Individual Patient Factors Associated with Effective Tinnitus Treatment

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Abstract

Background—Little is known about patient factors that might influence outcomes of tinnitus interventions. Determining such factors would offer insights into why some individuals benefit from tinnitus intervention whereas others do not.

Purpose—The purpose of this study was to evaluate selected patient factors that may be associated with outcomes of tinnitus intervention. Factors studied include demographics, tinnitus characteristics, psychoacoustic tinnitus measures, audiometric data, and overall physical/emotional health status.

Research Design—A retrospective analysis was performed on data obtained from a controlled clinical study that compared factors associated with tinnitus relief after tinnitus masking and tinnitus retraining therapy.

Study Sample—A total of 126 military veterans participated in this controlled clinical study. Of these, 89 completed outcome measures at both baseline and 12 mo and were included in the present analysis.

Data Collection and Analysis—A "responder" to intervention was identified as having a decrease (improvement) of 20 or more points on the Tinnitus Handicap Inventory between baseline and 12 mo. A "nonresponder" did not achieve a 20-point improvement on the Tinnitus Handicap Inventory. Individual patient factors were examined using independent *t*-tests or χ^2 analysis. A logistic regression model was used to determine how well each factor predicted treatment outcome (responder or nonresponder) while controlling for each of the other factors.

Results—Five patient factors were significantly different (p 0.05) between responders and nonresponders. Responders tended to (1) be younger in age; (2) have better low-frequency hearing sensitivity; (3) have greater problems with overall hearing; (4) be more likely to have tinnitus for

shorter durations; and (5) perceive their tinnitus to be located "in the head" versus "in the ears." A logistic regression was then performed to determine how well each factor predicted the treatment outcome (responder versus nonresponder) while controlling for each of the other factors. Results from the logistic regression revealed two of the five factors, localization of tinnitus and self-report of hearing problems, to be statistically significant.

Conclusions—Examining the association of individual patient factors to a specific tinnitus intervention yielded several significant findings. Although these findings are not definitive, they reveal the capability that exists to perform these kinds of analyses to investigate relationships between individual patient characteristics and outcomes of intervention for tinnitus. Prospective research using systematic approaches is needed to identify these relationships that would contribute toward the ability to differentially predict outcomes of various tinnitus interventions. Obtaining this information would lead to more targeted therapy and ultimately more effective intervention.

Keywords

Tinnitus; logistic regression; psychoacoustics; treatment

INTRODUCTION

Tinnitus is the perception of sound in the absence of external acoustic stimuli and is experienced by 10–15% of the adult population (Hoffman and Reed, 2004). Only approximately 20% of those who experience tinnitus consider it to be a significant problem (Jastreboff and Hazell, 1998; Davis and Refaie, 2000). A great variety of tinnitus interventions are available for clinicians to use; however, most of the methods have not been verified by controlled clinical trials (Dobie, 2004a; Hobson et al, 2010; Martinez-Devesa et al, 2010). It is likely that no one form of intervention is effective for all patients with tinnitus, i.e., individual characteristics and circumstances may predispose patients to respond differentially to the available interventions (Tyler et al, 2008). The present study was conducted to examine patient variables as possible predictors of outcomes of intervention for tinnitus.

Identifying factors associated with clinical outcomes falls under the category of prognostic factor research (Riley et al, 2013). One aspect of such research is to inform clinical treatment recommendations. Randomized clinical trials (RCTs) are the "gold standard" for the evaluation of different therapies (Gallin and Ognibene, 2007). Numerous RCTs have been conducted to evaluate different tinnitus interventions (Tyler et al, 2007; Hesser et al, 2011; Hoare et al, 2011). If factors that predict prognosis are known, then participants in an RCT for tinnitus can be stratified accordingly (Dobie, 2004a). Because such factors are not known, RCTs for tinnitus may not achieve prognostic balance among treatment groups, which can result in both false-positive and false-negative errors. The lack of known prognostic factors also confounds efforts to compare results of RCTs. For example, participants in one study might be amenable to treatment, whereas those in another study might be more resistant to treatment. Outcomes of such studies cannot be directly compared because of the different prognostic categories. Because of these concerns, Dobie (2004a) recommended, "Until we know more about prognostic variables, tinnitus RCTs should be

limited to patients who are unlikely to improve spontaneously: those with severe, long-standing tinnitus." (p. 270)

In an attempt to predict outcomes of tinnitus therapies, some researchers have examined aspects of the tinnitus (e.g., psychoacoustic measures of tinnitus characteristics) and of individuals presenting with tinnitus (e.g., psychological factors) to better understand what factors might lead to increased tinnitus-related distress. Results have varied, but offer some insight into possible predictors of tinnitus-related distress and treatment outcomes. Jastreboff et al (1994) investigated possible predictive capabilities of tinnitus psychoacoustic testing for treatment outcomes. Results were consistent with previous research in that none of the initial psychoacoustic measures correlated with outcomes. Measures of tinnitus maskability (minimal amount of noise required to render the tinnitus perception inaudible), however, were seen to decrease for patients whose tinnitus condition improved, and to increase for patients whose condition either worsened or remained the same. The authors concluded that measures of tinnitus maskability could be useful for monitoring the effectiveness of tinnitus treatment, but that initial psychoacoustic measures were not useful for predicting outcomes. Andersson et al (2001) examined whether baseline tinnitus psychoacoustic testing could be used to predict long-term tinnitus distress, finding that tinnitus maskability was predictive of later distress. In a review of psychoacoustic measures of tinnitus, Henry and Meikle (2000) noted that studies have consistently shown poor correlations between these measures and subjective ratings of tinnitus severity. Further research is needed to determine if tinnitus maskability is predictive of outcomes or if it correlates with outcomes.

In addition to the study by Jastreboff et al (1994), other studies have focused on prognostic factors for predicting outcome with tinnitus retraining therapy (TRT). Studies by both Herraiz et al (2007) and Koizumi et al (2009) found that patients had better results with TRT if, before receiving treatment, they reported higher levels of tinnitus loudness and greater distress levels. Ariizumi et al (2010) reported that lower tinnitus loudness and a positive attitude were predictive of favorable results with TRT.

Kleinjung et al (2007) reported tinnitus duration and degree of hearing loss to be factors associated with responsiveness to transcranial magnetic stimulation (TMS). Specifically, individuals with normal hearing and shorter duration of tinnitus were more likely to respond to TMS as a treatment of tinnitus.

Kröner-Herwig et al (2006) examined whether the presence of specific patient variables, including mental disorders, dysfunctional cognitions relating to tinnitus, and other variables were associated with reduced benefit in one of two tinnitus interventions: cognitive-behavioral tinnitus coping training, or habituation-based training. None of these variables had predictive capabilities with respect to the two interventions.

Kaldo-Sandström et al (2004) evaluated predictors of outcome for patients who participated in Internet-based cognitive-behavioral therapy. The only patient factor associated with outcome was the number of earlier treatments of tinnitus. Graul et al (2008) studied patient factors for "responders" and "nonresponders" to a multimodal cognitive-behavioral inpatient

treatment. Factors that were different between these two groups were age and the extent of psychosocial stress.

Although limited in their scope, all of these studies contributed to the available knowledge as to why some individuals respond better to tinnitus interventions than others. The present study further explored this avenue of research, hypothesizing that multiple relationships exist between patient factors (i.e., demographics, tinnitus characteristics, psychoacoustic tinnitus measures, hearing ability, and overall physical and emotional health) and tinnitus treatment outcomes. The goal of this study was to retrospectively identify patient factors associated with differential responsiveness to tinnitus intervention. A secondary goal was to bring awareness regarding the diversity of approaches used to examine patient factors and outcomes of tinnitus treatment.

METHODS

Data were analyzed retrospectively from a controlled clinical study that was conducted at the National Center for Rehabilitative Auditory Research to evaluate the clinical efficacy of tinnitus masking (TM) and TRT (Henry et al, 2006). TM and TRT both provide "sound therapy," but they differ in their approach (Henry et al, 2002). TM primarily uses ear-level sound generators ("maskers") to induce an immediate sense of relief from tinnitus (Vernon and Meikle, 2000). TRT is a counseling-based technique that also makes use of ear-level sound generators for patients with more severe tinnitus (Jastreboff and Jastreboff, 2004). Sound therapy with TRT is intended to promote habituation to the tinnitus, and not to induce a sense of relief. The counseling component of TRT is fairly extensive, and uses the "neurophysiologic model" as a guide to describe the underlying causes of tinnitus distress and therefore to "demystify" the tinnitus. TM also involves counseling but in a less structured manner and mainly focuses on how to use maskers to achieve relief. Differences between TM and TRT have been described in detail (Henry et al, 2002; Henry et al, 2006).

The study from which the present data were analyzed (Henry et al, 2006) used the Tinnitus Handicap Inventory (THI) (Newman et al, 1996) as the primary instrument to assess outcomes. THI data were collected at 0, 3, 6, 12, and 18 mo. Psychoacoustic and audiometric testing were performed at baseline and then every 6 mo (baseline, 6, 12, and 18 mo). Both groups showed significant reduction (improvement) in THI scores with TRT showing relatively greater effects than TM at 12 and 18 mo.

Participants

Of the 126 participants enrolled in the controlled study, 89 completed the THI at both baseline and at 12 mo and were included in the present analysis. These included 44 males (mean age = 59.0 yr; standard deviation [SD] =10.7) in the TRT group, and 41 males and four females (mean age = 61.0 yr; SD = 9.9) in the TM group. Mean age was not significantly different between groups ($p = 0.37$), nor was the duration of tinnitus ($p = 0.92$).

Primary Outcome Measure

The THI is a 25-item outcome measure that determines the level of self-perceived handicap caused by tinnitus, based on a 0–100 increasing handicap scale (with 100 being total

handicap and 0 being no handicap) (Newman et al, 1996). The THI aids the clinician in identifying patients who would benefit from tinnitus-specific intervention. Regarding demographic data, the THI shows no statistically significant differences for age or gender. The THI has been validated psychometrically, showing high internal consistency ($\alpha = 0.93$) and high test-retest reliability for each subscale: Functional, Emotional, Catastrophic (r =0.94, 0.88, and 0.84, respectively) (Newman et al, 1998).

Determining Responder versus Nonresponder—Different methods exist to determine whether a clinically significant change has occurred after treatment (suggestive of treatment benefit or responsiveness). For example, Norman et al (2003) established the threshold to detect changes in health-related quality of life for chronic diseases to be half of an SD. For the current study, the main outcome measure was the THI. Newman et al (1998) evaluated the test-retest reliability of the THI and determined that a reduction (between test and retest) of at least 20 points was necessary for tinnitus therapy to be considered effective based on the 95% confidence intervals associated with a significant change in perceived handicap. The current study used this criterion (change of at least 20 points on the THI) to establish "responders" to tinnitus treatment (either TM or TRT). Individuals who did not reach that criterion were classified as "nonresponders."

The outcome time point used for this analysis was 12 mo. It was important to use a time point that would allow for responsiveness to treatment to occur. Using a time point earlier than 12 mo might have been too soon for any change—improvement or otherwise—to be detected. Selecting a time point later than 12 mo, such as the 18 mo time point, risked reducing the number of subject data available because of loss of follow-up, a common concern in longitudinal studies.

Individual Patient Factors

The variables most often examined in previous related studies include sociodemographic information, self-reported hearing loss, localization of tinnitus (individual ear versus in the head), and tinnitus loudness (Andersson et al, 2001; Langenbach et al, 2005; Kröner-Herwig et al, 2006; Wallhäusser-Franke et al, 2012). Each of these variables was considered when determining which patient factors to select for analysis. Audiometric and psychoacoustic measures of tinnitus have also been examined for their potential to predict treatment responsiveness and therefore were included in the present study. Selected factors were grouped in the following categories: demographics, self-reported tinnitus characteristics, psychoacoustic tinnitus measures, audiometric measures, self-reported hearing and sound tolerance concerns, physical health status, and emotional health status.

Demographics—Four demographic factors were examined: age, marital status, employment, and education. For all factors but age, the distribution of response categories was skewed with few participants in some of the categories; those factors were dichotomized to increase the likelihood of detecting significant differences: (1) Age was analyzed as continuous data. (2) Marital status was collected categorically with respect to married, single, divorced, widowed, or not married (these groups were collapsed into dichotomous categories, married and not married). (3) Participants reported their employment in terms of

retired, employed, unemployed, or part-time (these were collapsed into employed and unemployed). (4) Participants were asked to report their education in the following categories: less than 9th grade, 9th–12th grade, high school graduate, some college, or college graduate (these categories were collapsed into two groups: high school or less and post high school education).

Self-Reported Tinnitus Characteristics—Eight self-reported tinnitus characteristics were examined: tinnitus loudness; tinnitus duration; perceived localization of tinnitus; number of tinnitus sounds; tinnitus onset sudden or gradual; fluctuation in tinnitus loudness; which is worse—hearing loss, tinnitus, or both; and strength of problem associated with tinnitus. Participants were asked to (1) rate the loudness of their tinnitus on a scale of 1–10, with 1 being very soft and 10 being very loud; (2) describe their tinnitus duration as occurring for less than 1 yr; 1–2 yr; 2–5 yr; 5–10 yr; 10–20 yr and more than 20 yr (these categories were collapsed into two groups: 20 and >20 yr); (3) characterize the localization of their tinnitus as being in the ears (right, left, or both) or in the head (right side, left side, or fills head); (4) report the number of tinnitus sounds as 1, 2, or 3 or more (these three categories were collapsed into two: one sound and two or more sounds); (5) report their tinnitus as having a sudden or gradual onset; (6) report the amount of fluctuation in tinnitus loudness as daily, weekly, monthly, rarely, or never (these were collapsed into two categories: daily or less than daily); (7) rate which is more of a problem—tinnitus, hearing, or both (only two participants reported hearing to be a bigger problem than tinnitus; therefore, categories were collapsed into tinnitus the worse problem, and tinnitus and hearing equally problematic); (8) rate the severity of their tinnitus as being a small, moderate, big, or very big problem (these were collapsed into a small to moderate problem and a big to very big problem).

Psychoacoustic Tinnitus Measures—Three psychoacoustic measures of tinnitus were selected: tinnitus loudness matching, minimal masking level (MML), and residual inhibition (RI); these measures are frequently used as part of a tinnitus assessment (Henry et al, 2005). For loudness matching, participants were asked to match the loudness of their tinnitus to the loudness of pure tones at audiometric frequencies. Loudness matching has been shown to be a reliable measure (Henry et al, 1999). MML is the lowest level at which broadband noise renders the tinnitus perception inaudible. MML was measured to the closest 1 dB and reported in dB sensation level (Henry et al, 2006). As mentioned in the Introduction section, MMLs have been shown to correlate with treatment outcomes; specifically, a reduction in the MML has correlated with successful treatment (Jastreboff et al, 1994). Residual inhibition (RI) is defined as the temporary suppression (partial RI) or elimination (complete RI) of tinnitus after an auditory stimulus (Vernon, 1982; Vernon and Meikle, 1988). For this study, RI was measured immediately after MML testing (Henry et al, 2006). A broadband noise was presented bilaterally for 1 min at 10 dB above the MML. When the stimulus was terminated, participants were asked to report if their tinnitus had changed. RI was analyzed as the number of seconds that either partial or complete RI occurred.

Audiometric Measures—Several audiometric measures were examined: low-frequency pure-tone average (LF-PTA; 0.5, 1, or 2 kHz); high-frequency PTA (HF-PTA; 3, 4, 6, or 8

kHz); and speech reception threshold (SRT). Audiometric testing was performed using calibrated equipment in a conventional sound-treated booth meeting established standards (American National Standards Institute, 1991). The LF-PTA and HF-PTA were computed separately for the left and right ears. SRTs were obtained in dB hearing level separately for the right and left ears.

Self-Report Hearing and Sound Tolerance Concerns—Factors related to participants' self-reported hearing ability included problem with sound tolerance (yes/no); use of hearing aids (yes/no); and self-reported hearing problem (none, mild, moderate, or severe). Categories for self-reported hearing problem were collapsed into two categories: mild to moderate problem and big to very big problem.

Physical Health Status—Four health status factors were examined: (1) number of coexisting health conditions; (2) self-rated health (compared with peers as "worse than people my age," "same as people my age," or "better than people my age"); (3) admitted as a patient in a hospital during the past 6 mo; and (4) received treatment at an emergency room or urgent care center during the past 6 mo. Responses for the last two factors were never, one time only, two to three times, or more than three times (these categories were collapsed into two groups: never and one or more times).

Emotional Health Status—Participants were administered the State-Trait Anxiety Inventory (STAI) (Spielberger, 1983) and the Beck Depression Inventory (BDI) (Beck et al, 1961). The raw scores from the STAI and BDI were collected and analyzed to determine if there was any association between these two measures and tinnitus treatment outcomes.

Data Analysis

Bivariate Analysis—Comparisons were initially made between responders and nonresponders for each treatment group separately (TM versus TRT), using χ^2 analysis for categorical factors and analysis of variance for factors with continuous data. Because of small sample sizes, the two treatment groups were then pooled for a secondary analysis to improve statistical power.

Some factors such as ethnicity and gender were excluded from these analyses because of a lack of variability within the participant population. All of the participants were military veterans, mostly male and Caucasian.

Multivariate Analyses—Factors exhibiting or approaching a statistically significant difference (p 0.05) between responders and nonresponders and demonstrating similar patterns across each treatment group, were further analyzed using multiple logistic regression. A logistic regression model was used to determine how well each factor predicted the treatment outcome (responder or nonresponder) while controlling for each of the other factors. Such a model is conceptually similar to multiple linear regressions inasmuch as statistical relationships between one dependent variable and several independent variables are evaluated. In multiple logistic regression, the dependent variable is binary (in this case, responder or nonresponder), and the actual probability of a participant responding is statistically modeled as an odds ratio.

The statistical analysis was conducted using the Statistical Package for Social Sciences v17.

RESULTS

Comparisons were initially made between responders and nonresponders for each treatment group separately (TM versus TRT). The mean THI score at baseline for the TRT group was 51.0 (SD = 20.0; range = 14–98); for the TM group, it was 52.0 (SD = 25.0; range = 10–94). Mean THI scores at 12 mo were 29.1 (SD = 17.8; range = 0–86) for the TRT group and 43.8 (SD = 26.6; range = 8–98) for the TM group. Tables 1 and 2 show comparisons of responders and nonresponders within each treatment group for continuous and categorical data, respectively. In general, distribution patterns across the two treatments groups were similar, with few exceptions. One exception was that depression and anxiety scores showed opposite results for TRT participants compared with TM participants with respect to treatment outcome. Again, because of the small sample sizes, observed differences between the two intervention groups should be interpreted with caution.

For the pooled treatment group, five patient factors were found to be significantly different (p　0.05) between responder and nonresponder groups (see Tables 3 and 4). Compared with nonresponders, responders tended to be younger in age (mean age = 56.2 yr, SD = 9.9 yr for responders versus 62.6 yr, SD = 9.8 yr for nonresponders), with better hearing thresholds in the low frequency range (mean = 16.9 dB HL, SD = 12.9 dB HL for responders versus 27.2 dB HL, SD = 19.7 dB HL for nonresponders) but greater problems with overall hearing (59% of responders versus 35% of nonresponders reporting big to very big problems with hearing). Responders also were more likely to have their tinnitus for a shorter duration (58% responders versus 35% of nonresponders with duration of tinnitus　20 yr) and to perceive the tinnitus to be in their head versus in their ears (61% of responders versus 36% of nonresponders reported localization of tinnitus to be "in the head"). To determine which of these factors or set of factors best predicted response to treatment, we performed a logistic regression analysis.

Logistic Regression Analysis

Results of the logistic regression analysis are presented in Table 5. After controlling for colinearity (the possibility of the predicting factors being correlated among themselves), only two of the five factors were statistically significant at the p　0.05 level: localization of tinnitus ($p = 0.04$) and self-report of hearing problems ($p = 0.01$). Localization of tinnitus had an odds ratio of 3.30, indicating that participants who perceived their tinnitus to be in their head were 3.3 times more likely to respond to treatment compared with those who perceived the tinnitus to be in their ears. Report of hearing problems had an odds ratio of 4.8, indicating that participants who reported big to very big problems with their hearing were 4.8 times more likely to respond to treatment than those who reported mild to moderate problems with their hearing ability. Duration of tinnitus and LF-PTA in the left ear approached significance ($p = 0.07$), indicating that shorter-duration tinnitus and low-frequency hearing loss may also be potential predictors of treatment success.

DISCUSSION

This study involved a retrospective analysis of data from a controlled clinical study (Henry et al, 2006). The analysis was conducted to determine if individual patient factors were associated with outcomes of interventions for tinnitus. Results of the analysis supported the hypothesis that certain patient factors would be significantly different between individuals who respond to intervention (20 point or better improvement in THI) compared with those who do not. Patient factors were categorized according to individuals' demographics, tinnitus characteristics, psychoacoustic tinnitus measures, audiometric data, and overall physical/emotional health status.

A preliminary analysis was performed revealing similar distribution patterns between responders and nonresponders across the two treatment groups. A few exceptions, however, were noted (see Table 2). Overall emotional health (depression and anxiety) differed between the two treatment groups such that TRT participants who had higher depression and anxiety scores at baseline were more likely to respond to treatment, whereas TM participants with high depression and anxiety scores at baseline were less likely to respond to treatment. This finding could be explained as a consequence of clinician variables. More specifically, one treatment specialist conducted TRT and one conducted TM (Henry et al, 2006). These clinicians had different personalities and different patient workloads, which could have affected outcomes. In addition, participants in the TRT group received more clinician contact time than participants in the TM group.

In general, results from the preliminary analysis found essentially no significant differences between responders and nonresponders across the two treatment groups. The few factors that showed opposite findings are of questionable significance because of the small sample size. To overcome this issue, we decided to pool the data from the two treatment groups to increase the statistical power. The preliminary analysis that informed this decision and patient factors that showed opposite results when the groups were analyzed separately (in essence, canceling out possible effects) were not included in the pooled data. Combining the data allowed for analyses to be conducted with sufficient power to identify patient factors predictive of treatment outcome (identify responder versus nonresponder).

On examining the pooled treatment group data, we found five factors to be significantly different between the responders and nonresponders: responders tended to (1) be younger in age; (2) perceive the tinnitus to be located in the head versus in the ears; (3) experience tinnitus for shorter periods (shorter duration of tinnitus); (4) have better low-frequency hearing sensitivity; and (5) have greater overall self-reported problems with hearing. Of these five factors, a logistic regression analysis revealed self-report of hearing problems and perceived tinnitus location to be most significant ($p = 0.01$ and $p = 0.04$, respectively; see Table 5). These results suggest that patients who perceive tinnitus to be located in the head and those who self-report more severe hearing problems may be more likely to respond positively to both TRT and TM than those who perceive tinnitus to be located in the ears and who self-report less severe hearing problems.

Participants who reported perceived tinnitus location as being inside the head were 3.3 times more likely to respond positively to therapy compared with those who perceived tinnitus to be located in their ears. Numerous studies have shown that only a small percentage of patients with tinnitus report the location of their tinnitus as "in the head." Stouffer and Tyler (1990) found that 9.8% of 528 patients described their tinnitus as being located "in head." Meikle and Taylor-Walsh (1984) reported that 11% of more than 1,800 clinic patients described their tinnitus location as "in the head." Meikle and Griest (1989) reported that 5% of 872 patients described their tinnitus as being located "in the head," whereas approximately 10% perceived their tinnitus location as "both in the head and ears." A tinnitus trial conducted by Henry et al (2007) found that 14.9% of 268 research participants described their tinnitus as being located "inside head."

It is clear that the location of tinnitus is perceived far more often in the ears than in the head. What is unknown is if this perceptual difference is related to etiologic factors. Meikle and Griest (1989) suggested that "men exposed to long-duration occupational noise tend to report tinnitus that is in 'both ears,' while tinnitus that is due to illness or other non-noise-related causes tends to be localized in the head." (p. 74) Vernon (1978) may have been the first to posit that tinnitus located within the head may be due to head injury. In a recent study (Henry et al, 2012), almost half of the participants with moderate to severe traumatic brain injury reported that their tinnitus was perceived "inside the head," whereas only 8% of the participants without traumatic brain injury reported this same perception. If these findings of differential tinnitus location are repeated in further trials, then this could have implications regarding underlying mechanisms of tinnitus generation. Different mechanisms might exist that generate tinnitus and help to explain why some people respond to treatment whereas others do not.

The other finding from the current study was that participants who perceived their hearing to be a big or very big problem were more likely to respond to treatment compared with those who did not. This finding could be explained because hearing aids and combination instruments (ear-level masking plus amplification devices) were provided to many participants as part of their treatment protocol. Therefore, these participants received treatment that addressed their hearing problem *in addition to* their tinnitus-related problems.

A potential confounder is that patients often blame their tinnitus for their hearing difficulties (Coles, 1995; Zaugg et al, 2002; Dobie, 2004b; Henry et al, 2008). These patients believe that the tinnitus interferes with their hearing, which is usually a misconception on their part (in very few cases, hearing ability may actually be impaired by tinnitus). Therefore, it is possible that some of the "responders" who reported hearing to be a problem received benefit primarily because their hearing needs were addressed. It is well known that hearing aids can be beneficial for mitigating the effects of tinnitus (Surr et al, 1985; Henry et al, 2008; Searchfield et al, 2010). The controlled clinical trial did not evaluate this potential confounder (i.e., attributing problems hearing to the tinnitus itself). Therefore, it is not possible to know how useful the patient factor "self-reported poorer hearing" by itself predicts outcomes of tinnitus therapy.

The potential for patients to ascribe their hearing problem to their tinnitus is a general concern whenever patients are evaluated to determine if intervention for tinnitus is warranted. A drawback of tinnitus outcome questionnaires is that they do not separate out hearing-related problems from tinnitus-related problems, resulting in artificially inflated index scores for some patients. Henry et al (2008) developed the Tinnitus and Hearing Survey to make this distinction at the time of the audiologic evaluation. Use of the Tinnitus and Hearing Survey helps to identify individuals who are candidates for tinnitus-specific therapy. All patients reporting both tinnitus and a hearing problem should first have their hearing problem addressed before considering tinnitus-specific intervention.

The present study highlights the need to develop systematic methodology for assessing individual patient factors that could be useful in determining the likelihood of successful therapeutic outcomes as well as the most appropriate form of therapy. Development of such methodology would also enable more direct comparisons among research studies. For example, Kröner-Herwig et al (2006) also examined hearing problems and duration of tinnitus as possible predictors of treatment outcome. Their results, however, did not reveal these to be significant patient factors. Without knowing how the current methods differ from those of Kröner-Herwig and colleagues, we can only speculate that the discrepant results could be attributed to different outcome measures being used as well as recruitment from different patient populations. Dobie (1999) addressed multiple caveats affecting direct comparison of research studies, including a lack of consensus regarding study design and use of a common outcome measure.

Future Directions

The patient factors evaluated in this study were selected retrospectively using data collected in a controlled clinical study (Henry et al, 2006). Prospective studies should be conducted to determine if the significant factors identified in this study are generalizable to other patient populations. More broadly, it will be necessary to standardize criteria for defining responders and nonresponders as well as methodologies used to determine the significance of individual factors.

Newman et al (1998) determined that a change of 20 points on the THI was clinically significant; the current study used this criterion change in the THI to classify an individual as a "responder." Other methods of identifying responders could include performing statistical analyses on selected variables to detect statistically significant differences among groups. Patient factors identified as significant may vary according to the specific intervention and the population sampled. In general, the question is how much improvement needs to occur to classify a patient as responding to treatment. A major component with respect to defining what constitutes "response to treatment" pertains to the outcome measure used. Indeed, different measures can result in the identification of different patient factors associated with treatment outcome. Furthermore, a specific amount of change may be significant for some patients but not for others. These issues necessitate standardizing (1) the method of identifying patient factors; (2) the outcome measures used to compare patient factors; and (3) the methods used to determine responders versus nonresponders. RCTs are needed to address these issues. In the current study, treatment-related changes were not

compared with a control group; using a control group would more definitively classify individuals responding to tinnitus therapy, above and beyond placebo effects, and validate patient factors associated with specific interventions. Results reported here are not meant to be suggestive of specific patient factors able to predict treatment benefit but, rather, that patient factors should be evaluated as possible variables leading to a better understanding of what factors contribute to responsiveness to treatment.

The need to standardize outcome measures used to evaluate tinnitus treatments led to the development of the Tinnitus Functional Index (TFI) (Meikle et al, 2012). The TFI is a 25-item self-report questionnaire that can be used to evaluate responsiveness to tinnitus treatment. As a standardized measure of tinnitus outcome, the TFI has certain advantages compared with other tinnitus outcome questionnaires. Mainly, the concept of responsiveness was central to the design of the TFI. All tinnitus questionnaires before the TFI, including the THI (Newman et al, 1996), Tinnitus Handicap Questionnaire (Kuk et al, 1990), Tinnitus Reaction Questionnaire (Wilson et al, 1991), Tinnitus Severity Index (Meikle et al, 1995), and many others were not validated for responsiveness. Another advantage of the TFI versus other questionnaires is the inclusion of multiple domains of tinnitus severity as well as an auditory/hearing subscale that can be used to distinguish between improvements in hearing versus tinnitus after completion of treatment. Overall, it is important for future research to look toward using a standardized outcome measure evaluating tinnitus treatment responsiveness, such as the TFI, to allow for comparisons across tinnitus treatments. Another benefit would be to guide in the selection of tinnitus therapies associated with responsiveness for specific patient factors and various types of tinnitus.

In the future, including factors related to tinnitus distress might yield different outcomes than those seen in our study. Wallhäusser-Franke et al (2012) evaluated a range of tinnitus characteristics, hearing, and psychological factors in individuals with tinnitus to determine the relationship between the perception of tinnitus loudness and tinnitus-related distress. Consistent with other studies (Henry and Meikle, 2000; Folmer et al, 2001), a modest relationship was reported to exist between tinnitus loudness and tinnitus-related distress. When considering responsiveness to treatment outcome, a benefit can be associated with reductions in tinnitus-related distress separate from any reduction in the perceptual characteristics of tinnitus. Using multiple outcome measures in future studies to differentiate between hearing-related problems, tinnitus-related problems, and tinnitus perceptions will assist in understanding the potential predictive qualities of certain patient factors and tinnitus treatment outcome. It is possible that certain patient factors might offer insight into whether an individual might respond to a specific treatment as well as being predictive of selecting one treatment versus another. Important and logical next steps include (1) examining patient factors associated with treatment benefit (responders); (2) looking at differences among tinnitus interventions; and (3) replicating these findings through inclusion of other outcome measures. More research is needed to further address these possibilities using prospective, randomized, controlled designs.

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Abbreviations

BDI	Beck Depression Inventory
HF-PTA	high-frequency pure-tone average
LF-PTA	low-frequency pure-tone average
MML	minimal masking level
RCTs	randomized clinical trials
RI	residual inhibition
SD	standard deviation
SRT	speech reception threshold
STAI	State-Trait Anxiety Inventory
TFI	Tinnitus Functional Index
THI	Tinnitus Handicap Inventory
TM	tinnitus masking
TRT	tinnitus retraining therapy

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Table 1

Comparison of Responders versus Nonresponders by Treatment Group (Continuous Data)

	Masking				TRT			
	N	Mean	SD	p-value	N	Mean	SD	p-value
Demographics								
Age of Participant (yr)								
Nonresponder	32	62.41	10.16	0.143	21	63.00	9.46	0.017
Responder	13	57.62	8.61		23	55.44	10.63	
Self-Reported Tinnitus Characteristics								
Tinnitus Loudness								
Nonresponder	31	7.66	1.37	0.334	18	7.47	1.14	0.256
Responder	11	8.14	1.42		20	8.03	1.77	
Psychoacoustic Tinnitus Measurements								
Loudness-Match								
Nonresponder	26	8.58	9.80	0.366	21	11.24	10.78	0.165
Responder	13	12.85	19.50		21	7.38	6.34	
RE MML (SL)								
Nonresponder	24	22.50	19.00	0.897	18	23.61	22.48	0.936
Responder	10	23.50	23.69		17	24.12	13.14	
LE MML (SL)								
Nonresponder	24	22.92	18.41	0.398	16	24.38	17.59	0.918
Responder	10	29.50	24.88		17	23.82	12.81	
RI duration								
Nonresponder	30	61.43	62.96	0.890	17	71.94	45.18	0.912
Responder	12	64.50	69.24		21	73.86	58.10	
Audiometric Measurements/Self-Reported Hearing Ability								
RE SRT (dB HL)								
Nonresponder	31	21.39	12.77	0.807	21	24.52	14.13	0.013
Responder	12	20.17	18.77		21	15.19	8.29	
LE SRT (dB HL)								
Nonresponder	32	20.78	11.46	0.994	21	22.62	13.84	0.124

	Masking				TRT			
	N	Mean	SD	p-value	N	Mean	SD	p-value
Responder	12	20.75	15.94		21	17.00	8.80	
RE PTA Low								
Nonresponder	32	27.45	23.03	0.175	21	26.90	13.69	0.008
Responder	13	17.82	15.64		23	16.38	11.38	
LE PTA Low								
Nonresponder	32	23.65	14.84	0.651	21	27.30	16.55	0.078
Responder	13	21.28	18.03		23	19.49	11.94	
RE PTA High								
Nonresponder	27	57.92	28.99	0.379	20	54.88	22.62	0.226
Responder	12	49.69	19.95		23	47.12	18.79	
LE PTA High								
Nonresponder	26	59.38	23.08	0.453	20	59.94	22.82	0.212
Responder	12	53.44	20.89		23	51.85	19.01	
Physical Health Status								
No. of Health Problems								
Nonresponder	32	2.78	1.79	0.792	21	2.14	1.80	0.095
Responder	13	2.62	2.14		23	3.26	2.51	
Emotional Health Status								
BDI								
Nonresponder	31	7.45	8.14	0.011	18	3.67	4.35	0.004
Responder	10	3.10	2.28		21	9.38	7.05	
STAI (Trait)								
Nonresponder	30	43.95	14.01	0.059	18	35.67	11.96	0.008
Responder	10	34.70	9.21		21	46.88	12.82	
STAI (State)								
Nonresponder	30	43.51	17.67	0.063	18	34.62	12.94	0.009
Responder	10	32.00	11.70		21	46.38	13.73	

Table 2

Comparison of Responders versus Nonresponders by Treatment Group (Categorical Data)

	Masking		χ^2	p-value	TRT		χ^2	p-value
Demographics								
Marital Status	Married	Not Married	0.27	0.608	Married	Not Married	0.01	0.933
Nonresponder	23 (72%)	9 (28%)			16 (76%)	5 (24%)		
Responder	7 (64%)	4 (36%)			17 (77%)	5 (23%)		
Employment Status	Employed	Not Employed	0.61	0.436	Employed	Not Employed	0.96	0.327
Nonresponder	12 (38%)	20 (62%)			7 (35%)	13 (65%)		
Responder	3 (25%)	9 (75%)			11 (50%)	11 (50%)		
Level of Education	HS or less	Post HS	0.06	0.810	HS or less	Post HS	0.60	0.438
Nonresponder	5 (17%)	25 (83%)			6 (35%)	11 (65%)		
Responder	2 (20%)	8 (80%)			5 (24%)	16 (76%)		
Self-Reported Tinnitus Characteristics								
Duration of Tinnitus	20 Years	>20 Years	2.20	0.141	20 Years	>20 Years	2.40	0.123
Nonresponder	12 (38%)	20 (62%)			7 (33%)	14 (67%)		
Responder	8 (62%)	5 (38%)			13 (57%)	10 (43%)		
Perceived Localization of Tinnitus	In the Ears	In the Head	2.20	0.141	In the Ears	In The Head	3.30	0.068
Nonresponder	20 (71%)	8 (29%)			14 (67%)	7 (33%)		
Responder	5 (19%)	22 (81%)			9 (39%)	14 (61%)		
Number of Tinnitus Sounds	One Sound	Multiple Sounds	1.90	0.167	One Sound	Multiple Sounds	2.20	0.141
Nonresponder	14 (48%)	15 (52%)			13 (68%)	6 (32%)		
Responder	2 (22%)	7 (78%)			8 (38%)	10 (63%)		
Tinnitus Onset: Sudden or Gradual	Sudden	Gradual	0.69	0.406	Sudden	Gradual	0.00	0.985
Nonresponder	7 (26%)	20 (74%)			7 (35%)	13 (65%)		
Responder	4 (40%)	6 (60%)			6 (35%)	11 (65%)		
Tinnitus Varies in Loudness	Not Daily	Daily	1.50	0.227	Not Daily	Daily	3.40	0.065
Nonresponder	21 (66%)	11 (34%)			10 (50%)	10 (50%)		
Responder	6 (46%)	7 (54%)			17 (77%)	5 (23%)		
Degree of Tinnitus Problem	Small-Moderate	Big-Very Big			Small-Moderate	Big-Very Big		

	Masking		χ^2	*p*-value	TRT		χ^2	*p*-value
Nonresponder	11 (35%)	20 (65%)	1.80	0.182	5 (25%)	15 (75%)	0.37	0.541
Responder	2 (15%)	11 (85%)			4 (17%)	19 (83%)		
Which is worse:								
	Tinnitus	Tinnitus & Hearing			Tinnitus	Tinnitus & Hearing		
Nonresponder	10 (37%)	17 (63%)	2.40	0.121	10 (63%)	6 (37%)	0.80	0.371
Responder	6 (67%)	3 (33%)			9 (47%)	10 (53%)		
Physical Health Status								
Self-Rated Health Status	Excellent-Good	Fair-Poor			Excellent-Good	Fair-Poor		
Nonresponder	15 (47%)	17 (53%)	0.18	0.672	15 (75%)	5 (25%)	0.49	0.486
Responder	7 (54%)	6 (46%)			15 (65%)	8 (35%)		
Admitted to Hospital Past 6 mo	No	Yes			No	Yes		
Nonresponder	26 (84%)	5 (16%)	0.80	0.777	14 (74%)	5 (26%)	0.90	0.342
Responder	8 (80%)	2 (20%)			18 (86%)	3 (14%)		
Admitted to ER Past 6 mo	No	Yes			No	Yes		
Nonresponder	19 (61%)	12 (39%)	0.01	0.942	13 (68%)	6 (32%)	0.01	0.915
Responder	6 (60%)	4 (40%)			14 (70%)	6 (30%)		
Self-Reported Hearing & Sound Tolerance Concerns								
Decreased Sound Tolerance	No	Yes			No	Yes		
Nonresponder	9 (28%)	23 (72%)	0.43	0.514	9 (43%)	12 (57%)	0.06	0.802
Responder	2 (18%)	9 (82%)			9 (39%)	14 (61%)		
Hearing Problems	Mild-Moderate	Big-Very Big			Mild-Moderate	Big-Very Big		
Nonresponder	18 (60%)	12 (40%)	0.06	0.812	13 (72%)	5 (28%)	5.27	0.022
Responder	5 (56%)	4 (44%)			7 (35%)	13 (65%)		
Hearing Aid Use	No	Yes			No	Yes		
Nonresponder	25 (81%)	6 (19%)	0.50	0.479	14 (74%)	5 (26%)	0.30	0.583
Responder	7 (70%)	3 (30%)			17 (81%)	4 (19%)		

Table 3

Pooled Data: Comparison of Responders versus Nonresponders (Continuous Data)

	N	Mean	SD	*p*-value
Demographics				
Age				
Nonresponder	53	62.6	9.8	**0.003**[*]
Responder	36	56.2	9.9	
Self-Reported Tinnitus Characteristics				
Self-report of tinnitus loudness				
Nonresponder	49	7.6	1.3	0.15
Responder	31	8.1	1.6	
Psychoacoustic Tinnitus Measurements				
Tinnitus loudness (loudness match)				
Nonresponder	47	60.9	21.6	0.79
Responder	34	62.3	25.6	
RE MML (SL)				
Nonresponder	42	23.0	20.3	0.85
Responder	27	24.0	17.3	
LE MML (SL)				
Nonresponder	40	23.5	17.9	0.59
Responder	27	26.0	18.0	
RI Duration				
Nonresponder	36	64.2	43.6	0.15
Responder	26	82.5	54.8	
Audiometric Measurements/Self-Report Hearing Ability				
RE SRT (dB HL)				
Nonresponder	52	22.7	13.3	0.06
Responder	33	17.0	13.0	
LE SRT (dB HL)				
Nonresponder	53	21.5	12.4	0.25
Responder	33	18.4	11.8	
RE PTA Low (0.5, 1, 2 kHz)				
Nonresponder	53	27.2	19.7	**0.007**[*]
Responder	36	16.9	12.9	
LE PTA Low (0.5, 1, 2 kHz)				
Nonresponder	53	25.1	15.5	0.13
Responder	36	20.1	14.2	
RE PTA High (3, 4, 6, 8 kHz)				
Nonresponder	47	56.6	26.2	0.10
Responder	35	48.0	18.9	
LE PTA High (3, 4, 6, 8 kHz)				
Nonresponder	46	59.6	22.7	0.14

	N	Mean	SD	*p*-value
Responder	35	52.4	19.4	
Physical Health Status				
Number of Health Problems				
Nonresponder	53	2.5	1.8	0.29
Responder	36	3	2.4	
Emotional Health Status				
BDI				
Nonresponder	49	6.1	7.2	0.42
Responder	31	7.4	6.6	
STAI (Trait)				
Nonresponder	48	40.8	13.8	0.50
Responder	31	42.9	13.0	
STAI (State)				
Nonresponder	48	40.2	16.5	0.67
Responder	31	41.7	14.6	

*
p 0.05 (indicated in bold).

Table 4

Pooled Data: Comparison of Responders versus Nonresponders (Categorical Data)

			χ^2	*p*-value
Demographics				
Marital Status	Married	Not Married		
Nonresponder	39 (74%)	14 (26%)	0.01	0.56
Responder	24 (73%)	9 (27%)		
Employment Status	Employed	Not Employed		
Nonresponder	19 (37%)	33 (63%)	1.61	0.45
Responder	14 (41%)	20 (59%)		
Level of Education	HS or less	Post HS		
Nonresponder	31 (66%)	16 (34%)	0.22	0.42
Responder	22 (71%)	9 (29%)		
Self-Reported Tinnitus Characteristics				
Duration of Tinnitus	20 Years	>20 Years		
Nonresponder	n = 19 (36%)	n = 34 (64%)	4.4	**0.03** *
Responder	n = 21 (58%)	n = 15 (42%)		
Perceived Localization of Tinnitus	In the Ears	In the Head		
Nonresponder	n = 34 (64%)	n = 19 (36%)	5.5	**0.02** *
Responder	n = 14 (39%)	n = 22 (61%)		
Number of Tinnitus Sounds	One Sound	Multiple Sounds		
Nonresponder	27 (56%)	21 (44%)	2.6	0.09
Responder	10 (37%)	17 (63%)		
Tinnitus Onset: Sudden or Gradual	Sudden	Gradual		
Nonresponder	14 (30%)	33 (70%)	0.41	0.35
Responder	10 (37%)	17 (63%)		
Tinnitus Varies in Loudness	Not Daily	Daily		
Nonresponder	31 (60%)	21 (40%)	0.33	0.57
Responder	23 (66%)	12 (34%)		
Degree of Tinnitus Problem	Small-Moderate	Big-Very Big		
Nonresponder	16 (31%)	35 (69%)	2.40	0.10
Responder	6 (17%)	30 (83%)		
Which is Worse: Tinnitus/Hearing	Tinnitus	Tinnitus & Hearing		
Nonresponder	20 (47%)	23 (53%)	0.39	0.63
Responder	15 (54%)	13 (46%)		
Physical Health Status				
Self-Rated Health Status	Excellent-Good	Fair-Poor		
Nonresponder	30 (58%)	22 (42%)	0.10	0.83
Responder	22 (61%)	14 (39%)		
Admitted to Hospital Past 6 mo	No	Yes		
Nonresponder	40 (80%)	10 (20%)	0.19	0.45
Responder	26 (84%)	5 (16%)		

			χ^2	*p*-value
Admitted to ER Past 6 mo	No	Yes		
Nonresponder	32 (64%)	18 (36%)	0.06	0.50
Responder	20 (67%)	10 (33%)		
Self-Report Hearing And Sound Tolerance Concerns				
Decreased Sound Tolerance	Yes	No		
Nonresponder	18 (34%)	35 (66%)	0.24	0.53
Responder	11 (32%)	23 (68%)		
Hearing Problems	Mild-Moderate	Big-Very Big		
Nonresponder	31 (65%)	17 (35%)	3.90	**0.05** [*]
Responder	12 (41%)	17 (59%)		
Hearing-Aid Use	No	Yes		
Nonresponder	39 (78%)	11 (22%)	0.00	0.58
Responder	24 (77%)	7 (23%)		

Notes: ER = emergency room.

[*] *p* 0.05 (indicated in bold).

Table 5

Coefficients and Wald Tests for Logistic Regression on Factors Associated with Treatment Response

Patient Factor	B	SE	Wald	df	p-value	OR	95% CI for OR Lower	Upper
Age	−0.007	0.034	0.037	1	0.85	0.99	0.93	1.06
Tinnitus duration (20 yr vs. >20 yr)	−1.105	0.601	3.380	1	0.07	0.33	0.10	1.10
Tinnitus location (in ears vs. in head)	1.200	0.582	4.300	1	**0.04****	3.30	1.10	10.50
LF-PTA (0.5, 1, 2 kHz) right ear	−0.055	0.030	3.400	1	0.07	0.95	0.89	1.00
Self-report of hearing problem (mild to moderate vs. big or very big problem)	1.6	0.64	6.000	1	**0.01****	4.80	1.40	16.60
Constant	0.219	1.900	0.013	1	0.91	1.20		

Note: CI = confidence interval; df = degrees of freedom; OR = odds ratio; SE = standard error.

** *p* 0.05 (indicated in bold).