Cognitive screening and hearing assessment in patients with chronic tinnitus

Running title: Cognition and hearing loss in tinnitus

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Acknowledgements

A.B.-R. is a PhD student in the Biomedicine Program at the School of Health Sciences at the University of Granada and this work is part of his Doctoral Thesis.

Authors contributions:

Conceptualization: JAL-E, PP-C. Formal analysis: AB-R, PP-C, JAL-E. Investigation: AB-R. Methodology: AB-R, PP-C and JAL-E. Supervision: PP-C and JAL-E. Writing—original draft: AB-R, PP-C and JAL-E. Writing—review and editing: AB-R, PP-C, BM, SS, DK, SS, BL, SW and JAL-E. All authors have revised all statistical analyses and approved the final version of the manuscript, and they are prepared to take total responsibility for the integrity of the content. All authors have read and agreed to the published version of the manuscript.

Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Granada Review Board, (1537-N-20).

Informed Consent Statement: Written informed consent was obtained from all subjects involved in the study.
Data Availability Statement: All data obtained in this study have been anonymized and are available from the corresponding author upon reasonable request.

Conflicts of Interest: The authors declare no conflict of interest.

Funding: This study has been funded by the European Union's Horizon 2020 Research and Innovation Programme, Grant Agreement Number 848261- H2020-SC1-BHC-2018-2020 (UNITI). P.P.-C. has received funds from the Andalusian Health Government (Grant RH-0150-2020).
Abstract

Objective: The study aims to assess the relationship between tinnitus and hyperacusis with cognitive impairment as indicated by the Montreal Cognitive Assessment (MoCA) tool.

Methods: A multicentre cross-sectional study including individuals with chronic tinnitus from the “Unification of Treatments and Interventions for Tinnitus” (UNITI) database. Four different tertiary clinical centres, located in Athens and Granada (Mediterranean group), Berlin and Regensburg (German group). Three hundred eighty individuals with a diagnosis of non-pulsatile chronic tinnitus (permanent and constant tinnitus > 6 months) and no evidence of severe cognitive impairment (MoCA > 22) were recruited and evaluated using the following tools: MoCA, Tinnitus Handicap Inventory (THI), Hyperacusis assessment (GÜF), Patient Health Questionnaire (PHQ-9) and European School for Interdisciplinary Tinnitus Research Screening Questionnaire (ESIT-Q).

Results: MoCA-scores were different between German and Mediterranean individuals (p<0.01), and both groups were analysed separately; MoCA-scores were significantly associated with the education level, age, hearing threshold at 8kHz and THI in both groups. Moreover, a significant correlation was found between PHQ-9 scores and THI and GÜF (p<0.01 in both Germans and Mediterranean).

Conclusion: Our data suggest an association between tinnitus handicap, high-frequency hearing loss and mild cognitive impairment. PHQ-9 scores are associated with tinnitus and hyperacusis scores, regardless of the hearing loss thresholds.
Highlights:

1. The MoCA questionnaire is a screening tool suitable for detection of cognitive impairment in patients with tinnitus regardless of hearing loss.

2. MoCA-scores suggest an association between tinnitus distress, high-frequency hearing loss and mild cognitive impairment.

3. PHQ-9 scores are associated with tinnitus and hyperacusis distress regardless of hearing loss.
Introduction

Tinnitus is a symptom defined by the conscious perception of a phantom, non-verbal tonal or composite sound in absence of any external stimuli [1]. Tinnitus can appear as a symptom associated with other common conditions, including hearing loss (HL), anxiety, depression or migraine[2]. More than 90% of patients with tinnitus show any type of HL[3], the most common being high-frequency sensorineural hearing loss (SNHL) observed in age-related hearing loss (ARHL) or noise-induced NIHL[3], but also otological diseases such as otosclerosis, vestibular schwannoma, or Meniere diseases [1,3–5].

The term “tinnitus disorder” has been proposed for tinnitus, that is associated with emotional distress, cognitive dysfunction, and/or autonomic arousal, leading to behavioral changes and functional disability [6].

Given the influence that other comorbidities have on tinnitus, a screening tool was generated to assess patients with tinnitus for personalization of diagnosis and treatment[1]. With this aim, the European School for Interdisciplinary Tinnitus Research (ESIT, https://esit.tinnitusresearch.net) [7] designed and validated the ESIT screening questionnaire (ESIT-SQ)[8]. Although this instrument has facilitated a standardized assessment of patients with chronic tinnitus[4], it does not evaluate cognition.

In this sense, there are several cross-sectional studies that have demonstrated a consistent association between cognitive decline and HL in different populations[9]. In fact, HL seems to aggravate cognitive deficits in the elderly and it may be a prognostic factor for mild cognitive impairment (MCI)[10]. Moreover, prospective cohort studies suggest that the use of hearing aids in patients with HL can reduce cognitive decline in elderly people[9]. Additionally, tinnitus-associated dysfunctional cognition, including
“catastrophic thinking” and “avoidance cognitions”, is strongly correlated with measures of tinnitus distress, anxiety and depression. This has been associated with impairment in executive functions, attention and memory [11]. Even mild cognitive symptoms can have a substantial impact on depression [11,12]. Furthermore, the elevated prevalence of depression among severely-impaired tinnitus sufferers has been reported to be as high as 60-80% [13].

Given the association of tinnitus and ARHL in elderly patients with cognitive impairment, and the increasing prevalence of dementia, including Alzheimer’s disease in elderly population, it may be useful to proactively diagnose HL and tinnitus in the middle-aged population; moreover, assessment of cognitive impairment is of great clinical importance and may improve the characterization of patients with tinnitus and HL [14].

The aims of this study are to assess cognitive function in a non-selected cohort of patients with chronic tinnitus using the Montreal Cognitive Assessment (MoCA) questionnaire and to investigate which aspects of tinnitus, its comorbidities and demographic variables are relevant for the extent of cognitive decline.

**Materials and Methods**

**Patients**

A total of 380 individuals with a diagnosis of non-pulsatile chronic tinnitus and no evidence of cognitive impairment (MoCA>22) were enrolled in a multi-center study. This cutoff point was established according to population studies, reporting that more than 60% of individuals obtained a score under 26 [11,15,16]. Tinnitus was defined as a permanent and constant tinnitus of at least 6 months of duration. Ninety-nine individuals were included from Berlin and 97 from Regensburg (Germany), 93 from Athens (Greece) and 91 patients from Granada (Spain) according to the inclusion and exclusion criteria.
published at the “Unification of Treatments and interventions for Tinnitus Patients” (UNITI) protocol in the UNITI randomised clinical trial (UNITI-RCT)[11].

The study was conducted according to the Declaration of Helsinki guidelines and approved by the Granada Review Board (1537-N-20). All participants agreed to participate after obtaining a written informed consent. Clinical and psychometric variables were obtained according to the UNITI-protocol [11]. Individuals underwent an assessment of audiological symptoms and pure tone hearing thresholds, and a neuropsychological screening based on the MoCA for cognition, the PHQ-9 for depression [12,17], the Tinnitus Handicap Inventory (THI) and the Test of Hypersensitivity to Sound (GÜF) for tinnitus and hyperacusis, respectively [18,19]. The ESIT-SQ was used to collect information on demographics, lifestyle and general medical and otological history [8].

The study was part of the UNITI-project [11] and used data gathered over the course of the UNITI-RCT.

**Audiological assessment**

Standard air and bone conduction hearing thresholds were obtained by using an audiometer (AC-40, Interacoustic, Middelfart, Denmark) in a soundproof booth (C-120, Diatec, Spain). The air-conduction hearing thresholds for the frequencies of 500Hz, 1KHz and 2KHz were retrieved from the audiograms and used to calculate the pure tone average (PTA) on each individual. The air conduction hearing thresholds at 4KHz and 8KHz were used as predictors of NIHL and ARHL respectively.

Individuals were categorised according to audiometric criteria defined in the UNITI-RCT protocol[11], distinguishing between bilateral SNHL (hearing thresholds >25dBHL in both ears for any frequency from 0.5-4KHz); unilateral-SNHL (hearing thresholds
>25dBHL in one ear for any frequency from 0.5-4KHz), or normal hearing (hearing thresholds ≤25dBHL in both ears at any frequency from 0.5-4KHz).

Cognitive and psychological assessment

Montreal Cognitive Assessment (MoCA) tool

The MoCA test was used for the assessment of cognitive functions. The MoCA test covers working memory, short-term memory, linguistic functions, visuospatial capability or time and space orientation [12]. The scores obtained can range between 0 and 30. A cut-off point of 26 yielded the best balance between sensitivity and specificity for detecting MCI, according to the MoCA reference scores (https://mocacognition.com/). The following ranges may be used to grade severity: 18–25: MCI (average MoCA-score: 22). 10–17: Moderate cognitive impairment and Alzheimer’s Diseases (average MoCA-score: 16). Fewer than 10: Severe cognitive impairment. This test includes a score correction according to the patient’s academic level[20].

Patient-Health Questionnaire depression scale (PHQ-9)

The PHQ-9 was used to assess depressive symptoms[21]. The PHQ-9 is a self-administered test, which consists of 9 items assessing depressive symptoms, according to DSM-V criteria. The options for each question are “never” (0 points), “some days” (1 point), “more than half of the days” (2 points) and “almost every day” (3 points). The sum of the scores can range from 0 to 27 points, (1-4: no depressive symptoms; 5-9: mild-depressive symptoms; 10-14: moderate-depressive symptoms; 15-27: severe-depressive symptoms)[17,21].

Assessment of auditory symptoms

Tinnitus Handicap Inventory (THI)
To assess the annoyance related to tinnitus, the THI was used. This questionnaire has 25 and 3 subscales: functional, emotional and catastrophizing tinnitus. Total scores range from 0 to 100 points, with 5 levels of severity: very mild (0-16), mild (18-36), moderate (38-56), severe (58-76) and catastrophic (78-100) [17, 21–23].

Hyperacusis assessment (Questionnaire on Hypersensitivity to Sound, GÜF-test)

This questionnaire consists of 15 questions and the total score obtained can range from 0 to 45 points. These scores can be organized into 4 handicap levels: grade-I (score 0-10, slight handicap), grade-II (11-17, moderate handicap), grade-III (18- 25, severe handicap), grade-IV (26-45, very-severe handicap)[19].

European School for Interdisciplinary Tinnitus Research Screening Questionnaire (ESIT-SQ).

ESIT-SQ is a self-administered questionnaire including 39 questions for clinical and tinnitus profiling: 17 general questions and 22 tinnitus-specific questions. It was developed with specific attention to questions about potential risk factors for tinnitus and tinnitus characteristics (including perceptual characteristics, modulating factors, and associations with co-existing conditions)[25].

Statistical analysis

The following demographic variables were retrieved from the ESIT-SQ: sex, age, educational level, episodes of vertigo and tinnitus-laterality.

First, we performed a descriptive analysis for the MoCA, PHQ-9, THI and GÜF scores (mean± standard deviation (SD). The Shapiro-Wilk test was used to determine if the MoCA-scores were normally distributed. Since MoCA-scores did not follow a normal
distribution, we used the non-parametric Mann Whitney-U test to compare the MoCA-scores across different centres and according to the hearing thresholds. Next, Spearman’s correlation coefficients were calculated to generate correlation matrices between all the variables, we performed a multiple lineal regression to estimate the effect of all variables in MoCA score. A p-value < 0.05 was considered statistically significant. All statistical analyses were performed using R-studio software (Version 4.1.3, R Foundation for Statistical Computing, Vienna, Austria).

We also tested several machine learning (ML) models to predict MoCA results (score<26 versus score≥26) based on audiological and psychometric variables. For this, individuals were randomly allocated into 2 groups: training (80%) and test groups (20%) to compare four supervised ML algorithms: Logistic[26], Extreme Gradient boosting (XGBoost)[27], Adaptive boosting (Adaboost)[28] and Gradient Boosted Decision Tree (GBDT)[29].

**Results**

The distribution of MoCA-scores was significantly different among participants recruited in the four centres (Figure 1). There were no differences between individuals recruited in Berlin and Regensburg (p=0.54) or Athens and Granada (p=0.29); however, when we compared the MoCA-scores between German and Mediterranean (MED) individuals, a statistically significant difference was found with lower values for the MED subjects (p<0.01). For this reason, we performed all statistical analyses separately in both groups.

**Sample description**

A descriptive analysis of the main sociodemographic, audiological and psychometric variables was performed (Table 1). The two groups (MED, n=184; and German, n=196) showed significant differences for age (MED: 50.16±12.21 years, German: 53.81±12.79 years), hearing thresholds (PTA for MED: 24.77±14.17 dB, PTA for German:
16.01± 10.49 dB), mean value of MoCA-scores (MED: 26.11±2.22, German: 27.07±1.84),
percentage of individuals with a MoCA-score under of the cut-off (MED: 42.4%, German:
24.4%) and educational level, where the greatest difference was found in individuals with
middle education level (MED: 9.3%, German: 33%) and university level (MED: 58.5%,
German: 41.8%, all p<0.01).

Both groups were stratified according to hearing threshold, and the individuals with
bilateral SNHL were the group with greatest differences for age (MED: 55.22±10.28
years, German: 59.19±10.04 years, p<0.01), PTA (MED: 32.11±14.15 dB, German:
21.08±10.15dB, p<0.01), MoCA-score (MED: 25.83±2.15, German: 27.03±1.86,
p<0.01), percentage of patients with a MoCA-score under of the cut-off (MED: 45%,
German: 22.4%, p<0.01) and educational level (MED: 14%, German: 34.8%, p<0.01).

For the unilateral SNHL group (MED, n=29; German, n=24), we also observed
significant differences for PTA and educational level.

Individuals with tinnitus and normal hearing (MED, n=55, German, n=56) also showed
significant differences for PTA (MED: 13.43±4.48 dB, German: 6.84±4.50 dB, p<0.01),
percentage of patients with a MoCA-score below the cut-off (MED: 40%, German: 16.1%,
p<0.01), and level of education (MED: 3.6%, German: 27.3%, p<0.01).

Cognitive screening and hearing threshold

MoCA-scores were compared between individuals with normal hearing, unilateral or
bilateral HL, but no significant differences were found either in then MED or the German
group (Suppl. tables 1 and 2).

Cognitive screening
To visualize the relationship among high-frequency HL, MoCA and THI-scores, 3D-scatter plot were designed for MED and German groups (Figure 2). Next, correlation matrices were calculated for all variables in MED (Table 2) and German groups (Table 3). For the MED group, MoCA-scores were associated with educational level (r=0.24, p<0.01), age (r=-0.19, p<0.01), THI-scores (r=-0.15, p<0.05), hearing thresholds at PTA (r= -0.16, p<0.05), at 4KHz (r=-16, p<0.05) and 8KHz (r=-0.15, p<0.05). For the German group, we observed statistically significant associations between MoCA-scores and educational level (r= 0.26, p<0.01), age (r=-0.25, p<0.01), THI-score (r= -0.22, p<0.01), hearing threshold at 8KHz (r=-0.18, p<0.05) and with GÜF-scores (r= 0.15, p<0.05).

A multiple linear regression model was generated to predict MoCA scores with THI, age and hearing threshold in the PTA, 4KHz and 8KHz. In the German group, the model explained a moderate proportion of variance (F (5, 190) = 5.80, p<.001, adj. R² = 0.11); however, for the MED group, the model explained a small proportion of variance (F (5, 177) = 3.10, p = 0.010, adj. R² = 0.05).

Since 70% of individuals with tinnitus had bilateral or unilateral SNHL, we analysed the impact on cognition of the covariates associated with the MoCA score (Table 4). We observed a significant effect of THI in both MED (p < 0.05), and German groups (p< 0.01) and a significant effect of age in both groups (p < 0.05) with a stronger effect in the German group (p< 0.01).

Depression screening (PHQ-9)

No correlation was observed between PHQ-9 and MoCA-scores either in MED (r=-0.14, p>0.05) nor German participants (r=-0.10, p>0.05). However, significant associations
were found between PHQ-9 and THI-scores, and also for PHQ-9 and GÜF-scores in both samples (all, p<0.01).

Machine Learning model

The XGBoost algorithm was the method that best predicted cognitive decline for both groups. For the MED group, the variables Age, GÜF-score, hearing threshold at 8KHz, THI-score, and educational levels were used as predictors, and XGBoost showed an accuracy of 0.65, 95% CI (0.47, 0.80), with precision and recall of 0.7. In the German group, the model used the variables THI-score, age, hearing threshold at 4KHz, hearing threshold at 8KHz and educational level as predictors, and XGBoost showed an accuracy of 0.76 95% CI (0.59, 0.88), with a precision of 0.84 and a 0.80 recall.

Discussion

Our results suggest an association between tinnitus distress and MCI. Higher THI scores are associated with lower MoCA-scores. Although additional factors such as education level, age and high-frequency HL need to be considered in each individual, from a clinical perspective it seems reasonable to perform a cognitive screening in individuals with severe or catastrophic scores in the THI. Additionally, PHQ-9 scores were associated with tinnitus and hyperacusis handicap, regardless of the HL. These findings were found in two sets of participants recruited within the UNITI-RCT: MED (Athens, Granada) and German (Berlin and Regensburg).

An unexpected finding was the significant differences in the patient samples from Germany and the Mediterranean countries. The MED group had lower MoCA-scores and higher PTA thresholds in the bilateral SNHL, unilateral-SNHL and normal hearing subgroups, than the German cohort. The association between higher HL and lower cognitive function is known from subjects with Alzheimer's disease who have worse
hearing thresholds in PTA than age-matched controls [32]. Our findings support an association of MoCA with the education level, age, hearing threshold at 8KHz and THI-scores and confirm previous studies that reported the association of high-frequency HL and cognitive impairment [33, 34].

Presbycusis is defined as bilateral, symmetric, progressive HL that increases with age, typically involving first the high-frequencies [31]. We did find an association between high-frequency HL (8KHz) in both groups with a lower MoCA-score. A moderate association between moderate/severe HL and memory performance has been previously reported[31]. Other studies also reported that people with HL had significantly lower MoCA-scores, compared to normal-hearing population, and this was related to a clinically significant effect[34].

We found an association between lower MoCA-scores and worse hearing threshold at 4KHz in the MED. HL at 4KHz has been related to noise exposure[36,37]. In this regard, a study in rodents reported a subset of younger animals with deficits in spatial learning after noise exposure. These findings suggest that noise exposure may be associated with an increased risk of cognitive impairment in spatial memory in vulnerable subjects[38].

This association between HL and cognitive impairment is consistent with current literature, which confirms that hearing impairment is an independent and modifiable risk factor for cognitive impairment, so it is necessary to understand the mechanisms underlying the correlation between hearing and cognition, in order to prevent the onset of hearing impairment and, therefore, cognitive impairment[39]. The differences found in hearing thresholds between German and MED may explain the lower scores found in MoCA, although a larger sample size will be needed to confirm these findings. Different studies suggest that the prevalence of Alzheimer’s Disease in Southern Europe is higher compared to Northern Europe[40]. In our study, the MoCA-scores were higher in the
German group than in the MED group; the percentage of individuals with MoCA-score below the cut-off was also lower in the German group (German 24%; MED: 42.4%). Moreover, the hearing thresholds were significantly better in German than in MED, for all participants, but also individuals with bilateral SNHL or unilateral SNHL.

We found a negative correlation between MoCA and THI-scores in both groups. These results confirm that the prefrontal region governs cognitive functions [9,41], and frontal neural dysfunction may hinder tinnitus habituation and trigger emotional distress linked to the limbic system [42]. Moreover, patients with chronic tinnitus exhibited difficulties in attention and memory tests. According to the Cognitive-perceptual load theory [43] continuous perception of tinnitus may consume perceptual resources like stimulus discrimination, contributing to an increased cognitive load [42,43]. In this sense, working memory issues could be related to the emotional distress caused by tinnitus than to a direct impairment [44].

From our data we can conclude that cognitive impairment in tinnitus patients is related to high THI-scores, which in turn reflect the emotional distress induced by tinnitus [44]. As we have no data from a control group without tinnitus, we cannot draw any conclusions about a possible relationship between the perception of tinnitus and cognitive impairment. Moreover, there are a large number of variables such as age or HL, which are directly associated with tinnitus and which all are associated with cognitive function[45].

In our study, no significant correlation was found between PHQ-9 score and MoCA-score. These results differ from the literature where Major Depression is often associated with MCI[46]. Nevertheless, a significant correlation has been found between PHQ-9, THI and GÜF-scores, which suggests that hyperacusis is a relevant factor in severe tinnitus.
A systematic review including 18 studies between 1982 and 2011 found a significant association between tinnitus and depression (p<0.01). The authors postulated that there may be at least three potential connections between depression and tinnitus: “depression affecting tinnitus, tinnitus predisposing to depression, and tinnitus appearing as a comorbidity in patients with depression”. The majority of these studies found that depression either predisposes to tinnitus or occurs as a consequence of this symptom.

Given the strong association of tinnitus with anxiety, depression, HL and hyperacusis, we should use a wide range of instruments to assess the full impact of tinnitus on the patient's quality of life and should refer a patient for treatment of depression, especially when the patient presents with severe anxiety and hyperacusis.

There is an association between tinnitus-distress severity and cognitive function, which could be a critical element in the process of characterizing the psychological impact of the tinnitus on each patient. This is particularly relevant, as impaired cognitive abilities and attention deficits have to be taken into account in individualized therapeutic management.

**Limitations**

This study had several limitations. The most relevant is the lack of a control group that can be used as a reference for MoCA-scores. However, most of the questionnaires included in this study were specific for symptom-orientated (e.g., THI for patients with tinnitus, GÜF for patients with hyperacusis), so the relevance of recording these questionnaires in healthy patients is limited.

In addition, the design of the UNITI-RCT, including audiological assessment and multiple questionnaires prevented the use of other relevant tests for the detection of cognitive impairment, such as the Weschler intelligence test (WAIS-IV) or Mini-
Mental State Examination (MMSE)[52,53], or the Beck Depression Inventory-II (BDI-II)[54,55].


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Figures legends and supplemental material

Figure 1. Cognitive screening in individuals with chronic tinnitus. (a) Frequency histogram of the MoCA-scores from each site. (b) Box-plots of the MoCA-score differences according to hearing threshold in Mediterranean and German individuals.

No differences are discernible.

Figure 2. Visualization of relationship between MoCA-scores, THI-scores and Average 8KHz frequency values (high-frequency hearing loss). Variables in Mediterranean and German group in a 3D scatter-plot. THI: Tinnitus Handicap Inventory; MoCA: Montreal Cognitive Assessment.

Supplemental material

Suppl. table 1. Correlation matrix for audiological, sociodemographic and psychometric variables in Mediterranean individuals with chronic tinnitus and bilateral SNHL (N=100).

Suppl. table 2. Correlation matrix for audiological, sociodemographic and psychometric variables in Mediterranean individuals with chronic tinnitus and unilateral SNHL (N=29)
Table 1. Audiological and psychometric variables in Mediterranean and German individuals with chronic tinnitus (n=380).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mediterranean</th>
<th>Total</th>
<th>p-value</th>
<th>Bilateral SNHL</th>
<th>Mediterranean</th>
<th>German</th>
<th>p-value</th>
<th>Unilateral SNHL</th>
<th>Mediterranean</th>
<th>German</th>
<th>p-value</th>
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<td>100%</td>
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<td>12.2%</td>
<td>30.4%</td>
<td>28.6%</td>
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<tr>
<td>Age</td>
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<td>&lt;0.01**</td>
<td>32.11±14.15</td>
<td>21.08±10.15</td>
<td>&lt;0.01**</td>
<td>20.97±10.27</td>
<td>12.88±4.86</td>
<td>0.02*</td>
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<td>&lt;0.01**</td>
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<tr>
<td>Average 4KHz</td>
<td>36.45±20.77</td>
<td>36.35±18.39</td>
<td>0.69</td>
<td>51.77±14.73</td>
<td>48.79±11.09</td>
<td>0.27</td>
<td>25.4±14.74</td>
<td>28.62±6.12</td>
<td>0.03*</td>
<td>14.41±6.05</td>
<td>13.88±7.72</td>
<td>0.77</td>
<td></td>
</tr>
<tr>
<td>Average 8KHz</td>
<td>42.98±24.43</td>
<td>42.15±20.76</td>
<td>0.93</td>
<td>58.26±19.51</td>
<td>54.01±14.83</td>
<td>0.06</td>
<td>31.8±16.88</td>
<td>34.23±13.75</td>
<td>0.31</td>
<td>21.09±13.74</td>
<td>20.96±14.40</td>
<td>0.84</td>
<td></td>
</tr>
<tr>
<td>THI Score</td>
<td>24.77±14.17</td>
<td>16.01±10.49</td>
<td>&lt;0.01**</td>
<td>55.22±10.28</td>
<td>59.19±10.04</td>
<td>0.01**</td>
<td>45.62±10.55</td>
<td>52.21±11.80</td>
<td>0.02*</td>
<td>43.35±12.16</td>
<td>43.36±11.73</td>
<td>0.75</td>
<td></td>
</tr>
<tr>
<td>MoCA Score</td>
<td>26.11±2.22</td>
<td>27.07±1.84</td>
<td>&lt;0.01**</td>
<td>25.83±2.15</td>
<td>27.03±1.86</td>
<td>&lt;0.01**</td>
<td>26.66±2.68</td>
<td>27.12±1.87</td>
<td>0.7</td>
<td>26.33±2.04</td>
<td>27.12±1.83</td>
<td>0.03**</td>
<td></td>
</tr>
<tr>
<td>MoCA Failure</td>
<td>42.4%</td>
<td>24.4%</td>
<td>&lt;0.01**</td>
<td>45%</td>
<td>22.4%</td>
<td>&lt;0.01**</td>
<td>37.9%</td>
<td>20.8%</td>
<td>0.17</td>
<td>40%</td>
<td>16.1%</td>
<td>&lt;0.01**</td>
<td></td>
</tr>
<tr>
<td>GÜF Score</td>
<td>14.18±8.56</td>
<td>12.69±7.15</td>
<td>0.17</td>
<td>15.3±8.63</td>
<td>12.96±7.80</td>
<td>0.06</td>
<td>14.14±9.53</td>
<td>13.08±6.86</td>
<td>0.92</td>
<td>12.24±7.67</td>
<td>11.96±5.86</td>
<td>0.87</td>
<td></td>
</tr>
<tr>
<td>PHQ-9</td>
<td>7.74±5.84</td>
<td>7.71±4.72</td>
<td>0.40</td>
<td>8.13±6.00</td>
<td>7.45±5.21</td>
<td>0.59</td>
<td>8.66±5.56</td>
<td>7.62±4.23</td>
<td>0.27</td>
<td>7.51±5.71</td>
<td>8.29±3.81</td>
<td>0.09</td>
<td></td>
</tr>
<tr>
<td>Bilateral tinnitus</td>
<td>73.3%</td>
<td>78.7%</td>
<td>0.23</td>
<td>74.7%</td>
<td>79.4%</td>
<td>0.43</td>
<td>50%</td>
<td>77.3%</td>
<td>0.05*</td>
<td>83.0%</td>
<td>78.0%</td>
<td>0.51</td>
<td></td>
</tr>
<tr>
<td>Vertigo episode</td>
<td>46.7%</td>
<td>58.1%</td>
<td>0.02*</td>
<td>51%</td>
<td>63.4%</td>
<td>0.06</td>
<td>32.1%</td>
<td>54.2%</td>
<td>0.1</td>
<td>45%</td>
<td>49.1%</td>
<td>0.73</td>
<td></td>
</tr>
<tr>
<td>Education (N,%)</td>
<td></td>
<td></td>
<td>&lt;0.01**</td>
<td></td>
<td></td>
<td>0.01**</td>
<td></td>
<td></td>
<td>0.02*</td>
<td></td>
<td>0.01**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elementary</td>
<td>13(7.1%)</td>
<td>16(8.4%)</td>
<td>0.57</td>
<td>8(8.8%)</td>
<td>13(11.6%)</td>
<td>0.27</td>
<td>2(7.4%)</td>
<td>1(4.2%)</td>
<td>0.5</td>
<td>3(5.4%)</td>
<td>2(3.6%)</td>
<td>0.65</td>
<td></td>
</tr>
<tr>
<td>Middle</td>
<td>17(9.3%)</td>
<td>63(33%)</td>
<td>&lt;0.01**</td>
<td>14(14%)</td>
<td>39(34.8%)</td>
<td>&lt;0.01**</td>
<td>1(3.7%)</td>
<td>9(37.5%)</td>
<td>&lt;0.01**</td>
<td>2(3.6%)</td>
<td>15(27.3%)</td>
<td>&lt;0.01**</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>46(25.1%)</td>
<td>32(16.8%)</td>
<td>0.11</td>
<td>23(23%)</td>
<td>14(12.5%)</td>
<td>0.13</td>
<td>7(25.9%)</td>
<td>6(25%)</td>
<td>0.78</td>
<td>16(29.1%)</td>
<td>12(21.8%)</td>
<td>0.4</td>
<td></td>
</tr>
<tr>
<td>University</td>
<td>107(58.5%)</td>
<td>80(41.8%)</td>
<td>0.04*</td>
<td>55(55.5%)</td>
<td>46(41.1%)</td>
<td>0.37</td>
<td>17(63%)</td>
<td>8(33.3%)</td>
<td>0.07</td>
<td>34(61.8%)</td>
<td>26(47.3%)</td>
<td>0.24</td>
<td></td>
</tr>
<tr>
<td>Smoker status</td>
<td></td>
<td></td>
<td>&lt;0.01**</td>
<td></td>
<td></td>
<td>0.01**</td>
<td></td>
<td></td>
<td>0.02*</td>
<td></td>
<td>0.01**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>38.6%</td>
<td>40.3%</td>
<td>0.62</td>
<td>34%</td>
<td>38.4%</td>
<td>0.30</td>
<td>32.1%</td>
<td>41.7%</td>
<td>0.81</td>
<td>50.0%</td>
<td>43.6%</td>
<td>0.57</td>
<td></td>
</tr>
<tr>
<td>Former</td>
<td>37.5%</td>
<td>46.1%</td>
<td>0.12</td>
<td>37%</td>
<td>49.1%</td>
<td>0.06</td>
<td>50%</td>
<td>58.3%</td>
<td>0.9</td>
<td>32.1%</td>
<td>34.6%</td>
<td>0.86</td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>23.9%</td>
<td>13.6%</td>
<td>0.03*</td>
<td>29%</td>
<td>12.5%</td>
<td>0.02*</td>
<td>17.9%</td>
<td>0%</td>
<td>0.01**</td>
<td>17.9%</td>
<td>21.8%</td>
<td>0.66</td>
<td></td>
</tr>
</tbody>
</table>

* Indicates p < .05. ** indicates p < .01. SNHL, Sensorineural hearing loss; PTA, pure tone average; THI, Tinnitus Handicap Inventory; MoCA, Montreal Cognitive Assessment; MoCA Failure, MoCA score < 26; GÜF, Hyperacusis questionnaire score; PHQ-9, Patient Health Questionnaire.
Table 2. Correlation matrix for audiological, sociodemographic and psychometric variables in Mediterranean individuals with chronic tinnitus (N=184).

<table>
<thead>
<tr>
<th>Variable</th>
<th>MoCA score</th>
<th>THI score</th>
<th>GÜF score</th>
<th>AV.PTA</th>
<th>AV.4KHz</th>
<th>AV.8KHz</th>
<th>PHQ-9 score</th>
<th>Education level</th>
<th>Smoking status</th>
</tr>
</thead>
<tbody>
<tr>
<td>THI score</td>
<td>-0.15*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GÜF score</td>
<td>-0.14</td>
<td>0.61**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AV.PTA</td>
<td>-0.16*</td>
<td>0.11</td>
<td>0.10</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AV.4KHz</td>
<td>-0.16*</td>
<td>0.11</td>
<td>0.12</td>
<td>0.73**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AV.8KHz</td>
<td>-0.15*</td>
<td>0.09</td>
<td>0.15*</td>
<td>0.62**</td>
<td>0.80**</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PHQ-9 score</td>
<td>-0.14</td>
<td>0.67**</td>
<td>0.55**</td>
<td>0.06</td>
<td>0.04</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education level</td>
<td>0.24**</td>
<td>-0.14</td>
<td>-0.11</td>
<td>-0.13</td>
<td>-0.16*</td>
<td>-0.09</td>
<td>-0.20*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking status</td>
<td>0.04</td>
<td>0.02</td>
<td>0.04</td>
<td>0.05</td>
<td>0.13*</td>
<td>0.14</td>
<td>-0.07</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>-0.19**</td>
<td>-0.08</td>
<td>-0.02</td>
<td>0.34**</td>
<td>0.46**</td>
<td>0.53**</td>
<td>-0.02</td>
<td>-0.10</td>
<td>0.07</td>
</tr>
</tbody>
</table>

* Indicates p < .05. ** indicates p < .01. MoCA, Montreal Cognitive Assessment; THI, Tinnitus Handicap Inventory; GÜF, Hyperacusis questionnaire score; AV, Average; PTA, pure tone average; PHQ-9, Patient Health Questionnaire
Table 3. Correlation matrix for audiological, sociodemographic and psychometric variables in German individuals with chronic tinnitus (N=196).

<table>
<thead>
<tr>
<th>Variable</th>
<th>MoCA score</th>
<th>THI score</th>
<th>GÜF score</th>
<th>AV.PTA</th>
<th>AV.4KHz</th>
<th>AV.8KHz</th>
<th>PHQ-9 score</th>
<th>Education level</th>
<th>Smoking status</th>
</tr>
</thead>
<tbody>
<tr>
<td>THI score</td>
<td>-0.22**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GÜF score</td>
<td>-0.15*</td>
<td>0.62**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AV.PTA</td>
<td>-0.06</td>
<td>0.16*</td>
<td>0.20**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AV.4KHz</td>
<td>-0.11</td>
<td>0.09</td>
<td>0.14</td>
<td>0.70**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AV.8KHz</td>
<td>-0.18*</td>
<td>0.08</td>
<td>0.11</td>
<td>0.58**</td>
<td>0.79**</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PHQ-9 score</td>
<td>-0.10</td>
<td>0.64**</td>
<td>0.50**</td>
<td>0.04</td>
<td>-0.08</td>
<td>-0.13</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education level</td>
<td>0.25**</td>
<td>0.17*</td>
<td>-0.18*</td>
<td>-0.11</td>
<td>-0.14</td>
<td>0.14*</td>
<td>-0.07</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking status</td>
<td>-0.03</td>
<td>0.09</td>
<td>-0.04</td>
<td>-0.03</td>
<td>-0.01</td>
<td>0.01</td>
<td>0</td>
<td>-0.09</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>-0.25**</td>
<td>0.01</td>
<td>0.04</td>
<td>0.43</td>
<td>0.60**</td>
<td>0.63**</td>
<td>-0.13</td>
<td>-0.18*</td>
<td>0.04</td>
</tr>
</tbody>
</table>

* Indicates p < .05. ** indicates p < .01. MoCA, Montreal Cognitive Assessment; THI, Tinnitus Handicap Inventory; GÜF, Hyperacusis questionnaire score; AV, Average; PTA, pure tone average; PHQ-9, Patient Health Questionnaire.
Table 4. Effects of covariates in multiple regression analysis for Mediterranean and German Group.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Variables</th>
<th>Unstandardized Coefficients</th>
<th>Standardized Coefficients</th>
<th>t</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mediterranean</td>
<td></td>
<td>B</td>
<td>Std. Error</td>
<td>Beta</td>
<td></td>
</tr>
<tr>
<td>(Constant)</td>
<td>28.949</td>
<td>0.826</td>
<td></td>
<td>35.034</td>
<td>&lt;.001**</td>
</tr>
<tr>
<td>THI</td>
<td>-0.018</td>
<td>0.007</td>
<td>-0.178</td>
<td>-2.431</td>
<td>0.016*</td>
</tr>
<tr>
<td>Av.PTA</td>
<td>-0.001</td>
<td>0.017</td>
<td>-0.008</td>
<td>-0.079</td>
<td>0.937</td>
</tr>
<tr>
<td>Av.4KHz</td>
<td>-0.013</td>
<td>0.015</td>
<td>-0.122</td>
<td>-0.881</td>
<td>0.379</td>
</tr>
<tr>
<td>Av.8KHz</td>
<td>0.004</td>
<td>0.012</td>
<td>0.045</td>
<td>0.348</td>
<td>0.728</td>
</tr>
<tr>
<td>Age</td>
<td>-0.032</td>
<td>0.016</td>
<td>-0.176</td>
<td>-2.045</td>
<td>0.042*</td>
</tr>
<tr>
<td>German</td>
<td></td>
<td>B</td>
<td>Std. Error</td>
<td>Beta</td>
<td></td>
</tr>
<tr>
<td>(Constant)</td>
<td>30.061</td>
<td>0.631</td>
<td></td>
<td>47.65</td>
<td>&lt;.001**</td>
</tr>
<tr>
<td>THI</td>
<td>-0.024</td>
<td>0.006</td>
<td>-0.255</td>
<td>-3.689</td>
<td>&lt;.001**</td>
</tr>
<tr>
<td>Av.PTA</td>
<td>0.011</td>
<td>0.016</td>
<td>0.06</td>
<td>0.663</td>
<td>0.508</td>
</tr>
<tr>
<td>Av.4KHz</td>
<td>0.017</td>
<td>0.013</td>
<td>0.166</td>
<td>1.333</td>
<td>0.184</td>
</tr>
<tr>
<td>Av.8KHz</td>
<td>-0.015</td>
<td>0.01</td>
<td>-0.167</td>
<td>-1.446</td>
<td>0.15</td>
</tr>
<tr>
<td>Age</td>
<td>-0.037</td>
<td>0.013</td>
<td>-0.256</td>
<td>-2.865</td>
<td>0.005**</td>
</tr>
</tbody>
</table>

Dependent Variable: MoCA score. Indicates p < .05. ** indicates p < .01.