Psychiatric (axis I) and personality (axis II) disorders and subjective psychiatric symptoms in chronic tinnitus

Hanna Sahlsten[1], Tero Taiminen[2], Max Karukivi[3], Noora Sjösten[4], Johanna Nikkilä[3], Juuso Virtanen[1], Janika Paavola[5], Juho Joutsa[8-11], Katri Niinivirta-Joutsa[8], Mari Takala[6], Anu Holm[6], Esa Rauhala[6], Eliisa Löyttyniemi[7], Reijo Johansson[4], Satu K. Jääskeläinen[8]

[1] Faculty of Medicine, University of Turku, Turku, Finland

[2] Department of Psychiatry, Turku University Hospital, Turku, Finland

[3] Unit of Adolescent Psychiatry, Satakunta Hospital District, Pori, Finland.

Department of Psychiatry, University of Turku and Turku University Hospital, Turku, Finland

[4] Department of Ear, Nose and Throat, Turku University Hospital, Turku, Finland

[5] Department of Medical Physics, Turku University Hospital, Turku, Finland

[6] Department of Clinical Neurophysiology, SataDiag, Satakunta Hospital District, Pori, Finland.

[7] Department of Biostatistics, University of Turku, Turku, Finland

[8] Department of Clinical Neurophysiology, Turku University Hospital and University of Turku, Turku, Finland

[9] Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital and Harvard Medical School, Charlestown, MA, USA

[10] Berenson-Allen Center for Noninvasive Brain Stimulation, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, USA

[11] Department of Neurology, University of Turku, Turku, Finland

Corresponding author: Hanna Sahlsten

Address: Kliininen Neurofysiologia (os.936), TYKS, PL 52, 20521 Turku, Finland

E-mail: hanna.sahlsten@hotmail.fi, hanna.sahlsten@luukku.com

Keywords: Tinnitus; Psychiatric disorder; Personality disorder; Structured clinical interview for DSM disorders, SCID

Abbreviations:

BDI Beck Depression Inventory

dB HL Decibel Hearing Level

DES Dissociative Experiences Scale

DSM-IV Diagnostic and Statistical Manual of Mental Disorders, 4th Edition

MRI Magnetic Resonance Image

NCS-R survey The US National Comorbidity Survey Replication

NRS Numeric Rating Scale

PTA Pure Tone Average

rTMS Repetitive Transcranial Magnetic stimulation

RCT Randomized Controlled Trial

SCID Structured Clinical Interview for DSM Disorders

SCL-90 Symptom Checklist-90

THI Tinnitus Handicap Inventory

TMS Transcranial Magnetic Stimulation

VAS Visual Analog Scale

ABSTRACT

Objective: Chronic tinnitus has been associated with several psychiatric disorders. Only few studies have investigated these disorders using validated diagnostic interviews. The aims were to diagnose psychiatric and personality disorders with structured interviews, to assess self-rated psychiatric symptoms and elucidate temporal relations between psychiatric disorders and tinnitus.

Design: Current and lifetime DSM-IV diagnoses of axis-I (psychiatric disorders) and axis-II (personality disorders) were assessed using structured clinical interviews (SCID-I and -II). Current subjective psychiatric symptoms were evaluated via self-rating instruments: the Symptom Check List-90 (SCL-90), the Beck Depression Inventory, and the Dissociative Experiences Scale (DES).

Study sample: 83 patients (mean age 51.7, 59% men) with chronic, disturbing tinnitus and a median Tinnitus Handicap Inventory score of 32.

Results: The rates of lifetime and current major depression were 26.5% and 2.4%. The lifetime rate of obsessive-compulsive personality disorder (type C) was 8.4%. None of the patients had cluster B personality disorder or psychotic symptoms. The SCL-90 subscales did not differ from the general population, and median DES score was low, 2.4.

Conclusions: Tinnitus patients are prone to episodes of major depression and often also have obsessive-compulsive personality features. Psychiatric disorders seem to be comorbid or predisposing conditions rather than consequences of tinnitus.

Clinical trial reference: ClinicalTrials.gov (ID NCT 01929837)

Introduction

Tinnitus is defined as the perception of sound in the absence of any external noise. It is a common disorder in the general population with a prevalence of 10-15%. While most habituate to this phantom sound, the condition creates severe distress in 1-2% of all people by impairing quality of life (Langguth, et al. 2013). The exact pathophysiology of tinnitus is still obscure. High-frequency cochlear hearing loss is one of the main risk factors of tinnitus, as it reduces cochlear nerve signaling, and thus down-regulates the inhibitory cortical processes, thereby leading to hyperexcitability within central auditory structures, especially the primary auditory cortex (Baguley, et al. 2013). The treatment of chronic tinnitus focuses on symptomatic relief, as there is no curative therapy (Tunkel, et al. 2014).

Both chronic tinnitus and neuropathic pain are disabling conditions wherein peripheral deafferentation induces widespread pathophysiologic alterations in brain function. Recent studies suggest that higher cognitive and affective brain circuits, including the frontostriatal (Leaver, et al. 2011, Rauschecker, et al. 2015) and basal ganglia (Jääskeläinen, et al. 2014) gating systems, are critically involved in both disorders. Similar pathophysiological mechanisms for chronic pain and tinnitus are possibly related to low brain dopamine tone (Hagelberg, et al. 2004, Jääskeläinen, et al. 2014, Rauschecker, et al. 2015). Dopamine is assumed to regulate auditory processing and gating; thus, dysfunction in these dopaminergic pathways has also been proposed as participating in the pathogenesis of tinnitus (Du & Jansen. 2011, Langguth, et al. 2011).

Like chronic pain, tinnitus has been associated with an increased rate of psychiatric disorders, but the reported frequencies vary widely. An electronic search on the Web of Science using the keywords “tinnitus” and “psychiatric” revealed over 180 articles. Most of the studies have used

only self-report symptom questionnaires (Geocze, et al. 2013, Pinto, et al. 2014, Pattyn, et al. 2016), such as the Symptom Check List 90 (SCL-90) (Derogatis. 1977) and the Beck's Depression Inventory (BDI) (Steer, et al. 1999). The self-report questionnaires were developed for screening psychiatric symptoms and follow-up on symptom severity during treatment. They are not validated for diagnostic evaluation, and thus, their results have varied widely. Few studies show a low prevalence rate of depressive symptoms in tinnitus patients(Figueiredo, et al. 2010, Ooms, et al. 2011), while other studies have shown significantly higher prevalence rates (up to 49%) of depressive symptoms (Folmer, et al. 2008), and a significant association between depression and tinnitus (Folmer, et al. 2001, Langguth, et al. 2007). The difference in these methods is crucial, since the detection of psychiatric symptoms using self-report scales does not mean that the diagnostic criteria for a psychiatric disorder are fulfilled.

To our knowledge, only 11 studies published in English (Belli, et al. 2008, Harrop-Griffiths, et al. 1987, Holgers, et al. 2005, Malakouti, et al. 2011, Marciano, et al. 2003, Shargorodsky, et al. 2010, Simpson, et al. 1988, Sullivan, et al. 1988, Zirke, et al. 2013, Zöger, et al. 2001, Zöger, et al. 2006) have investigated axis I psychiatric disorders in tinnitus patients using a structured diagnostic interview, like the Structural Clinical Interview for DSM-IV disorders (SCID) (First, et al. 1997a) that was developed for accurate psychiatric diagnostics (Table 1). Diagnostic interviews indicate that 60-78% of tinnitus patients have at least one lifetime psychiatric disorder (Malakouti, et al. 2011, Zöger, et al. 2001); 32.5-77.5% have lifetime depression (Malakouti, et al. 2011, Sullivan, et al. 1988), and approximately 45% have a lifetime anxiety disorder (Holgers, et al. 2005, Malakouti, et al. 2011, Zöger, et al. 2001) (Table 1). Dissociative disorders have not yet systemically been investigated in tinnitus patients. The temporal relationship of psychiatric disorders and the occurrence of tinnitus are only rarely reported, so no conclusions can be drawn from the existing

literature on whether tinnitus predisposes one to psychiatric disorders or vice versa or whether they are just comorbid conditions.

To our knowledge, only two studies have evaluated the prevalence of personality disorders (PD) in tinnitus patients using a validated diagnostic interview (SCID axis II). These have shown incongruent rates of 3% (Belli, et al. 2008) and 50% (Erlandsson & Persson. 2006). Thus, it cannot be concluded whether the rate of PDs in chronic tinnitus actually differ from the estimates in general population studies (Lenzenweger, et al. 2007); see also Table 2. Self-report questionnaires have revealed similarly differing rates of PDs, ranging from 19% (Marciano, et al. 2003) to 61% (Zöger, et al. 2001). These widely ranging figures indicate either methodological shortcomings in the assessments of PD, very diverse patient populations, or the major effects of cultural factors. PDs can cause significant impairment in functioning and are highly comorbid with other mental disorders, and patients with PD are usually heavy users of health services (Lenzenweger, et al. 2007).

This current study was a part of a larger project that evaluated transcranial magnetic stimulation (TMS) in the treatment of chronic tinnitus (Sahlsten, et al. 2017). The aims of this study were to examine the current and lifetime prevalence of psychiatric axis I (main psychiatric diagnoses) and axis II (personality) disorders using the standardized SCID tool in patients with disturbing, chronic tinnitus and investigate the temporal relationship of psychiatric disorders and the occurrence of tinnitus. Current subjective psychiatric symptoms, including dissociative experiences, were evaluated using questionnaires to further analyze tinnitus patients' mental well-being and draw a comparison between SCID and self-reported symptoms. In addition, as chronic pain and tinnitus have been proposed to share similar pathophysiological central nervous system mechanisms, we wanted to compare the axis I and II diagnoses for these two chronic patient groups to further

elucidate any potential common pathways of vulnerability that are possibly related to low brain dopamine tone (Taiminen, et al. 2011, Jääskeläinen, et al. 2014). A psychological profile may serve as a biomarker for the treatment response to therapeutic neuromodulation.

Methods

The Ethical Committee for the Hospital District of South-Western Finland (73/1800/2013) consented to this study, which was registered on ClinicalTrials.gov (ID NCT 01929837). All patients also gave their written informed consent. The trial was conducted in the Departments of Ear, Nose and Throat Diseases (ENT) and Psychiatry at Turku University Hospital (TUCH) and Satakunta Central Hospital (SatKS) in Finland during the years 2013–2016.

Patients

In TUCH, tinnitus patients born between 1948 and 1995 treated in the Department of ENT between January 2009 and March 2013, and in SatKS between January 2012 and March 2013, were searched using the patient archives for the study project that investigated therapeutic repetitive transcranial magnetic stimulation (rTMS) for chronic tinnitus. The inclusion criteria were chronic (6 months–10 years), uni- or bilateral, non-pulsatile subjective tinnitus in patients age 18–65 years. None of these patients had any auditory hallucinations, such as understandable speech. The exclusion criteria were magnetically active, metallic intra-corporeal appliances (e.g., cochlear implants), epilepsy, or an increased risk of seizure (e.g., brain tumour or active alcohol abuse), bipolar disorder (as TMS may induce mania), severe heart disease, migraine, and pregnancy. The exclusion criteria were selected based on the guidelines for the safe use of rTMS (Rossi, et al. 2009). Of a total of 622 patients, 329 were eligible for the study. Patients were recruited with a letter that included a complete description of the rTMS study (consisting of 10 treatment sessions of TMS and a 6-month follow-up) and a

telephone call a few days later during which patients were interviewed about whether they still had disturbing tinnitus with an average intensity at least 4/10 on the Numeric Rating Scale (NRS), ranging from 0 (no tinnitus) to 10 (the worst tinnitus the patient could imagine). There were 120 suitable patients who were willing to participate in the study, and of those, 86 patients with the highest NRS scores were selected for the trial so as to treat at least 80 patients with rTMS.

All patients were examined by an ENT specialist. Head magnetic resonance imaging (MRI) was taken, to rule out possible treatable causes for their tinnitus. There were no tumour findings or other serious pathologies in the MRIs, but a few patients did have minor unspecific signal changes, mild leucoaraiosis or atrophy, or a small benign cyst in the brain. Of the 86 patients, the SCID was conducted on 83 patients. Two patients withdrew from the trial before attending the SCID because of their busy work schedule, and one patient was excluded because she suffered a transient ischemic brain attack before the first session of TMS. During the course of this study, one patient was discovered to have bipolar disorder, but it was stable, and that individual was willing to continue in the study group.

Eighty-three patients (49 men, 59% and 34 women, 41%) ages 19-65 (mean 51.7, SD 11.5, median 56.0) with mean tinnitus duration of 5.5 (SD 2.9, median 5.0) years completed this study and were analysed. Table 3 lists the characteristics of these patients.

Evaluation of tinnitus and hearing

Patients were evaluated using the Tinnitus Handicap Inventory (THI), which consists of cut-off scores of 0–16 for slight (grade 1), 18–36 for mild (grade 2), 38–56 for moderate (grade 3), 58–76 for severe and 78–100 for catastrophic (grade 5) tinnitus (Newman, et al. 1996) and the Visual Analog Scale (VAS), with a score between 0 (no tinnitus) and 100 (the worst tinnitus the patient

could imagine) for self-ratings of tinnitus intensity, annoyance, and distress in everyday life (Adamchic, et al. 2012). An audiogram (both air and bone thresholds) was measured for decibels hearing level (dB HL) and pure tone average (PTA) of 500–4000 Hz calculated for both ears.

Psychiatric diagnostic evaluation

Psychiatric interviews were conducted either by a psychiatrist or a psychologist who was trained to use the instruments. Axis I disorders, in the DSM-IV (American Psychiatric Association. 1994) indicate psychiatric diagnoses like depression, anxiety, or social phobia. Diagnoses of axis I disorders, both current (previous month) and lifetime, were done using the structured clinical interview for DSM-IV disorders (SCID-I) (First, et al. 1997a). Axis II disorders in DSM-IV (American Psychiatric Association, 1994) indicate personality disorders. They are divided into three clusters; A represents odd and eccentric; B dramatic, erratic or emotional; and C fearful and neurotic. Personality disorders were evaluated independently of the axis I disorders using the SCID-II interview (First, et al. 1997b). The duration of the SCID interviews ranged from 2 to 4 hours. A further division of lifetime axis I and II disorders was done for onset before and after the onset of tinnitus. In addition, patients' personal and somatic histories were recorded. Patients' medical records for TUCH or SatKS were available for both the interviewers and the ENT specialist.

Evaluation of subjective psychiatric symptoms

Self-report questionnaires were used to assess subjective psychiatric symptoms and these included the Beck's Depression Inventory (BDI) (Steer, et al. 1999), the Symptom Check List 90 (SCL-90) (Derogatis. 1977), and the Dissociative Experiences Scale (DES) (Bernstein & Putnam. 1986). The BDI has 21 questions and measures the severity of depression with cut-off scores of 0–13 for minimal, 14–19 for mild, 20–28 for moderate, and 29–63 for severe depression.The SCL-90 uses 90 questions on a 5-point scale from 1 (not at all) to 5 (extremely) to evaluate psychological problems

and symptoms of psychopathology for primary symptom dimensions of somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, psychoticism, and additional items. The SCID-I does not include dissociative disorders. The DES with 28 questions screens the different types of dissociation, including both problematic dissociative disorders and normal dissociative experiences, such as day dreaming. As the DES is not a diagnostic instrument, a high score suggests that a clinical assessment for dissociation may be warranted.

Statistical analysis

All variables under examination were checked for normality by a visual inspection of the data distribution and the Shapiro-Wilk -test. Tinnitus intensity, annoyance, and distress were normally distributed, thus the mean and standard deviation were reported. All other variables were not normally distributed, and therefore, the median values and the first and the third quartiles were reported. Exact 95% confidence intervals for the binomial distribution were obtained from the literature. P=0.05 was chosen as the level of statistical significance. Associations between the categorical variables were cross-tabulated and evaluated, using the two-sided Fisher's exact test. For this aim, the tinnitus intensity (VAS) was divided into categories where a score of 0–40 represented mild, >40–70 represented moderate, and >70–100 indicated severe tinnitus. Statistical analyses were performed using SPSS 22.

Results

Tinnitus and hearing

The mean tinnitus intensity was 60.5 (SD 13.7), annoyance 53.7 (SD 18.8), and distress 52.1 (SD 17.9) in the VAS scores. The median THI score was 32 (quartiles 18–56, range 2–94), which indicated THI grade 2, mild tinnitus (Table 3).

The median PTA was 14.0 dB (quartiles 6.0–27.5, range 0–78) in the right ear and 14.0 dB (quartiles 6.0–28.8, range 0–83) in the left ear, so the median PTA in both ears was within the normal range (0–20 dB).

Psychiatric axis I disorders

Results of the SCID interviews (axis I and II) are shown in Table 2. Of the 83 patients evaluated, 37 (44.6%) had at least one lifetime axis I disorder. The most common lifetime disorder was major depression found in 22 patients (26.5%). Lifetime chronic depression occurred in 6 patients (7.2%); thus altogether, 28 patients (33.7%) suffered from some lifetime depressive disorder. The severity of tinnitus intensity (p=0.34) or annoyance (p=0.27) on the VAS scale or the grade of THI scores (p=0.30) was not associated with lifetime depressive disorders. Although the lifetime depressive disorder rate was high, only two patients (2.4 %) suffered from current major depression. Panic disorder was the second most common lifetime disorder for 7 patients (8.4%); 6 of them (7.2%) without agoraphobia (AG) and one with AG (1.2%). Active alcohol abuse was an exclusion criterion that affected the results; only 4 patients (4.8%) were found to have suffered from lifetime alcohol dependence. Two patients (2.4%) suffered from lifetime drug abuse; one patient had temporarily used amphetamine, cannabis and hallucinogen in his youth, and another patient had a current mild addiction to lorazepam. The number of patients suffering from other axis I disorders listed in Table 2, ranged from one to five. None of the patients had any psychotic disorders.

The SCID I results shown in Table 2 are given, together with the lifetime prevalence rates in the general population of the US National Comorbidity Survey Replication (NCS-R) for comparison (Kessler, et al. 2005a, Kessler, et al. 2005b, Kessler, et al. 2006). The lifetime prevalence rates did not differ significantly from the general population (Kessler, et al. 2005a), except for a higher rate

of lifetime major depressive disorder (26.5% vs. 16.6%) and lower lifetime specific phobia (1.2% vs. 12.5%) seen in tinnitus patients (Table 2). The rate of lifetime chronic depression was also somewhat higher in our patients (7.2%) than it was in the NCS-R survey (2.5%). Further, we compared the current prevalence rates in our study with the 12-month rates for the general population in the NCS-R survey (Kessler, et al. 2005b). Most of the rates did not differ except for a higher prevalence of current chronic depression (6.0% vs. 1.5%), and a lower prevalence of current specific phobia (1.2% vs. 8.7%) in our study. The prevalence rate of any lifetime axis I disorder was very similar in our patients (44.6%) as in the NCS-R survey (46.4%) (Kessler, et al. 2005a), but the current prevalence rate was somewhat lower in our study (18.1%), compared to the 12-month rate (26.2%) (Kessler, et al. 2005b).

Most of the axis I disorders occurred before tinnitus in 25 patients (30.1%) compared to 12 patients (14.5%) for whom the onset of psychiatric disorder was after tinnitus. Only 15 patients (18.1%) suffered from a current axis I disorder. Of the 83 patients assessed, 16 (19.3%) had comorbidity among their lifetime axis I disorders; 12 patients had 2, three patients had 3 and one patient 5 comorbid axis I disorders.

Personality disorders

Lifetime personality disorders were discovered in 9 patients (10.8%) (Table 2); all of them had occurred before tinnitus, and 8 of them (9.6%) were current. One patient had previously been diagnosed with an avoidant and obsessive-compulsive personality in a SCID-II interview, but in the recent interview for this current study, the diagnostic criteria for any personality disorder were not fulfilled. The lifetime personality disorders were obsessive-compulsive personality in 7 patients (8.4%), avoidant personality in 2 (2.4%) and schizoid personality in one patient (1.2%). Further, 8 patients had any cluster C personality disorder, and only one patient had a cluster A personality

disorder; none of the patients had any cluster B personality disorder. The severity of tinnitus intensity (p=0.53) or annoyance (p=0.43) on the VAS scale or the grade of THI scores (p=0.69) was not associated with lifetime obsessive-compulsive disorder.

The results are shown in Table 2 and Figure 1, together with the prevalence rates in the general population for the NCS-R survey for comparison (Lenzenweger, et al. 2007). Figure 1 illustrates the similarities between the distributions of personality disorders in our tinnitus patients and chronic neuropathic pain patients (Taiminen, et al. 2011).The prevalence rates did not differ significantly from the NCS-R survey results, but the prevalence rate of cluster C personality disorders was somewhat higher in our study, 9.6% vs. 6.0%, especially concerning the obsessive-compulsive personality disorder at 8.4% vs. 2.4%. The prevalence rate for any personality disorder in our study was almost similar as that found in the general population, 10.8% vs. 9.1% (Lenzenweger, et al. 2007).

Comorbidity among lifetime personality disorders was found only in one patient (who had both an obsessive-compulsive and an avoidant disorder). Of the 83 patients, 6 had both a lifetime axis I and II disorder. Further, 6 out of 9 patients (66.7%) with any lifetime personality disorder also had some comorbid lifetime axis I disorder.

Self-rated current psychiatric symptoms

The median BDI score was 5 (quartiles 2–9, range 0–24), which belonged to the category of minimal depression; 64 (77.1%) patients scored minimal, 14 (16.9%) mild, 5 (6.0%) moderate, and none had severe depression. The median DES score was 2.4 (quartiles 1.1–4.7, range 0–30) implying a very low likelihood of a dissociative disorder. The results for different dimensions of the SCL-90 are shown in Table 4, together with the values of a Finnish validation study of the SCL-90

including a Finnish community sample (Holi, et al. 1998) for comparison. The mean values for the tinnitus patients were almost identical to those of the community sample although the tinnitus patients had a little less interpersonal sensitivity (1.41 vs. 1.74), hostility (1.37 vs. 1.58) and paranoid ideation (1.37 vs. 1.53) (Table 4).

Discussion

The main findings of this study were relatively high prevalence rates of lifetime major depression and obsessive-compulsive personality disorder in patients with chronic tinnitus. Low rates of specific phobia and current major depression were found, but also an elevated rate of current chronic depression. Most of the axis I disorders occurred before tinnitus. Further, there was a lack of both cluster B personality disorders and psychotic disorders, as well as a very low likelihood of any dissociative disorder.

In our patients, the rate of lifetime major depression (MD), 26.5%, was significantly higher than that found in the general population of the NCS-R survey, 16.6% (Kessler, et al. 2005a) (Table 2). This finding is noteworthy, especially considering that 59% of our study population were men, and generally, women are more prone to mood disorders, such as depression, in the general population studies (Kessler, et al. 2005a). However, the rate of current (previous month) MD was lower than the 12-month rate in the NCS-R survey, 6.7% (Kessler, et al. 2005b). Thus, although these patients were prone to episodes of major depression, they seemed to recover well, as the current rate was low. However, the rate of current chronic depression, 6.0% was significantly higher than the 12-month rate seen in the NCS-R survey, 1.5%. Yet the lifetime rates did not differ significantly, although they were higher in our study (Table 2). In our study, the prevalence rates of major and chronic depression were the same before and after the onset of tinnitus, a finding that implies that

tinnitus does not predispose patients to depression. The rather high lifetime rate of depressive disorders (33.7%) in our tinnitus patients was in line with a study applying SCID (Malakouti, et al. 2011), but even rates up to 77.5% (Sullivan, et al. 1988) have been reported (Table 1). Sullivan et al (1988) investigated only 40 patients with disabling tinnitus, so a smaller sample size and possibly different symptom severity may explain the differences when compared to our results here.

In the present study, the lifetime prevalence rates of anxiety disorders did not differ from the general population (Table 2), except for the very low rate of specific phobia seen in our study; only one patient suffered from lifetime specific phobia (against snakes) compared to the significantly higher general population prevalence at 12.5% (Kessler, et al. 2005a). This finding may be coincidental and partially based on the gender distribution in our study, as women are more prone to anxiety disorders, such as phobias (Kessler, et al. 2005a). Both the lifetime prevalence rate of anxiety disorders, 21.7% and the current rate, 13.3%, in this study were markedly lower than that found in other studies on tinnitus, using validated diagnostic interviews and reporting lifetime prevalence, at around 45% (Holgers, et al. 2005, Malakouti, et al. 2011, Zöger, et al. 2001), with a 28–49% current rate (Belli, et al. 2008, Zöger, et al. 2006) (Table 1). Our tinnitus patients had rather mild symptomatology (median THI score 32), which may explain the difference in the amount of anxiety disorders.

Most of these, axis I disorders occurred before tinnitus in 25 patients, compared to 12 for whom the onset occurred after tinnitus. Only 15 patients suffered from a current axis I disorder. Thus, tinnitus did not seem to predispose patients to psychiatric disorders.

Regarding axis II disorders, in the present study, 10.8% of the patients had at least one personality disorder (PD) (Table 2, Figure 1). This rate is about the same as that found in the NCS-R general

population survey (Lenzenweger, et al. 2007), but higher than the prevalence rate of 3% in one of the two previous studies investigating tinnitus patients using the SCID tool (Belli, et al. 2008), and much lower than the 50% rate in the other study (Erlandsson & Persson. 2006) (Table 1). Belli et al (2008), evaluated 90 patients with "annoying tinnitus", but symptom severity was not assessed using any numerical measure, so it may be that those patients had even milder tinnitus symptomatology than our patients did. In addition, they excluded all patients with significant medical and/or psychiatric pathologies, such as schizophrenia and dementia. Further, cross-cultural differences may also partly explain the very different results in our study. Erlandsson and Persson (2006) investigated a sub-group of only 18 tinnitus patients with depressed mood (an average BDI score of 19.9), which may explain the differences in those findings compared to our larger group of patients. The prevalence rate of PDs in the present study utilizing SCID was also lower than the previous 19% rate that was based on a self-report questionnaire (Marciano, et al. 2003).

In our study, most of the PDs belonged to the cluster C, and only one had a cluster A disorder (Table 2). The rate of obsessive-compulsive personality (O-CPD), 8.4% in our patients, was somewhat higher than that in the NCS-R survey (Table 2) and for Belli et al (2008), but markedly lower than that in Erlandsson and Persson (2006) (Table 1). Zöger et al (2001) reported a 49% prevalence rate of cluster C personality traits in tinnitus patients; however, personality traits are not directly comparable to a psychiatric diagnosis of personality disorder. As O-CPD is defined as an extensive pattern of preoccupation with perfectionism and mental control, at the cost of efficiency and flexibility (American Psychiatric Association. 1994), it is thus understandable that uncontrollable tinnitus can cause severe distress for patients with O-CPD. Further, because of high subjective distress, patients with O-CPD may also be prone to seek help for their tinnitus. In our sample, there were no patients in the cluster B personality disorder, although the NCS-R survey did report a 1.5% prevalence rate. The lack of cluster B personality disorders may have been partially

due to the high age of our patients (median 56.0 years), as cluster B disorders usually decline with advancing age (Reich, et al. 1988).

In all 9 subscales of the SCL-90,the mean values of our patients were almost identical or only a little lower than those in a Finnish community sample (Holi, et al. 1998), thus supporting our conclusion that tinnitus patients are psychologically quite resilient (Table 4). Compared to the other two studies on tinnitus patients evaluated with SCL-90-R (Belli, et al. 2008, Malakouti, et al. 2011), the mean values in all the subscales were rather similar in our patients, with only some minor exceptions related to obsessive-compulsive symptoms, anxiety, paranoid ideation, and psychoticism. These slight discrepancies may partly be due to cross-cultural differences, as the Finnish validation study discovered that the Finnish community sample scoring was consistently higher on all subscales than, for example, the American scoring (Holi, et al. 1998).

In our study, the median DES score was only 2.4. That is lower than the median score of 4.38 reported for adults (Bernstein & Putnam. 1986). Thus, our study implies that tinnitus patients are resilient to dissociative experiences, and tinnitus is not associated with dissociative auditory hallucinations. Further, there was no connection between tinnitus and psychotic disorders, as none of the patients suffered from psychotic disorders.

Generally, tinnitus patients seem to be psychologically somewhat healthier than chronic pain patients, and yet the psychiatric and personality disorders that do occur in these two conditions are remarkably similar. In a previous study on 63 patients with chronic orofacial neuropathic pain (Taiminen, et al. 2011), SCID-I and –II indicated an increased rate of lifetime major depression (30.2%) and current major depression (12.7%). In addition, the rate of any personality disorder was increased (19.0%), but only due to an increase in cluster C disorders as was the case in most of the

tinnitus patients. The prevalence rates in pain patients were somewhat higher than in the present study, especially the rate of obsessive-compulsive personality (14.3%), but the profiles of axis I and II disorders and disorders with increased rates compared to the population samples seemed to be very similar (Figure 1).

Major depression has been associated with decreased brain dopamine levels (Lambert, et al. 2000), and obsessive-compulsive personality disorder with dysfunctional brain dopamine activity (Olver, et al. 2009). In general, cluster C personality disorders are characterized by low novelty seeking, neuroticism, and fearfulness, all of which have been associated with low brain dopamine activity (Zald, et al. 2008). To the contrary, cluster B personality disorders, which were totally absent in our sample, are characterized by extroversion, high novelty seeking, and low harm avoidance, all traits that have been connected to high brain dopamine activity (Hess, et al. 2009). Further, dopamine is assumed to regulate auditory processing and gating (Du & Jansen. 2011). Dopaminergic receptors that are located both in the cochlea and in the central nervous system network are involved in tinnitus. Further, dysfunction in these dopaminergic pathways has been proposed as participating in the pathogenesis of tinnitus (Langguth, et al. 2011, Rauschecker, et al. 2015). The present findings on psychiatric axis I and II disorders in tinnitus, which are most associated with brain dopamine hypo- or dysfunction, lend further support to the importance of frontostriatal dopamine circuits in chronic tinnitus and neuropathic pain. Low brain dopamine tone with subsequent deficient top-down inhibition might serve as a common predisposing factor for these chronic deafferentation conditions and the psychiatric comorbidity associated with them.

In our study, patients were prone to episodes of major depression (MD), but they remitted well from depressive episodes, which implies good neuronal plasticity and resilience (Castren. 2013). Patients participated in the trial investigating repetitive transcranial magnetic stimulation (rTMS) for chronic

tinnitus. rTMS exerts its effects by altering neuronal plasticity by releasing dopamine and endogenic opioids (Lamusuo, et al. 2017), and has been successfully used for the treatment of depression and chronic pain (Lefaucheur, et al. 2014). However, more research is needed to establish its therapeutic efficacy for tinnitus. If rTMS will be applied for tinnitus in the future, it will be useful to screen for depression (for example with the BDI), as it is possible to treat comorbid depression and tinnitus during the same rTMS session

Strengths and limitations of the study

The strengths of our study are the elaborate diagnostic evaluation of a large sample of patients by a multidisciplinary research team, and the application of structured instruments to analyze both axis I and II psychiatric disorders, including presenting both lifetime and current disorders, and the temporal relationship of those disorders and the occurrence of tinnitus.

This study has some limitations. Due to the nature of the rTMS study, certain exclusion criteria, such as active alcohol abuse and bipolar disorder, may have affected the results. Also, the lack of a comparison group can be viewed as a limitation. However, the present results were compared to other studies on tinnitus and pain patients, as well as the large national studies on the healthy population. It is usually more productive to compare the broad confidence of intervals (CI) of a relatively small sample to the narrow CIs of a large population study than to the broad CIs of a small comparison group.

Conclusion

This study offers a psychological profile for chronic tinnitus patients who show rather high prevalence rates of lifetime depression and cluster C personality disorders, low rates of current major depression and a lack of both cluster B personality disorders and psychotic disorders,

together with a very low likelihood of any dissociative disorder. Patients were prone to episodes of major depression, but their capability to remit from that depression was good. The rate of depressive disorders was similar both before and after tinnitus implying that, in general, tinnitus was not causing the depression. Instead, our results indicate that tinnitus and comorbid depression, anxiety, and cluster C personality disorders may actually share common predisposing factors that are related to an inefficient function of brain dopaminergic circuitries, as in chronic deafferentation pain. Tinnitus is prone to be an even bigger problem in the future, as the population is getting older, and the popular use of headphones and earpieces is predisposing even young people to have cochlear damage and tinnitus. The need for new and innovative interventions is obvious. The results of this study imply that tinnitus patients are psychologically quite resilient, and thus, suitable for receiving novel treatment options, such as therapeutic brain stimulation.

Conflicts of Interest

Dr Sahlsten has received travel grant from Nexstim for an international Congress on therapeutic use of rTMS. Dr. Taiminen has received a lecturer honorarium from Astra-Zeneca, Bayer, Bristol-Myers Squibb, Efeko, Eisai, GlaxoSmithKline, Lilly, Lundbeck, Nexstim, Orion Pharma, Pfizer, Schering-Plough and UCB. Dr. Joutsa received a lecturer honorarium from Boehringer-Ingelheim, travel grants from Abbvie and research grants from Lundbeck and the Orion Research Foundation. PhD Holm has received a travel grant from ResMed. Professor Jääskeläinen has received lecturer honoraria from Nexstim, Orion Pharma, Pfizer, and Ratiopharm as well as a grant for academic research from Orion Pharma. Others involved in the study declared no conflicts of interest.

Funding

This study was supported by Finnish governmental University Hospital grants (EVO), the Finnish Research Foundation of Ear Diseases, and State research funding from the Hospital District of Southwest Finland.

References

Adamchic I., Langguth B., Hauptmann C. & Tass P.A. 2012. Psychometric Evaluation of Visual Analog Scale for the Assessment of Chronic Tinnitus. *Am.J.Audiol.*, 21, 215-225.

American Psychiatric Association (ed.) 1994. *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). 4th Ed.* Washington, DC: APA.

Baguley D., McFerran D. & Hall D. 2013. Tinnitus. *Lancet,* 382, 1600-1607.

Belli S., Belli H., Bahcebasi T., Ozcetin A., Alpay E., et al 2008. Assessment of psychopathological aspects and psychiatric comorbidities in patients affected by tinnitus. *Eur.Arch.Oto-Rhino-Laryn.,* 265, 279-285.

Bernstein E. and Putnam F. 1986. Development, Reliability, and Validity of a Dissociation Scale. *J.Nerv.Ment.Dis.,* 174, 727-735.

Castren E. 2013. Neuronal Network Plasticity and Recovery From Depression. *JAMA Psychiatry,* 70, 983-989.

Derogatis L. (ed.) 1977. *SCL-90: Administration, Scoring and Procedure Manual-I for the Revised Version.* Baltimore: John Hopkins University, School of Medicine, Clinical Psychometric Unit.

Du X. and Jansen B.H. 2011. A neural network model of normal and abnormal auditory information processing. *Neural Networks,* 24, 568-574.

Erlandsson S. and Persson M. 2006. A longitudinal study investigating the contribution of mental illness in chronic tinnitus patients. *Audiol Med,* 4, 124-133.

Figueiredo R.R., Rates M.A., de Azevedo A.A., de Oliveira P.M. & de Navarro P.B.A. 2010. Correlation analysis of hearing thresholds, validated questionnaires and psychoacoustic measurements in tinnitus patients. *Braz.J.Otorhinolaryngol.,* 76, 522-526.

First M., Spitzer R., Gibbon M. & Williams J. (eds.) 1997a. *Structured Clinical Interview for DSM-IV Axis I disorders (SCID-I, 4/97 Version).* New York, NY: Biometrics Research Department, New York State Psychiatric Institute.

First M., Spitzer R., Gibbon M., Williams J. & Benjamin L. (eds.) 1997b. *Structured Clinical Interview for DSM-IV Axis II Disorders (SCID-II).* New York, NY: Biometrics Research Department, New York State Psychiatric Institute.

Folmer R., Griest S. & Martin W. 2008. Obsessive-compulsiveness in a population of tinnitus patients. *Int.Tinnitus J.,* 14, 127-130.

Folmer R., Griest S. & Martin W. 2001. Chronic tinnitus as phantom auditory pain. *Otolaryngol.Head.Neck.Surg.,* 124, 394-400.

Geocze L., Mucci S., Abranches D.C., de Marco M.A. & Penido N.d.O. 2013. Systematic review on the evidences of an association between tinnitus and depression. *Brazilian Journal of Otorhinolaryngology,* 79, 106-111.

Hagelberg N., Jaaskelainen S., Martikainen I., Mansikka H., Forssell H., et al 2004. Striatal dopamine D2 receptors in modulation of pain in humans: a review. *Eur.J.Pharmacol.,* 500, 187-192.

Harrop-Griffiths J., Katon W., Dobie R., Sakai C. & Russo J. 1987. Chronic Tinnitus - Association with Psychiatric Diagnoses. *J.Psychosom.Res.,* 31, 613-621.

Hess C., Reif A., Strobel A., Boreatti-Huemmer A., Heine M., et al 2009. A functional dopamine-beta-hydroxylase gene promoter polymorphism is associated with impulsive personality styles, but not with affective disorders. *J.Neural Transm.,* 116, 121-130.

Holgers K., Zoger S. & Svedlund K. 2005. Predictive factors for development of severe tinnitus suffering-further characterisation. *International Journal of Audiology,* 44, 584-592.

Holi M., Sammallahti P. & Aalberg V. 1998. A Finnish validation study of the SCL-90. *Acta Psychiatr.Scand.,* 97, 42-46.

Jääskeläinen S.K., Lindholm P., Valmunen T., Pesonen U., Taiminen T., et al 2014. Variation in the dopamine D2 receptor gene plays a key role in human pain and its modulation by transcranial magnetic stimulation. *Pain,* 155, 2180-2187.

Kessler R., Berglund P., Demler O., Jin R. & Walters E. 2005a. Lifetime prevalence and age-of-onset distributions' of DSM-IV disorders in the national comorbidity survey replication. *Arch.Gen.Psychiatry,* 62, 593-602.

Kessler R., Chiu W., Demler O. & Walters E. 2005b. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Arch.Gen.Psychiatry,* 62, 617-627.

Kessler R., Chiu W., Jin R., Ruscio A., Shear K., et al 2006. The epidemiology of panic attacks, panic disorder, and agoraphobia in the National Comorbidity Survey Replication. *Arch.Gen.Psychiatry,* 63, 415-424.

Lambert G., Johansson M., Agren H. & Friberg P. 2000. Reduced brain norepinephrine and dopamine release in treatment-refractory depressive illness - Evidence in support of the catecholamine hypothesis of mood disorders. *Arch.Gen.Psychiatry,* 57, 787-793.

Lamusuo S., Hirvonen J., Lindholm P., Martikainen I.K., Hagelberg N., et al 2017. Neurotransmitters behind pain relief with transcranial magnetic stimulation - positron emission tomography evidence for release of endogenous opioids. *Eur.J.Pain,* .

Langguth B., Kleinjung T., Fischer B., Hajak G., Eichhammer P., et al 2007. Tinnitus severity, depression, and the big five personality traits. *Prog.Brain Res.,* 166, 221-225.

Langguth B., Kreuzer P.M., Kleinjung T. & De Ridder D. 2013. Tinnitus: causes and clinical management. *Lancet Neurol.,* 12, 920-930.

Langguth B., Landgrebe M., Kleinjung T., Sand G.P. & Hajak G. 2011. Tinnitus and depression. *World J.Biol.Psychiatry,* 12, 489-500.

Leaver A.M., Renier L., Chevillet M.A., Morgan S., Kim H.J., et al 2011. Dysregulation of Limbic and Auditory Networks in Tinnitus. *Neuron,* 69, 33-43.

Lefaucheur J.P., Andre-Obadia N., Antal A., Ayache S.S., Baeken C., et al 2014. Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS). *Clin.Neurophysiol.,* 125, 2150-2206.

Lenzenweger M.F., Lane M.C., Loranger A.W. & Kessler R.C. 2007. DSM-IV personality disorders in the National Comorbidity Survey Replication. *Biol.Psychiatry,* 62, 553-564.

Malakouti S., Mahmoudian M., Alifattahi N. & Salehi M. 2011. Comorbidity of chronic tinnitus and mental disorders. *Int.Tinnitus J.,* 16, 118-122.

Marciano E., Carrabba L., Giannini P., Sementina C., Verde P., et al 2003. Psychiatric comorbidity in a population of outpatients affected by tinnitus. *Int.J.Audiol.,* 42, 4-9.

Newman C., Jacobson G. & Spitzer J. 1996. Development of the tinnitus handicap inventory. *Archives of Otolaryngology-Head & Neck Surgery,* 122, 143-148.

Olver J.S., O'Keefe G., Jones G.R., Burrows G.D., Tochon-Danguy H.J., et al 2009. Dopamine D-1 receptor binding in the striatum of patients with obsessive-compulsive disorder. *J.Affect.Disord.,* 114, 321-326.

Ooms E., Meganck R., Vanheule S., Vinck B., Watelet J., et al 2011. Tinnitus Severity and the Relation to Depressive Symptoms: A Critical Study. *Otolaryngology-Head and Neck Surgery,* 145, 276-281.

Pattyn T., Van den Eede F., Vanneste S., Cassiers L., Veltman D.J., et al 2016. Tinnitus and anxiety disorders: A review. *Hear.Res.,* 333, 255-265.

Pinto P.C.L., Marcelos C.M., Mezzasalma M.A., Osterne F.J.V., de Melo Tavares de Lima,M.A., et al 2014. Tinnitus and its association with psychiatric disorders: systematic review. *J.Laryngol.Otol.,* 128, 660-664.

Rauschecker J.P., May E.S., Maudoux A. & Ploner M. 2015. Frontostriatal Gating of Tinnitus and Chronic Pain. *Trends Cogn.Sci.(Regul.Ed.),* 19, 567-578.

Reich J., Nduaguba M. & Yates W. 1988. Age and Sex Distribution of Dsm-Iii Personality Cluster Traits in a Community Population. *Compr.Psychiatry,* 29, 298-303.

Rossi S., Hallett M., Rossini P.M., Pascual-Leone A. & Safety TMS Consensus Grp 2009. Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. *Clinical Neurophysiology,* 120, 2008-2039.

Sahlsten H., Virtanen J., Joutsa J., Niinivirta Joutsa K., Löyttyniemi E., et al 2017. Electric field-navigated transcranial magnetic stimulation for chronic tinnitus: a randomized, placebo-controlled study. *Int J Audiol,* 1-9.

Shargorodsky J., Curhan G.C. & Farwell W.R. 2010. Prevalence and Characteristics of Tinnitus among US Adults. *Am.J.Med.,* 123, 711-718.

Simpson R., Nedzelski J., Barber H. & Thomas M. 1988. Psychiatric Diagnoses in Patients with Psychogenic Dizziness Or Severe Tinnitus. *J.Otolaryngol.,* 17, 325-330.

Steer R.A., Ball R., Ranieri W.F. & Beck A.T. 1999. Dimensions of the Beck Depression Inventory-II in clinically depressed outpatients. *J.Clin.Psychol.,* 55, 117-128.

Sullivan M., Katon W., Dobie R., Sakai C., Russo J., et al 1988. Disabling Tinnitus - Association with Affective-Disorder. *Gen.Hosp.Psychiatry,* 10, 285-291.

Taiminen T., Kuusalo L., Lehtinen L., Forssell H., Hagelberg N., et al 2011. Psychiatric (axis I) and personality (axis II) disorders in patients with burning mouth syndrome or atypical facial pain. *Scand J Pain,* 2, 155-160.

Tunkel D.E., Bauer C.A., Sun G.H., Rosenfeld R.M., Chandrasekhar S.S., et al 2014. Clinical practice guideline: tinnitus. *Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery,* 151, S1-S40.

Zald D.H., Cowan R.L., Riccardi P., Baldwin R.M., Ansari M.S., et al 2008. Midbrain Dopamine Receptor Availability Is Inversely Associated with Novelty-Seeking Traits in Humans. *J.Neurosci.*, 28, 14372-14378.

Zirke N., Seydel C., Arsoy D., Klapp B.F., Haupt H., et al 2013. Analysis of mental disorders in tinnitus patients performed with Composite International Diagnostic Interview. *Qual.Life Res.*, 22, 2095-2104.

Zöger S., Svedlund J. & Holgers K.M. 2001. Psychiatric disorders in tinnitus patients without severe hearing impairment: 24 month follow-up of patients at an audiological clinic. *Audiology*, 40, 133-140.

Zöger S., Svedlund J. & Holgers K. 2006. Relationship between tinnitus severity and psychiatric disorders. *Psychosomatics*, 47, 282-288.

Figure Legends

Figure 1. The percentages (+SE) of patients with different personality disorders. The results of this study are presented (Tinnitus patients, n=83), then compared to chronic facial pain patients, Taiminen et al 2011 (Pain patients, n=63) and a normal population sample, Lenzenweger et al 2007 (Population sample, n=214). There were no significant differences between the percentages of tinnitus patients and the population sample. None of the tinnitus or pain patients suffered from any cluster B personality disorders.

Table 1. Summary of the studies published in English that have investigated psychiatric disorders in tinnitus patients with a structured diagnostic interview. N/A not applicable.
SCID=Structured Clinical Interview for DSM-III/IV disorders, NIMH DIS=National Institute of Mental Health Diagnostic Interview Schedule, MINI=Mini International Neuropsychiatric Interview
CIDI=Composite International Diagnostic Interview, PD=personality disorder, O-CPD=obsessive-compulsive personality disorder
[B] The rate of lifetime major depression, [E] The rate of current major depression

Authors and year Axis I psychiatric disorders	Sample	Instrument	Any lifetime axis I disorder (%)	Lifetime depression (%)	Lifetime anxiety (%)	Any current axis I disorder (%)	Current depression (%)	Current anxiety (%)	Comments
Belli et al 2008	90	SCID-I	N/A	N/A	N/A	24.4	7.8	27.8	
Harrop-Griffiths et al 1987	21	NIMH DIS	N/A	61.9[B]	N/A	N/A	47.6[E]	28.6	
Holgers at al 2005	127 (82)	SCID-P	76.8	61.0	45.1	65.9	39.0	45.1	SCID-P was conducted for 82 patients
Malakouti et al 2011	400	SCID-I	60.0	32.5[B]	45.8	55.2	N/A	N/A	
Marciano et al 2003	75	MINI	N/A	N/A	N/A	77.3	N/A	29.3	Affective disorders were analysed (27%), but depression not separately. Personality disorders were not analysed with a diagnostic interview.
Shargorodsky et al 2010	2265	CIDI	N/A	N/A	N/A	N/A	N/A	N/A	Only major depression (9.3%) and generalized anxiety disorder (20.4%) were analysed using CIDI with no division to lifetime or current.
Simpson et al 1988	24	SCID	N/A	N/A	N/A	62.5	54.2	29.2	
Sullivan et al 1988	40	NIMH DIS	N/A	77.5[B]	N/A	N/A	60.0[E]	N/A	
Zirke et al 2013	100	CIDI	N/A	N/A	N/A	46.0	N/A	32.0	Affective disorders were analysed (37%), but depression not separately.
Zöger et al 2001	82	SCID-P	78.0	62.2	45.1	54.9	39.0	45.1	Personality traits were also evaluated.
Zöger et al 2006	224 (80/144)	SCID-P	N/A	N/A	N/A	46/81	33[E]/52[E]	45/49	80 consecutive and 144 high-risk tinnitus patients were evaluated.

Axis II psychiatric disorders			Any PD (%)	Any cluster A PD (%)	Any cluster B PD (%)	Any cluster C PD (%)	O-CPD (%)	Avoidant PD (%)	
Belli et al 2008	90	SCID-II	3.3	0	1.1	4.4	1.1	2.2	
Erlandsson&Persson 2006	70 (18)	SCID-II	50.0	0	38.9	27.8	16.7	11.1	SCID-II was conducted only to a sub-group of 18 patients. Majority of patients had comorbidity of personality disorders.

Table 2

The prevalence rates of DSM-IV axis I and II psychiatric disorders in SCID-I and -II interviews, by onset, in 83 patients with chronic, disturbing tinnitus.
[o]Bipolar disorder and [a]active alcohol dependence were exclusion criteria for TMS treatment; during the study course one patient was discovered to have a bipolar disorder, though.
In order to compare the results to the general population, the rates of the National Comorbidity Survey Replication (Kessler et al, 2005 & 2006; Lenzenweger et al, 2007) are also shown.

Diagnosis	Onset before tinnitus		Onset after tinnitus		Current (previous month)		Lifetime		Lifetime, Kessler et al
	N	% (95% CI)	N	% (95% CI)	N	% (95% CI)	N	% (95% CI)	% (95% CI)
Axis I disorders									
Major depressive disorder	11	13.3 (6.8-22.5)	11	13.3 (6.8-22.5)	2	2.4 (0.3-8.4)	22	26.5 (17.4-37.3)	16.6 (15.8-17.4)
Chronic depression	3	3.6 (0.8-10.2)	3	3.6 (0.8-10.2)	5	6.0 (2.0-13.5)	6	7.2 (1.6-12.8)	2.5 (2.2-2.8)
Bipolar disorder[o]	1	1.2 (0-6.5)	0	0 (0-4.4)	0	0 (0-4.4)	1	1.2 (0-6.5)	3.9 (3.5-4.3)
Generalized anxiety disorder	2	2.4 (0.3-8.4)	2	2.4 (0.3-8.4)	2	2.4 (0.3-8.4)	4	4.8 (1.3-11.9)	5.7 (5.3-6.2)
Specific phobia	1	1.2 (0-6.5)	0	0 (0-4.4)	1	1.2 (0-6.5)	1	1.2 (0-6.5)	12.5 (11.9-13.1)
Social phobia	4	4.8 (1.3-11.9)	1	1.2 (0-6.5)	4	4.8 (1.3-11.9)	5	6.0 (2.0-13.5)	12.1. (11.5-12.7)
Agoraphobia without panic	0	0 (0-4.4)	0	0 (0-4.4)	0	0 (0-4.4)	0	0 (0-4.4)	1.4 (1.2-1.6)
Panic disorder	5	6.0 (2.0-13.5)	2	2.4 (0.3-8.4)	4	4.8 (1.3-11.9)	7	8.4 (3.5-16.6)	4.7 (4.3-5.1)
Panic disorder without agoraphobia	4	4.8 (1.3-11.9)	2	2.4 (0.3-8.4)	3	3.6 (0.8-10.2)	6	7.2 (1.6-12.8)	3.7 (1.7-5.7)
Panic disorder with agoraphobia	1	1.2 (0-6.5)	0	0 (0-4.4)	1	1.2 (0-6.5)	1	1.2 (0-6.5)	1.1 (0-3.1)
Post-traumatic stress disorder	1	1.2 (0-6.5)	0	0 (0-4.4)	0	0 (0-4.4)	1	1.2 (0-6.5)	6.8 (6.3-7.3)
Binge-eating disorder	2	2.4 (0.3-8.4)	0	0	1	1.2 (0-6.5)	2	2.4 (0.3-8.4)	
Alcohol dependence[a]	4	4.8 (1.3-11.9)	0	0 (0-4.4)	0	0 (0-4.4)	4	4.8 (1.3-11.9)	5.4 (4.9-5.9)
Drug dependence	2	2.4 (0.3-8.4)	0	0	1	1.2 (0-6.5)	2	2.4 (0.3-8.4)	3.0 (2.7-3.3)
Any psychotic disorder	0	0 (0-4.4)	0	0 (0-4.4)	0	0 (0-4.4)	0	0 (0-4.4)	
Any axis I disorder	25	30.1 (20.5-41.2)	12	14.5 (7.7-23.9)	15	18.1 (10.5-28.0)	37	44.6 (33.6-55.9)	46.4 (45.1-47.7)
Axis II personality disorders									Lenzenweger et al
Any cluster C personality disorder	8	9.6 (4.3-18.1)	0	0 (0-4.4)	7	8.4 (3.5-16.6)	8	9.6 (4.3-18.1)	6.0 (5.4-6.6)
Obsessive-compulsive personality	7	8.4 (3.5-16.6)	0	0 (0-4.4)	6	7.2 (1.6-12.8)	7	8.4 (3.5-16.6)	2.4 (0.8-4.0)
Avoidant personality	2	2.4 (0.3-8.4)	0	0 (0-4.4)	1	1.2 (0-6.5)	2	2.4 (0.3-8.4)	5.2 (2.0-8.3)
Any cluster A personality disorder	1	1.2 (0-6.5)	0	0 (0-4.4)	1	1.2 (0-6.5)	1	1.2 (0-6.5)	5.7 (5.1-6.3)
Schizoid personality	1	1.2 (0-6.5)	0	0 (0-4.4)	1	1.2 (0-6.5)	1	1.2 (0-6.5)	4.9 (0.6-9.2)
Any cluster B personality disorder	0	0 (0-4.4)	0	0 (0-4.4)	0	0 (0-4.4)	0	0 (0-4.4)	1.5 (1.2-1.8)
Any personality disorder	9	10.8 (5.1-19.6)	0	0 (0-4.4)	8	9.6 (4.3-18.1)	9	10.8 (5.1-19.6)	9.1 (8.4-9.9)

Table 3 Characteristics of 83 patients with chronic tinnitus. "Blue collar" refers to manual labor and "white collar" to office work.

Sex	
Men (%)	49 (59.0)
Women (%)	34 (41.0)
Age years, median (quartiles, range)	56.0 (47-61, 19-65)
Smoking patients (%)	9 (10.8)
Anti-depressive medication for mood or insomnia (%)	15 (18.1)
Medication for insomnia (other than anti-depressive), regular or irregular	9 (10.8)
Pain medication, regular or irregular (%)	16 (19.3)
Sosioeconomic class (%)	
Unskilled	1 (1.2)
Blue collar	43 (51.8)
White collar	16 (19.3)
Managerial	23 (27.7)
Duration of tinnitus years, median (quartiles, range)	5.0 (3.0-8.0, 1-10)
Audiogram, PTA right ear in decibel, median (quartiles)	14.0 (6.0-27.5)
Audiogram, PTA left ear in decibel, median (quartiles)	14.0 (6.0-28.8)
Tinnitus intensity in VAS, mean (SD)	60.5 (13.7)
Tinnitus annoyance in VAS, mean (SD)	53.7 (18.8)
Tinnitus distress in VAS, mean (SD)	52.1 (17.9)
Tinnitus Handicap Inventory (THI), median (quartiles)	32 (18-56)
THI grade 1 (%)	20 (24.1)
THI grade 2 (%)	27 (32.5)
THI grade 3 (%)	16 (19.3)
THI grade 4 (%)	19 (22.9)
THI grade 5 (%)	1 (1.2)