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Identifying Tinnitus Subgroups With Cluster Analysis

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Abstract

Purpose—We believe it is important to uncover tinnitus subgroups to identify subsets of patients most likely to benefit from different treatments. We review strategies for subgrouping based on etiology, subjective reports, the audiogram, psychoacoustics, imaging, and cluster analysis.

Method—Preliminary results of a 2-step cluster analysis based on 246 participants from whom we had 26 categorical and 25 continuous variables were determined.

Results—A 4-cluster solution suggested the following subgroups: (a) constant distressing tinnitus, (b) varying tinnitus that is worse in noise, (c) tinnitus patients who are copers and whose tinnitus is not influenced by touch (somatic modulation), and (d) tinnitus patients who are copers but whose tinnitus is worse in quiet environments.

Conclusions—Subgroups of tinnitus patients can be identified by using statistical approaches. The subgroups we identify here represent a preliminary attempt at identifying such patients. One next step would be to explore clinical trials of tinnitus treatments based on subgroup analyses or on using subgroups in the selection criteria.

Keywords

tinnitus; subgroups; cluster analysis

Tinnitus is a symptom but likely has many causes. It may be the case that any single treatment will not be effective for treating all tinnitus patients but that different treatments will be needed for different subgroups. There is a long-standing interest in the identification of these subgroups. For example, Tyler and Baker (1983) observed that some tinnitus sufferers avoided noisy situations, whereas others avoided quiet situations. They postulated that ”these contrasts may suggest two subcategories of tinnitus [patients]” (Tyler & Baker, 1983, p. 152). Tyler (1984) observed that ”psychophysical masking studies suggests there are different types of tinnitus” (p. 43).

In this article, we briefly review some possible strategies for determining tinnitus subgroups and then focus on some preliminary data from questionnaires and psychoacoustic measures using a cluster analysis.

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Strategies for Subgrouping

Etiology

Many of the causes and mechanisms involved in hearing loss are likely involved in tinnitus. Some of the more common and widely accepted causes are noise, aging, medications, head injury, and Ménière's disease. Unfortunately, many of the causes of tinnitus are unknown. Stouffer and Tyler (1990) found that 23% of their male participants reported that noise exposure had likely caused their tinnitus, but 46% of the 528 tinnitus patients had no idea what might have caused their tinnitus. It may also be that the cause of tinnitus varies within these categories. For example, impulsive noise might create a different kind of tinnitus compared with tinnitus caused by continuous noise. In addition, the aging process might affect people differently. Different medications are likely to have different effects on individuals with different metabolisms, and the category of tinnitus caused by head injuries might depend on where in the brain the injury occurs.

Subjective Reports

Because tinnitus is a subjective phenomenon, the patients' own descriptions of their problem provide valuable insights. Stouffer and Tyler (1990), for example, noted that 38% of their tinnitus patients reported hearing a ringing sound and 11% heard a buzzing sound.

We have recently (Tao et al., 2008) grouped these descriptions into the following:

- tonal (including hissing, musical note, ringing, steam whistle, whistling)
- noise (including buzzing, humming, roaring, rushing, whooshing)
- crickets (including clicking, cricket-like)
- pulsing
- other

One can imagine that noise-like tinnitus might activate a large array of fibers, or that a tonal or cricket-like tinnitus might be represented by periodic activity. But patients' descriptions of their tinnitus are likely influenced by their personal experiences, and some are not very articulate.

Audiogram

Tinnitus is closely linked to hearing loss, and some of the proposed models of tinnitus are linked to hearing loss (e.g., Salvi, Lockwood, & Burkard, 2000; Salvi, Wang, & Powers, 1996) and audiogram shape (Norena, Micheyl, Chery-Croze, & Collet, 2002). We have been exploring different audiogram shapes in tinnitus patients (Tao et al., 2008) and have identified the following shapes:

- flat loss
- low-frequency hearing loss
- normal hearing
- notch
- others (shape not typical)
- gradual slope loss
- steep slope loss
- inverted U shape

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However, similar audiograms might be produced by different causes. Furthermore, it may be that hearing thresholds at octaves are insufficient to provide an adequate characterization of the details of hair cell and nerve fiber survival. It could even be the case that hearing thresholds below 125 Hz and above 8000 Hz are helpful.

Psychoacoustics

We have suggested for some time that detailed psychoacoustic studies should provide an important basis for identifying subgroups (e.g., Tyler, Babin, & Niebuhr, 1984; Tyler, 2000).

Some potential leads for psychoacoustic-based subgroups are (a) tonal masking patterns (Feldmann, 1971; Formby & Gjerdingen, 1980; Tyler & Conrad-Armes, 1984); (b) ipsilateral and contralateral masking (Henry, Fausti, Flick, Helt, & Ellingson, 2000; Tyler, Kuk, & Mims, 1987); (c) postmasking effects of level and duration (Feldmann, 1971; Tyler Babin, & Niebuhr, 1984; Vernon & Meikle, 1988); (d) contralateral postmasking (Tyler, Conrad-Armes, & Smith, 1984); and (e) adaptation of masking (Penner & Bilger, 1995; Penner, Brauth, & Hood, 1981).

Imaging

Obtaining ”images” of the auditory area and related systems might also help to understand different subgroups of tinnitus patients. Researchers have used magnetoencephalography (e.g., Weisz, Moratti, Meinzer, Dohrnann, & Elbert, 2005), event-related potentials (Jacobson et al., 1991; Muhlnickel, Elbert, Taub, & Flor, 1998; Weisz, Voss, Berg, & Elbert, 2004), magnetic resonance imaging (De Ridder, De Mulder, Menovsky, Sunaert, & Kovacs, 2007; Melcher, Sigalovsly, Guinan, & Levine, 2000; Muhlau et al., 2006), and positron emission tomography (Arnold, Bartenstein, Oestreicher, Romer, & Schwaiger, 1996; Lockwood, Salvi, & Burkard, 2001; Lockwood et al., 1998; Reyes et al., 2002). Unfortunately, only a few of these studies have used hearing impaired controls. It is unclear whether differences between the images from tinnitus and control groups are attributable to tinnitus or to hearing loss. It is important that any approach to modify the tinnitus (to create a tinnitus and nontinnitus condition within the same patient) does not also change the image itself.

Cluster Analysis

Yet another approach to finding subgroups involves many measurements and a statistical analysis called cluster analysis. Cluster analysis is an approach to identify homogeneous subgroups from a set of common variables without making presumptions about what variables are important. Generally, measurements are made from a large number of participants, and the analysis attempts to group those participants that perform similarly.

Preliminary Results of Cluster Analysis

We have performed a cluster analysis on patients enrolled in some clinical trials at the University of Iowa. Some of the variables that were included were (a) the Tinnitus Handicap Questionnaire (Kuk, Tyler, Russell, & Jordan, 1990); (b) the Tinnitus Activities Questionnaire (Tyler, Gehringer, et al., 2006); (c) portions of the Tinnitus Intake Questionnaire (Stouffer & Tyler, 1990); (d) biographical variables; and (e) psychoacoustic tinnitus measurements (pitch and loudness matching).

We have found that the Tinnitus Handicap Questionnaire and the Tinnitus Activities Questionnaire are particularly helpful because they are scored on a 0−100 ordinal scale (Tyler, Oleson, Noble, Coelho, & Ji, 2007). They therefore have advantages over questionnaires that use only a 3-point scale, such as the Tinnitus Handicap Inventory (Newman, Jacobson, & Spitzer, 1996). Because we use the Tinnitus Handicap and Tinnitus Activities Questionnaire, we include in our analysis some responses to individual questions. Other behavioral tests, such as measuring postmasking effects and tonal masking patterns, might be additionally helpful. We did not have data on a sufficient number of patients, and therefore they could not be utilized in the cluster analysis.

Prliminary Cluster Analysis

Data were reviewed from 246 participants, from whom we had 26 categorical and 25 continuous variables. The analysis was conducted using a two-step cluster method (SPSS Version 15.0) because it accepts continuous and categorical variables. We prespecified four, five, and six clusters, and show results here for a four-subgroup solution as it resulted in about equal numbers in each subgroup (*n* 44, 37, 40, and 32, respectively). We had to exclude 93 participants due to missing data, resulting in an analysis performed on 153 patients.

We highlight some of the results from the categorical variables and show ”clusterwise importance” and responses within clusters. Thirteen of 26 categorical variables and 19 of 25 continuous variables were significant.

Table 1 shows the output from the cluster analysis for the continuous variables. Each row shows a continuous variable and the average scores for this variable in each of the four clusters. For example, the average loudness rating for the four subgroups was 83%, 67%, 66%, and 68%, respectively. Therefore, those patients who were assigned to Cluster 1 reported a higher tinnitus loudness measure.

We next show examples of detailed responses for each of the clusters.

Cluster 1

Figure 1 shows results from the request to ”Rate the loudness of your tinnitus on a scale from I to 100.” The bottom indicates the average loudness rating for each of the four clusters. It can be seen that Cluster 1 patients have higher loudness ratings. The overall mean of 71% averaged across all participants is also shown. The top panel indicates the statistical significance (using Student's *t* test with a significance level of .05). Overall, the loudness assigned by tinnitus patients varies across a wide continuum. In this preliminary study, only those in Cluster 1 showed a loudness score that was highly significant.

Figure 2 shows results from the Emotional subscale of the Tinnitus Activities Questionnaire (Tyler, Gehringer, et al., 2006). In the bottom panel, the average score for Cluster 1 patients was over 80%, which was statistically significant (see top panel). Those participants in Cluster 3 had a significantly lower score than the other participants (about 45%).

Patients assigned by the analysis to Clusters 3 and 4 had very similar scores on the Tinnitus Handicap and Tinnitus Activities Questionnaire. Their scores were significantly lower than those patients assigned to the other clusters and are therefore referred to as ”copers” (see below). Cluster 1 patients had higher scores than those in Cluster 2, and we therefore included ”distressed” as a label for Cluster 1.

Figure 3 shows results from the Sleep subscale of the Tinnitus Activities Questionnaire. In the bottom panel, the average score of about 77% for Cluster 1 patients was significantly higher than for the other clusters (see top panel).

Figure 4 shows results from the Concentration subscale of the Tinnitus Activities Questionnaire. In the bottom panel, Cluster 1 patients report concentration difficulties of about 80%, which is significantly higher than for the other clusters (see top panel).

Combining the results from these figures and from Table 1, we suggest that Cluster 1 patients have (a) loud tinnitus; (b) loudness hyperacusis; (c) a tinnitus that is present all day, everyday; (d) the highest Tinnitus Handicap and Tinnitus Activities Questionnaire scores; (e) the highest anxiety and depression scores; and (f) the highest emotional, sleep, hearing, and concentration scores on the Tinnitus Activities Questionnaire. Thus, it appears that Cluster 1 represents patients who have loud, persistent, and distressing tinnitus, and who suffer from loudness hyperacusis.

Cluster 2

Figure 5 shows results from the question to patients regarding whether the pitch of their tinnitus varied. In the bottom panel, Cluster 2 patients were the only ones who were more likely to report yes to this question, and their responses were statistically signficantly different from scores represented in any of the other clusters (using a chi-square test to see how much the distribution within each cluster differs from what would be expected). The dashed lines in the top panel represent tie significant differences. Combining the results from this figure and from Table 1, we suggest that for Cluster 2 patients (a) pitch and loudness vary, (b) noise makes it worse, and (c) relaxation helps somewhat. Thus, it appears that Cluster 2 represents patients whose tinnitus varies in pitch and loudness, and whose tinnitus is worse in noise.

Cluster 3

Figure 6 shows results from the question to patients regarding whether touch or movement in the head or neck region or their hands or arms influenced their tinnits. Over 90% of patients assigned to Cluster 3 responded no to this question, and none responded positively. A tentative observation is that Cluster 2 patients had the highest proportion of patients who responded yes, that touch or movement did affect their tinnitus (over 60%). However, most of the patients in Cluster 2 did not have their tinnitus modulated by touch or movement. Note that over 80% of the entire sample indicated that touching or movement did not change their tinnitus. Combining the results from this figure and from Table 1, we suggest that Cluster 3 patients (a) have the lowest scores on the Tinmitus Handicap and Tinnitus Activities Questionnaires; (b) have no loudniess hyperacusis; (c) have had no recent life changes; (d) do not have too much stress; and (e) do not have their tinnitus changed by touching or movement. Thus, it appears that Cluster 3 represents patients who are not too distressed by their tinnitus. They do not have loudness hyperacusis, and their tinnitus is not influenced by touch.

Cluster 4

Figure 7 shows results from the question to patients regarding whether being in a quiet place made their tinnitus worse. In the bottom panel, almost 100% of patients in Cluster 4 responded yes. Most patients assigned to Clusters 2 and 3 responded no to this question. These observations were all statistically significant.

Figure 8 shows results from the question regarding whether being in a noisy place reduced their tinnitus. In the bottom panel, about 80% of patients in Cluster 4 said yes. In contrast, for patients who fell into Cluster 2, 100% said no. Note that when all the responses of all the patients in the study are combined (ignoring the clusters), about 80% of patients said no to this question. Noteworthy for Cluster 4 is (a) being in a quiet environment makes their tinnitus worse; (b) noise reduces their tinnitus; (c) they do not have loudness hyperacusis; (d) they experience low anxiety; (e) many things make their tinnitus better; and (f) they report a soft tinnitus loudness. Thus, it appears that Cluster 4 represents patients whose tinnitus is worse in quiet and better in noise. They report a soft tinnitus loudness and are not too distressed by their tinnitus.

Contrasting Clusters

The Appendix provides an overall summary of some of the main features of the clusters. It does appear that this initial cluster analysis produced four distinct groups. Some of the main factors that seem to distinguish groups include the loudness of the tinnitus, whether it varies, how it is influenced by background noise or quiet, and the amount of distress experienced by patients.

Possible Applications of Cluster Analysis

There are several possible applications of this cluster analysis and of approaches to tinnitus subgrouping. These include the following:

- Designing clinical trials for a single subgroup instead of all tinnitus patients
- Analyzing a large amount of data of heterogeneous tinnitus patients based on subgroups
- Using subgroups to search for clues for the mechanism; for example, there might be a common modifier gene for a depression subgroup (Tyler, Coelho, & Noble, 2006)
- Identifying subgroups (e.g., those most distressed) who might require more specific collaborative counseling and sound therapy, such as Tinnitus Activities Treatment (Tyler, Gehringer, et al., 2006)
- Understanding specific effects of treatment by monitoring changes in clusters following a treatment

Summary

We continue to believe that identifying subgroups is necessary to find appropriate treatments (Tyler, 1992). We have reviewed several approaches to define and discover subgroups. We also present a preliminary cluster analysis approach intended to identify possible subgroups Our intent was not to propose these as *the* subgroups but only to demonstrate the potential importance of the technique. As a preliminary step, our analysis suggests the following four subgroups of tinnitus patients:

1. Constant distressing tinnitus
2. Varying tinnitus that is worse in noise
3. Tinnitus patients who are copers and whose tinnitus is not influenced by touch
4. Tinnitus patients who are copers and whose tinnitus is worse in quiet environments

It is possible, perhaps likely, that a patient falling within a particular subgroup might change over time. For example, it might be that the tinnitus magnitude (as measured by its loudness) does not change over time, but the reactions to the tinnitus do. Tyler and Baker (1983) observed that the number of problems identified by tinnitus patients decreased since the time of tinnitus onset. It might also be that the central neurophysiological representation of tinnitus changes with time. When imaging studies are included in such an analysis, the brain regions activated might change over time.

One intriguing and dramatic distinction among tinnitus patients is the difference reported on the effect of background noise. Noise makes tinnitus worse for some patients but reduces tinnitus for others (see Stouffer & Tyler, 1990; Tyler & Baker, 1983). This might represent a fundamental difference in the neural mechanisms underlying tinnitus and an opportunity for different treatment approaches.

Acknowledgments

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Appendix

Descriptions of Four Subgroups Based on Preliminary Cluster Analysis

Cluster 1	Cluster 2	Cluster 3	Cluster 4
Constant distressing tinnitus •Loud tinnitus •Loudness hyperacusis •Present all day, everyday •The highest Tinnitus Handicap and Tinnitus Activities Questionnaire •The highest anxiety and depression scores •Highest emotional, sleep, hearing, and concentration difficulty on Tinnitus Activities Questionnaire	Varying tinnitus that is worse in noise •Pitch and loudness varies •Noise makes it worse •Relaxation helps somewhat	Tinnitus patients who are copers and whose tinnitus is not influenced by touch •The lowest scores on Tinnitus Handicap and Tinnitus Activities Questionnaire •No loudness hyperacusis •No recent life changes •Stress not so bad •Touching or movement does not change their tinnitus	Tinnitus patients who are copers and whose tinnitus is worse in quiet •Being in quiet makes their tinnitus worse •Noise reduces their tinnitus •They do not have loudness hyperacusis •They experience low anxiety •Many things make their tinnitus better •They report a soft tinnitus loudness

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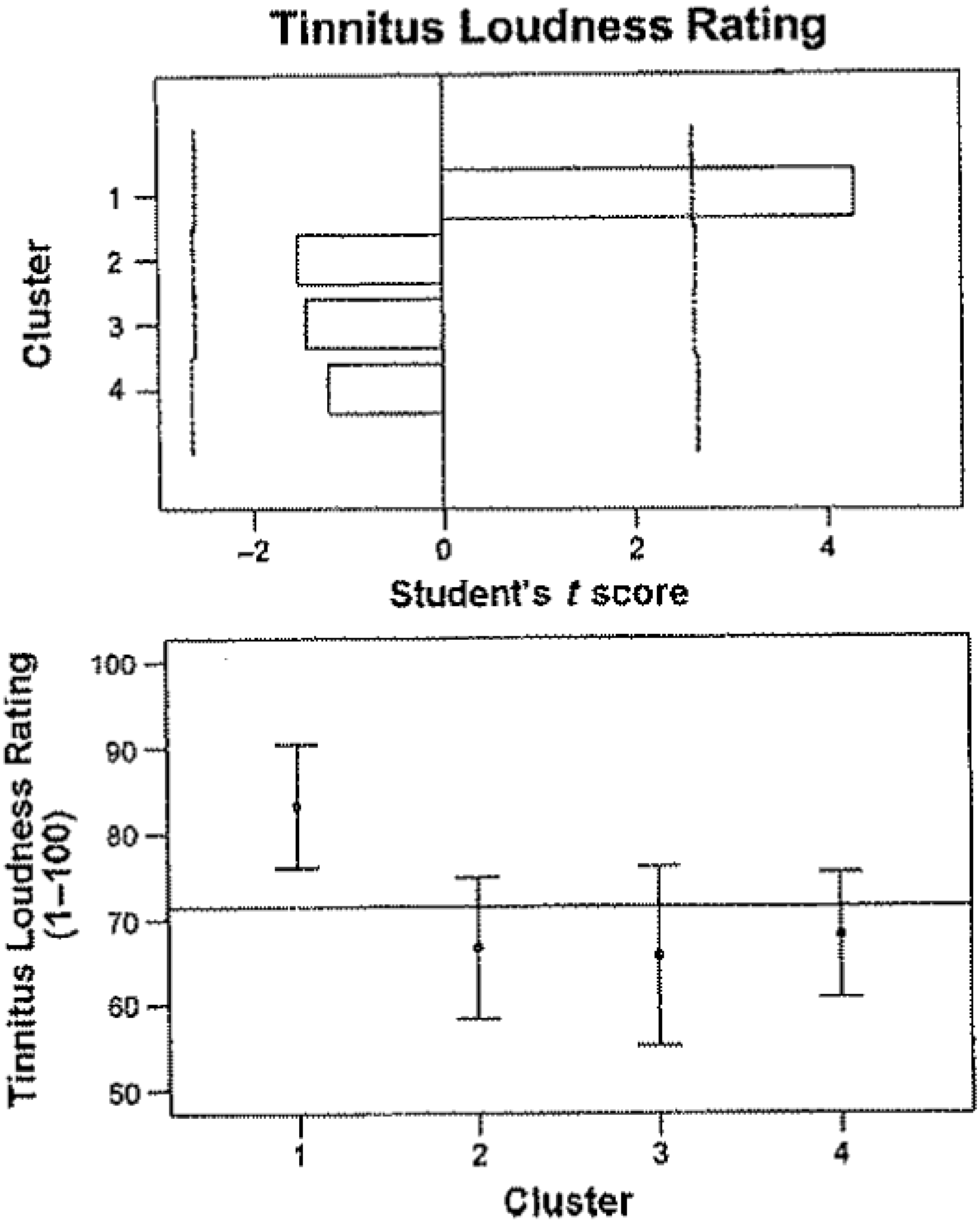

Figure 1.
Cluster results for the question regarding tinnitus loudness (1%-100%). The bottom panel shows the mean scores and standard deviations for each of the clusters. The horizontal line depicts the mean for all participants. The top panel plots the Student *t* scores for each of the clusters. The significance levels ($p < .05$; Bonferroni adjustment applied) are shown with vertical dashed lines.

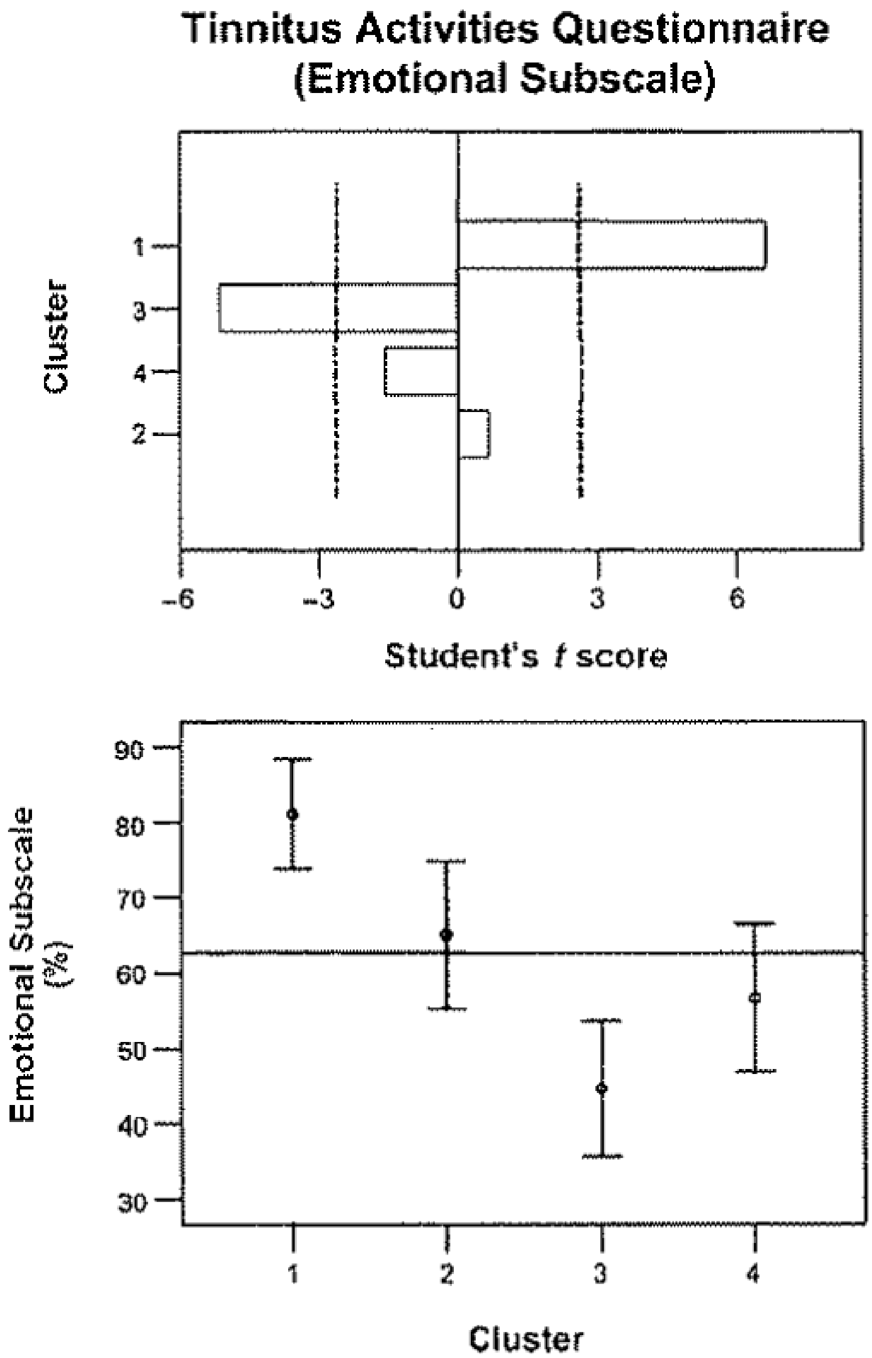

Figure 2.
Cluster results for the Emotional subscale of the Tinnitus Activities Questionnaire (see Figure 1 for details of graphing clusters based on continuous variables).

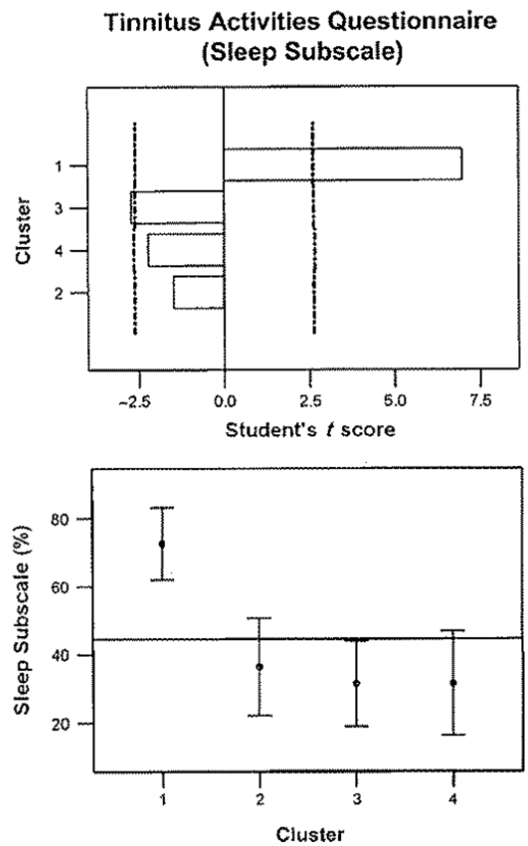

Figure 3.
Cluster results for the Sleep subscale of the Tinnitus Activities Questionnaire (see Figure 1 for details of graphing clusters based on continuous variables).

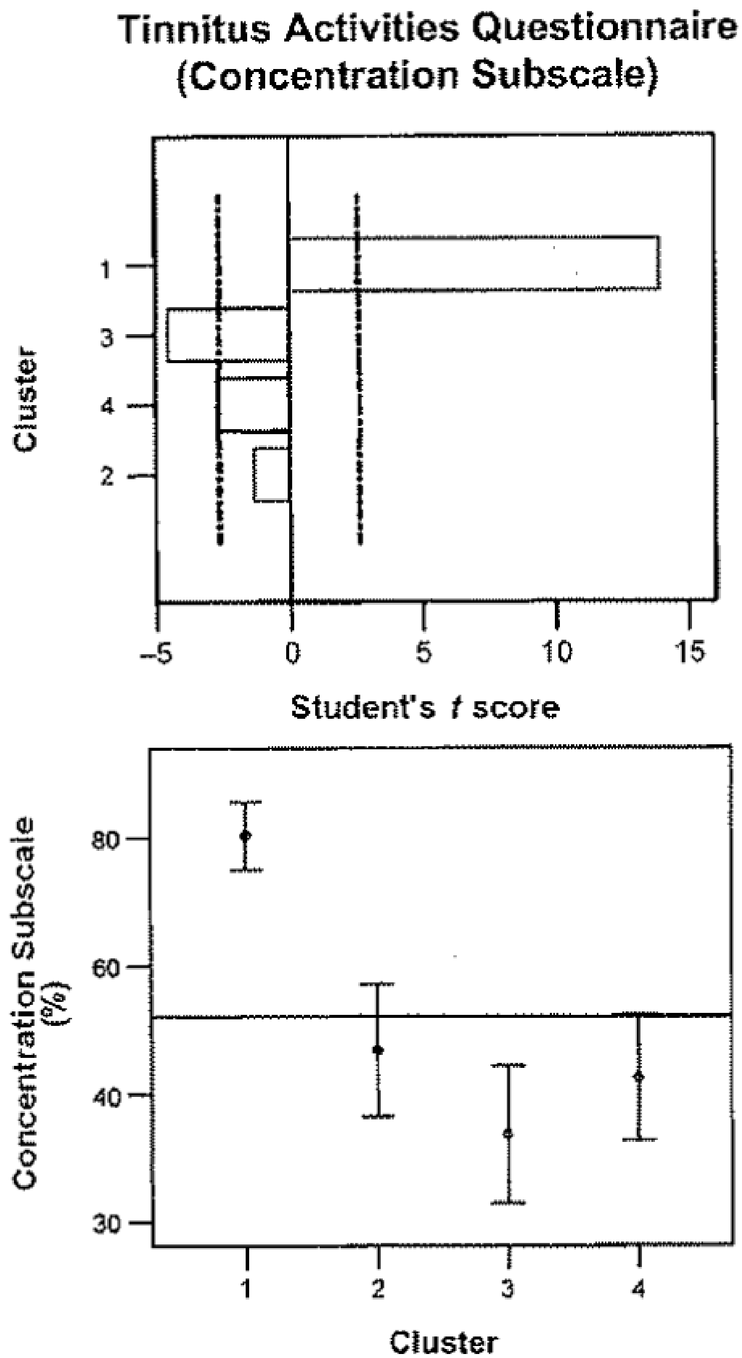

Figure 4.
Cluster results for the Concentration subscale of the Tinnitus Activities Questionnaire (see Figure 1 for details of graphing clusters based on continuous variables).

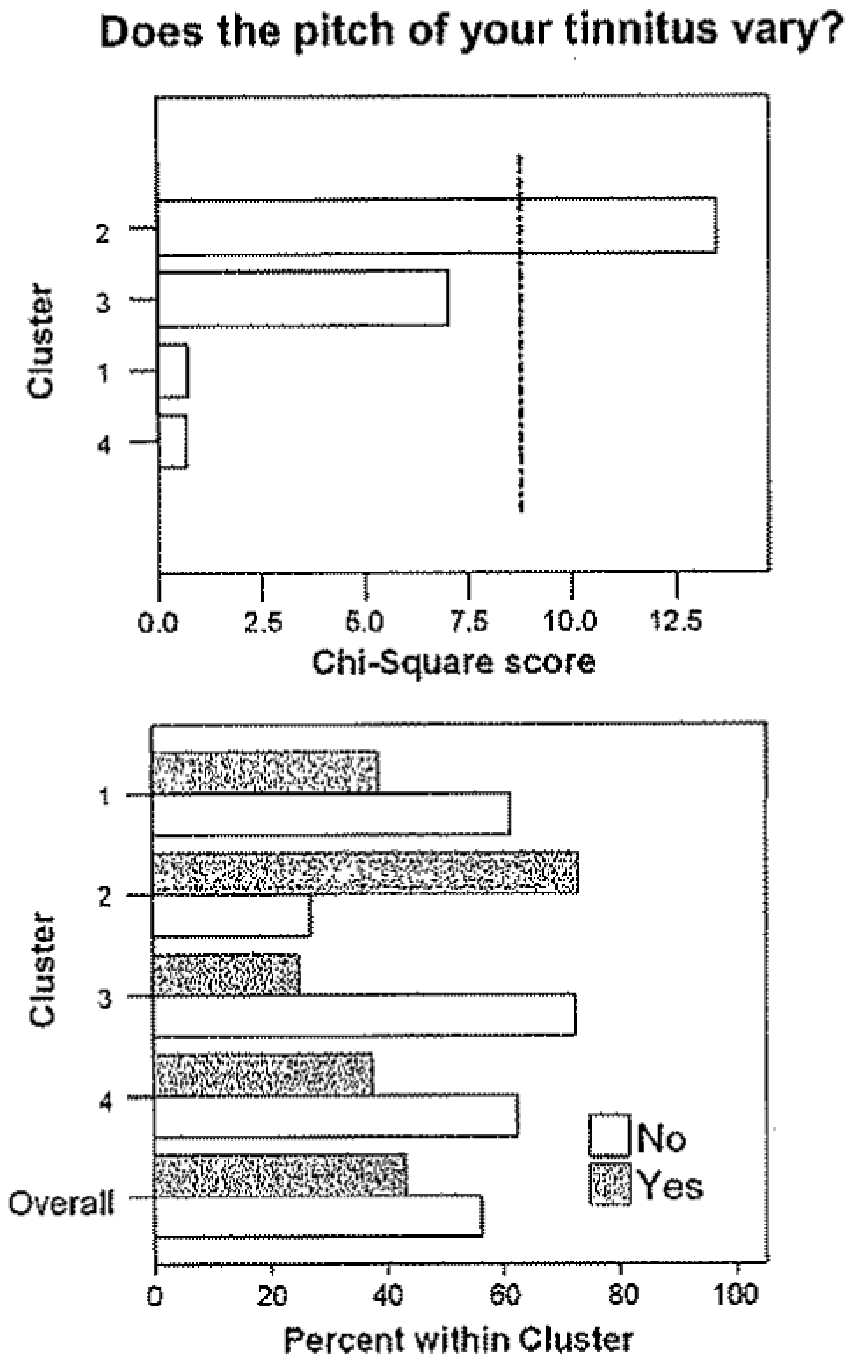

Figure 5.

Cluster results for the question to patients regarding whether their tinnitus pitch varied from day to day; yes or no (categorical variable). The bottom panel shows the percentage of participants who responded yes or no for each of the clusters and in all patients combined. The top panel plots the chi-square scores for each of the clusters. The significance levels ($p < .05$; Bonferroni adjustment applied) are shown with vertical dashed lines.

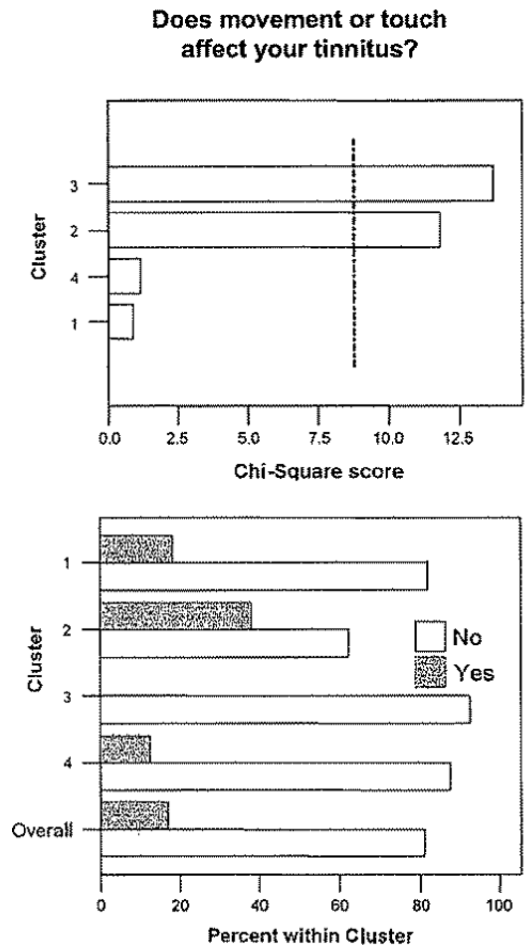

Figure 6.

Cluster results for the question regarding whether touch or movement in the head or neck region or hands or arms influenced tinnitus (see Figure 5 for details of graphing clusters based on categorical variables).

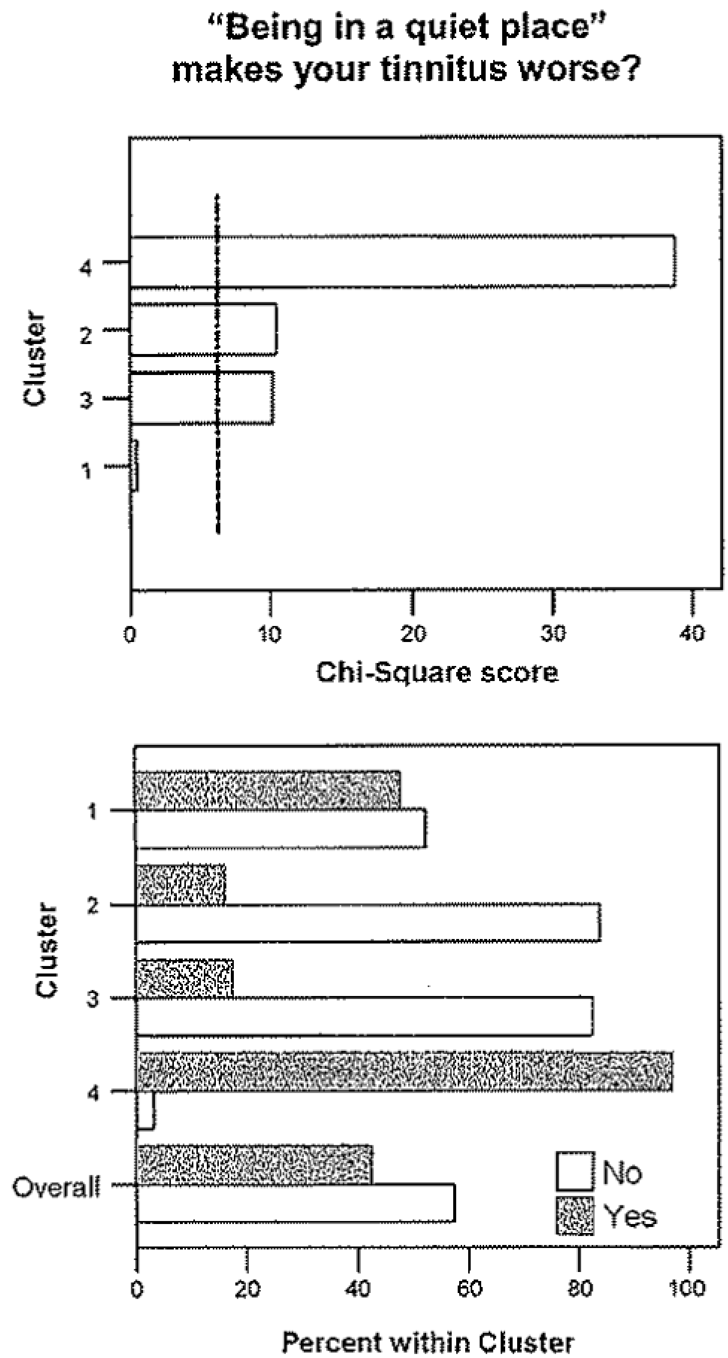

Figure 7.

Cluster results for the question regarding whether being in a quiet place made the tinnitus worse (see Figure 5 for details of graphing clusters based on categorical variables).

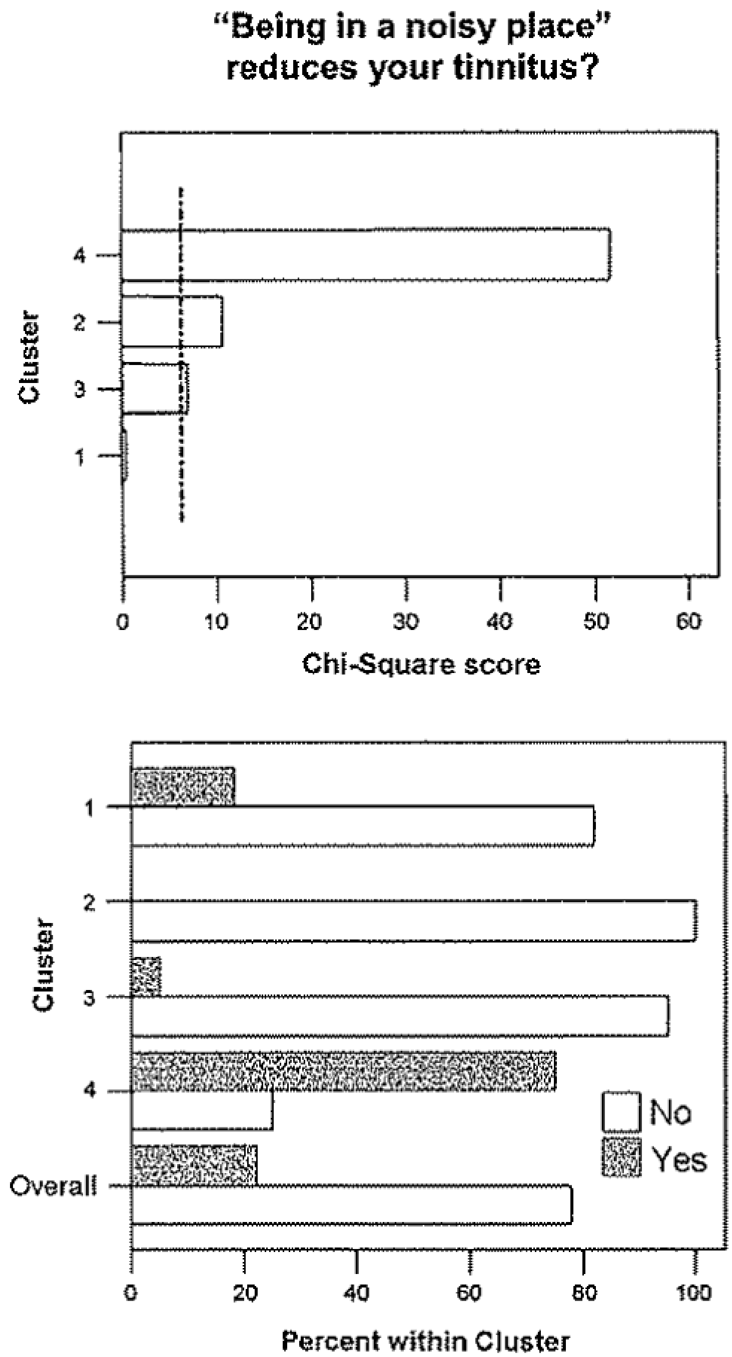

Figure 8.

Cluster results for the question regarding whether being in a noisy place reduced the tinnitus (see Figure 5 for details of graphing clusters based on categorical variables).

Table 1

Variable scores (means and standard deviations) for each of the four profiles and for the total group (n = 246).

		Cluster				
		1	**2**	**3**	**4**	**Combined**
Age (years)	*M*	54.2	55.6	58.7	54.9	55.9
	SD	10.8	10.6	10.3	9.4	10.4
Many everyday sounds are unbearably loud to me.	*M*	60.6	49.5	15.9	14.1	36.5
	SD	36.5	35.0	22.8	22.8	36.5
Sounds that others believe are moderately loud are too loud to me.	*M*	63.2	56.8	19.3	18.6	40.8
	SD	35.8	31.8	25.2	25.1	36.4
I hear very soft sounds that others with normal hearing do not hear.	*M*	21.9	15.5	7.4	15.3	15.2
	SD	32.7	30.8	21.4	26.1	28.5
Describe the most prominent PITCH of your tinnitus by using a scale from 1 to 10.	*M*	8.6	7.9	7.6	8.1	8.1
	SD	1.7	1.9	2.3	1.1	1.9
Describe the LOUDNESS of your tinnitus by using a scale from 1 to 100.	*M*	83.2	66.6	65.6	68.0	71.4
	SD	18.3	19.2	25.4	15.7	21.3
During the time you are awake, what percentage of the time is your tinnitus present?	*M*	96.7	91.2	91.8	91.7	92.8
	SD	9.3	20.2	17.3	18.8	16.6
On the average, how many days per month are you bothered by tinnitus?	*M*	29.3	25.5	28.5	25.3	27.3
	SD	3.4	8.9	4.5	8.7	6.8
How many months have you had tinnitus?	*M*	114.2	141.2	141.4	127.2	130.5
	SD	121.3	193.12	156.2	170.8	159.2
Pitch average (Hz)	*M*	4957.4	4774.8	4962.5	4834.7	4888.9
	SD	2845.9	2949.2	2968.5	2602.1	2828.4
Loudness match (dB HL)	*M*	56.1	47.4	52.3	40.4	49.7
	SD	16.2	17.8	14.3	11.2	16.2
Sensation level of loudness match (loudness match – threshold)	*M*	31.2	25.0	30.7	21.2	27.5
	SD	16.4	15.3	15.7	8.3	15.0
Iowa Tinnitus Handicap Questionnaire	*M*	67.1	50.7	34.3	36.5	48.1
	SD	11.3	15.5	15.4	12.8	19.3
Iowa Tinnitus Handicap Questionnaire (THQ) Factor 1	*M*	68.8	46.3	28.2	33.8	45.4
	SD	15.1	21.0	19.8	17.2	24.3

		Cluster				
		1	**2**	**3**	**4**	**Combined**
Iowa Tinnitus Handicap Questionnaire (THQ) Factor 2	*M*	64.4	54.6	35.2	31.7	47.6
	SD	22.7	20.6	23.0	18.1	25.2
Trait Anxiety Questionnaire (20–80)	*M*	49.6	42.9	33.8	35.3	40.8
	SD	11.3	9.7	8.2	7.3	11.4
Iowa Tinnitus Activities Questionnaire (Concentration subscale)	*M*	80.2	46.8	33.6	42.3	52.0
	SD	13.4	24.0	25.9	20.7	28.2
Iowa Tinnitus Activities Questionnaire (Emotional subscale)	*M*	81.1	65.0	44.7	56.8	62.6
	SD	18.5	22.6	21.9	20.8	24.9
Iowa Tinnitus Activities Questionnaire (Hearing subscale)	*M*	74.5	58.5	44.6	49.1	57.5
	SD	22.2	23.9	23.8	27.8	26.8
Iowa Tinnitus Activities Questionnaire (Sleep subscale)	*M*	72.5	36.4	31.4	31.6	44.5
	SD	26.7	33.0	30.2	32.7	35.2
Iowa Tinnitus Activities Questionnaire (overall score)	*M*	77.1	51.7	38.6	44.9	54.1
	SD	11.9	19.6	17.6	15.5	22.2
Beck Depression Inventory Questionnaire (0–59)	*M*	15.6	8.4	5.2	4.8	8.9
	SD	8.3	6.1	4.3	3.2	7.4
Recent Life Change Questionnaire (0–3,545)	*M*	279.5	218.1	112.3	196.5	203.6
	SD	227.9	171.6	111.9	156.4	183.8
Somatic Perception (0–39)	*M*	10.0	5.5	3.6	3.0	5.8
	SD	6.9	4.5	3.8	2.6	5.6

Note. Unless otherwise noted, the scales go from 0 to 100.