



Personality traits associated with tinnitus: A systematic review and contributing genetic variants

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ABSTRACT

Chronic tinnitus is a multifaceted condition associated with auditory (hearing loss, hyperacusis), neurological (headache) and psychological disorders (anxiety, depression). Personality traits may determine how tinnitus is perceived, and common genetic variation contributes to shape personality. The goal of this systematic review is to analyze evidence supporting a link between personality traits and tinnitus. Published articles about tinnitus and personality related to the Big Five Traits were included. Based on 7 studies, this systematic review identified the neuroticism trait as the main potential connection between personality and tinnitus suffering. The consistency of this relationship is evident across different Big Five personality tools, with similar outcomes observed regardless of the instrument used, reinforcing the consistency of this association. In order to establish a genetics association, a GWAS based search revealed common genetic variants in the *GRM5*, *XKR6*, *GRM8*, *TCF4*, and *SLC39A8* genes, with *SLC39A8* identified as a shared missense variant rs13107325 (C/T, p.Ala391Thr) between neuroticism and tinnitus. The role of these genes in important neural functions points to possible shared mechanisms underlying both conditions.

1. Introduction

Tinnitus is defined as the perception of sound without an external stimulus to trigger it. Tinnitus is a common affection, reported in at least 15 % of the total population, nevertheless, only 1–2 % reports high emotional distress (Mazurek et al., 2023). Evidence from epidemiological studies in twins, adoptees, and familial aggregation supports a genetic contribution to tinnitus that may help distinguish environmental effects from heritability (Cederroth et al., 2019; Gallego-Martinez et al., 2022; Lopez-Escamez and Amanat, 2020).

Tinnitus is related to different symptoms such as sensorineural hearing loss (SNHL) hyperacusis, cognitive impairment and several tinnitus studies have demonstrated the impact of anxiety and depression on the tinnitus perception (Trevis et al., 2018). The psychological process associated with persistent awareness in generalized anxiety disorder and the perceived severity of tinnitus is often described as a feedback

loop which is represented with a catastrophic perception closely linked to feelings of anxiety and depression (McKenna et al., 2014; Ridder et al., 2011; Trevis et al., 2018).

This psychological process may also be related to personality traits, affective disorders such as anxiety and depression have been associated with different personality traits in various studies (Durai and Searchfield, 2016; Mazurek et al., 2023). Most individual differences in personality can be understood in terms of five basic dimensions, commonly known as the Big Five personality traits, which are usually used to describe human personality (Costa and McCrae, 1992). Neuroticism, also referred to as negative emotionality, reflects a predisposition to experience persistent negative emotions such as worry, anger, frustration, and envy. It is often associated with anxiety and depressive symptoms. Agreeableness describes the tendency to maintain positive interpersonal relationships and to be cooperative and compassionate toward others. Extraversion is characterized by sociability,

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assertiveness, and a tendency to seek stimulation through social engagement. Conscientiousness refers to a tendency to be organized, disciplined, and goal-oriented, and is marked by a strong sense of responsibility and diligence. Finally, openness to experience, or simply openness, is associated with intellectual curiosity, creativity, and a willingness to embrace new ideas, perspectives, and experiences (Babcock and Wilson, 2020; Yoneda et al., 2023).

Among these, neuroticism is the Big Five trait of personality which have been most studied due to its strong correlation with depression and anxiety (Lyon et al., 2020; Naragon-Gainey and Watson, 2011; Uliaszek et al., 2010) and can be related with the ongoing of the suffering

Personality traits have an important implication in thought, feelings and behavior. Environmental factors play a fundamental role in shaping personality phenotypes (Briley and Tucker-Drob, 2014). However, there is also a genetic component, as research has demonstrated that certain personality traits exhibit heritability (Sanchez-Roige et al., 2018). Study based on genome-wide analyses for personality traits have identified SNVs in *XKR6* and *L3MBTL2* genes as predictive for Neuroticism and in *GBE1*, *MTMR9*, *PCDH15*, *WSCD2* and *RBFOX1* for Extraversion (Lo et al., 2017; Sanchez-Roige et al., 2018).

The Big Five personality traits provide more specific information about individuals and their behavior. One of the key factors in tinnitus suffering is how people respond and perceive the stimuli (Schaaf et al., 2010). Therefore, using a specific tool to analyze the personality traits that influence behavior can provide valuable insights for better understanding the condition and treatment outcomes.

In this context, our goal is to explore which personality traits are most commonly associated with tinnitus distress and based on the results, we will further examine the genetic variants that may explain the higher prevalence of tinnitus in individuals with specific personality traits, to explore potential causal relationships.

2. Methods

This review has followed the guidelines from “Preferred Reported Items for Systematic Reviews and Meta-Analyses”, and has been registered in PROSPERO (ID: CRD42025610502)

2.1. Study design

This study was designed as a systematic review. This review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Table S1). Based on the results obtained in our review, we also described the main genetic variants that could explain the relationship between each personality trait and the development of the tinnitus. In accordance with the methodology for systematic reviews, our PICOS question was structured around the following components:

- Participants: Studies reporting on the main personality trait in patients with chronic tinnitus.
- Intervention or variable of interest: Tinnitus distress, personality traits in patients with tinnitus; Identification of genetic variants related to tinnitus and severe tinnitus).
- Comparison: Controlled and uncontrolled studies were included.
- Outcomes (Primary results): Distribution of personality traits and tinnitus distress based on the main quality of life questionnaires: Big Five questionnaires, Tinnitus Handicap Inventory (THI), Visual Analog Scale (VAS) and/or Tinnitus questionnaire (TQ) and association between Neurotic disorder SNVs and Tinnitus disorder SNVs using GWAS Catalog.
- Secondary outcomes: A description of the main features used in the models, such as demographic information, rates obtained in the tinnitus questionnaires.
- Type of Studies: Observational studies, cross-sectional and longitudinal studies were included.

2.2. Search strategy

The bibliographic search was conducted in March 14, 2025. International databases, PubMed, Scopus and Web of Science were used with the following combination of terms: (tinnitus [Title/Abstract]) AND ((big five inventory) OR (bfi) OR (neuroticism) OR (agreeableness) OR (extraversion) OR (conscientiousness) OR (openness) OR (“negative emotion”)). Once the search was performed in both databases, duplicates were eliminated and articles whose title, or abstract did not adjust to the objectives of the review were discarded. The selected records were revised by 2 independent reviewers (ABR, MDCM) and those that did not meet the inclusion criteria were excluded. Discrepancies were resolved by a senior reviewer (PPC). Studies which have not used any questionnaire related to big five traits were excluded.

2.3. Selection criteria

First, we gathered all articles related to relationships between the five personality traits and tinnitus, with the inclusion criteria being that they were in English and had the full text available. Only studies assessing chronic tinnitus using the THI score and the Big Five personality traits were included. Additionally, studies employing various versions of the Big Five Inventory (BFI) and the NEO-FFI, which are based on the Big Five model, were also considered

In addition, the following exclusion criteria were established:

- Animal studies.
- Studies published in languages other than English or Spanish.
- Single case reports.

2.4. Data extraction

Two reviewers (A.B-R and M.D.C.M) independently extracted study characteristics and outcomes from all included studies and then compared the data. In cases where consensus could not be reached, a third reviewer (P.P-C) was consulted. Each paper was reviewed to extract the most relevant information according to the objective of this review. Specifically, data extraction focused on identifying details related to study design, participant demographics, methodology, and outcome measures. Information was systematically collected on each of the Big Five personality traits (agreeableness, conscientiousness, extraversion, neuroticism, and openness) and their reported associations with tinnitus. Additionally, results concerning tinnitus severity, distress levels, and psychological comorbidities such as anxiety and depression were extracted.

The bibliographic search was conducted using Mendeley and Zotero.

2.5. Data synthesis

General information on the sample age, THI score was expressed as mean $\pm$ standard deviations (SD). Sample size, population, sex, and Big Five Inventory tools were also obtained with the results. All statistical analysis and figures were performed using R-studio software (Version 4.2.2, R Foundation for Statistical Computing, Vienna, Austria).

2.6. Quality assessment

The quality of each study was analyzed according to the type of study. For this case, all studies were analyzed using the “Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies” from National Heart, Lung, and Blood Institute (Study Quality Assessment Tools | NHLBI, NIH (n.d.)). A color scale was used to determine the answer to each question (Green-Yes; Red-No; Orange-Not applicable), as summarized on Table 2.

2.7. Genetic data extraction

A search was conducted in the GWAS Catalog (Cerezo et al., 2025) to identify single nucleotide variants (SNVs) associated with neuroticism, neurotic disorder or post-traumatic stress disorder and tinnitus. The search was performed without restrictions on publication year or population. Studies were included if they reported genome-wide significant variants ($p < 10^{-5}$) in human participants, while studies in which tinnitus was induced by ototoxic drugs were excluded. Extracted data included study characteristics (author, year, population, sample size, and phenotype) and variant annotation (rsID, chromosomal position, alleles, gene symbol, effect size, and p-value). SNVs were classified based on their association with tinnitus or neuroticism, and overlaps were analyzed at both the gene and variants levels.

3. Results

3.1. Study selection

According to the eligibility criteria, 7 studies (1260 individuals Female 475 (37,7 %) and male 785 (62,3 %) with an average age of 50.57 were included. Five studies recruited patients in hospitals from Germany (European population) (Langguth et al., 2007; Conrad et al., 2015; Simoes et al., 2019; Schlee et al., 2020), two selected patients from Taiwan and Korea (East Asian Population) (Huang et al., 2022; Jeong et al., 2024) and one study recruited half of the participants in the outpatient clinic (Lithuania, European population) and half via internet (Strumila et al., 2017). The flowchart with the steps followed in this search is shown in Fig. 1.

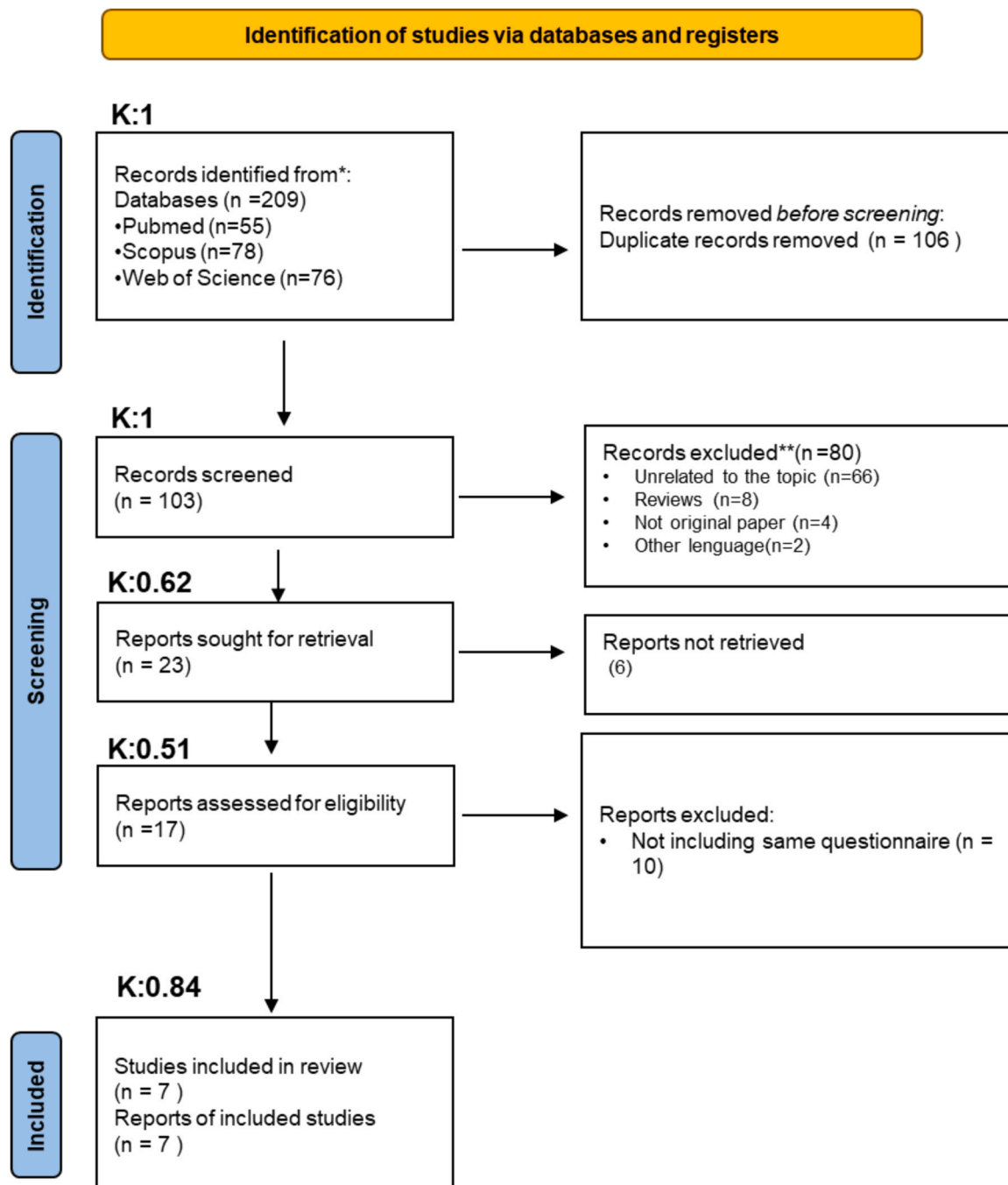


Fig. 1. Flow diagram for study selection.

3.2. Tinnitus and personality traits

All studies have shown a correlation between tinnitus distress and one or more personality traits. BFI-N (Big Five Inventory - neuroticism) has been the most associated trait with tinnitus, not only related to THI score, but also using other questionnaires for tinnitus distress such as VAS) or TQ have been related to personality traits.

Nevertheless, studies performed in Europe have found correlations with two or more traits. In contrast, studies performed in Asia have demonstrated relationships with two or less traits. Table 1 summarizes the main descriptive information and the correlation analysis between tinnitus impact and personality traits.

3.3. Use of the big five inventory tools

A total of 6 different versions of BFI have been used in these articles (Fig. 2a). We found that the most correlated trait is neuroticism (Fig. 2b). The questionnaires most strongly associated with tinnitus distress were the BFP-DS, which showed correlations with four traits. Similarly, results were found using BFI-2 and BFI-10 which found correlations in three traits, The NEO-FFI, BFI-44 and BFI showed correlations with two or fewer traits (Fig. 2c).

3.4. GWAS extraction

A total of 322 SNVs associated with tinnitus were identified across eight genome-wide association studies (GWAS) (Table S2), while 242 SNVs related to neuroticism, neurotic disorder or post-traumatic stress were reported in twenty studies (Table S3). Using the conventional genome-wide significance threshold ($p < 5 \times 10^{-8}$), the total number of identified SNVs was reduced to 66 for tinnitus (from seven studies) and 145 for neuroticism (from ten studies).

A comparative analysis of these datasets showed nine genomic regions shared between tinnitus and neuroticism traits, regardless of whether they are the same SNVs (Table 2). Among these, five variants

were located within protein-coding genes, including *XKR6*, *GRM5*, and *GRM8*, *SLC39A8*, and *TCF4*. The remaining four regions were intergenic, defined by their closest flanking genes (*LINC02571* - *HLA-B*, *RPSAP2* - *NOP56P1*, *FBXL17* - *LINC01023*, and *HMGNA4* - *ABT1*). Notably, the common variant rs13107325 (NC_000004.12:g.102267552 C>T, p. Ala391Thr) was independently found to be associated with 2 GWAS (Clifford et al., 2024; Gong et al., 2023; Zhou et al., 2023), located in the *SLC39A8* gene. When applying the more stringent threshold ($p < 5 \times 10^{-8}$), the overlap between tinnitus and neuroticism was reduced to four coincidences: *FBXL17* - *LINC01023*, *HMGNA4* - *ABT1*, *SLC39A8*, and *TCF4*.

3.5. Quality assessment

A comprehensive assessment of the risk of bias and associated concerns has been performed for each study (Table 3).

The overall risk of bias for each questionnaire was low, but the main bias was that the selected studies did not involve any exposures and were conducted without a control group, making the assessment of bias not applicable.

4. Discussion

Our findings indicate a strong influence of personality traits on tinnitus distress, with Neuroticism showing the most significant correlation across all studies. While other personality traits also appear to affect tinnitus distress, the impact of neuroticism stands out as the most prominent. In terms of population differences, Neuroticism was the only trait consistently observed as a significant factor, suggesting a genetic contribution.

4.1. Neuroticism trait relation with tinnitus

Neuroticism is not only the most strongly correlated but also demonstrates the strongest relationship with tinnitus distress (Schlee et al.,

Table 1
Summary of the main findings in Personality traits associated with tinnitus studies.

Authors, Year	Population	Sample (Female)	Age ($\bar{x}$, SD)	THI score ($\bar{x}$ $\pm$ SD)	Questionnaires	Personality traits effects in Tinnitus	Statistics
Langguth B, et al. 2007	European (German)	77 (22)	Female: 49.47 $\pm$ 13.1; Male: 49.37 $\pm$ 13.0	40.30 $\pm$ (24.11)	NEO-FFI	Positive correlation between TQ score and BFI-N; Negative correlation between BFI-A and THI score	BFI-N: $r = 0.276$, $p = 0.028$; BFI-A: $r = -0.367$, $p = 0.028$
Conrad I, et al. 2015	European (German)	373 (155)	51.66 $\pm$ (12.14)	41.33 $\pm$ (18.46)	Big Five Inventory-10	Moderate correlation with BFI-N and Tinnitus Cognitions Scale, BFI-E, and BFI-O significant but weak	BFI-N: $r = 0.29$ ($p < 0.001$), $r = 0.11$ (0.041); BFI-E: -0.17 (0.001); BFI-O: $r = -0.19$ ($p < 0.001$)
R. Strumila et al. (2017)	European (Lithuanian)	212(104)	48.33 $\pm$ (14.02)	48.30 $\pm$ (22.54)	Big Five Personality Dimensions Scale	Correlation between Tinnitus distress and personality traits; High VAS scores predicted high scores in BFI-E, Conscientiousness, BFI-A, BFI-N	OR and 95 % CI: BFI-E = 1.36 (1.12–1.64); BFI-C = 1.47 (1.12–1.89); BFI-A = 1.37 (1.03–1.82); BFI-N = 0.82 (0.68–0.97), $p < 0.05$
Simões, J. et al. 2019	European (German)	388(146)	55.9 $\pm$ (11.9)	49.5 $\pm$ (23.3)	Big Five Index 2 (BFI-2)	both BFI-N and BFI-A positive correlation with THI score, while BFI-E had a negative correlation with THI score	BFI-E, $R^2 = -0.47$, $p < 0.01$; BFI-N, $R^2 = 1.56$, $p < 0.001$; BFI-A, $R^2 = 0.62$, $p < 0.01$
Schlee, W. et al. 2020	European (German)	122(42)	54.0 $\pm$ (10.9)	45.89 $\pm$ (23.47)	Big Five Index 2 (BFI-2)	BFI-E, BFI-C and BFI-O negative correlated with Tinnitus distress; BFI-N positive correlation with tinnitus distress	BFI-N: $r = 0.617$, $p < 0.001$; BFI-E: -0.353 , $p < 0.001$; BFI-C: $r = -0.305$, $p = 0.002$; BFI-O: $r = -0.265$, $p = 0.008$
Huang, Chii-Yuana. Et al. 2022	Asian (Taiwanese)	33(15)	48.3 $\pm$ (15.8)	42.9 $\pm$ (26.2)	BFI-44	Positive correlation between Tinnitus distress and BFI-N	BFI-N: $r = 0.56$, $p < 0.01$
Jeong, H. et al. 2024	Asian (Korean)	33(13)	Mild: 47.9 $\pm$ 12.2 Severe: 50.2 $\pm$ 7.4	Mild: (24.5 $\pm$ 8.6) Severe: (62.9 $\pm$ 12.8)	Big Five Inventory	Positive correlation between Tinnitus distress and BFI-N; negative correlation with BFI-A	BFI-N: $r = 0.377$, $p = 0.043$, BFI-A: $r = -0.279$, $p = 0.020$

BFI-N to specify Neuroticism; BFI-A, Agreeableness; BFI-E, Extraversion; BFI-O, Openness, and BFI-C, Conscientiousness

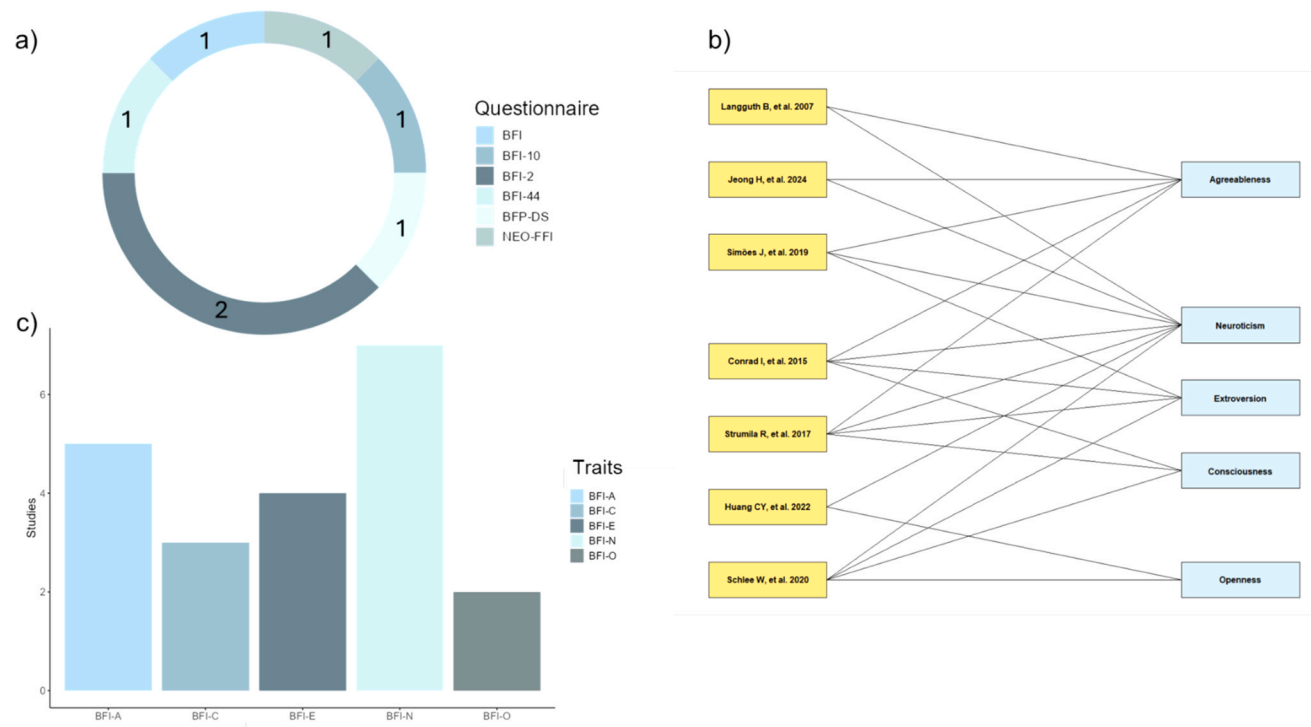


Fig. 2. Distribution of questionnaires, studies, and personality traits. (a) Number of questionnaires used in the analyzed studies. (b) Number of studies reporting an association between personality traits and tinnitus. (c) Frequency of each personality trait appearing in the reviewed studies. BFI: Big Five Inventory; BFI-10: Big Five Inventory-10; BFI-2: Big Five Inventory-2; BFI-44: Big Five Personality Dimension Scale; NEO-FFI: NEO Five-Factor Inventory. BFI-N: Neuroticism; BFI-A: Agreeableness; BFI-E: Extraversion; BFI-O: Openness; BFI-C: Conscientiousness.

Table 2
Genetic overlap between neuroticism and tinnitus identified through GWAS studies.

Neuroticism studies	Sample	Trait	Genes/regions with associated SNPs	Tinnitus studies	Sample	Trait	Common SNPs found
Cai N	274,107 British ancestry individuals	Neuroticism	GRM5 XKR6	Shahbazi M.	19,907 European ancestry cases, 114,930 European ancestry controls	Tinnitus	No
				Wells HRR	91,424 British ancestry individuals	Tinnitus	No
			GRM8	Bhatt IS	132,164 European ancestry individuals	Tinnitus-related distress	No
			FBXL17 - LINC01023	Clifford RE	481,874 European ancestry individuals	Tinnitus	No
Wendt FR	497,803 European ancestry individuals	Post-traumatic stress disorder (mental health questionnaire or predicted)	TCF4 FBXL17 - LINC01023	Clifford RE	481,874 European ancestry individuals	Tinnitus	No
Gong W	54,854 European ancestry gastroesophageal reflux disease cases, 23,212 European ancestry PTSD cases, 552,920 European ancestry controls	Gastroesophageal reflux disease or posttraumatic stress disorder (pleiotropy)	SLC39A8	Clifford RE	481,874 European ancestry individuals	Tinnitus	rs13107325
Zhou S	At least 23,212 European ancestry cases, at least 151,447 European ancestry controls (MTAG boosted by gastrointestinal tract disorder samples)	Post-traumatic stress disorder (MTAG)	HMGN4 - ABT1 SLC39A8	Clifford RE	481,874 European ancestry individuals	Tinnitus	No
			RPSAP2 - NOP56P1	Shahbazi M.	19,907 European ancestry cases, 114,930 European ancestry controls	Tinnitus	No
Nievergelt CM	23,212 European ancestry cases, 4363 African ancestry cases, 1981 Latino and Native American ancestry cases, 151,447 European ancestry controls, 10,976 African ancestry controls, 3722 Latino and Native American ancestry controls	Post-traumatic stress disorder	LINC02571 - HLA-B	Shahbazi M.	19,907 European ancestry cases, 114,930 European ancestry controls	Tinnitus	No

Table 3
Risk of bias assessment according to the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies from Study Quality Assessment Tools | NHLBI, NIH, n.d.

References	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14	OVERALL
Langguth B, et al. 2007															
Conrad I, et al 2015															
R. Strumila et al. 2017															
Simões, J. et al 2019															
Schlee, W. et al 2020															
Huang, Chii-Yuana. Et al 2022															
Jeong, H. et al 2024															

Green=Yes; Red=No; Orange=Not applicable. According to the guidelines “Not Applicable” does not represent a negative score.

2020; Simoes et al., 2019). These results are consistent with the existing literature (Langguth et al., 2007; McCormack et al., 2014; Strumila et al., 2017). Both Strumila et al. (2017) and Simões et al. (2019) found that the high levels of neuroticism can predict a high THI score, indicating that individuals with a predominant neuroticism trait are more susceptible to experiencing greater tinnitus distress (Simoes et al., 2019; Strumila et al., 2017). Furthermore, neuroticism is closely associated with depressive and stress-related behavior. These findings help explain how individuals cope with tinnitus over time. As we mentioned previously, the perception of tinnitus is subjective, individuals with lower tolerance tend to demonstrate a significant worsening in their perception and related behaviors.

Neuroticism has also been associated with various psychological disorders (Dukalski et al., 2019; Streit et al., 2022). Sahlsten H. et al. (2018) highlight that individuals with chronic tinnitus may exhibit trait associated with obsessive-compulsive personality disorder, which seems to be a predisposing conditions for tinnitus (Sahlsten et al., 2018). The impact of personality traits has also been linked to suicidal behavior (Bi et al., 2017). High neuroticism could be a risk factor for suicidal behavior in people with psychiatric disorders. According with the literature, individuals suffering from tinnitus have been also linked with suicidal ideation, with a reported prevalence of 20,6 % for suicidal ideation in tinnitus populations (Tailor et al., 2021; Tov et al., 2016). A scoping review on tinnitus and suicidal ideation (MacDonald et al., 2023) highlights the importance of developing a theory-informed model of tinnitus and suicide, as there are identifiable risk factors and an association between suicidal ideation, suicidal behavior, and tinnitus.

4.2. Agreeableness and extraversion trait relation with tinnitus

Traits such as agreeableness and extraversion have been associated with tinnitus, although to a lesser extent than neuroticism. The impact of these personality traits on tinnitus-related distress may be attributed to the underlying characteristics and psychological mechanisms associated with these traits. Extraversion is defined by the degree of engagement with the external world and involves traits such as being outgoing or being solitary and agreeableness is defined as a general concern for social harmony including traits such as friendliness and antagonism (Redelmeier et al., 2021). Both traits are linked to social isolation, depression, and anxiety, which are behavioral conditions known to exacerbate tinnitus distress. In some cases, these conditions may even contribute to the onset of tinnitus (Chirakkal et al., 2021). Moreover, the seeking of social support can mitigate tinnitus distress through the mediating effects of resilience and self-esteem (Wang et al., 2021). This highlights the importance of social connections in buffering the

psychological impact on individuals experiencing tinnitus.

4.3. Genetic association between tinnitus and neuroticism

The findings suggest a potential genetic link between tinnitus and neuroticism, with different common variants in nine shared genomic regions identified across studies. The presence of the common variant (rs13107325) within the *SLC39A8* gene highlights a possible molecular intersection between both traits supporting pleiotropic effects. *SLC39A8* encodes a zinc transporter involved in neurophysiological processes, including inflammation (Liu et al., 2013) and synaptic plasticity (S. Li et al., 2022), which have been previously implicated in both tinnitus (Guillon, 2012; Henry et al., 2014; Mennink et al., 2022, 2022) and neuroticism (Dima et al., 2015). In addition, this variant has been also associated with schizophrenia (Tseng et al., 2021; S. Li et al., 2022). While these associations do not imply causality, they support the concurrent observation of tinnitus and neuroticism in the same individuals.

Furthermore, although no further overlapping SNVs have been found, other variants have been found in the same genes. *GRM5* and *GRM8* encode metabotropic glutamate receptors mGluR5 and mGluR8, respectively, which are involved in glutamatergic neurotransmission (Xu et al., 2021). Dysregulation of this pathway has been implicated in the pathogenesis of tinnitus, as excessive glutamate activity can lead to excitotoxicity in auditory pathways (Imsuwansri et al., 2016). Additionally, alterations in glutamatergic signaling have been associated with psychiatric disorders (C.-T. Li et al., 2018), such as schizophrenia, suggesting a potential link between these receptors with tinnitus and neuroticism. *TCF4* is a key transcription factor in brain development as well as synaptic plasticity, verbal memory and language development (Kennedy et al., 2016). Genetic variants in *GRM5* (Matosin et al., 2018), *GRM8*, and *TCF4* (Tavakkoly-Bazzaz et al., 2018; Teixeira et al., 2021)) have been associated with schizophrenia. *XKR6* encodes a membrane protein involved in phosphatidylserine exposure during apoptosis, but its role in the central nervous system remains unclear, although it has been associated with tinnitus and neuroticism (Clifford et al., 2020).

The identification of distinct variants within *GRM5*, *XKR6*, *GRM8*, *TCF4* and *SLC39A8* genes underscores the complex genetic architecture underlying tinnitus and neuroticism. Although only one shared variant in the gene *SLC39A8* was found, the involvement of these genes in key neural processes suggests potential convergent mechanisms contributing to both conditions.

4.4. Future directions and conclusions

Although this review is focused on the association of Big Five Traits

with tinnitus, most of the studies reviewed have not shown a specific causal effect between them or are not included as potential factors to predict the tinnitus experienced. However, given the known genetic basis associated with both neuroticism and tinnitus, it is plausible that shared genetic factors might partly explain their correlation. Since severe tinnitus have not been studied exclusively, possible directions include the analysis of rare variants and their relationship with the most extreme phenotypes. Further exploration of other comorbidities, such as cognitive impairment, depression and anxiety disorders, associated with neuroticism and tinnitus, as well as their possible genetic causes.

As a conclusion, neuroticism seems to play a key role in how strongly individuals are affected by tinnitus, with higher levels of this trait being associated with increased emotional distress and reduced ability to cope. The fact that similar results have been observed across various Big Five personality assessment tools reinforce the reliability of this relationship. Additionally, the discovery of a common genetic variant in the *SLC39A8* gene associated with both tinnitus and neuroticism points to a possible shared biological mechanism that may help explain why these traits often occur together.

5. Limitations

Regarding the limitations of this review, one major issue is the heterogeneity of personality questionnaires, as not all studies use the same version. Additionally, the variable used to measure tinnitus-related distress is assessed through different questionnaires, making comparisons between studies more challenging. Furthermore, the substantial variability in study designs, populations, and outcome measures prevented the use of a meta-analytic approach. As a result, this review adopts a descriptive and exploratory perspective.

Authors contributions

Conceptualization: JAL-E and PP-C. Formal analysis: AB-R, AMP-P, PP-C. Methodology: AB-R, AMP-P, MCM, PP-C. Supervision: JAL-E and PP-C. Writing—original draft: AB-R, AMP-P, MCM, JAL-E and PP-C. Writing—review and editing: AB-R, AMP-P, MCM, JAL-E, PP-C. 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.

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Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work the author(s) used ChatGPT in order to improve the readability of certain sentences. After using this tool, the author(s) reviewed and edited the content as needed and take (s) full responsibility for the content of the published article.

Declaration of Competing Interest

The authors declare no conflict of interest.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.neubiorev.2025.106389.

Data availability

No data was used for the research described in the article.

References

- Babcock, S.E., Wilson, C.A., 2020. Big five model of personality. In: *The Wiley Encyclopedia of Personality and Individual Differences*. John Wiley & Sons, Ltd, pp. 55–60. <https://doi.org/10.1002/9781119547174.ch186>.
- Bi, B., Liu, W., Zhou, D., Fu, X., Qin, X., Wu, J., 2017. Personality traits and suicide attempts with and without psychiatric disorders: analysis of impulsivity and neuroticism. *BMC Psychiatry* 17 (1), 294. <https://doi.org/10.1186/s12888-017-1453-5>.
- Briley, D.A., Tucker-Drob, E.M., 2014. Genetic and environmental continuity in personality development: a meta-analysis. *Psychol. Bull.* 140 (5), 1303–1331. <https://doi.org/10.1037/a0037091>.
- Cederroth, C.R., PirouziFard, M., Trpchevska, N., Idrizbegovic, E., Canlon, B., Sundquist, J., Sundquist, K., Zöller, B., 2019. Association of genetic vs environmental factors in Swedish adoptees with clinically significant tinnitus. *JAMA Otolaryngol. Head. Neck Surg.* 145 (3), 222–229. <https://doi.org/10.1001/jamaoto.2018.3852>.
- Cerezo, M., Solis, E., Ji, Y., Lewis, E., Abid, A., Bircan, K.O., Hall, P., Hayhurst, J., John, S., Mosaku, A., Ramachandran, S., Foreman, A., Ibrahim, A., McLaughlin, J., Pendlington, Z., Stefancsik, R., Lambert, S.A., McMahon, A., Morales, J., Harris, L. W., 2025. The NHGRI-EBI GWAS catalog: standards for reusability, sustainability and diversity. *Nucleic Acids Res.* 53 (D1), D998–D1005. <https://doi.org/10.1093/nar/gkac1070>.
- Chirakkal, P., Al Hail, A.N., Zada, N., Vijayakumar, D.S., 2021. COVID-19 and tinnitus. *Ear Nose Throat J.* 100 (2), 160S–162S. <https://doi.org/10.1177/0145561320974849>.
- Clifford, R.E., Maihofer, A.X., Stein, M.B., Ryan, A.F., Nievergelt, C.M., 2020. Novel risk loci in tinnitus and causal inference with neuropsychiatric disorders among adults of European ancestry. *JAMA Otolaryngol. Head. Neck Surg.* 146 (11), 1015–1025. <https://doi.org/10.1001/jamaoto.2020.2920>.
- Clifford, R.E., Maihofer, A.X., Chatzinakos, C., Coleman, J.R.I., Daskalakis, N.P., Gasperi, M., Hogan, K., Mikita, E.A., Stein, M.B., Tcheandjieu, C., Telese, F., Zuo, Y., Ryan, A.F., Nievergelt, C.M., 2024. Genetic architecture distinguishes tinnitus from hearing loss. *Nat. Commun.* 15 (1), 614. <https://doi.org/10.1038/s41467-024-44842-x>.
- Conrad, I., Kleinstaub, M., Jasper, K., Hiller, W., Andersson, G., Weise, C., 2015. The role of dysfunctional cognitions in patients with chronic tinnitus. In: *Ear and Hearing*, 36. Scopus, pp. e279–e289. <https://doi.org/10.1097/AUD.000000000000168>.
- Costa, P.T., McCrae, R.R., 1992. The five-factor model of personality and its relevance to personality disorders. *J. Personal. Disord.* 6 (4), 343–359. <https://doi.org/10.1521/pedi.1992.6.4.343>.
- Dima, D., Friston, K.J., Stephan, K.E., Frangou, S., 2015. Neuroticism and conscientiousness respectively constrain and facilitate short-term plasticity within the working memory neural network. *Hum. Brain Mapp.* 36 (10), 4158–4163. <https://doi.org/10.1002/hbm.22906>.
- Dukalski, B., Suslow, T., Egloff, B., Kersting, A., Dinges, U.-S., 2019. Implicit and explicit self-concept of neuroticism in borderline personality disorder. *Nord. J. Psychiatry* 73 (3), 159–168. <https://doi.org/10.1080/08039488.2019.1582694>.
- Durai, M., Searchfield, G., 2016. Anxiety and depression, personality traits relevant to tinnitus: a scoping review. *Int. J. Audiol.* 55 (11), 605–615. <https://doi.org/10.1080/14992027.2016.1198966>.
- Gallego-Martinez, A., Escalera-Balsara, A., Trpchevska, N., Robles-Bolivar, P., Roman-Naranjo, P., Frejo, L., Perez-Carpena, P., Bulla, J., Gallus, S., Canlon, B., Cederroth, C.R., Lopez-Escamez, J.A., 2022. Using coding and non-coding rare variants to target candidate genes in patients with severe tinnitus. *NPJ Genom. Med.* 7 (1), 70. <https://doi.org/10.1038/s41525-022-00341-w>.
- Gong, W., Guo, P., Li, Y., Liu, L., Yan, R., Liu, S., Wang, S., Xue, F., Zhou, X., Yuan, Z., 2023. Role of the Gut-Brain axis in the shared genetic etiology between gastrointestinal tract diseases and psychiatric disorders: a Genome-Wide pleiotropic analysis. *JAMA Psychiatry* 80 (4), 360–370. <https://doi.org/10.1001/jamapsychiatry.2022.4974>.
- Guitton, M.J., 2012. Tinnitus: pathology of synaptic plasticity at the cellular and system levels. *Front. Syst. Neurosci.* 6, 12. <https://doi.org/10.3389/fnsys.2012.00012>.
- Henry, J.A., Roberts, L.E., Caspary, D.M., Theodoroff, S.M., Salvi, R.J., 2014. Underlying mechanisms of tinnitus: review and clinical implications. *quiz 126 J. Am. Acad. Audiol.* 25 (1), 5–22. <https://doi.org/10.3766/jaaa.25.1.2>.
- Huang, C.-Y., Cheng, Y.-F., Yang, A.C., Lin, C.-J., Leong, P.-I., Hsueh, C.-Y., 2022. The moderating effect of personality traits on acute tinnitus sensation in idiopathic sudden sensorineural hearing loss. In: *Journal of the Chinese Medical Association*, 85. Scopus, pp. 633–638. <https://doi.org/10.1097/JCMA.0000000000000710>.
- Imsuwansri, T., Hoare, D.J., Phaisaltuntiwongs, W., Srisubut, A., Snidvongs, K., 2016. Glutamate receptor antagonists for tinnitus. *Cochrane Database Syst. Rev.* 2016 (10), CD012391. <https://doi.org/10.1002/14651858.CD012391>.

- Jeong, H., Kim, I., Kim, S.H., Lee, J.B., Kim, H., 2024. Effects of personality traits on the severity of chronic subjective tinnitus: a Cross-Sectional analysis. *Med. (Kaunas. Lith.)* 60 (8). <https://doi.org/10.3390/medicina60081259>.
- Kennedy, A.J., Rahn, E.J., Paulukaitis, B.S., Savell, K.E., Kordasiewicz, H.B., Wang, J., Lewis, J.W., Posey, J., Strange, S.K., Guzman-Karlsson, M.C., Phillips, S.E., Decker, K., Motley, S.T., Swayze, E.E., Ecker, D.J., Michael, T.P., Day, J.J., Sweatt, J.D., 2016. Tcf4 regulates synaptic plasticity, DNA methylation, and memory function. *Cell Rep.* 16 (10), 2666–2685. <https://doi.org/10.1016/j.celrep.2016.08.004>.
- Langguth, B., Kleinjung, T., Fischer, B., Hajak, G., Eichhammer, P., Sand, P.G., 2007. Tinnitus severity, depression, and the big five personality traits. *Prog. Brain Res.* 166, 221–225. [https://doi.org/10.1016/S0079-6123\(07\)66020-8](https://doi.org/10.1016/S0079-6123(07)66020-8).
- Li, C.-T., Yang, K.-C., Lin, W.-C., 2018. Glutamatergic dysfunction and glutamatergic compounds for major psychiatric disorders: evidence from clinical neuroimaging studies. *Front. Psychiatry* 9, 767. <https://doi.org/10.3389/fpsy.2018.00767>.
- Li, S., Ma, C., Li, Y., Chen, R., Liu, Y., Wan, L.P., Xiong, Q., Wang, C., Huo, Y., Dang, X., Yang, Y., Lv, L., Chen, X., Sheng, N., Li, W., Luo, X.-J., 2022. The schizophrenia-associated missense variant rs13107325 regulates dendritic spine density. *Transl. Psychiatry* 12 (1), 1–12. <https://doi.org/10.1038/s41398-022-02137-z>.
- Liu, M.-J., Bao, S., Gálvez-Peralta, M., Pyle, C.J., Rudawsky, A.C., Pavlovicz, R.E., Killilea, D.W., Li, C., Nebert, D.W., Wewers, M.D., Knoell, D.L., 2013. ZIP8 regulates host defense through zinc-mediated inhibition of NF- κ B. *Cell Rep.* 3 (2), 386–400. <https://doi.org/10.1016/j.celrep.2013.01.009>.
- Lo, M.-T., Hinds, D.A., Tung, J.Y., Franz, C., Fan, C.-C., Wang, Y., Smeland, O.B., Schork, A., Holland, D., Kauppi, K., Sanyal, N., Escott-Price, V., Smith, D.J., O'Donovan, M., Stefansson, H., Björnsdóttir, G., Thorgerisson, T.E., Stefansson, K., McEvoy, L.K., Chen, C.-H., 2017. Genome-wide analyses for personality traits identify six genomic loci and show correlations with psychiatric disorders. *Nat. Genet.* 49 (1), 152–156. <https://doi.org/10.1038/ng.3736>.
- Lopez-Escamez, J.A., Amanat, S., 2020. Heritability and genetics contribution to tinnitus. *Otolaryngol. Clin. North Am.* 53 (4), 501–513. <https://doi.org/10.1016/j.otc.2020.03.003>.
- Lyon, K.A., Juhasz, G., Brown, L.J.E., Elliott, R., 2020. Big five personality facets explaining variance in anxiety and depressive symptoms in a community sample. *J. Affect. Disord.* 274, 515–521. <https://doi.org/10.1016/j.jad.2020.05.047>.
- MacDonald, C., Caimino, C., Burns-O'Connell, G., Hartley, D., Lockwood, J., Sereda, M., Whitmer, W., Cima, R., Turton, L., Hoare, D.J., 2023. Tinnitus, suicide, and suicidal ideation: a scoping review of primary research. *Brain Sci.* 13 (10), 1496. <https://doi.org/10.3390/brainsci13101496>.
- Matosin, N., Newell, K.A., Quidé, Y., Andrews, J.L., Teroganova, N., Green, M.J., Fernandez, F., 2018. Effects of common GRM5 genetic variants on cognition, hippocampal volume and mGluR5 protein levels in schizophrenia. *Brain Imaging Behav.* 12 (2), 509–517. <https://doi.org/10.1007/s11682-017-9712-0>.
- Mazurek, B., Böcking, B., Döbel, C., Rose, M., Brüggemann, P., 2023. Tinnitus and influencing comorbidities. *Laryngo Rhino Otol.* 102 (S 01), S50–S58. <https://doi.org/10.1055/a-1950-6149>.
- McCormack, A., Edmondson-Jones, M., Fortnum, H., Dawes, P., Middleton, H., Munro, K. J., Moore, D.R., 2014. The prevalence of tinnitus and the relationship with neuroticism in a middle-aged UK population. *Int. J. Journal of Psychosomatic Research*, 76. Scopus, pp. 56–60. <https://doi.org/10.1016/j.jpsychores.2013.08.018>.
- McKenna, L., Handscomb, L., Hoare, D.J., Hall, D.A., 2014. A scientific cognitive-behavioral model of tinnitus: novel conceptualizations of tinnitus distress. *Front. Neurol.* 5. <https://doi.org/10.3389/fneur.2014.00196>.
- Mennink, L.M., Aalbers, M.W., van Dijk, P., van Dijk, J.M.C., 2022. The role of inflammation in tinnitus: a systematic review and Meta-Analysis. *J. Clin. Med.* 11 (4), 1000. <https://doi.org/10.3390/jcm11041000>.
- Naragon-Gainey, K., Watson, D., 2011. The anxiety disorders and suicidal ideation: accounting for co-morbidity via underlying personality traits. *Psychol. Med.* 41 (7), 1437–1447. <https://doi.org/10.1017/S0033291710002096>.
- Redelmeier, D.A., Najeeb, U., Etchells, E.E., 2021. Understanding patient personality in medical care: Five-Factor model. *J. Gen. Intern. Med.* 36 (7), 2111–2114. <https://doi.org/10.1007/s11606-021-06598-8>.
- Ridder, D.D., Elgoyhen, A.B., Romo, R., Langguth, B., 2011. Phantom percepts: tinnitus and pain as persisting aversive memory networks. *Proc. Natl. Acad. Sci. USA* 108 (20), 8075–8080.
- Sahlsten, H., Taiminen, T., Karukivi, M., Sjosten, N., Nikkila, J., Virtanen, J., Paavola, J., Joutsa, J., Niinivirta-Joutsa, K., Takala, M., Holm, A., Rauhalä, E., Loyttyniemi, E., Johansson, R., Jaaskelainen, S.K., 2018. Psychiatric (Axis I) and personality (Axis II) disorders and subjective psychiatric symptoms in chronic tinnitus. *Int. J. AUDIOLOGY* 57 (4), 302–312. <https://doi.org/10.1080/14992027.2017.1409440>.
- Sanchez-Roige, S., Gray, J.C., MacKillop, J., Chen, C.-H., Palmer, A.A., 2018. The genetics of human personality. *Genes Brain Behav.* 17 (3), e12439. <https://doi.org/10.1111/gbb.12439>.
- Schaaf, H., Eichenberg, C., Kastellis, G., Hesse, G., 2010. Treatment of tinnitus needs a combined neurootological and psychosomatic approach. *Otolaryngol. Pol. = Pol. Otolaryngol.* 64 (2), 78–82. [https://doi.org/10.1016/S0030-6657\(10\)70039-1](https://doi.org/10.1016/S0030-6657(10)70039-1).
- Schlee, W., Hølleland, S., Bulla, J., Simoes, J., Neff, P., Schoisswohl, S., Woelflick, S., Scheckmann, M., Schiller, A., Staudinger, S., Probst, T., Langguth, B., 2020. The effect of environmental stressors on tinnitus: a prospective longitudinal study on the impact of the covid-19 pandemic. In: *Journal of Clinical Medicine*, 9. Scopus, pp. 1–11. <https://doi.org/10.3390/jcm9092756>.
- Simoes, J., Schlee, W., Scheckmann, M., Langguth, B., Farahmand, D., Neff, P., 2019. Big five personality traits are associated with tinnitus improvement over time. *Sci. Rep.* 9. <https://doi.org/10.1038/s41598-019-53845-4>.
- Streit, F., Witt, S.H., Awasthi, S., Foo, J.C., Jungkunz, M., Frank, J., Colodro-Conde, L., Hindley, G., Smeland, O.B., Maslahati, T., Schwarze, C.E., Dahmen, N., Schott, B.H., Kleindienst, N., Hartmann, A., Giegling, I., Zillich, L., Sirignano, L., Poisel, E., Andreassen, O.A., 2022. Borderline personality disorder and the big five: molecular genetic analyses indicate shared genetic architecture with neuroticism and openness. *Transl. Psychiatry* 12 (1), 153. <https://doi.org/10.1038/s41398-022-01912-2>.
- Strumila, R., Lengvenytė, A., Vainutienė, V., Lesinskas, E., 2017. The role of questioning environment, personality traits, depressive and anxiety symptoms in tinnitus severity perception. In: *Psychiatric Quarterly*, 88. Scopus, pp. 865–877. <https://doi.org/10.1007/s11126-017-9502-2>.
- Study Quality Assessment Tools | NHLBI, NIH. (n.d.). Retrieved 16 January 2025, from <https://www.nlm.nih.gov/health-topics/study-quality-assessment-tools>.
- Taylor, B.V., Thompson, R.E., Nunney, I., Agius, M., Phillips, J.S., 2021. Suicidal ideation in people with tinnitus: a systematic review and meta-analysis. *J. Laryngol. Otol.* 135 (12), 1042–1050. <https://doi.org/10.1017/S0022251521003066>.
- Tavakkoly-Bazzaz, J., Azarnehad, A., Mousavi, N., Salehipour, P., Shahsavand Ananloo, E., Alizadeh, F., 2018. TCF4 and GRM8 gene polymorphisms and risk of schizophrenia in an Iranian population: a case-control study. *Mol. Biol. Rep.* 45 (6), 2403–2409. <https://doi.org/10.1007/s11033-018-4406-2>.
- Teixeira, J.R., Szeto, R.A., Carvalho, V.M.A., Muotri, A.R., Papes, F., 2021. Transcription factor 4 and its association with psychiatric disorders. *Transl. Psychiatry* 11 (1), 1–12. <https://doi.org/10.1038/s41398-020-01138-0>.
- Tov, W., Nai, Z.L., Lee, H.W., 2016. Extraversion and agreeableness: divergent routes to daily satisfaction with social relationships. *J. Personal.* 84 (1), 121–134. <https://doi.org/10.1111/jopy.12146>.
- Travis, K.J., McLachlan, N.M., Wilson, S.J., 2018. A systematic review and meta-analysis of psychological functioning in chronic tinnitus. *Clin. Psychol. Rev.* 60, 62–86. <https://doi.org/10.1016/j.cpr.2017.12.006>.
- Tseng, W.C., Reinhart, V., Lanz, T.A., Weber, M.L., Pang, J., Le, K.X.V., Bell, R.D., O'Donnell, P., Buhl, D.L., 2021. Schizophrenia-associated SLC39A8 polymorphism is a loss-of-function allele altering glutamate receptor and innate immune signaling. *Transl. Psychiatry* 11 (1), 136. <https://doi.org/10.1038/s41398-021-01262-5>.
- Uliaszek, A.A., Zinbarg, R.E., Mineka, S., Craske, M.G., Sutton, J.M., Griffith, J.W., Rose, R., Waters, A., Hammen, C., 2010. The role of neuroticism and extraversion in the stress-anxiety and stress-depression relationships. *Anxiety Stress Coping* 23 (4), 363–381. <https://doi.org/10.1080/10615800903377264>.
- Wang, X., Qi, M., Zeng, X., Cai, W., Yin, G., Zhang, S., Cen, J., Gu, J., Yuan, L., Fang, B., Lu, A., Li, Z., 2021. Social support and tinnitus distress: the importance of developing positive psychological qualities in patients with chronic tinnitus. *AUDIOLOGY NEUROOTOLOGY* 26 (4), 246–256. <https://doi.org/10.1159/000511254>.
- Xu, J., Marshall, J.J., Kraniotis, S., Nomura, T., Zhu, Y., Contractor, A., 2021. Genetic disruption of Grm5 causes complex alterations in motor activity, anxiety and social behaviors. *Behav. Brain Res.* 411, 113378. <https://doi.org/10.1016/j.bbr.2021.113378>.
- Yoneda, T., Lozinski, T., Turiano, N., Booth, T., Graham, E.K., Mroczek, D., Muniz Terrera, G., 2023. The big five personality traits and allostatic load in middle to older adulthood: a systematic review and meta-analysis. *Neurosci. Biobehav. Rev.* 148, 105145. <https://doi.org/10.1016/j.neubiorev.2023.105145>.
- Zhou, S., Luo, H., Tian, Y., Li, H., Zeng, Y., Wang, X., Shan, S., Xiong, J., Cheng, G., 2023. Investigating the shared genetic architecture of post-traumatic stress disorder and gastrointestinal tract disorders: a genome-wide cross-trait analysis. *Psychol. Med.* 53 (16), 7627–7635. <https://doi.org/10.1017/S0033291723001423>.