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Factors Associated with Depression in Patients with Tinnitus and Hyperacusis

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Short title: Depression in tinnitus and hyperacusis sufferers

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Abbreviations

BDI	Beck Depression Inventory
CI	95% confidence interval
HADS	Hospital Anxiety and Depression Scale
HQ	Hyperacusis Questionnaire
ICF	International Classification of Functioning Disability and Health
ISI	Insomnia severity index
NHS	National Health Service
PHQ	Patient Health Questionnaire
PTA	Pure tone average
SD	Standard deviation
TDI	Tinnitus Disability Index
THI	Tinnitus Handicap Inventory
THTSC	Tinnitus and Hyperacusis Therapy Specialist Clinic
ULL	Uncomfortable Loudness Level
ULLmin	Average ULL across the audiometric frequencies for the ear with the lower average
VAS	Visual Analogue Scale
WHO	World Health Organization

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Abstract

Purpose: To assess factors associated with depression for patients with tinnitus and hyperacusis.

Method: Data were gathered from the records of 620 consecutive patients who sought help concerning their tinnitus or hyperacusis from an audiology clinic in the UK.

Results: One third of patients had borderline abnormal or abnormal scores on the depression subscale of the hospital anxiety and depression scale (HADS-D). Linear regression models showed that HADS-D scores were related to scores for tinnitus handicap, tinnitus loudness, and uncomfortable loudness levels (ULLs). Mediation analyses showed that: (1) The influence of tinnitus handicap scores on HADS-D scores was mainly mediated via the effects of insomnia, hyperacusis, and anxiety; (2) The influence of tinnitus loudness scores on HADS-D scores was fully mediated via the effects of tinnitus handicap, insomnia, hyperacusis handicap, and anxiety; (3) The small influence of ULLs on HADS-D scores was fully mediated by hyperacusis handicap and anxiety.

Conclusions: Those involved in the management of patients with tinnitus and/or hyperacusis should use a wide range of instruments to assess the full impact of tinnitus on a patient's life and should be prepared to refer a patient for treatment for depression, especially when the patient has anxiety, hyperacusis, and/or insomnia.

INTRODUCTION

Tinnitus is the sensation of sound without any external acoustic sound source. Hyperacusis is an intolerance to everyday sounds that causes significant distress and impairment in social, occupational, recreational, and other day-to-day activities (Aazh, Moore, Lammaing, & Cropley, 2016). Sounds may be perceived as uncomfortably loud, unpleasant, frightening, or painful (Tyler et al. 2014). Tinnitus and hyperacusis often occur together (Schecklmann, Landgrebe, Langguth, & T. R. I. Database Study Group, 2014; Tyler, Noble, Coelho, Roncancio, & Jun, 2015). Tinnitus handicap has been shown to be related to the loudness of tinnitus, hyperacusis, insomnia, anxiety, and depression (Hiller & Goebel 2007; Hiller & Goebel 2006; Kehrle et al. 2016; Ooms et al. 2012; Andersson et al. 2004; Hu et al. 2015; Tyler & Baker 1983; Juris et al. 2013; Aazh & Allott 2016; Hebert et al. 2012; Probst et al. 2016; Folmer & Griest 2000). It has been suggested that anxiety symptoms are more likely to lead to depressive symptoms than depressive symptoms are to lead to anxiety symptoms (Lenze & Wetherell 2011; Wetherell et al. 2001). Therefore, the anxiety produced by tinnitus and hyperacusis could be a risk factor for depression in affected individuals.

Symptoms of depression are common in patients with tinnitus and hyperacusis and there is an overlap between the factors associated with depression and with tinnitus, such as insomnia and anxiety (Langguth et al. 2011; Durai & Searchfield 2016; Schecklmann et al. 2014). However, only a few studies have examined the factors that predict depression in patients with tinnitus and hyperacusis (Zeman, Koller, Langguth, & Landgrebe, 2014; Trevis, McLachlan, & Wilson, 2016). Exploration of the factors predicting depression is important as it can guide audiologists to screen for such factors in patients with tinnitus and hyperacusis and to refer patients for psychiatric management of co-morbid depression. In addition, deeper understanding of the processes mediating the relationship between tinnitus and depression is important as it may guide development of specific therapeutic interventions for this population.

Zeman et al. (2014) reported that tinnitus handicap as measured via the Tinnitus Handicap Inventory (THI; Newman et al. 1996) significantly predicted depression as measured via the Beck Depression Inventory (BDI) (Beck & Steer 1984); the regression coefficient was b = 0.26 (p<0.001). Although in their model the THI scores explained 42% of the variance in BDI scores, they did not take into account other factors that are known to influence

depression, such as anxiety and insomnia (Lenze & Wetherell, 2011; Bhatt, Bhattacharyya, & Lin, 2017). The inclusion of such factors in the model might explain part or all of the relationship between THI and BDI scores. Trevis et al. (2016) also reported that depression as measured via the BDI was predicted by tinnitus handicap as measured via the THI (regression coefficient $b = 0.31$, $p<0.001$). They too did not take into account the possible effect of intervening factors on the relationship between depression and tinnitus handicap. Neither of these studies assessed the effect of tinnitus loudness on BDI scores (Zeman et al. 2014; Trevis et al. 2016). The perceived loudness of tinnitus is an important factor leading to tinnitus distress from the patient's perspective (Tyler et al. 2006; 2007).

It is not clear whether tinnitus loudness is related to depression. Probst et al. (2016) assessed the relationship between tinnitus loudness and tinnitus distress using regression models and mediation analysis. Mediation analysis estimates the direct and indirect effects of variables on an outcome (see methods for details). They reported that the direct effect of tinnitus loudness on tinnitus distress was considerable; the regression coefficient was $b = 0.65$ ($p<0.001$). The indirect effect of tinnitus loudness on tinnitus distress, mediated via stress level, arousal, and valance, was only 0.11 (95% confidence interval, CI: 0.08 to 0.14). That study did not assess the relationship between tinnitus loudness and depression. In addition, they used only a single question to measure tinnitus loudness and tinnitus distress, as opposed to using validated questionnaires or a clinical interview.

Hyperacusis can lead to a high level of disability and is co-morbid with a wide range of psychological disorders (Aazh et al. 2014). Goebel and Floezinger (2008) reported that 42% of 163 patients with hyperacusis suffered from depression. Juris et al. (2013) reported that 15% and 8% of patients with hyperacusis ($n = 62$) had an affective disorder and major depression, respectively. Schecklmann et al. (2014) reported that the mean score on the BDI was 12.8 (standard deviation, SD = 9.4) for patients with tinnitus combined with hyperacusis ($n = 867$). This was significantly higher than the mean score of 9.3 (SD = 8.0) for patients with tinnitus only ($n = 716$, $p<0.001$). Aazh and Moore (2017) reported that the relative risk ratio of abnormal depression scores on the Patient Health Questionnaire (PHQ-9; Kroenke et al. 2001) increased by factors of 2.7 (95% CI: 1.04 to 7.13) for patients with hyperacusis handicap as measured via the Hyperacusis Questionnaire (HQ; Khalfa et al. 2002) compared to patients with no hyperacusis handicap.

Audiologists often use uncomfortable loudness levels (ULLs), also called loudness discomfort levels, to determine the lowest sound level at which sounds are perceived to be "too loud"; for people with normal-hearing the average ULL across the audiometric frequencies is about 100 dB HL (Sherlock & Formby 2005). People with hyperacusis often have lower than normal ULLs in one or both ears (Tyler et al. 2014). ULLs can be used both to diagnose hyperacusis and to assess the severity of hyperacusis. However, to our knowledge there is no study in the literature that assessed the mechanisms underlying the relationship between reduced ULLs and depression.

The aims of this study were to assess, for patients seeking help for tinnitus and/or hyperacusis in an audiology clinic, whether:

(1) the relationship between tinnitus handicap and depression, as reported by Zeman et al. (2014) and Trevis et al. (2016), remains significant after taking into account the intervening effects of other factors, namely, insomnia, anxiety and hyperacusis.

(2) there is a relationship between self-reported tinnitus loudness and depression and the factors mediating any such relationship.

(3) there is a relationship between ULLs and depression and the factors mediating any such relationship.

METHODS

Study Design and Patients

This was a retrospective cross-sectional study conducted at the Tinnitus and Hyperacusis Therapy Specialist Clinic (THTSC), Royal Surrey County Hospital, Guildford, UK, which is part of the National Health Service in the UK. The data for patients who attended the THTSC from January 2012 to October 2013 were included (n = 620). The average age of the patients was 57 years (SD = 17 years) and 49% (306/620) were male. Demographic data for the patients and the outcomes of their audiological investigations and self-report questionnaires were imported from their records held at the Audiology department. All the data are based on the initial assessment of the patients prior to any treatment.

Evaluation Instruments

Assessment of anxiety and depression

Anxiety and depression were evaluated using the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith 1983). The HADS consists of 14 items, each rated from 0 to 3 according to the severity experienced. Eight items require reversed scoring, after which anxiety (HADS-A) and depression (HADS-D) subscale totals can be obtained. The total score for each subscale ranges from 0 to 21. Scores from 0-7 are classified as normal, scores from 8-10 are classified as borderline abnormal, and scores from 11-21 are classified as abnormal (Zigmond & Snaith 1983).

Audiological measurements

Pure-tone audiometry was conducted using the procedure recommended by the British Society of Audiology (BSA 2004). The severity of hearing loss was categorized based on the values of the PTA at the frequencies 0.25, 0.5, 1, 2, and 4 kHz, as recommended by the British Society of Audiology (BSA 2004): Mild (20–40 dB HL), Moderate (41–70 dB HL), Severe (71–95 dB HL) and Profound (over 95 dB HL). ULLs were measured using the BSA recommended procedure (BSA 2011). The average ULL at 0.25, 0.5, 1, 2, 4 and 8 kHz for the ear with the lower average ULL is denoted ULLmin. Hyperacusis was considered as present if ULLmin was ≤77 dB HL (Aazh & Moore 2017b).

Assessment of tinnitus and hyperacusis handicap

The Tinnitus Handicap Inventory (THI; Newman et al. 1996) was used to assess the impact of tinnitus on each patient's life. The THI has 25 items, and response choices are "no" (0 points), "sometimes" (2 points) and "yes" (4 points). The overall score ranges from 0 to 100. Scores from 0–16 indicate no handicap, scores from 18–36 indicate mild handicap, scores from 38–56 indicate moderate handicap, and scores from 58–100 indicate severe handicap (Newman et al. 1996).

The Visual Analogue Scale (VAS; Maxwell 1978) was used in order to assess the loudness of tinnitus. VAS scores are ratings on a scale from 0 to 10. The VAS score for loudness of tinnitus was assessed by asking the patient to rate the loudness of tinnitus during their waking hours over the last month. It was explained that 0 corresponds to no tinnitus being heard and 10 is the loudest sound that they can imagine.

The Hyperacusis Questionnaire (HQ; Khalfa et al. 2002) was used to assess the effect of hyperacusis on each patient's life. The HQ comprises 14 items and the response choices are

"no" (0 points), "yes, a little" (1 point), "yes, quite a lot" (2 points), and "yes, a lot" (3 points). The overall score ranges from 0 to 42. Scores of 22 or more were taken as indicating hyperacusis handicap (Aazh & Moore 2017b).

Assessment of insomnia

The Insomnia Severity Index (ISI; Bastien et al. 2001) was used to assess insomnia. The ISI comprises seven items that assess the severity of sleep difficulties and their effect on the patient's life. Each item is rated on a scale from 0 to 4 and the total score ranges from 0 to 28. Scores from 0-7 indicate no clinically significant insomnia, scores from 8-14 indicate slight insomnia, scores from 15-21 indicate moderate insomnia, and scores from 22-28 indicate severe insomnia (Bastien et al. 2001).

Ethical Approval

This study was approved by the South West Cornwall and Plymouth Research Ethics Committee and the Research and Development Department at the Royal Surrey County Hospital.

Data Analysis

The STATA program (version 13) was used for statistical analyses. Descriptive statistics, means, SDs, 95% CIs, and scores for the self-report questionnaires are reported. The *p*-value required for statistical significance was set at $p<0.05$.

Linear regression models were created to assess the one-to-one relationship between the tinnitus- and hyperacusis-related independent variables and depression. Then, multiple mediation analysis (Bollen 1987) was conducted in order to explore the nature of the relationship between specific independent variables and depression (dependent variable). The mediation analysis assessed the direct and indirect effects of each independent variable on the dependent variable. This was achieved by determining whether the relationship between a given independent variable and the dependent variable changed when other independent variables were added. If the other variables changed this relationship, and if they themselves were related to the dependent variable, they were defined as mediator variables (Baron & Kennedy 1986). The total effect of each independent variable on the dependent variable was assessed by calculating the regression coefficient (*b*) between them. A relationship was indicated by a regression coefficient that was significantly different from zero. If the

relationship between a given independent variable, X, and the dependent variable became insignificant after including the effect of the mediator variable(s), this was defined as full mediation. Full mediation implies that the effect of X on the dependent variable is determined entirely through the mediator(s). A remaining significant effect of X after including the effect of the mediator(s) is called a direct or residual effect, and it is assumed to reflect the direct influence of X on the dependent variable (Chen & Hung 2016).

The indirect effect of a specific independent variable, X, was calculated by multiplication of the regression coefficient between X and the mediator variable, also defined as the first stage effect, and the regression coefficient between the mediator variable and the dependent variable, also defined as the second stage effect (Brown 1997). The method described by Preacher and Hayes (2008) for assessing indirect effects in multiple mediator models was used. All of the necessary coefficients were calculated via "seemingly unrelated regression" (Zellner 1962). The individual indirect effects were calculated via the "nonlinear combinations of estimators command" in STATA (Preacher & Hayes 2008). The total indirect effect was calculated by summing up the individual indirect effects (Brown 1997).

Three mediation models were developed. The first model assessed the relationship between THI scores and HADS-D scores. The independent (potential mediator) variables were scores for the HADS-A, ISI, and HQ. The second model assessed the relationship between tinnitus loudness as measured via the VAS and HADS-D scores. The potential mediator variables were scores for the THI, HADS-A, ISI, and HQ. The third model assessed the relationship between ULLmin values and the HADS-D score. The potential mediator variables were scores for the HQ and HADS-A. Tinnitus-related variables were not included in this model as some of the patients with hyperacusis did not have tinnitus, and not all patients with hyperacusis completed the THI and VAS. The inclusion of tinnitus-related variables would have led to the exclusion of such patients from the model, leading to reduced statistical power and generalisability. Although the relationship between insomnia and depression is well established, ISI scores were not included in the model, as there is no evidence supporting the idea that ULLs are related to insomnia. The analyses were restricted to patients with complete data on all variables required for a particular analysis. The number of patients included in each analysis (*n*) is reported.

RESULTS

The means and SDs of scores on the HADS, VAS, THI, HQ, and ISI are shown in Table 1. For the depression subscale of the HADS, 67% (355/499) of patients had normal scores, 15% (76/499) had borderline abnormal scores, and 18% (88/499) had abnormal scores. For the anxiety subscale of the HADS, 43% (215/499) of patients had normal scores, 24% (120/499) had borderline abnormal scores, and 33% (164/499) had abnormal scores.

TABLE 1 HERE

Means and Distributions of Scores

Based on scores for the THI, 13% of patients (66/492) had no tinnitus handicap, 28% (139/492) had a mild tinnitus handicap, 27% (134/492) had a moderate tinnitus handicap, and 31% (153/492) had a severe tinnitus handicap.

The mean pure-tone average (PTA) hearing loss at the frequencies 0.25, 0.5, 1, 2, and 4 kHz across the ears was 25 dB HL (SD = 17 dB). Based on the PTA for the better ear, 56% of patients (269 out of 483 with audiograms) had no hearing loss, 33% (160/483) had mild hearing loss, 10% (50/483) had moderate hearing loss, and 0.8% (4/483) had severe hearing loss.

The average value of ULLmin across patients was 82 dB HL (SD = 15 dB). Thirty three percent (108/326) of patients had ULLmin values of 77 dB HL or lower, which indicates hyperacusis handicap. Based on scores for the HQ, 29% (131/455) of patients experienced hyperacusis handicap.

Based on scores for the ISI, 30% (128/421) of patients did not have insomnia, 29.5% (124/421) had mild insomnia, 26% (111/421) had moderate insomnia, and 14% (58/421) had severe insomnia.

FIGURE 1 HERE

Relationship between tinnitus handicap and depression

Linear regression analysis showed a small but statistically significant relationship between tinnitus handicap as measured via the THI and depression as measured via the HADS-D (b = 0.12, 95% CI: 0.11 to 0.13) (path “a” in Figure 1), after allowing for the effect of age and gender. This model explained 43% of the variance of the scores on the HADS-D. Mediation

analysis was conducted to explore how much of this effect was direct and how much of it was mediated through other variables. The mediation analysis (n = 374) showed that the regression coefficients for the indirect effects of tinnitus handicap on depression were as follows: via anxiety as measured using the HADS-A score (path "e"), b = 0.05 (95% CI: 0.04 to 0.06); via insomnia as measured using the ISI score (path "b"), b = 0.02 (95% CI: 0.01 to 0.03); and via hyperacusis as measured using the HQ score (path "c"), b = 0.01 (95% CI: 0.005 to 0.02). The coefficient for the total indirect effect was b = 0.08 (95% CI: 0.07 to 0.095). The regression coefficient for the direct effect of tinnitus handicap on depression (path "d") was only b = 0.04 (95% CI: 0.02 to 0.05), a small but significant effect. In summary, the relationship between tinnitus handicap and depression was largely mediated via anxiety, insomnia, and hyperacusis.

FIGURE 2 HERE

Relationship between tinnitus loudness and depression

Linear regression analysis showed a statistically significant relationship between tinnitus loudness as measured via the VAS and the HADS-D score (b = 0.74, 95% CI: 0.55 to 0.94), after allowing for the effects of age and gender (path "a" in Figure 2). This model explained 12% of the variance in the HADS-D scores. A mediation analysis (n = 359) showed that the regression coefficients for the indirect effects of tinnitus loudness on depression were as follows: via tinnitus handicap as measured using the THI score (path "b"), b = 0.20 (95% CI: 0.09 to 0.32); via insomnia as measured using the ISI score (path "c"), b = 0.17 (95% CI: 0.09 to 0.25); via hyperacusis as measured using the HQ score (path "e"), b = 0.05 (95% CI: 0.006 to 0.085); and via anxiety as measured using the HADS-A score (path "f"), b = 0.31 (95% CI: 0.19 to 0.42). The regression coefficient for the total indirect effect was b = 0.73 (95% CI: 0.55 to 0.92). The direct effect of tinnitus loudness on depression (path "d") was not statistically significant (b = –0.04, 95% CI: –0.2 to 0.12). In summary, the relationship between tinnitus loudness and depression was fully mediated via tinnitus handicap, insomnia, hyperacusis, and anxiety.

FIGURE 3 HERE

Relationship between ULLmin and depression

Linear regression analysis showed a small but statistically significant negative relationship between the ULLmin and depression as measured via the HADS-D (b = –0.06, 95% CI: –0.1 to –0.03) after allowing for the effects of age and gender (path "a" in Figure 3). This model

explained 5% of the variance in HADS-D scores. A mediation analysis (n = 297) showed that the regression coefficients for the indirect effects of ULLmin on depression were as follows: via anxiety as measured using the HADS-A (path "b"), b = –0.03 (95% CI: –0.05 to –0.013); via hyperacusis handicap as measured using the HQ (path "d"), b = –0.03 (95% CI: –0.04 to –0.014). The regression coefficient for the total indirect effect was b = –0.06 (95% CI: –0.09 to –0.03). The direct effect of the ULLmin on depression (path "c") was not statistically significant (b = 0.02, 95% CI: –0.007 to 0.04). In summary, the relationship between ULLmin and depression was fully mediated via hyperacusis handicap and anxiety.

DISCUSSION

In our sample of patients, 33% had borderline abnormal or abnormal scores on the HADS-D. This prevalence of depression is comparable with the value of 36% for a tinnitus self-help group reporting feelings of depression (Tyler & Baker 1983) and 27% of tinnitus patients who self-reported depression (Folmer et al. 1999). Our prevalence is slightly lower than the prevalence of 42% reported by Goebel and Floezinger (2008) for patients whose primary complaint was hyperacusis. Overall, it appears that the prevalence of depression is high among patients seeking treatment for tinnitus and/or hyperacusis.

As described in the Introduction, some studies have reported an association between tinnitus and depression. Zeman et al. (2014) and Trevis et al. (2016) reported that THI scores significantly predicted depression as measured via the BDI (b = 0.26, p<0.001 for Zeman et al. and b = 0.31, p<0.001 for Trevis et al.). In our study, the regression coefficient for the relationship between THI and depression as measured via the HADS-D was smaller but still significant at b = 0.12 (p<0. 001). The discrepancy in the regression coefficients between our study and those of Zeman et al. and Trevis et al. could be due to differences in the instruments used for the assessment of depression. The HADS-D used in the present study gives a total score between 0 and 21 while the BDI used by Zeman et al. (2014) and Trevis et al. (2016) gives a total score between 0 and 63. Due to the smaller range of numbers with the HADS-D than with the BDI, a 1-unit increase in THI score is associated with a smaller change in the HADS-D score than in the BDI score. In addition, Trevis et al. (2016) recruited participants through advertisement, so their study population may have differed from ours. Their mean THI score was 26% (95% CI: 21.8% to 30.8%) which was lower than the value

of 44% (95% CI: 42.3% to 46.5%) found in our study. Their population was also significantly younger than ours. The mean age of our study population was 57 years (SD = 17), while that of their study population was 45 years (SD = 16).

While these studies are consistent in finding a link between tinnitus and depression, the first mediation model used in our study revealed that most of the effect of THI scores on HADS-D scores was explained by the mediating effects of scores on the HADS-A, ISI, and HQ. This highlights the need for audiologists who are specialised in tinnitus and hyperacusis rehabilitation to use instruments such as the HADS, ISI, and HQ, in addition to the THI, to fully explore the effect of tinnitus on a patient's life and to decide whether the patient needs to be referred to mental health services for further assessment and management of their depression symptoms. Consistent with this, Aazh and Moore (2017) suggested the use of psychological questionnaires assessing anxiety disorders and depression for patients with tinnitus and hyperacusis. They reported that psychological questionnaires are acceptable to such patients and that the patients find the questionnaires to be relevant to their problems.

The second mediation model revealed that the effect of tinnitus loudness on depression, while significant, was fully mediated through scores for the THI, HQ, HADS-A and ISI. This is consistent with the idea that high tinnitus loudness is associated with tinnitus handicap, hyperacusis handicap, anxiety, and insomnia, and these in turn lead to depression. The clinical implication for audiologists is that for patients who suffer from tinnitus, depressive symptoms may be alleviated if tinnitus-induced anxiety, tinnitus handicap and hyperacusis are managed adequately, even if the self-perceived tinnitus loudness remains unchanged. Past research has shown that although tinnitus loudness as measured via the VAS is only minimally reduced following various forms of tinnitus rehabilitation, THI scores typically improve (Aazh et al. 2008; Aazh et al. 2013; Aazh & Moore 2016). This improvement may be sufficient to reduce the severity of depression.

The third mediation model assessed the relationship between ULLmin and depression. The total effect of ULLmin values on HADS-D scores was minimal: the ULLmin values explained only 5% of the variance in HADS-D scores. Furthermore, the mediation model revealed that the relationship between ULLmin and HADS-D scores was mediated by hyperacusis handicap and anxiety rather than being a direct relationship. Although it has been reported that people with hyperacusis often have lower than normal ULLs in one or both ears

(Tyler et al. 2014) and 42-47% of them may also suffer from depression (Goebel & Floezinger 2008; Aazh & Moore 2017), the mechanism that produces depression in patients with hyperacusis does not seem to be explained by reduced ULLs. Therefore, future research should focus on factors that might lead to depression in patients with hyperacusis.

As this was a cross-sectional study, the analyses conducted here do not directly indicate that anxiety, insomnia and hyperacusis lead to depression. However, the results do suggest that those involved in the management of patients with tinnitus and/or hyperacusis should screen for insomnia, hyperacusis handicap, and anxiety and depression symptoms in addition to assessing tinnitus handicap. Patients with anxiety and depression symptoms may need to be referred for further psychological or psychiatric evaluation and treatment when needed.

CONCLUSIONS

Among patients seeking treatment for tinnitus and/or hyperacusis, 33% had borderline abnormal or abnormal scores on the depression sub-scale of the HADS. Our results showed that:

(1) Although depression as measured via the HADS-D was predicted by tinnitus handicap, most of this effect was mediated by insomnia, hyperacusis handicap, and anxiety.

(2) The relationship between depression as measured by the HADS-D and tinnitus loudness as measured via the VAS was fully mediated by tinnitus handicap, insomnia, hyperacusis, and anxiety. Hence treatments focusing on minimizing tinnitus handicap, insomnia, hyperacusis, and anxiety might alleviate depressive symptoms in this population.

(3) ULLmin values had only a minimal effect on HADS-D scores, and the effect was mediated by hyperacusis handicap and anxiety.

We conclude that those involved in the management of patients with tinnitus and/or hyperacusis should use a wide range of instruments to assess the full impact of tinnitus on a patient's life and should be prepared to refer a patient for treatment of depression, especially when the patient has severe anxiety, hyperacusis, and/or insomnia.

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Figure captions

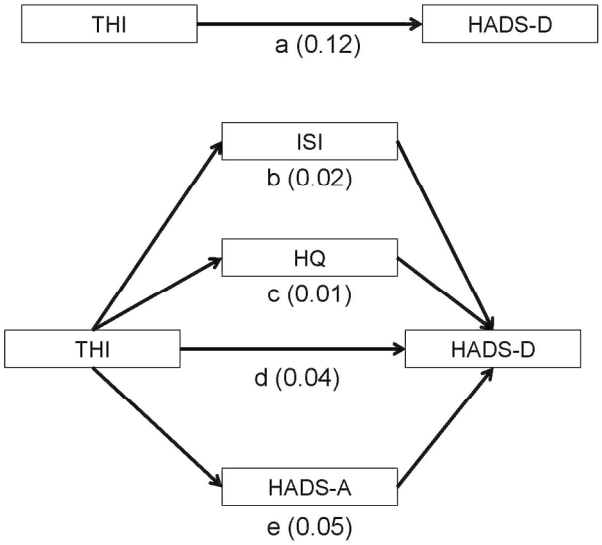
Figure 1: Multiple mediation model for the relationship between depression as measured via the HADS-D and tinnitus handicap as measured via the THI. Numbers in parentheses are regression coefficients; see text for details. (HADS-D= depression subscale of hospital anxiety and depression scale, HADS-A= anxiety subscale of hospital anxiety and depression scale, ISI= insomnia severity index, THI=tinnitus handicap inventory, HQ=hyperacusis questionnaire)

Figure 2: As Fig. 1 but for the relationship between depression as measured via the HADS-D and tinnitus loudness as measured by the VAS. (VAS=visual analogue scale, HADS-D= depression subscale of hospital anxiety and depression scale, HADS-A= anxiety subscale of hospital anxiety and depression scale, ISI= insomnia severity index, THI=tinnitus handicap inventory, HQ=hyperacusis questionnaire)

Figure 3: As Fig. 1 but for the relationship between depression as measured via the HADS-D and ULLmin values. (HADS-D= depression subscale of hospital anxiety and depression scale, HADS-A= anxiety subscale of hospital anxiety and depression scale, HQ=hyperacusis questionnaire, ULLmin= average ULL across the audiometric frequencies for the ear with the lower average)

TABLE 1. Means and SDs of scores on the hospital anxiety and depression scale (HADS-D and HADS-A), visual analogue scale (VAS) of tinnitus loudness, tinnitus handicap inventory (THI), hyperacusis questionnaire (HQ), and insomnia severity index (ISI). The number of patients for whom scores were available for each questionnaire is indicated by *n*.

Questionnaire	*n*	Mean	SD
HADS (Depression)	499	6.0 (out of 21)	4.4
HADS (Anxiety)	499	8.5 (out of 21)	4.5
VAS (Tinnitus loudness)	456	6.0 (out of 10)	2.0
THI	493	44.4 (out of 100)	24
HQ	455	17.3 (out of 42)	9.2
ISI	421	12.4 (out of 28)	7.1



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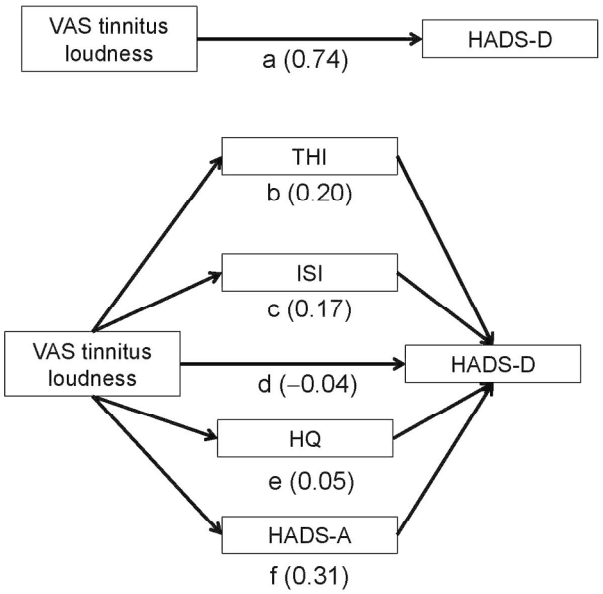

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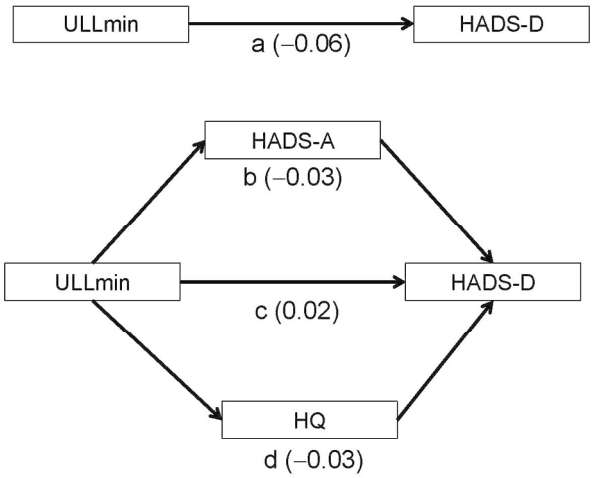

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