotonergic activation, and dopaminergic transmission in the basal ganglia. It is conceivable that similar non-linear patterns may also apply to its effects on the peripheral auditory pathway.

It is particularly noteworthy that the SP–Base interlatency demonstrates excellent diagnostic accuracy (AUC=1.000) in the left ear. Because this parameter reflects cochlear proximal mechanisms independently of the middle ear and external auditory canal, it may serve as a potential biomarker for OSAS-related peripheral auditory system dysfunction. The current ECochG literature has primarily evaluated the SP–Base interlatency in the context of Meniere’s disease and endolymphatic hydrops; prospective studies are needed to assess the clinical value of this parameter in the OSAS population.

6.Possible Pathophysiological Mechanisms

In light of the findings of our study, three main mechanisms that mediate the adverse effects of OSAS on the inner ear can be discussed:

Intermittent Hypoxia and Reactive Oxygen Species (ROS): The hypoxia-reoxygenation cycles that occur during recurrent sleep in OSAS increase oxidative stress and ROS production ([Meliante, P. G., et al. (2023)], [Li, P., et al. (2023)]). Li et al. demonstrated that ROS-induced mitochondrial dysfunction and NLRP3 inflammasome activation play a central role in cochlear hair cell damag([Li, P., et al. (2023)]). It has been

demonstrated that ROS can induce apoptotic pathways in cochlear neurons([Kishimoto-Urata, et al. (2022)., Johns, J., et al.(2023)]). The AP–Base interlatency prolongation and AP amplitude changes documented in this study may be indicative of the electrophysiological reflection of this ROS-mediated damage at the level of spiral ganglion neurons or the auditory nerve.

Stria Vascularis and Cochlear Microvascular Dysfunction: The stria vascularis is of significant importance in this regard, given its role as a critical energy source for the inner ear. This phenomenon can be explained by the elevated metabolic demands and extensive capillary network of the subject([Thulasiram, M. R., et al. (2022)., Lang, H.,et al. (2023)]). In addition to this, the stria vascularis also acts as the primary component of the blood-labyrinth barrier([Thulasiram, M. R., et al. (2022)., Lang, H.,et al. (2023)]). Hypoxia and oxidative stress can disrupt the integrity of the blood–labyrinth barrier by reducing the expression of tight junction proteins in stria vascularis endothelial cells ([Fischer, A. Q., et al. (1992)]). This situation may pave the way for disruption of endolymphatic ion homeostasis, a decrease in the endocochlear potential, and consequently, changes in SP. In our study, the notably high SP/AP area ratio observed particularly in the mild OSAS group may serve as an early electrophysiological indicator of this microvascular dysfunction.

Increased Intracranial Perfusion Changes: Changes in intrathoracic pressure occurring alongside apnea during OSAS episodes may cause fluctuations in cerebral venous return and intracranial pressure. It has been suggested that this may contribute to increased endolymphatic pressure by disrupting venous drainage to the inner ear([Wardly D. E. (2014). Ferraro, J. A., & Durrant, J. D. (2006)]). It is also thought that the intermittent hypoxia and hypercapnia observed in OSAS may alter cochlear blood flow via vasodilation; it is anticipated that this mechanism may be reflected in peripheral nerve conduction parameters such as the AP–Base interlatency.

7.Comparison with Current ECochG Studies

Studies on ECochG findings in patients with OSAS are quite limited. Sun et al. reported significant changes in AP latency and AP amplitude in their study involving 31 patients with moderate-to-severe OSAS; however, they did not detect a significant difference in the SP/AP amplitude ratio[4].In our current study, the SP/AP amplitude ratio differed significantly between groups ($p<0.001$, $\varepsilon^2=0.199$); this inconsistency may stem from two primary methodological differences: Sun et al.'s study included only moderate and severe OSAS patients; the mild OSAS group was not included([Sun, W. T., et al. (2018)]). In our current study, in addition to the amplitude ratio, the area ratio was also calculated, and this parameter alone provided stronger differentiation. It is known that the area ratio is a more sensitive indicator of endolymphatic hydrops compared to the amplitude ratio([Bawazeer, N., et al.(2024)., Ferraro, J. A., & Tibbils, R. P. (1999)]) and the data from our study support this finding in the context of OSAS as well.

Matsumura et al. evaluated the peripheral auditory pathways in individuals with OSAS and demonstrated conduction delays using auditory brainstem response([Matsumura, E.,et al. (2016)]). While Wave I in ABR primarily corresponds to the distal portion of the auditory nerve, the AP–Base interlatency in ECochG reflects the conduction velocity at a more peripheral—cochlear output—level; thus, the two techniques

are complementary. Kalathingal et al. investigated the association between AHI and hearing loss, reporting a correlation between the severity of AHI and a reduction in OAE responses at high frequencies([Kalathingal, N., et al. (2023)]). The present study makes a contribution to the extant literature by demonstrating the potential of ECochG parameters as a cochlear electrophysiology panel that is sensitive to OSAS.

8.ROC Analysis and Clinical Evaluation

ROC analysis has shown that parameters such as the SP/AP area ratio and the SP area can reach AUC values of 1.000 for the Mild OSAS group. While these results are highly promising in terms of high diagnostic accuracy, they should be evaluated in light of certain methodological limitations. Firstly, the sample size of the mild OSAS group (n=19) is relatively limited, leading to variability in the bootstrap AUC confidence interval estimates. AUC values of 1.000 give rise to concerns regarding the risk of overfitting in small samples; as such, these results must be confirmed by external validation studies. However, the fact that the same parameters also yield high AUC values for the Moderate OSAS group (SP/AP area ratio: AUC=0.879; AP–Base interlatency: Right 0.909; Left 0.925) indicates that these measurements hold clinical value independent of OSAS severity. In this context, ECochG may be considered a useful supplementary tool, particularly in the early stages of OSAS monitoring when audiological tests are still within normal limits.

9.Strengths and Limitations of the Study

The study's principal strengths can be identified in its four-group comparative design, the extensive variety of ECochG parameters (22 for both right and left ears), the application of contemporary statistical methodologies (including effect sizes and the bootstrap ROC) and the validation of OSAS diagnosis by PSG.

However, it is imperative to acknowledge the limitations of the study when interpreting the findings. Due to the cross-sectional design, a causal relationship cannot be established; the effect of OSAS duration and treatment (CPAP) on ECochG parameters could not be assessed. The fact that it is a single-center study limits generalizability. The absence of gender data in the mild OSAS group undermines demographic homogeneity. The relatively small sample size (particularly in the Mild and Severe OSAS groups, where n=19) necessitates caution when interpreting the results of the ROC analysis. In conclusion, the absence of concomitant presentation of pure-tone audiometry and OAE data hinders the capacity to engage in discourse concerning the role of ECochG alterations within a comprehensive audiological profile. Additionally, it should be noted that the multiple comparisons performed on 22 ECochG parameters in this study may increase the study-specific Type I error rate; addressing this limitation using the False Discovery Rate(FDR) method in future studies would be appropriate.

Conclusion

This study provides one of the most comprehensive comparative analyses of ECoChG parameters according to OSAS severity. The findings suggest that OSAS may adversely affect the peripheral auditory system at a subclinical level, and that these changes can be detected by ECoChG beyond the limits of standard audiological tests.

All three hypotheses were largely confirmed: most ECoChG parameters differed in OSAS, severity showed a non-linear effect with consistent AP–base interlatency changes, and recurrent hypoxia with microvascular dysfunction led to subclinical cochlear alterations.

AP-based interlatency, SP/AP area ratio, and SP area are powerful biomarkers that objectively detect inner ear dysfunction in early-stage OSAS. Inclusion of ECochG in routine audiological follow-up can enable both early detection of cochlear damage and objective monitoring of the effectiveness of CPAP or surgical interventions.

It is asserted that future studies with larger sample sizes, prospective designs evaluating the long-term effects of CPAP therapy on ECochG parameters, concurrent assessment with OAE and pure-tone audiometry, and the use of multi-center data will make significant contributions to filling the knowledge gaps in this field. In particular, prospective studies incorporating longitudinal ECochG follow-up according to OSAS severity groups could clarify whether AP–Base interlatency and SP/AP area ratio can be used as a biomarker for monitoring the course of OSAS.

Declarations

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Conflict of interest: The authors have no conflicts of interest to declare.

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Availability of data and materials: All the data generated or analyzed during this study are included in this published article.

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Tables

Tables 1 to 3 are available in the supplementary files section

Figures

Figure 1 – ECochG Waveforms

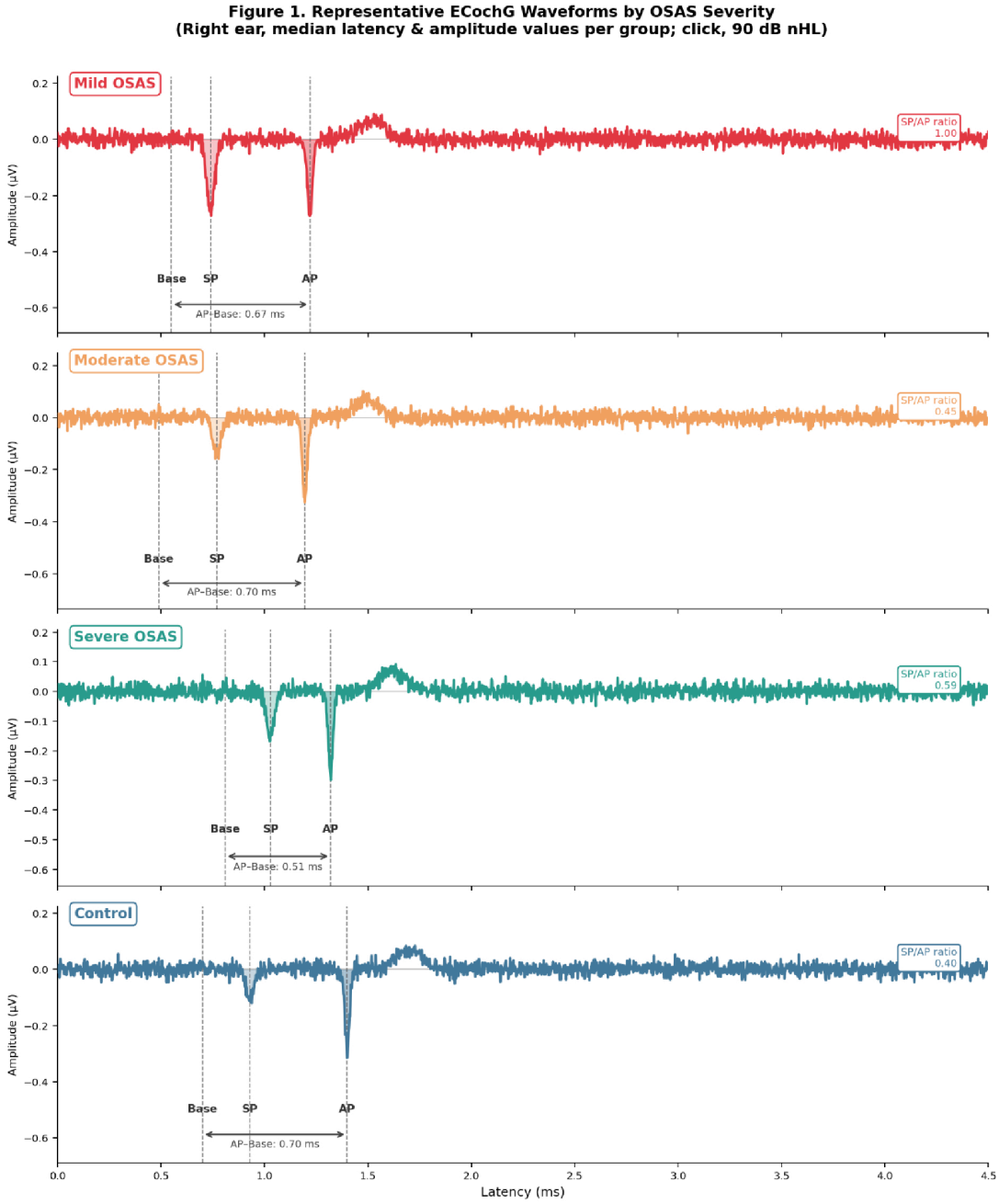


Figure 1

See image above for figure legend.

Figure 2 – Violin + Strip Plots

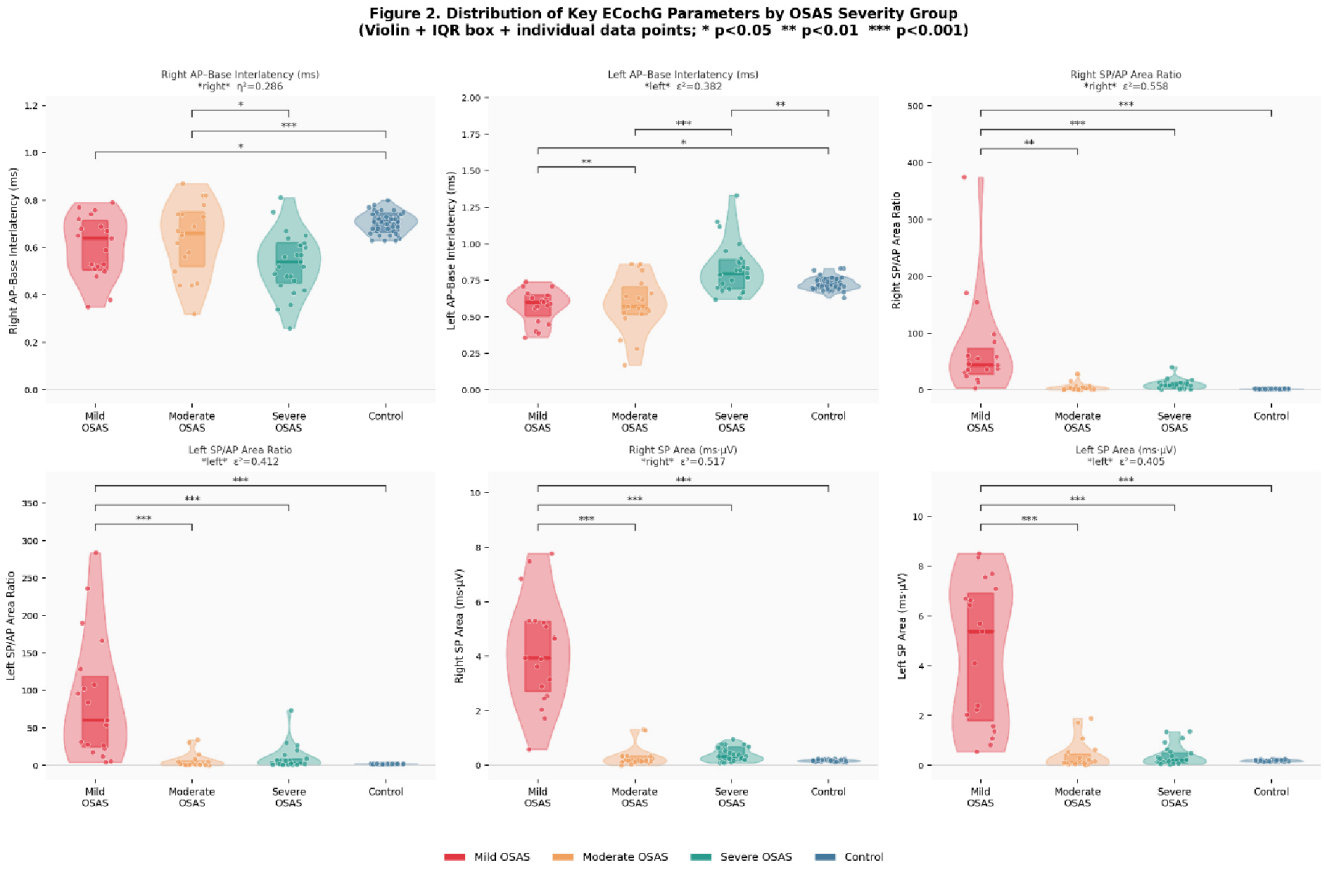


Figure 2

See image above for figure legend.

Figure 3 – Right vs Left Ear Comparison & Effect Size Heatmap

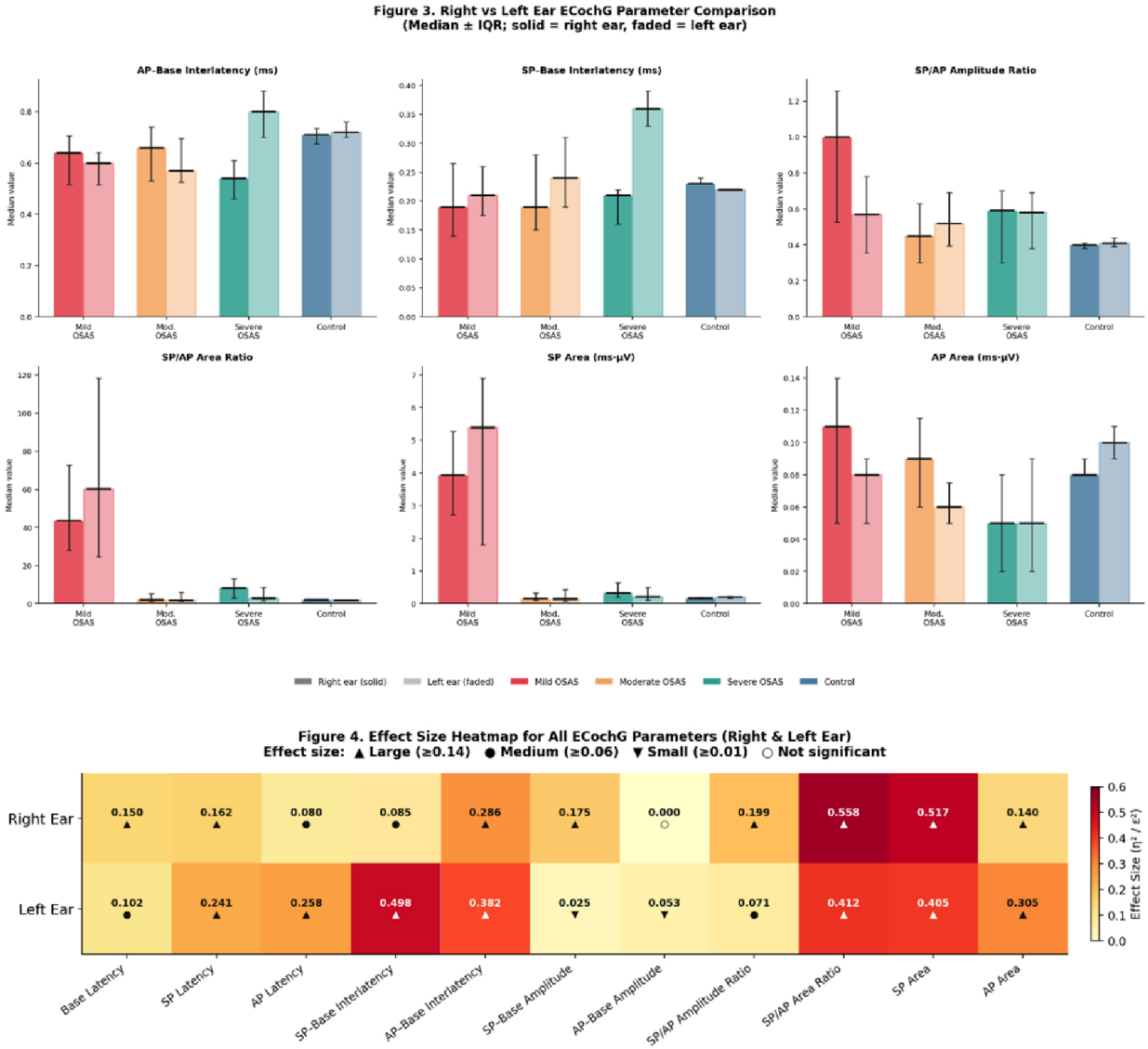


Figure 3

See image above for figure legend.

Figure 4 – ROC Curves

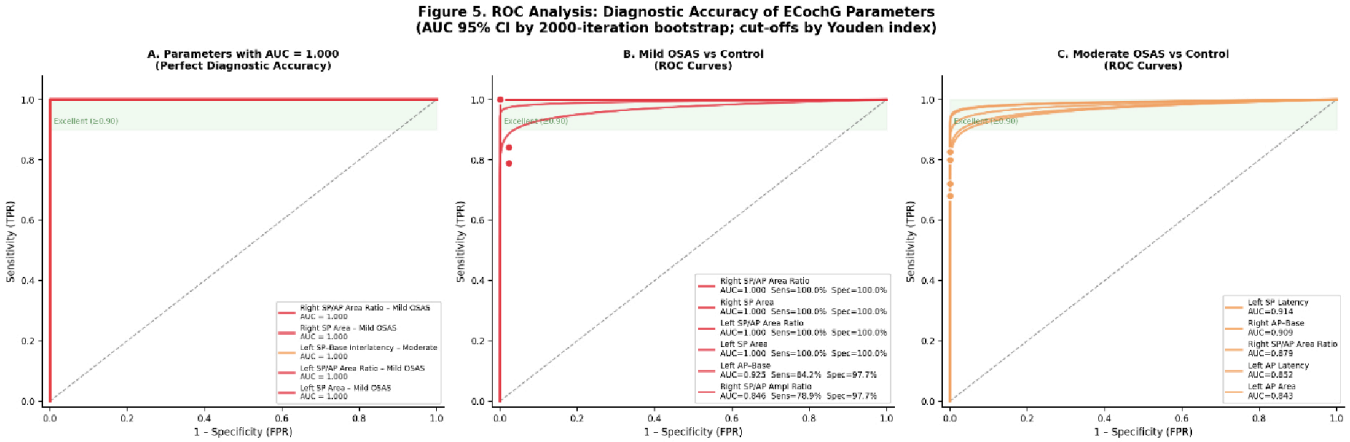


Figure 4

See image above for figure legend.

Figure 5 – Radar Chart & Scatter / AHI Spectrum

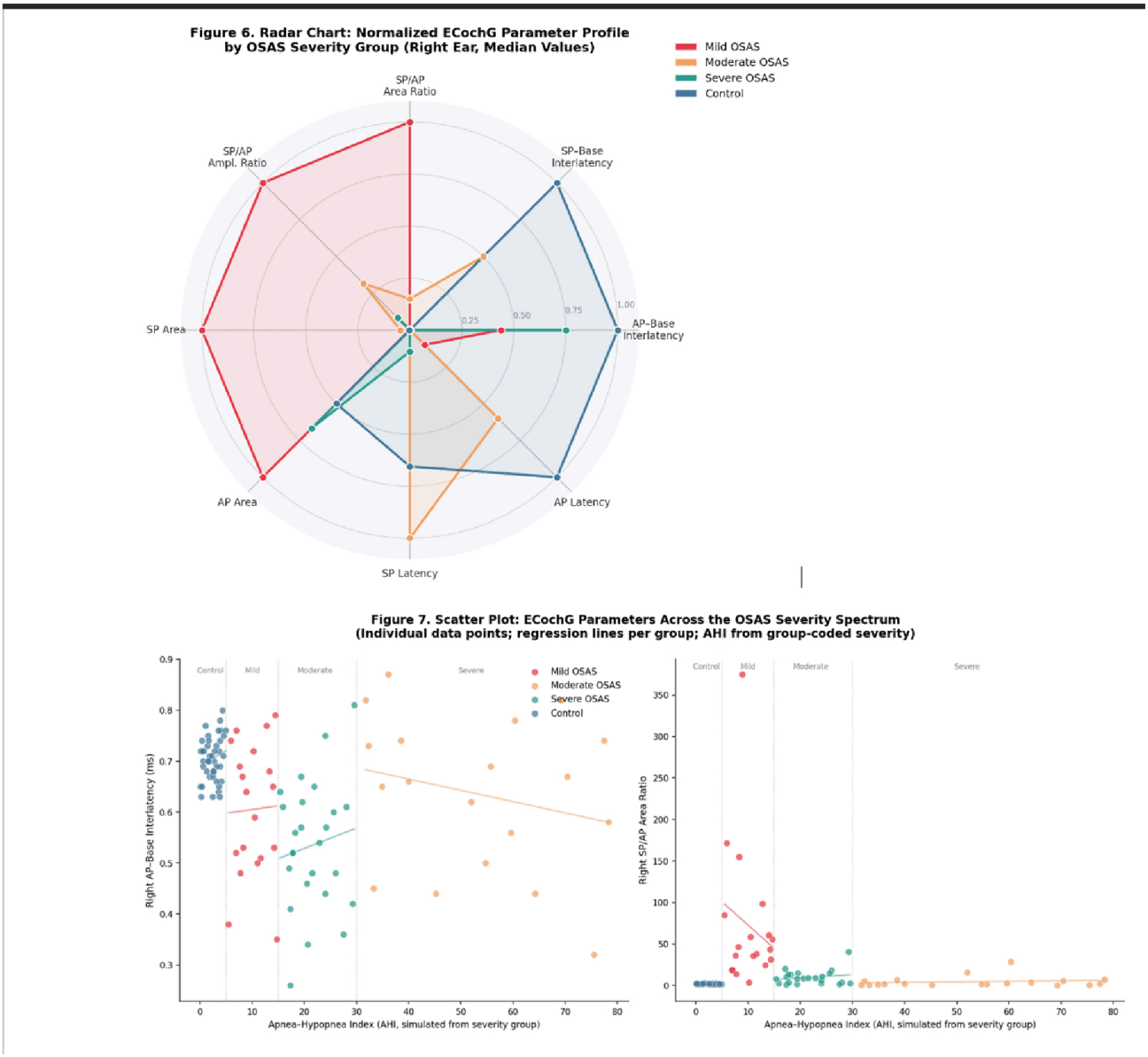


Figure 5

See image above for figure legend.

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